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EINSTEIN

THE MAGAZINE FOR ALUMNI AND FRIENDS OF ALBERT EINSTEIN COLLEGE OF MEDICINE



FORGING THE FUTURE OF MEDICINE

Einstein and Montefiore scholars
meld research with data to improve
patient care

INSIDE: Mapping a Roundworm's Nervous System • The Physician Investigators

A Message from the Dean

As 2019 came to a close, we learned that Einstein researchers had secured \$178 million in grants from the National Institutes of Health (NIH)—our largest annual total ever (page 14). The grants included funds to study the Ebola virus and HIV, to continue research on neuroscience and genetics, and to improve health among minority groups.

The year's end also brought news that Philip O. Ozuah, M.D., Ph.D., has become the new chief executive officer of Montefiore Medicine, the umbrella organization for Montefiore Health System and Einstein (page 2). Dr. Ozuah has decades of experience in leadership positions at Montefiore and a strong commitment to research and medical education. He replaces Steven M. Safyer, M.D., who retired after 40 years of service to Einstein and Montefiore.

Moving medicine forward is the focus of our cover story (page 22). The article describes a talented group of Einstein and Montefiore faculty scholars who epitomize what a learning health system can do: influence complex health systems to adapt and change behavior thanks to evidence obtained from rigorous research and data collection. The scholars are members of a new center of excellence established with a \$3.3 million NIH grant. It is one of only 11 such centers in the nation and the only one in New York State.

Another example of outstanding research can be found in the work of Einstein scientist Scott Emmons, Ph.D., who has been mapping the nervous



system of the worm *C. elegans* for the better part of two decades. The story of his success in completing the first wiring diagram of an animal's entire nervous system—a major milestone in biology—begins on page 36.

For the past 20 years, Einstein's Clinical Research Training Program has trained dozens of physicians in a variety of specialties. Five of those scholars talk about their research (page 16).

New funding, new leadership, and new research add up to bright days ahead at Einstein. I'm looking forward to them.

GORDON F. TOMASELLI, M.D.
*The Marilyn and Stanley M. Katz Dean
Albert Einstein College of Medicine
Executive Vice President, Chief Academic Officer
Montefiore Medicine*

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Science at the Heart of Medicine

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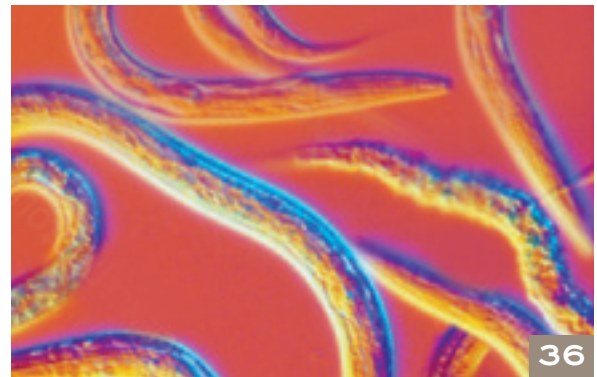
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ON THE COVER: A depiction of a learning health system, where research and data collection are used to help change behavior and more quickly benefit patients. Illustration concept by Tatyana Starikova Harris.



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Dr. Philip O. Ozuah Named CEO of Montefiore



"I look forward to continuing to expand inclusive access to state-of-the-art care and to furthering Montefiore's role as a global leader in healthcare and biomedical research."

— DR. PHILIP O. OZUAH

Philip O. Ozuah, M.D., Ph.D., has been named the chief executive officer (CEO) of Montefiore Medicine, the umbrella organization for Montefiore Health System (MHS) and Albert Einstein College of Medicine. He started his new role on Nov. 15, 2019, succeeding Steven M. Safyer, M.D., who retired after 40 years of service to Einstein and Montefiore.

As CEO, Dr. Ozuah will lead Montefiore's next phase of growth and evolution as a global healthcare leader, renowned for its excellent medical school, groundbreaking research and technology, and highly specialized, coordinated care of diverse populations in the New York region, across the country, and globally.

"We are thrilled that Dr. Philip Ozuah, a proven senior executive and strong strategic thinker, will lead Montefiore into the next decade," says Dan Tishman, chair of the Board of Trustees of Montefiore Medicine. "What stood out was his impressive record of success, his intellect and warmth as a physician, his strength as a leader and manager, and his deep commitment to Montefiore's mission. I'd also like to thank our outgoing CEO, Dr. Steven Safyer, for putting our organization on a path of excellence."

Dr. Ozuah joined Montefiore in 1989. "It will be a privilege to lead an organization with a clear purpose—to heal, to teach, to discover, and to advance the health of the communities we serve," he says. "We are an

organization of exceptionally talented and compassionate people. Working closely with the board, I look forward to continuing to expand inclusive access to state-of-the-art care and to furthering Montefiore's role as a global leader in healthcare and biomedical research."

Dr. Safyer, who has worked alongside Dr. Ozuah for the past 25 years, says, "I know I am leaving our institution in the best possible hands. I have consistently been impressed by Dr. Ozuah's strategic vision for the Montefiore Health System. His appointment as CEO will guarantee a smooth transition, and I know he'll continue to uphold the standard of excellence on which Montefiore has built its reputation."

Gordon F. Tomaselli, M.D., the Marilyn and Stanley M. Katz Dean at Einstein, says, "Dr. Ozuah has a long and storied history at Einstein, and we could not have hoped for a better choice to lead our joint enterprise. His vision, commitment to excellence, and dedication to social justice will undoubtedly provide the direction and support for Einstein to thrive in the coming years."

Dr. Ozuah previously served as

president of Montefiore and physician-in-chief of the Children's Hospital at Montefiore (CHAM), where he worked to deliver best-in-class clinical care with a commitment to healthcare access for the underserved. *U.S. News & World Report* has ranked MHS's medical specialties, under his leadership, in the top 1% of the nation's hospitals and CHAM as one of "America's Best Children's Hospitals."

Dr. Ozuah has a strong commitment to medical education as well as deep academic medical research expertise, including as a National Institutes of Health-funded investigator and as a professor and the university chair of pediatrics at Einstein.

In these roles, Dr. Ozuah expanded access for underserved communities, recruited and cultivated outstanding talent, advanced programs of excellence, fostered innovations in medical education, and improved financial and operational performance by integrating care across a rapidly growing and evolving Montefiore system that sees more than 6 million patient interactions a year.

He has been recognized regionally and nationally for excellence in teaching and patient care, including as an inductee into the Alpha Omega Alpha Honor Medical Society and a two-time recipient of the Academic Pediatric Association's prestigious Helfer Award for Innovation in Medical Education. Along with receiving various awards for teaching and clinical excellence, Dr. Ozuah has been recognized by *Modern Healthcare* magazine as one of the "Top 25 COOs in Healthcare."



Philip Ozuah, M.D., Ph.D., with a young patient at the Children's Hospital at Montefiore. Under his leadership, CHAM was named one of "America's Best Children's Hospitals" by *U.S. News & World Report* magazine.

Dr. Ozuah earned his medical degree from the University of Ibadan, Nigeria, a master's degree in education from the University of Southern California, Los Angeles, and a Ph.D. in educational leadership and administration from the University of Nebraska, Lincoln. He completed his pediatric internship and residency at Einstein and Montefiore, and his postdoctoral fellowship in medical education at the University of Southern California School of Medicine, Los Angeles.



WATCH THE VIDEO

View Dr. Ozuah's message:

magazine.einstein.yu.edu/ozuah20

Einstein Joins With CUNY to Offer M.D./M.P.H.



Einstein and the City University of New York Graduate School of Public Health & Health Policy (CUNY SPH) have collaborated to offer Einstein medical students an opportunity to complete a five-year program resulting

in a doctor of medicine (M.D.) degree from Einstein and a master's degree in public health (M.P.H.) from CUNY.

In its Best Public Health Schools list, *U.S. News & World Report* ranks CUNY SPH 23rd in the nation—making it the

second-highest-ranked school in New York State.

With the October 2019 announcement of its new M.D./M.P.H. program, Einstein joins about 80 medical schools across the nation with similar programs available at a single institution or in collaboration with another. Einstein first offered this opportunity to the Class of 2023 and made it available to all subsequent incoming M.D. students.

Physicians with M.P.H. degrees work in a variety of settings, including departments of health, nonprofit organizations, and research institutions.

Earning a separate M.P.H. degree typically takes two years. The new program's structure will allow Einstein students to complete both their M.D. and M.P.H. degrees in five years.

DoSA Marks 50 Years With Opioid Conference

Scientists, clinicians, policymakers, and community activists discussed opioid-use disorder's past, present, and future at a daylong conference at Einstein and Montefiore in September 2019 featuring a keynote address by Michael Botticelli, M.Ed., former director of the Office of National Drug Control Policy under President Barack Obama.

The event, "On the Front Lines of the Opioid Epidemic," highlighted Einstein and Montefiore's leadership in the field of opioid-use disorder, from basic and clinical research to community care and outreach services. It also marked the 50th anniversary of the Division of

Substance Abuse (DoSA), which was established as an Einstein methadone treatment program and—as a part of Montefiore—has evolved into a leading provider of comprehensive outpatient care at multiple locations for more than 3,400 adults in the Bronx.

Einstein and Montefiore researchers and clinicians discussed recent discoveries, from neuroscientific advances on the brain's role in reward-seeking behavior to effective, evidence-based opioid-use-disorder treatment strategies. Panel discussions also addressed public policy concerns and the need for reducing the stigma of addiction and structural barriers to care.



Joyce Lowinson, M.D., was honored for her decades of service to DoSA. With her are Jonathan Alpert, M.D., Ph.D., left, and Montefiore CEO Philip Ozuah, M.D., Ph.D.

3 Physicians Win National Honors

Dr. Cristina Gonzalez Gets New Investigator Award



Cristina Gonzalez, M.D. '04, an associate professor of medicine at Einstein, an internist at Montefiore, and an activist in the fight against health disparities, received the 2018 New Investigator Award from the Association of American Medical Colleges in November 2019.

The award was given in recognition of the publication of a paper for which she was the lead author, “How to Make or Break Implicit Bias Instruction: Implications for Curriculum Development,” in a November 2018 online supplement to the journal *Academic Medicine*.

Implicit bias refers to subconscious, unintentional assumptions about other people, which can often lead to disparities in healthcare for disadvantaged populations.

Many medical schools offer their students instruction about avoiding bias, and Dr. Gonzalez has made significant contributions to such programming at Einstein. Teachers, however, have not been on the receiving end of these educational efforts, and in her paper Dr. Gonzalez explores faculty members’ personal challenges, the role of institutions, and strategies for helping educators.

Her goals are to see the topic recognized as a faculty-development priority and to change the culture around implicit bias in medical education and healthcare.

Mentor Award Goes to Dr. Michal Melamed

Michal Melamed, M.D., M.H.S., was given the Distinguished Mentor Award by the American Society of Nephrology (ASN) at its annual Kidney Week meeting in November 2019. Earlier in the year, Dr. Melamed, associate professor of medicine and of epidemiology & population health at Einstein and a nephrologist at Montefiore, also received a mentoring award from Einstein’s department of medicine. Since joining the faculty at Einstein, she has mentored multiple junior faculty members, fellows, residents, and Einstein medical students.



Several of Dr. Melamed’s colleagues nominated her for the ASN mentorship award. They lauded her reputation as a national expert in studying risk factors for chronic kidney disease progression and praised her drive, enthusiasm, patience, and advocacy for her mentees. “I try especially to mentor women and people who may be underrepresented in medicine because I think that it’s important to get more people with diverse backgrounds into research,” Dr. Melamed says. Her research interests include the epidemiology of, and ethnic and racial disparities in, chronic kidney disease, vitamin D deficiency, and the health consequences of metabolic acidosis.

Dr. Irene Blanco Named Hispanic Health Leader



Last November, the National Hispanic Health Foundation (NHHF) recognized **Irene Blanco, M.D. '04, M.S.**, associate dean for diversity enhancement at Einstein and a rheumatologist at Montefiore, with its Hispanic Health Leadership Award.

The NHHF is part of the National Hispanic Medical Association, a nonprofit organization that represents 50,000 licensed Hispanic physicians in the United States and is a partner organization of the National Institutes of Health.

Dr. Blanco, associate professor of medicine at Einstein and director of the Lupus Clinic at Montefiore, was chosen for the honor because of her leadership in improving healthcare. She works with the American College of Rheumatology’s Lupus Initiative on information sheets distributed to Hispanic patients. With the help of a two-year federal grant, she is recruiting more minority patients for lupus clinical trials. The disease is two to three times more prevalent among women of color, particularly Hispanics, than among Caucasian women.

Enhancing Einstein, Inside and Out



From new outdoor benches and lighting to completely refurbished lobbies, several projects begun in 2019 are making Einstein a better place to work and live.

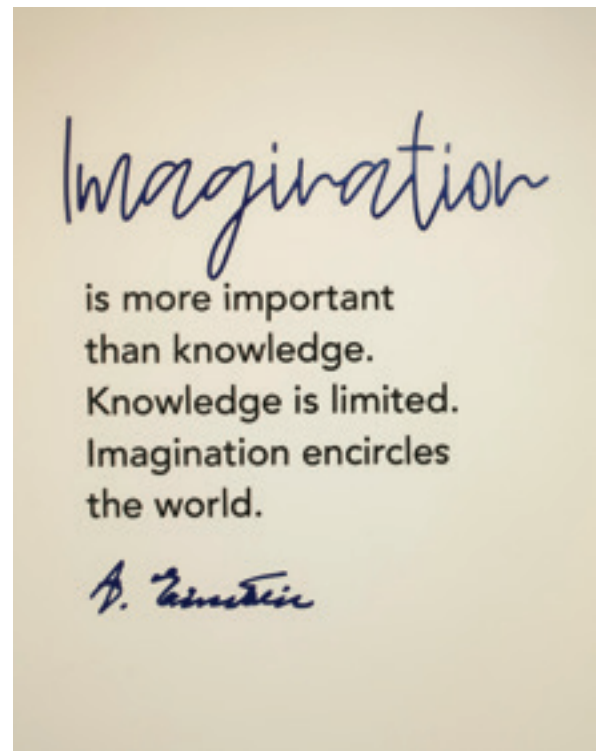
“Upgrading and modernizing our grounds and facilities and investing in enhancements to our campus community are a priority,” says Gregg Tarquinio, Einstein’s associate dean for administration and finance.

The renovations have included adding new furniture and lighting to student housing, the Belfer Educational Center, and the D. Samuel Gottesman Library study area. Necessary structural improvements have involved upgrading elevators and replacing air conditioners in several buildings. Audiovisual equipment has been replaced in auditoriums, lecture halls, and conference rooms; wireless and wired networking technology is currently being overhauled campus-wide; and additional automated external defibrillator units have been placed in all buildings.

In addition to those projects, the Clinical Research Center has moved from the Jack D. Weiler Hospital and the Leo Forchheimer Medical Science Building to space within the Van Etten Building, and the Magnetic Resonance Research Center has received a new 3T magnet and had its infrastructure upgraded.

THIS PAGE, at top: The renovated Belfer lobby welcomes visitors with new Einstein signage and terrazzo flooring. At left: New tables and chairs adorn the lobby at the 1925/1935 Eastchester Road Residence Complex.

OPPOSITE PAGE, at top: First-year medical students assemble before class in the renovated Belfer basement. Middle left: First-year medical student Christina Pil does some laptop work on a new couch in the Belfer basement. Middle right: Inspiring words from Albert Einstein decorate the Belfer lobby. Two bottom photos: Students convene on new couches in the expansive 1925 student housing lobby.



MONTEFIORE AND EINSTEIN MAVENS OF MEDICINE



Ensuring Diversity in Mental Health Research

Q&A with
Dr. Jonathan Alpert

Jonathan E. Alpert, M.D., Ph.D., is the Dorothy and Marty Silverman Chair in Psychiatry and chair of the department of psychiatry and behavioral sciences at Einstein and Montefiore. Dr. Alpert arrived in 2017 from Massachusetts General Hospital, where he was associate chief of psychiatry and director of the depression research program. He was also the first incumbent of the Joyce Tedlow Chair in the field of depression studies at Harvard Medical School.

Why did you specialize in psychiatry?

It is a remarkable field that spans basic neuroscience, clinical pharmacology, and social, emotional, and cognitive development. It engages fundamental questions such as what it means to be human and to live a good life. On a more personal level, I think clinicians are drawn to different forms of human suffering. As long as I can remember, I've been drawn to suffering related to psychiatric conditions and to people traditionally marginalized in society and in healthcare due to mental illness or addiction.

What influenced you to leave Boston?

My wife and I were empty nesters, with two young-adult sons off at school, so we were at an inflection point when I was contacted about the department chair opportunity here. I was grateful for the wonderful career, outstanding colleagues, and formative opportunities I'd had in Boston. But with, I hope, a decade or more of active professional life ahead, it seemed like an ideal time to make a meaningful contribution elsewhere.

Were you familiar with Einstein and Montefiore?

I knew of Einstein and Montefiore by reputation and of Montefiore's leading national role in behavioral-health integration in primary care and school health. And when I came here for interviews I was inspired by what I saw: a special place where commitments to advancing social justice and science—two values very important to me—are seamlessly interwoven and fully embraced across campuses.

Was the Einstein and Montefiore consolidation an attraction?

Yes, very much. Among other things it created the opportunity for psychiatry to partner with Einstein's exceptional department of neuroscience—one of the world's first freestanding neuroscience departments. Working with neuroscience, we've launched PRIME (Psychiatry Research Institute at Montefiore and Einstein) in a refurbished research space on the fourth floor of Van Etten.

What does PRIME do?

PRIME will allow us to greatly increase clinical and translational research in psychiatry. Our health-equity research program within PRIME will enable us to study how factors such as socioeconomic status, ethnicity, and sexual or gender orientation affect mental health outcomes. PRIME brings together clinically focused people like me and outstanding basic scientists, many of whom share a devotion to unraveling the mysteries of mental illness. We're fortunate that our clinical programs serve diverse communities that are exceedingly underrepresented in studies on mental illness and addiction. We have the obligation to ensure that these diverse voices are better represented in psychiatry research.

What other programs have you started?

We have many new programs, thanks mainly to strong interdepartmental collaborations. We've worked with the Children's Hospital at Montefiore emergency department to develop a specialized pediatric psychiatry emergency service to improve the care of children presenting with psychiatric problems. We've also joined with the dean's office and Montefiore leadership to create the

Einstein Student Mental Health Center, which provides expert, accessible evaluation and treatment for medical and graduate students on the Einstein campus.

Do people in the Bronx face unique mental health challenges?

Many patients we see have experienced some kind of major trauma. It might be physical violence, poverty, housing insecurity, dislocation from their country of origin—significant burdens that increase the risk of mental illness and addiction.

Could more be done to prevent mental health problems from developing?

Certainly. We can do more to impart practical coping and resilience skills in our school systems and to support good parenting skills, particularly for parents who've experienced early life adversity and trauma and aren't fully equipped to be the parents they want to be. We need to enhance access to affordable, high-quality mental health services to address problems early on before they become severe and chronic.

What has been the main focus of your research?

I've been interested in mood disorders, particularly treatment-resistant major depressive disorder. Available therapies don't work well enough for far too many individuals, and those gaps in knowledge and treatment continue to motivate me.

Have you read any good books lately?

I'm now reading *Sapiens: A Brief History of Humankind*, by Yuval Noah Harari. It raises fascinating, provocative questions about our improbable ascendancy as the dominant species on the planet. **E**

RESEARCH NOTES

Firefighter Heart Disease Linked to WTC Exposure

Photo by Neville Elder/CORBIS/Corbis via Getty Images



A study of nearly 10,000 New York City firefighters has found that exposure to 9/11 World Trade Center (WTC) dust is associated with a significantly increased long-term risk of cardiovascular disease (CVD). The study was conducted by researchers at Einstein, Montefiore, and the Fire Department of the City of New York (FDNY). Firefighters who arrived first at the WTC site—when the airborne

dust was thickest—have a 44% increased risk of CVD compared with those who arrived later in the day. The study was published in September 2019 in *JAMA Network Open*.

“The increase in risk was signif-

icant, even taking into account known CVD risk factors such as age, hypertension, elevated cholesterol, diabetes, and smoking,” says study leader David J. Prezant, M.D., professor of medicine at Einstein, a pulmonary disease specialist at Montefiore, and chief medical officer of the FDNY.

This study’s finding of an increased risk of CVD with WTC exposure—as well as the researchers’ earlier studies identifying an increased risk for

autoimmune rheumatologic diseases and for a blood-cancer precursor that can lead to the cancer multiple myeloma—“highlights the need to add these health conditions to the list of WTC-related diseases that are coverable under the James L. Zadroga 9/11 Health and Compensation Act,” Dr. Prezant adds.

Other studies have linked both acute and prolonged exposure to air pollution to CVD. The authors noted that the firefighters’ exposure to dust and products of combustion could have triggered persistent disease processes involving chronic inflammation that increased their risk for CVD years later.

“Our results emphasize why it is crucial to monitor the long-term health of anyone exposed to massive environmental disasters, even many years after the event,” says co-lead author Rachel Zeig-Owens, Dr.P.H., research assistant professor of epidemiology & population health at Einstein and an epidemiologist at Montefiore and the FDNY.

Promising Treatment for Cancer-Caused Anemia

In myelodysplastic syndrome (MDS), a cancer of the bone marrow, anemia occurs because the proliferation of abnormal blood cells leaves people with too few normal ones. An experimental cancer drug called galunisertib may offer a way to treat anemia in low- to intermediate-risk MDS patients without the need for blood transfusions.

The findings, published in September

2019 in *Clinical Cancer Research*, come from an international phase 2 clinical trial conducted at 14 centers in Italy, Spain, and Germany. The study’s principal investigator was Amit K. Verma, M.B.B.S., professor of medicine and of developmental and molecular biology at Einstein and director of the division of hemato-oncology at Montefiore.

Dr. Verma and colleagues developed galunisertib using tumor samples from patients at Montefiore. The drug inhibits a molecule called ALK5 that plays a role in activating defective MDS stem cells.

The research was co-led by Valeria Santini, M.D., associate professor of hematology at the University of Florence in Italy.

Unexpected Origin of Hospital Infections

The intestinal bacterium *Clostridium difficile* can be lethal and is difficult to treat. Each year it sickens about half a million Americans and causes about 30,000 deaths. *C. diff*, as it's called, has long been thought to infect people hospitalized or in other healthcare facilities. But in a study published in December 2019 in *Infection Control and Hospital Epidemiology*, researchers report that nearly one in 10 patients admitted to the hospital is already infected with *C. diff*, even though they do not have symptoms.

The researchers, led by Sarah Baron, M.D., M.S., tested 220 incoming hospital patients with no symptoms of *C. diff* and found that 21 were infected. Within

six months, 38% of those carriers progressed to symptomatic *C. diff*; by contrast, only 2% of initially noninfected patients ended up with symptomatic *C. diff*.

The U.S. Centers for Disease Control and Prevention considers the prospective identification of *C. diff* carriers a “supplemental intervention” but doesn’t recommend it as a prevention strategy. This study suggests that prospectively identifying and treating carriers could help prevent *C. diff*-related illnesses and deaths. Dr.

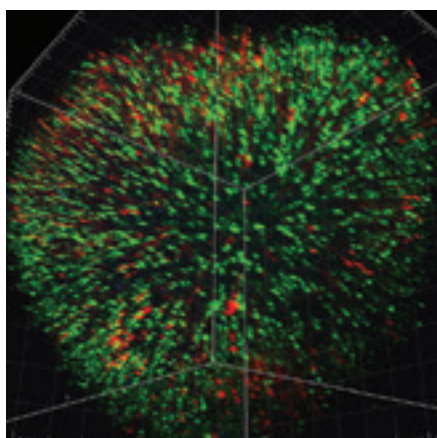


Baron is an assistant professor of medicine at Einstein and director of inpatient quality improvement in the department of medicine at Montefiore.

Growing Retinas in the Lab

It's not easy to study the retina and its diseases—in particular, macular degeneration, the leading cause of irreversible vision loss in people over 60. The retina's macula, a small spot in the center of the retina where vision is the sharpest, is crucial for both central vision and visual acuity. It is also rich in cones, the photoreceptors that enable color vision. But the macula is unique to primates, and nonhuman primates are extremely costly to study.

Now, as reported in May 2019 in the *Proceedings of the National Academy of Sciences*, Einstein scientists have for the first time successfully produced cone-rich retinal organoids that resemble the human macula. The research was led by Wei Liu, Ph.D., assistant professor of



Cones (red) and rods (green) in a retinal organoid cultured for about 7 months.

ophthalmology and visual sciences and of genetics at Einstein.

Organoids—tiny clumps of cells grown in tissue culture that

resemble human tissues or organs—have emerged as powerful models for studying human development and disease. They are derived from stem cells—in this case, human embryonic stem cells, which Dr. Liu and his colleagues coaxed to develop into retinal organoids.

Cone-rich retinal organoids could be a valuable resource for studying the biology of the human retina and may help reveal the molecular glitches that affect the retina, leading to treatments for macular degeneration and other blinding retinal diseases.



WATCH THE VIDEO

See photoreceptor cells in a retinal organoid come to life in 3-D. magazine.einstein.yu.edu/retina20

RESEARCH NOTES

Lab Chat

Michael Berney, Ph.D., is a microbiologist who studies *Mycobacterium tuberculosis* (*Mtb*), the microbe that causes TB. Dr. Berney was born in Switzerland, where he studied environmental sciences and microbiology at the Swiss Federal Institute of Technology in Zurich, which was also Albert Einstein's alma mater. After completing a postdoctoral fellowship in bacterial bioenergetics in New Zealand, he came to Einstein to collaborate with TB pioneer William Jacobs, Ph.D. Dr. Berney joined the Einstein faculty in 2016, where he is an assistant professor of microbiology & immunology.

How did you become interested in microbiology?

During my education in Switzerland, I was a visiting student in environmental sciences at the Massachusetts Institute of Technology, and we studied a polluted lake outside Boston. Industrial toxic chemicals were leaking in but, oddly, toxins weren't flowing out. We learned that bacteria, and not some inorganic process, were degrading the chemicals. That opened my eyes to the importance of microbes in shaping the environment.

Why did you become a TB researcher?

I was looking for a postdoc where I could dive into a bacterium that matters to human health and found a position at the University of Otago in New Zealand with Gregory Cook, an expert in mycobacterial bioenergetics.

And what led you to Einstein?

A paper we published in 2010 caught Dr. Jacobs' eye, and we started to talk about possible collaborations. Two years later, I asked Dr. Jacobs if I could work in his lab. I didn't anticipate that I'd end up on the faculty. But that's what you get with a scientific career. It takes you to unexpected places, and if you work hard and stay focused you can end up in a great place to do science.

For TB researchers, what is special about Einstein?

We have world-class infrastructure for TB research and various groups studying TB from every angle, from bacteriology to immunology to clinical epidemiology. You get to learn about so many aspects of the disease.

What are you studying now?

We've uncovered vulnerable components of *Mtb* metabolism: the aspartate pathway and the respiratory chain. In papers published in 2019 in *Nature Communications* and in 2017 in *PNAS*, we wrote about finding ways to eradicate *Mtb* persisters—the bacteria that resist conventional treatment. We're now testing combinations of existing and novel enzyme inhibitors in vitro and in animal models.

Is there anything about you that people would be surprised to know?

I was a ski instructor in Switzerland and then in New Zealand during my days at university.

Do you have any hobbies?

I have three children, ages 7, 9, and 11. They keep me very busy. But when I have time, I love running, biking, and skiing.



Dr. Berney wears a protective Tyvek suit as he enters Einstein's Biosafety Level 3 facility to study *Mycobacterium tuberculosis*.

Have you read anything interesting lately?

Currently, I am reading *The ONE Thing: The Surprisingly Simple Truth Behind Extraordinary Results* [by Gary W. Keller and Jay Papasan]. I also like to read biographies of great scientists, such as Albert Einstein and Craig Venter. And I just read *The Remedy* [by Thomas Goetz], about the quest to cure TB.

Bolstering Biopsies: Testing Single Cells in Lupus Patients

Scientists have used a powerful new tool to zero in on individual cells in a patient's diseased organ and reveal the cells' underlying abnormalities in gene expression—information that may allow for more-precise and more-effective treatment. The findings, made by scientists at Einstein, Montefiore, and other medical institutions, were published in May 2019 in *Nature Immunology*.

The study involved 21 patients with lupus nephritis (kidney inflammation), which affects half of all people who have systemic lupus erythematosus (SLE), a chronic autoimmune disease that inflames and damages tissues and organs throughout the body.

"Lupus inflammation can destroy kidney tissue and is a leading cause of death among patients with SLE," says Chaim Putterman, M.D., the paper's co-corresponding author, professor of medicine and of microbiology & immunology, and chief of rheumatology at Einstein and Montefiore.

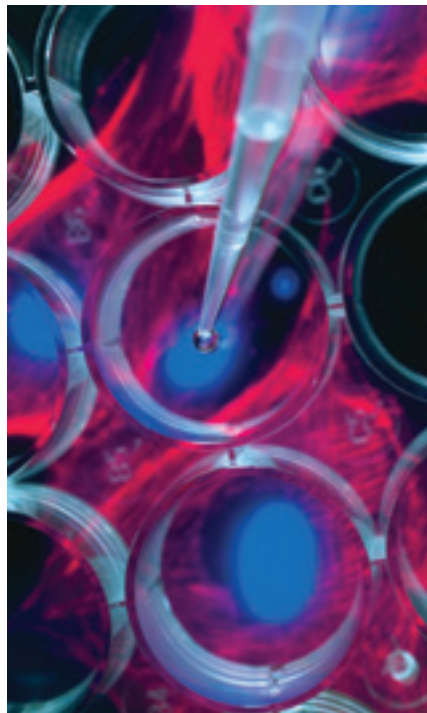
The kidney biopsy has been the gold standard for diagnosing the condition, assessing its severity, and monitoring patients' response to therapy. But it requires interpretation of stained tissue sections, which is not always sufficiently accurate for assessing disease severity or guiding treatment decisions.

By contrast, Dr. Putterman says, "we used a much more sensitive tool called single-cell RNA sequencing, or scRNA-seq, which requires only a tiny amount of clinically obtained tissue to reveal the gene expression of individual

cells. With scRNA-seq, we can see the inner workings of different types of kidney cells and identify disease-associated genetic 'signatures' within those cell types."

The researchers found that scRNA-seq testing of skin cells mirrored the results obtained with kidney cells—opening up the possibility that patients with lupus nephritis may one day be able to avoid kidney biopsies altogether.

"While our study focused on the kidney," Dr. Putterman says, "we're optimistic that scRNA-seq can potentially be similarly employed to improve on results obtained from many other types of clinical biopsies, such as those done on the prostate, breast, and skin."



Novel Therapy for Acute Migraine Shows Promise in Phase 3 Clinical Trial

A drug belonging to a new generation of acute migraine headache treatments eliminated pain and reduced symptoms in a large-scale trial reported in July 2019 in *The New England Journal of Medicine*. The drug, rimegepant, is awaiting U.S. Food and Drug Administration approval and may offer advantages over currently available migraine medications. The study, led by researchers at Einstein and Montefiore, involved more than 1,000 men and women with migraine.

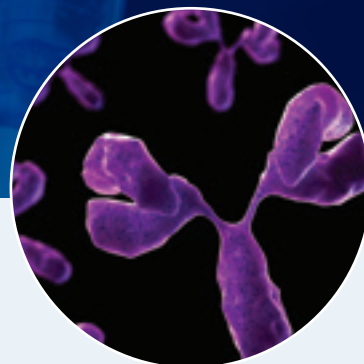
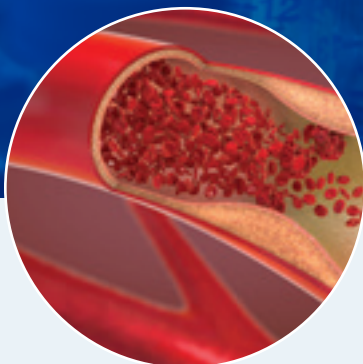
"For the first time in nearly three decades, people with migraine not helped by existing medications may have a new option to find relief during attacks," says Richard B. Lipton, M.D., the study's first author and the Edwin S. Lowe Chair in Neurology, vice chair of the Saul R. Korey Department of Neurology at Einstein, and director of the Montefiore Headache Center.

Currently, many people with migraine take triptan drugs (examples include sumatriptan, eletriptan, and rizatriptan), which were introduced in the 1990s. People not helped by triptans may benefit from the new class of drugs called gepants, which includes rimegepant.

Gepants work by targeting the receptors for the small protein CGRP, long implicated in migraine. During migraine attacks, CGRP is released, resulting in pain. Gepants relieve the pain and other symptoms of migraine by blocking the CGRP pathway.

RESEARCH NOTES

MAJOR NIH RESEARCH AWARDS



Einstein and Montefiore investigators received \$178 million in research funding from the National Institutes of Health (NIH) during federal fiscal year 2019—the largest annual total in the College of Medicine’s history.

Detecting Arterial Disease in the Legs

Lower extremity arterial disease (LEAD) is a debilitating but under-recognized condition usually caused by fatty plaque buildup in arteries carrying blood from the heart to the legs. LEAD typically isn’t diagnosed until people experience cramping or pain while walking. The National Institutes of Health has awarded a five-year, \$8 million grant to Einstein’s Robert Kaplan, Ph.D., and a Johns Hopkins co-investigator to identify early symptoms of LEAD so it can be promptly diagnosed and treated. Some 6,000 participants in a community health study will first undergo diagnostic testing for LEAD. They’ll then be fitted with wristwatch monitors to measure daily activity. Comparing the monitor results with the diagnostic-test results may reveal telltale patterns of activity associated with LEAD. Dr. Kaplan is a professor of epidemiology & population health and the Dorothy and William Manealoff Foundation and Molly Rosen Chair in Social Medicine at Einstein.

Understanding How Antibodies Protect Against TB

Tuberculosis (TB) ranks among the 10 leading causes of death worldwide. To develop an effective vaccine and new immunotherapies against TB, researchers need to better understand how the immune system works to prevent and control *Mycobacterium tuberculosis* (*Mtb*) infection. The NIH has awarded Jacqueline Achkar, M.D., M.S., a five-year, \$3.7 million grant to investigate the role of antibodies in protecting against TB.

Dr. Achkar and colleagues are focusing on the surface glycans of *Mtb*, some of which elicit an antibody response. The researchers particularly want to learn where on the glycans the antibodies attach. Findings could fill a critical gap in the current knowledge about TB immunity and lead to new strategies for developing both vaccines and antibody-based immunotherapies against TB. Dr. Achkar is an associate professor of medicine and of microbiology & immunology at Einstein.



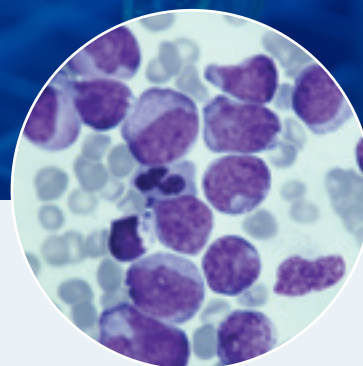
Curbing Heart Disease Among Those With HIV

Antiretroviral therapy has turned HIV into a chronic disease in the United States. Lifelong HIV infection, however, greatly increases the risk of age-related diseases, including cardiovascular disease (CVD). Chronic inflammation triggered by the body's immune response to HIV infection contributes to CVD, but it's not yet known which genes are altered in this immune response. Robert Kaplan, Ph.D., has received a four-year, \$3.3 million grant from the NIH to identify the genes that are over- or under-expressed in immune cells of people living with HIV. Researchers hope to find differences in blood cells that can be targeted by existing medicines or to identify new targets for which drugs can be developed. Dr. Kaplan is a professor of epidemiology & population health and the Dorothy and William Manealoff Foundation and Molly Rosen Chair in Social Medicine at Einstein.



Preventing Diabetes in Minority Men

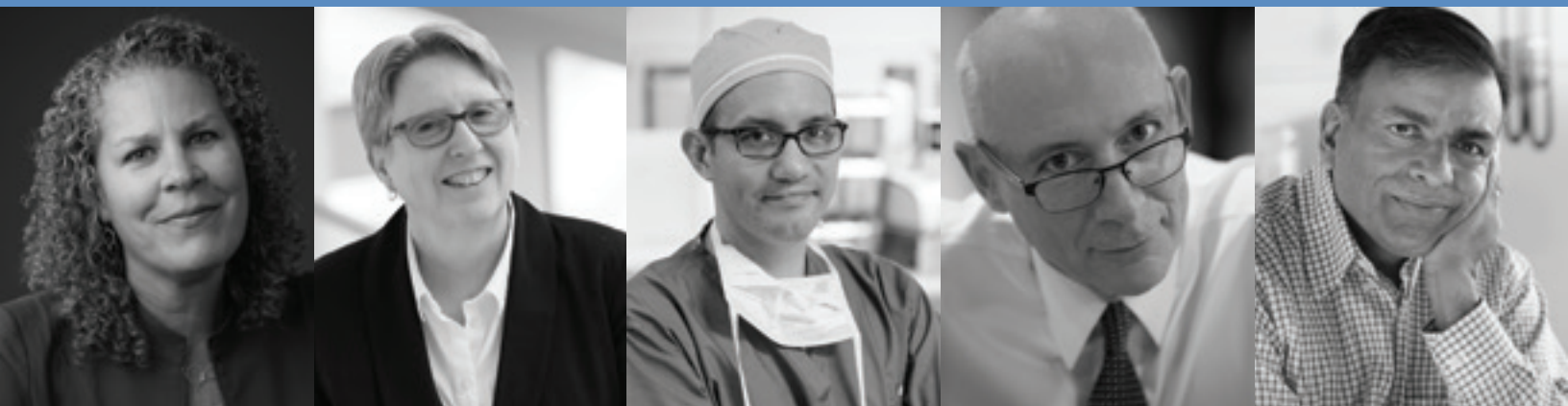
For people with prediabetes, a lifestyle intervention called the Diabetes Prevention Program (DPP) has been shown to reduce their risk of developing type 2 diabetes by 60% to 70%. Men of color, however, are far less likely to enroll in the 12-month DPP and to remain engaged if they do enroll. The NIH has awarded Earle Chambers, Ph.D., and Jeffrey Gonzalez, Ph.D., a five-year, \$3.1 million grant to evaluate Power-Up, a version of DPP tailored to black and Latino men. Men with prediabetes will be randomly assigned to a traditional coed DPP program or to Power-Up. The researchers will evaluate the participants' engagement, as well as weight loss and levels of hemoglobin A1c (a blood test indicative of diabetes). Dr. Chambers is an associate professor of family and social medicine and of epidemiology & population health at Einstein; Dr. Gonzalez is a professor of medicine and of epidemiology & population health at Einstein.



Finding an Enzyme's Role in Blood Stem-Cell Disorders

Myelodysplastic syndrome (MDS) is a bone-marrow disorder arising from defective hematopoietic (blood-forming) stem cells (HSCs). The enzyme TET2 controls how HSCs produce healthy blood cells and is frequently mutated in MDS. TET2's normal catalytic activity is essential for suppressing MDS. Keisuke Ito, M.D., Ph.D., and Meelad Dawlaty, Ph.D., have found evidence that TET2 also suppresses MDS through noncatalytic means. The scientists have received a four-year, \$2.8 million NIH grant to conduct further research into how TET2 acts noncatalytically to suppress MDS. Discovering additional ways in which TET2 influences MDS could lead to new treatments. Dr. Ito is the director of scientific resources of the Einstein Stem Cell Institute and an associate professor of cell biology and of medicine at Einstein; Dr. Dawlaty is an assistant professor of genetics and a member of the Einstein Stem Cell Institute. **E**

THE PHYSICIAN INVESTIGATORS



Einstein's Clinical Research Training Program (CRTP) marks 20 years of giving doctors the right skills for study success

BY GARY GOLDENBERG

In 1998 Einstein created its first terminal master's degree program, leading to an M.S. in clinical research methods. At that time there were very few training programs for physicians like it across the country. In the two decades since then, under the guidance of director Aileen McGinn, Ph.D., and former directors Ellie Schoenbaum, M.D.,

and Paul Marantz, M.D., M.P.H., the program has trained dozens of clinical research scholars in a variety of specialties.

On the following pages five of those scholars from across the years talk about CRTP and how it has made all the difference in making their research possible.



CHINAZO O. CUNNINGHAM, M.D., M.S.

C RTP Class of 2009; associate division chief of general internal medicine at Einstein and Montefiore and professor of medicine, of family and social medicine, and of psychiatry and behavioral sciences at Einstein

It was in the early 2000s when I first started to think critically about how best to deliver care to people struggling with homelessness, drug use, and HIV. I was collecting data but didn't know how to analyze the information. When I look back at my first study, I cannot believe it was published, and I shudder at the thought of my name on it. I'm proud I was able to do it, but the level of rigor was terrible. I finally realized I had to go back to school.

Perhaps the most valuable things I learned in CRT P were how to do

statistics, use statistical software, and write code. For the previous three or four years, I had all these questions about research methods, and all of a sudden they were being answered.

Nowadays, I do less and less hands-on work with statistics, only because I work with statisticians who do it for me. What's important is that I have the ability to discuss things with them. It eliminates any miscommunication.

During CRT P, I continued my studies of marginalized populations and published about 10 papers on that work. My thesis project was to write a large, multisite National Institutes of Health (NIH) grant. It didn't get funded, mainly because I was ahead of the curve in terms of addressing this population. Nonetheless, that effort was a turning point—the beginning of my NIH-funded research career. This is what I've always wanted to do. I love it.

"Twenty or 30 years ago, M.D.s usually didn't pursue formal research training. Programs like CRT P didn't exist. Today, one might think that one could do research without this training, but there's no way."

— DR. CHINAZO CUNNINGHAM

One of my goals now is to make sure that junior faculty don't take the same path I did. If they're interested in research, I tell them they have to get the right skill set. Four years ago, we developed a general internal medicine research fellowship, and all of our fellows are required to enroll in CRT P.

It's a different world now for clinical researchers. Twenty or 30 years ago, M.D.s usually didn't pursue formal research training. Programs like CRT P didn't exist. Today, one might think that one could do research without this training, but there's no way.

Dr. Cunningham is currently the principal or co-principal investigator on four NIH grants: "Mentoring Researchers on Drug Abuse and HIV," "Resilience in HIV-Infected Drug Users," "Does Medical Cannabis Reduce Opioid Analgesics in HIV+ and HIV- Adults With Pain?" and "The Center of Excellence in Promoting Learning Health System Operations and Research at Einstein/Montefiore (EXPLORE)" (see page 22).

M. DIANE MCKEE, M.D., M.S.

C RTP Class of 1999; professor and chair, department of family medicine and community health, University of Massachusetts Medical School, Worcester

Those who stand to benefit most from CRT P are researchers on the verge of becoming independently funded investigators. That describes me in the late 1990s. I was starting to do clinical research, but I soon realized there were significant gaps in my knowledge of research methods, particularly in study design and statistics. CRT P offered a unique opportunity to focus on these and other core competencies—much more so than in a conventional master of public health program.

During CRT P, I was able to continue to strengthen my research. It involved seeing how clinicians in community health settings communicate results to patients about mildly abnormal Pap smears and what patients understood about those results. Several papers came out of that work.

It was incredibly valuable having not one but several mentors during CRT P. One helped me with statistics, another with qualitative methods. My primary mentor was Michael Mulvihill [then director of the division of research in family medicine, and now professor emeritus], who was, and still is, my most important mentor in terms of my overall career development.

Immediately after the program, I received a Robert Wood Johnson Generalist Physician Faculty Scholar Award, which I used to explore barriers that adolescent girls face in starting

gynecologic care. The award was a major career milestone, and I would have been far less likely to receive it without my formal research training. The CRT P credential says to grant reviewers, “This person really does have the skills to be an investigator.”

There was another side effect of CRT P as well. By staying here, as opposed to going to an outside master’s degree program, I was exposed to researchers across multiple departments in the Einstein and Montefiore world. It was like becoming part of a family. There’s a real leap of faith that you’re

going to be able to support part of your salary as a clinician-investigator. Being able to network with more-senior faculty bolstered my confidence that I could be successful in this career path.

Dr. McKee is the former director of the New York City Research and Improvement Networking Group, sponsored by Einstein’s department of family and social medicine, where she oversaw a wide range of practice-based research and quality-improvement efforts, with the goal of improving care for the urban underserved.





“That’s the sign of a true mentor: someone who knows what’s good for you and pushes you in directions that you might not otherwise go.”

— DR. THOMAS OW

THOMAS J. OW, M.D., M.S.

CRTP Class of 2017; associate professor of otorhinolaryngology–head & neck surgery and of pathology at Einstein and Montefiore

I was hired at Einstein and Montefiore in 2012 to be a surgeon-scientist. I’d had some experience in basic and translational science and wanted to continue building our head and neck cancer research program, which has a strong relationship with the department of pathology.

In 2015, I was accepted as a K12 Paul Calabresi scholar, which required work in career development. One of my senior colleagues, Mark Einstein, was a CRTP graduate, and he strongly suggested that I enroll in CRTP. It wasn’t an ultimatum, but he wisely advised that I needed more experience with statistics, clinical research study design, and grant

writing. That’s the sign of a true mentor: someone who knows what’s good for you and pushes you in directions that you might not otherwise go.

My primary mentors were (and still are) Evripidis Gavathiotis [professor of biochemistry and of medicine], who has helped me stay current with experimental therapeutics and cancer cell signaling, and Chandan Guha [professor of radiation oncology, of pathology, and of urology], whose expertise in radiation biology, immunology, and stem-cell biology has helped me move my research into those fields. Having a basic scientist and a translational investigator as my mentors is critical for someone like me, who is balancing a career that combines lab work and patient care.

At the end of CRTP, I received a National Institutes of Health K23 Mentored Research-Scientist Career Development Award. My project focuses on the association between key genetic

and molecular characteristics of head and neck squamous-cell cancer and tumor-cell resistance to cisplatin and radiation.

CRTP was instrumental in helping me develop my research and submit a competitive grant application. It has truly improved my ability to differentiate outstanding research from work that has inherent design flaws. I feel like a true expert when I discuss clinical and translational research with my peers and leaders in the field. If programs such as CRTP were universally available, I think science and research would advance more quickly.

Dr. Ow specializes in the surgical treatment of head and neck tumors, including those that occur in the mouth, throat, larynx, neck, sinuses, salivary glands, and thyroid gland, and of skin cancers that occur on the scalp, face, and neck. He is a translational investigator who is focused on molecular and genomic alterations in head and neck squamous-cell cancer that can be used to develop important biomarkers and treatment targets.



**WILLIAM SOUTHERN, M.D.,
M.S.**

C RTP Class of 2007; chief of the division of hospital medicine at Einstein and Montefiore and professor of medicine (hospital medicine) at Einstein

I'd been working as a hospitalist for 10 years, mostly providing clinical care and teaching. Then I decided it would be a good idea to study the relative effectiveness of hospitalist versus nonhospitalist care, based on data from electronic health records. I didn't know much about how to design a study, collect data in a rigorous way, do statistical analyses,

or even write a paper—and I guess it showed. Before sending the paper off to a journal, I gave it to my division chief, who gently said, "Maybe you'll get it published someday, but if you want to do research, you'll need additional training." After that humbling experience, I enrolled in CRT P.

It would be hard to single out which CRT P course was the most important. The statistics courses were certainly invaluable, where I learned statistical principles and how to use statistical software, among many other things. So, too, were the courses in epidemiology and grant writing. Almost immediately, I was able to apply what I was learning

"CRT P changed absolutely everything. It would be hard to overstate the effect it had on my life."

— DR. WILLIAM SOUTHERN

in class to my CRT P research project—a redo of that hospitalist versus nonhospitalist study, with a new study design, new data analysis, new everything.

I ultimately did publish my work in 2007, the year I graduated from the CRT P course. That was only the beginning. I've published dozens of papers since then. CRT P changed absolutely everything. It would be hard to overstate the effect it had on my life. I once thought conducting research was inaccessible to me, but it has turned out to be an extraordinarily rewarding part of my career, personally and professionally.

Today, my job entails running the medicine services at Montefiore's Moses, Weiler, and Wakefield campuses. The skills that I took away from CRT P have allowed that work to flourish. As before, I have access to patient data, but now I have the ability to draw valid conclusions about the type of care we offer and how we can do it better. I would never have been able to do that before CRT P.

In May 2019, Dr. Southern was the senior author of a study showing that patient safety is not compromised by allowing physicians to view multiple electronic patient records at the same time—a practice barred at 40% of the hospitals across the nation. The paper was published in the Journal of the American Medical Association.

JOE VERGHESE, M.B.B.S., M.S.

CRTP Class of 2000; professor in the Saul R. Korey Department of Neurology, the Murray D. Gross Memorial Faculty Scholar in Gerontology, and director of the Jack and Pearl Resnick Gerontology Center

I didn't go to medical school because I wanted to become a doctor; I went because I was good at my studies. In time I realized that what I really wanted to be was a researcher. I started doing clinical research during my residency in neurology here at Montefiore, but I was a bit worried because my computing and math skills weren't all that great.

As luck would have it, CRTP was just getting started when I was finishing my fellowships [in aging and dementia and in neurophysiology]. Since I was already familiar with Einstein and Montefiore, I didn't want to go elsewhere to learn more about clinical research.

Right from the beginning, the program had a practical emphasis. It gave us the tools to succeed as clinical researchers—tools such as statistics and epidemiology and study design—and I could see immediate applications in my studies.

One of the best aspects of CRTP is that it can accommodate each student's needs. For example, I decided to change my thesis when I came up with a better study idea. I was already halfway through the program, but the faculty were supportive. As it happened, one day a colleague told me that he saw two older women walking and talking and they were so engrossed in their conversation that, when they came to a door, they didn't know what to do.

It was fascinating, this idea that doing two things can interfere with your ability to do a third thing. There were a few case reports in the literature about this, showing that those nursing home residents who had to stop walking while talking were the ones who fell most often.

I decided to create my own walking-while-talking divided-attention test. I discovered that elderly people whose walking had slowed down by a third had a huge risk of falling during the next year. This idea led me in many different directions, and I've incorporated it into many of my studies.

CRTP was a real eye-opener.

Interacting with students and faculty from different disciplines and in different stages of their careers gave me a broader perspective on research life, on the intersection of clinical and research duties, and on possible career paths.

Dr. Vergheese serves as clinical director of the NIH-funded Einstein Aging Study, a longitudinal study examining both normal aging and the special challenges of Alzheimer's disease and other disorders involving cognitive decline. He is a three-time recipient of the CRTP Mentor of the Year Award. **E**





collect data

analyze

knowledge

research

health
history

quality

care

practice
change

FORGING THE FUTURE OF MEDICINE

Einstein and Montefiore scholars meld research with data to improve patient care

BY TERESA CARR

All too often, cancer cells can break away from breast, prostate, and other tumors and travel through the bloodstream to different parts of the body. For some 330,000 Americans, that means living with cancer that has metastasized, or spread, to their bones.

Metastases can crop up anywhere in the skeleton, most commonly in the spine, where they can weaken bones and lead to fractures. Identifying and treating spinal tumors early—before they can cause severe pain and disability—helps people live longer and better lives. But that’s easier said than done.

“Early symptoms, such as back pain or fatigue, caused by bone metastases are so subtle and common that they’re easily overlooked,” says Parsa Mirhaji, M.D., Ph.D., director of clinical research informatics at Einstein and Montefiore and director of the Center for Health Data Informatics. He notes that the tumors themselves are rare and, in the earliest stages, hard to spot on images—even by highly skilled radiologists.

“A radiologist may review 50,000 MRIs of patients with back pain and only 10 will have a spine metastasis; it’s like looking for the proverbial needle in a haystack,” Dr. Mirhaji says. “And even when scans reveal a possible tumor, it can take weeks to follow up and get patients to the appropriate specialist for treatment—a critical delay that can allow tumors to progress.”



FORGING THE FUTURE OF MEDICINE



EXPLORE grant co-principal investigators, from left, Chinazo Cunningham, M.D., M.S.; Michael Rinke, M.D., Ph.D.; and Paul Marantz, M.D., M.P.H.

“In the simplest terms, an LHS is a system where research and data collection inform practice and, in turn, practice influences research.”

— DR. MICHAEL RINKE

A STRATEGY FOR COMPLICATED CASES

In order to solve complex medical problems, a talented group of young researchers at Einstein and Montefiore is harnessing the power of something called a learning health system (LHS). Combining research, data, and a culture dedicated to continuous improvement, the LHS educates physicians and develops ways to more efficiently care for people. Not only do patients benefit from state-of-the-art care, but their experiences are helping drive the future of medical research.

“In the simplest terms, an LHS is a system where research and data collection inform practice and, in turn, practice influences research,” says Michael Rinke, M.D., Ph.D., associate professor of pediatrics at Einstein and co-director of the Health Research Implementation

Core at the Harold and Muriel Block Institute for Clinical and Translational Research at Einstein and Montefiore. “With an LHS, you’re constantly improving and innovating to achieve best practices, which you incorporate into the healthcare you deliver.”

An LHS “epitomizes evidence-based medicine and is the best way to get at complex medical issues like detecting spinal metastases,” says Vijay Yanamadala, M.D., M.B.A., M.S., assistant professor of neurological surgery at Einstein and director of the Center for Surgical Optimization at Montefiore. In fact, he says, the logic behind an LHS is not unique to healthcare.

“To devise a game plan, football coaches use what they learn from trying different configurations and plays during practice,” Dr. Yanamadala says. “After game day, the team goes over the films to see what worked and didn’t work, and it then builds on its analysis of those data to develop a better strategy.”

But medicine has been reluctant to let data steer it toward better healthcare. “Multiple studies show that when a new and better way to treat patients comes out, it takes about 17 years to be widely adopted,” Dr. Rinke says. “The classic example we give in quality improvement is that we’ve all tried to change something about ourselves—exercise more, for instance, or get more sleep—and it’s really challenging. Changing things in a workplace can be just as hard.”

One of the main goals of LHS research is to greatly shorten that

17-year lag time, he says. And Einstein and Montefiore are at the forefront of this approach. “We have incredible researchers who analyze data—primarily information from patients’ electronic health records—to continuously generate information aimed at solving problems,” Dr. Rinke says. “But just as important, once a new treatment or tool has been rigorously tested, we have an equally strong operations group to integrate it into our systems to make sure that all patients benefit.”

Dr. Yanamadala, in collaboration with Dr. Mirhaji, is using LHS practices to detect and treat spinal tumors. Dr. Mirhaji is creating a machine-learning algorithm to do what no human can: analyze millions of pieces of data—images, lab results, doctors’ notes, and more—to uncover the patterns indicating that a patient’s cancer may have spread.

“Physicians are only human, so they can factor only about seven variables—things like blood pressure, pulse rate, and body temperature—into their decision-making process,” Dr. Mirhaji says. “But the algorithm can look at hundreds of different variables and draw conclusions regarding a patient’s condition from that information.”

Dr. Yanamadala, for his part, is interviewing patients and their providers and collecting other patient-care data to uncover roadblocks that cause delays. The goal is to create a center staffed by a variety of specialists, including neurosurgeons, radiation oncologists, and physiatrists. The new center will enable patients to receive prompt, appropriate treatment in one place for spinal metastases.

“This way of operating—constantly collecting and analyzing data and



Parsa Mirhaji, M.D., Ph.D., processes data generated by the EXPLORE scholars. Physicians can factor about seven variables into their decision-making process, he says.

using what you learn to continually improve—is where medicine is headed,” Dr. Yanamadala says. “And Einstein and Montefiore are at the cutting edge, which is what drew me here.”

THE NEW FACES OF MEDICAL RESEARCH

Dr. Yanamadala is one of four scholars who’ve recently joined the new Einstein and Montefiore LHS center—known as the Excellence in Promoting LHS Operations and Research at Einstein and Montefiore, or EXPLORE. It was established in November 2018 with a \$3.3 million federal grant—one of only

11 LHS Centers of Excellence in the nation and the only one in the state of New York.

“This is the first federal grant to train investigators in the LHS model,” says Dr. Rinke, who is also a co-principal investigator for the EXPLORE grant. Traditionally, promising physician-scientists such as Dr. Yanamadala approach medical institutions with research questions they’d like to pursue. EXPLORE turns that model on its head, Dr. Rinke says. It first identifies high-priority questions—such as how to detect bone metastases early—and then seeks applicants with the experience and

FORGING THE FUTURE OF MEDICINE



“This way of operating—constantly collecting and analyzing data and using what you learn to continually improve—is where medicine is headed.”

— DR. VIJAY YANAMADALA

the intense curiosity to answer those questions.

“A major advantage to that approach is that we can have all the resources in place for the scholars to hit the ground running,” says Paul Marantz, M.D., M.P.H., associate dean for clinical research education and a co-principal investigator on the grant. He notes that each scholar will have both clinical and health-systems mentors, plus access to expertise in sophisticated data processing.

The abundance of medical data now stored digitally “amounts to a treasure trove for an LHS center like EXPLORE,” Dr. Marantz says. “At the heart of the LHS model is the notion

EXPLORE scholar Vijay Yanamadala, M.D., M.B.A., M.S., uses learning health system practices to detect and treat spinal metastases.

that we can use all those data—not only to figure out the right things to do clinically, but to influence complex health systems to adapt and be willing to implement new evidence.” To that end, he says, EXPLORE brings together professionals from all parts of the healthcare system—from physicians and nurses to data scientists and pharmacists. “Their collaboration is key in a learning health system,” he emphasizes.

“There’s great value in having people from different disciplines and different levels of the health system leadership sitting around the same table,” says Chinazo Cunningham, M.D., M.S., a co-principal investigator for the EXPLORE grant. “That takes discussions to another level where we’re able to see beyond our respective roles and consider how best to make changes in a complex system. And by publishing what we’ve learned about improving clinical practice, we’re helping patients at other hospitals and health systems benefit as well.”

The EXPLORE program “reflects the changing culture of medical research,” says Shalom Kalnicki, M.D., chair of radiation oncology at Einstein and Montefiore and one of Dr. Yanamadala’s mentors. “Research done at wet-lab benches using test tubes and animal models is vital,” he says. “But research increasingly is being done by computer modeling, with results that can be fed into an LHS. I feel that these young investigators we’re training and mentoring in collaborative research represent the future of medicine.”

FOUR SCHOLARS AND THEIR COMPLEX CHALLENGES

The four Einstein and Montefiore EXPLORE scholars (three more will be selected next year) take courses and undergo training in three areas essential for a career as an LHS investigator: health-information technology, quality improvement, and clinical research. Applying their new skills and their previous experience, the scholars work with mentors to solve thorny healthcare problems.

As noted above, Dr. Yanamadala's EXPLORE project leverages the power of an LHS to research ways to detect and treat spinal metastases. "Vijay is a skilled spine neurosurgeon, but he's dedicated to improving care by reducing the need for surgery," Dr. Kalnicki says. "From the bottom of his physician heart, he feels compelled to find ways to improve patients' quality of life, to really make a difference."

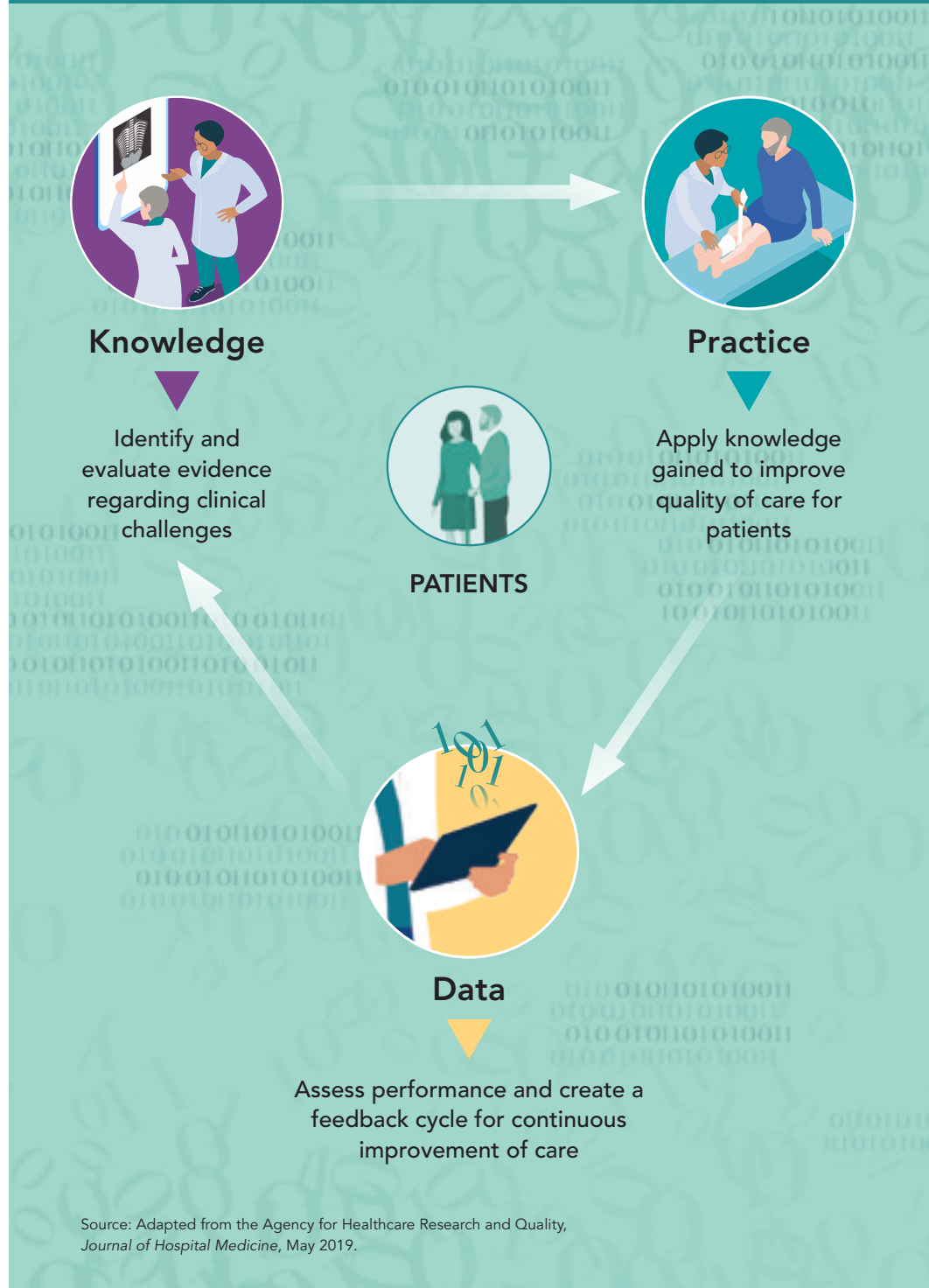
The projects of the other three EXPLORE program scholars are described below.

Using Electronic Health Records to Spot Sepsis

Sepsis—the body's overwhelming and potentially fatal response to infection—is the most expensive inpatient problem in American hospitals, costing an estimated \$27 billion yearly. Kaitlyn Philips, D.O., M.S., assistant professor of pediatrics at Einstein and an attending physician at the Children's Hospital at Montefiore (CHAM), is pursuing an EXPLORE project aimed at improving the care of sepsis patients.

Dr. Philips says that her experience treating sepsis in children, who often display more-subtle symptoms than adults, helps in her effort to recognize

WHAT IS A LEARNING HEALTH SYSTEM?



FORGING THE FUTURE OF MEDICINE

“Being able to predict which patients are at risk and to prompt doctors to quickly take preventive action can save lives.”

— DR. KAITLYN PHILIPS

sepsis at an early, treatable stage. “I’m able to act as a liaison between the pediatric and adult worlds in sepsis research,” she says.

One-third of patients who die in hospitals have sepsis. But according to Dr. Philips, the challenge is diagnosing sepsis early enough to save lives—before the heart weakens and organs start shutting down. For her project, Dr. Philips is sifting through the electronic health records of patients whose organs have failed due to sepsis.

Sepsis can progress rapidly, and it’s not known why one patient develops it and another, similar patient doesn’t. “Once we can identify early signs and symptoms that these patients have in common we can modify electronic

alerts and make them more usable to help physicians identify patients at high risk for sepsis and treat them,” Dr. Philips says. “Being able to predict which patients are at risk and to prompt doctors to quickly take preventive action can save lives.”

Connecting At-Risk Patients Via Big Data

After a divorce, Montefiore outpatient Fatoumata Camara lost her apartment, and she and her four children wound up living in a homeless shelter for a year. Montefiore community health worker Janet Gonzalez was determined to find the family a place to live—and succeeded. “Now that we have a home, we’re sleeping better, eating better—I’ve even lost weight,” Ms. Camara says.

Research confirms that the health of people like Ms. Camara improves when healthcare systems link them with community resources. But what’s the best way to identify those outpatients, like Ms. Camara, most in need of a community health worker’s help?

Asking all Montefiore outpatients to fill out a social-needs survey isn’t practical. So for his EXPLORE project, Kevin Fiori, M.D., M.S., M.P.H., assistant professor of pediatrics and of family and social medicine at Einstein and an attending physician at Montefiore Medical Group Pediatric Practice, is using data to identify people most likely to need social services and then developing strategies to alert clinical teams to administer surveys and, when

EXPLORE scholar Kaitlyn Philips, D.O., M.S., uses electronic health records to predict which patients are most at risk of developing sepsis.





EXPLORE scholar Kevin Fiori, M.D., M.S., M.P.H., uses social-needs data on more than 50,000 Montefiore patients to identify people most in need of help from community health workers.

warranted, connect those patients to various community health workers in the clinic.

Dr. Fiori recently spent 15 years directing a nongovernmental organization in Togo that uses community health workers to address health disparities and improve care. His insights from Africa should help with his EXPLORE project.

“Montefiore already has social-needs data on over 50,000 patients—an impressive amount of information,” Dr. Fiori says. “If the algorithm reveals which of those patients could benefit from taking a social-needs survey, the next step is to find the best way to efficiently integrate into a busy clinic the screening and subsequent referrals to

community health workers.”

A key aspect of the research is what’s known as “implementation science,” he says. “It involves repeatedly tweaking processes to work out all the details.” For example, who’s responsible for inputting data on patients coming in for appointments so that doctors can discover who should be screened? And what’s the best way to alert physicians to administer a survey?

“Once we have optimized the screening process in our pilot clinic, we will be able to incorporate that process throughout the Montefiore system,” Dr. Fiori says. He adds that he hopes the findings from his EXPLORE research will eventually benefit patients in the larger world.

“Montefiore already has social-needs data on over 50,000 patients—an impressive amount of information.”

— DR. KEVIN FIORI



HOW A LEARNING SYSTEM CAN SAVE LIVES



Using data from more than 68,000 patient encounters at Montefiore and the Mayo Clinic, Michelle Gong, M.D., helped develop the Accurate Prediction of Prolonged Ventilation (APPROVE) score for predicting respiratory failure or death in critically ill patients.

A multidisciplinary group at Einstein and Montefiore has proved that the LHS model can help medical advances reach patients faster—and save lives.

Respiratory failure causes severe breathing problems and is a leading cause of death for hospitalized patients. “Knowing that a patient has a high risk of developing acute respiratory failure allows doctors to take steps to address it,” says Michelle Ng Gong, M.D., chief of the divisions of pulmonary medicine and of critical care medicine at Einstein and Montefiore.

In 2014, Dr. Gong and her LHS colleagues received a five-year, \$1.9 million grant from the National Heart, Lung, and Blood Institute

(NHLBI) to develop and test a program that would (1) provide an early warning regarding which hospitalized patients were at high risk for respiratory failure and (2) prompt providers to administer proven therapies to those patients.

To create their early-warning system, the researchers worked with artificial-intelligence experts to comb through data collected from more than 68,000 patient encounters at Montefiore and the Mayo Clinic. The researchers determined which signs, symptoms, and other factors could predict risk and then looked for patterns of data indicating that respiratory failure or death was likely.

The result: an algorithm called the Accurate Prediction of Prolonged

Ventilation (APPROVE) score.

APPROVE continuously monitors the records of hospitalized patients and can alert doctors, raising red flags up to 48 hours before symptoms become life threatening. In validating APPROVE, the researchers found that 20% of patients with high APPROVE scores at any time during their hospital stays either will develop respiratory failure requiring mechanical ventilation or will die in the hospital, compared with only 1% of patients with low scores.

A 2018 study, conducted at multiple medical centers, compared existing early-warning measures with APPROVE. Results showed that APPROVE was the most accurate, with fewer false alarms, in identifying hospitalized patients at risk of death or in need of breathing machines.

“One of the most exciting outcomes of this study is that we were able to demonstrate that APPROVE works in a variety of complex hospital settings,” Dr. Gong says. “That means that patients elsewhere, as well as those at Montefiore, can benefit from it.”

APPROVE scores should help even more if doctors are notified about the best-possible treatments for their patients. That’s where the second fruit of Dr. Gong’s NHLBI-funded research comes in: a patient-specific checklist, called PROOFCheck (Prevention of Organ Failure Checklist), of interventions considered appropriate for that patient. Physicians also have the option to call on critical-care specialists for assistance. APPROVE and PROOFCheck are now both in use at Montefiore.

FORGING THE FUTURE OF MEDICINE

Using Decision Tools to Prescribe Pain Medicine

Opioid pain medications can effectively relieve pain after surgery. But opioids are often started without a clear plan for transitioning patients to safer forms of pain relief. As a result, as many as 1.6 million Americans who have surgery each year wind up taking opioids over the long term, increasing the risk of serious side effects such as opioid-use disorder and overdose. For her EXPLORE project, Justina Groeger, M.D., assistant professor of medicine at Einstein and an internist at Montefiore, is trying to figure out how to prescribe the right amount of opioids to surgical patients.

"The severity of pain is highly dependent on the individual patient," Dr. Groeger says, "so a one-size-fits-all approach doesn't work when prescribing pain medication." She is researching how to tailor opioid prescribing, starting with the amount of pain medication a patient was taking before leaving the hospital and tapering the dose over several days at home.

Using the LHS approach, Dr. Groeger is working with a team of clinicians, performance-improvement experts, and researchers to develop a protocol, test it in small groups of patients, and refine it based on feedback. "It's exciting to pull together a multidisciplinary team to work on a project like this," Dr. Groeger says.

Initially, Dr. Groeger is studying people who've had knee replacements. But

once the prescribing protocol is solid, she plans to integrate it into Montefiore's electronic-record system. "Ideally, the provider who is discharging a patient will be prompted with a recommended dose and tapering schedule for opioid pain medication as well as customized instructions for patients," she says.

Dr. Groeger's project also involves developing a clinical decision tool to help physicians tailor their pain medication prescribing to patients' individual needs. Ultimately, she envisions using the clinical decision tool for other purposes as well, such as customizing doses of insulin for patients with diabetes.

MINING DATA FOR BETTER HEALTH

"Having an LHS means recognizing that every patient's experience is an opportunity to learn as much as possible to help the next person," Dr. Rinke says. "As

"It's exciting to pull together a multidisciplinary team to work on a project like this."

— DR. JUSTINA GROEGER

data from electronic records accumulate and our ability to analyze those data improves, we'll be relying on a pipeline of rigorously trained researchers to harness data and take us into the future. Thanks to the EXPLORE grant, we're fortunate to have this crack squad of researchers focused on finding the best possible healthcare strategies and delivering them to patients." **E**

EXPLORE scholar Justina Groeger, M.D., works with a team of clinicians, performance-improvement experts, and researchers to develop a protocol for prescribing the right amount of opioids to surgical patients.





READY FOR ROTATIONS

Einstein's new Transition to Clerkship program helps third-year medical students shift from the classroom to the clinic

BY SUE BYRNE

A 10-month-old girl sits in a pediatrician's office with her grandmother. Two days ago she was in the hospital because a piece of a candy bar was lodged in the air-way leading to her right lung. Doctors removed it successfully and she's breathing comfortably now, but her grandmother, who speaks limited English, has some questions.

She doesn't understand the handout about choking hazards that they were given when they left the hospital or why they received it. She also wonders if the mold in their apartment might be contributing to the baby's wheezing and to her other granddaughter's asthma.

As the baby's physician, what do you focus on during this visit? The choking risks, certainly. But what about addressing what you suspect is food insecurity? And what about the mold problem?

Cases like the real-life one above happen regularly in medicine. Third-year Einstein medical students used it as an opportunity last summer to learn about what they might face as they began their clerkships at various clinics and hospitals in the Bronx. "We want students to start thinking about all the aspects that

contribute to the overall picture of their patients' health and what they can do to help," says Todd Cassese, M.D., assistant dean for clinical sciences at Einstein.

FROM SCHOOL TO HOSPITAL

The first two years of medical school are much like regular college work—lots of studying, memorization, classwork, and practice exams with volunteers and actors. But things change with the start of the third year, when medical students begin a series of clerkships on hospital wards to learn how to take care of patients under the supervision of medical professionals.

"Students have to apply their classroom knowledge in ways they haven't been asked to before," Dr. Cassese explains. "Now they will need to go on rounds with doctors and residents, make oral presentations, and create daily progress notes. That can be stressful and involve long hours. And as the most junior members of the team, they won't have as much say regarding what they have to do and when they have to do it as they did in years one and two."

An increasing number of medical schools are recognizing the importance



"We want students to start thinking about all the aspects that contribute to the overall picture of their patients' health and what they can do to help."

— DR. TODD CASSESE



OPPOSITE PAGE, clockwise from left: Third-year medical students Xavier Quezada, left, and Marouf Hossain use a ventilation device on an adult mannequin as part of basic life-support training; Eden Gelman practices on a baby model; and a student tries out lifesaving compression techniques on an adult model. THIS PAGE: Stephen Baum, M.D., distinguished professor of microbiology & immunology, leads a workshop on clinical reasoning.

READY FOR ROTATIONS



Above, Natalie Ramsey practices a physical exam on fellow third-year medical student Nisha Shah in the Clinical Skills Center in the Van Etten Building.

of better orienting students to the rigors of the clerkship years. To help students cope with the demands of their new roles, Einstein's senior associate dean for medical education, Joshua Nosanchuk, M.D., asked the offices of medical education and student affairs to develop a plan to expand Einstein's student training from one day to a full week. "We convened focus groups of third- and fourth-year medical students, and many told us that they faced challenges in the hospital they weren't prepared to manage," Dr. Nosanchuk says.

A working group spearheaded by Dr. Cassese asked colleagues nationwide to come up with authentic experiences that would give students the tools needed to succeed once they started their rotations.

Introduced last June to 196 third-year students, the Transition to Clerkship program involved five days of classes and hands-on workshops and

help from more than 150 Einstein and Montefiore physicians, nurses, social workers, respiratory therapists, and other volunteers.

ESSENTIAL EXERCISES

To third-year student Deborah Schwartz one of the week's most important exercises involved the clinical reasoning session on how to present patient cases to other health professionals on rounds.

"Learning how to summarize all the relevant patient information and condense it into a short, informal presentation was very helpful to a third-year, because that is an essential skill on the wards," Ms. Schwartz says. "Without that workshop, I would not have understood what was expected of me, how to structure my presentations, or what content to put in them."

M.D./Ph.D. candidate Niloy Jafar Iqbal says that learning clinical science is quite different from learning basic science. "There is a change in mentality. You're applying your scientific

knowledge to human patients," he explains. The session on seeking and receiving feedback was among the most helpful, he says. "We learned to take feedback as constructive criticism and not to be defensive about it. You can voice your opinion, but you have to be open to the idea that you still have a lot to learn."

APPLYING SCIENCE TO PATIENTS

The Transition to Clerkship week began with a disease-mapping exercise. Students were presented with a fictional patient who had acute rhinosinusitis, a common inflammatory condition of the upper airways that affects nearly 40 million Americans every year.

Third-year students were given key clinical features of the condition, such as congestion, loss of sense of smell, and nasal drainage; then, working in small groups, they mapped those features to their possible causes—for example, a viral infection, an allergic reaction, or



Alan Engler, M.D., shows third-year medical student Lucy Oh how to conduct a physical exam of "patient" Shayon Mottahed, also a third-year.

nasal polyps. Using those maps, the students were asked to list four medications that could potentially be effective in treating the root causes of rhinosinusitis and not just its symptoms.

"This session was meant to help students better understand how basic-science principles are linked to clinical reasoning," Dr. Cassese says.

Another exercise focused on the hypothesis-driven physical exam, in which students practiced physical examination maneuvers on their peers in the Clinical Skills Center in the Van Etten Building. As a leader of one of the small-group sessions, Alan Engler, M.D., a clinical assistant professor in the department of surgery, presented a scenario to the third-years: "I'm having trouble breathing. What should you do? Examine my abdomen? My neck? What questions should you ask me?"

Students took part in basic life-support training, also in the Clinical Skills Center, practicing effective compression techniques using different ventilation devices on adult and baby mannequins. Other sessions included work-life balance (see "A Stressful Learning Environment," at right), best practices regarding electronic health records, note writing in different specialties, clinical informatics at the bedside, medical interpreters, the student's role on the interdisciplinary healthcare team, developing a professional identity, and career planning.

Now many weeks into his clerkship, Mr. Iqbal reports that "the days are long but the weeks are short. Medicine is one of the hardest careers as far as hours per week, but it's one of the most gratifying. So far it has been an amazing experience. Nothing beats learning on the job." **E**



A STRESSFUL LEARNING ENVIRONMENT

The hospital environment can be intense for medical students.

"Being in an acute-care setting, you will encounter shouting, temper tantrums, and rudeness," Allison Ludwig, M.D., Einstein's associate dean for student affairs, told the medical students assembled in Lubin Dining Hall as part of their Transition to Clerkship training. "It may not be directed at you. But it erodes the learning environment," she said.

She cautioned students to not confuse being embarrassed with being mistreated. "On rounds, we go from the lowest up, which means the student speaks first" when giving a patient assessment, Dr. Ludwig said. This is meant to be a learning experience—not an exercise in humiliation. She noted that mistreatment, which can include public belittling, will not be tolerated at Einstein. "We have a zero-tolerance policy, and an 'ombuds' panel of faculty and students will confidentially investigate your complaint without risk of retaliation," she said.

Dr. Ludwig offered other advice to the third-years:

- Use your time wisely during clerkships. "At the end of the day, ask 'Is there anything else I can do today?' If the answer is no, then you should leave. You don't get bonus points for staying when the work is done, so ask to be dismissed."
- Advocate for yourself. "Part of a strategy for maintaining work-life balance is being proactive," she said. "You're entitled to a doctor's appointment or a sick day. And inform people as soon as you know that you have an important function you have to attend."
- Seek out Einstein's mental-health resources if needed. The new Student Mental Health Center in the Van Etten Building is set up with staff trained to help with such issues as stress, anxiety, and depression. "You can be more effective in caring for others when you attend to your own well-being first," she said.



CONNECTING the DOTS

With the help of a tiny worm, Einstein scientists complete the first wiring diagram of an animal's entire nervous system

BY GARY GOLDBERG

Who doesn't have fond memories of the childhood puzzle Connect the Dots? With the stroke of a pencil, you could create order from disorder by transforming a seemingly random series of numbered points into a line drawing of a fish, a rabbit, or a tree. Einstein scientist Scott Emmons, Ph.D., has never outgrown his fascination with that sort of magic.

For almost two decades, Dr. Emmons, professor of genetics and in the Dominick P. Purpura Department of Neuroscience and the Siegfried Ullmann Chair in Molecular Genetics, has been connecting many thousands of dots—each representing a neural structure—visible on thousands of serial electron micrographs of the tiny roundworm *Caenorhabditis elegans*.

Dr. Emmons' painstaking pointillist portraiture has culminated in the first complete wiring diagram of the nervous system of any animal—in this case, an animal used by scientists worldwide as a model organism for studying the basics of biology and disease.

Dr. Emmons' magnum opus—featured on the July 4, 2019, cover of the prestigious journal *Nature*—marks a major milestone in the field of “connectomics,” the effort to map the myriad neural connections in a brain, brain region, or nervous system, with the goal of finding the specific nerve connections responsible for particular behaviors.

“Structure is always central in biology,” Dr. Emmons says. “The structure of DNA revealed how genes work, and the structure of proteins revealed how enzymes function. Now the structure of the nervous system is revealing how animals behave and how neural connections go wrong to cause disease.”

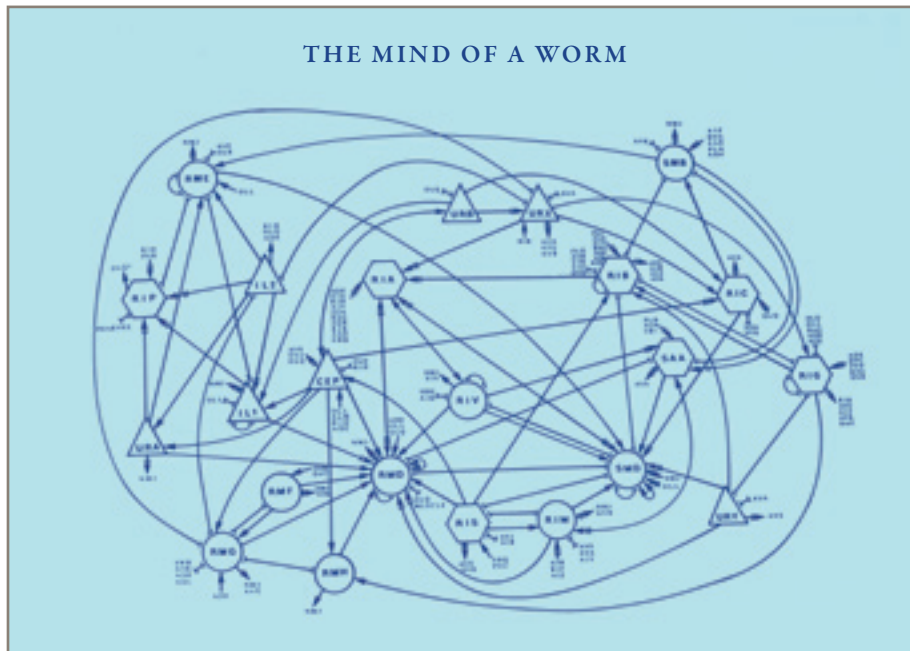
NEW FIELD WITH A LONG PAST

Although the word *connectomics* began to be used only some 15 years ago, the field dates back at least to the Renaissance. Fascinated with anatomy, Leonardo da Vinci dissected a variety of organisms, from frogs to oxen to humans, seeking to



At left: *C. elegans* adults, colorized and greatly magnified beyond their actual 1 mm length.

CONNECTING THE DOTS



A figure from "The Structure of the Nervous System of the Nematode *Caenorhabditis elegans* (The Mind of a Worm)," by Dr. Sydney Brenner and colleagues. The 450-page manuscript mapped a significant portion of the *C. elegans* nervous system.

understand how the nervous system's interconnected structures give rise to the senses and perhaps even the soul. With his crude tools and razor-sharp mind, he developed an original model of sensory physiology. (The soul, alas, eluded his grasp.)

Connectomics began in earnest in the 1960s with Sydney Brenner, a South African-born molecular biologist based at the Medical Research Council in Cambridge, England. Early in his career, Dr. Brenner made important discoveries regarding how genes replicate and convey information. In the late 1960s, he turned his attention to the genetic and neural bases of behavior.

Dr. Brenner's first order of business was describing the structure of a nervous system: a network of connected neurons. He realized that figuring out how those neurons are connected would be essential (although not sufficient) for

understanding how that nervous system functions. Or to paraphrase one neuroscientist: You won't fully understand the brain *with* a wiring diagram, but you likely won't understand the brain *without* one.

Dr. Brenner needed a suitable experimental organism, one with accessible genetics but relatively advanced behaviors. The fruit fly *Drosophila* met both criteria, but its 100,000-neuron nervous system was too complex. He ultimately chose *C. elegans*, a benign, nearly translucent, millimeter-long roundworm. It can be found the world over, dining on microbes that live on rotting vegetation, especially fruit. ("It really should be called the fruit worm," Dr. Emmons says.)

Although *C. elegans* lacks circulatory and respiratory systems, its nervous system—which includes a rudimentary brain—is capable of several functions:

basic learning, memory, experiencing fear, sensing and squirming away from predators, navigating toward food, and mating and reproducing using its sperm and eggs. All those activities occur in one tiny animal containing only about a thousand cells, one-third of them dedicated to the nervous system.

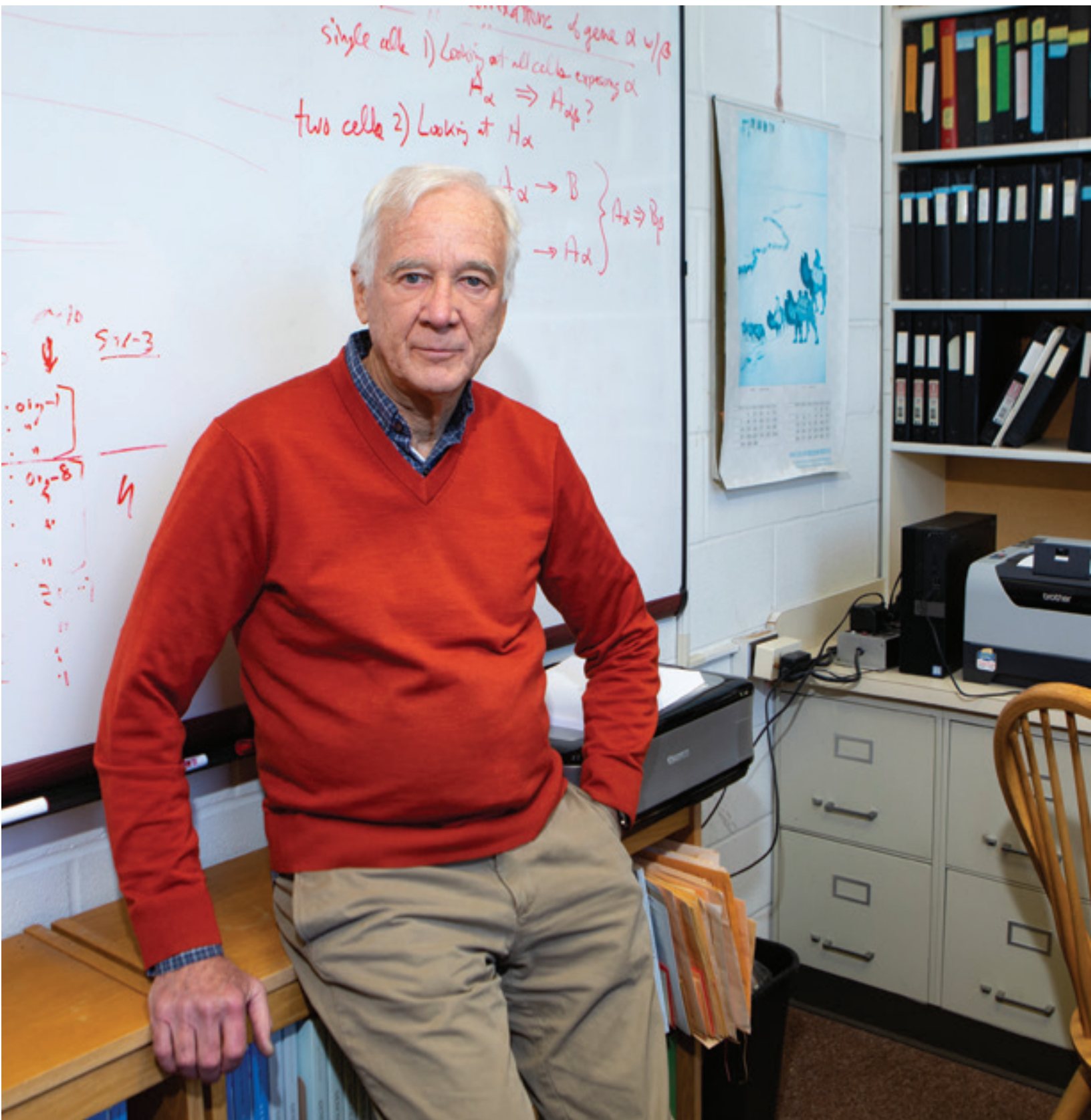
FINDING THE RIGHT MICROSCOPE

Although the worm was small, the task ahead loomed large. Details of its nervous system were beyond the resolving power of the light microscope, so Dr. Brenner and his colleagues would need to use electron microscopy (EM). EM works by passing electrons through razor-thin slices of tissue to produce magnified images. Some 20,000 cross-sectional slices—each one-thousandth the width of a human hair—would be required to cover the roundworm's nervous system from "head" to "toe."

Further complicating things, each slice contained numerous anatomical details—slivers of chemical and electrical synapses and neuromuscular junctions. (A synapse is the junction where a neuron passes an electrical or chemical signal to another neuron, or where a neuron connects with another type of cell. For example, a neuromuscular junction is a synapse at which a neuron transmits a signal to a muscle fiber, triggering muscle contraction.)

Making a wiring diagram required scrutinizing every slice, identifying each neural structure, and connecting that structure to the corresponding structure

Einstein's Scott Emmons, Ph.D., and colleagues completed the effort begun by Nobel laureate Sydney Brenner to completely map the *C. elegans* nervous system.



CONNECTING THE DOTS

Thousands of laboratories around the world would adopt the roundworm as an essential animal model.

in the previous slice—all by hand.

Led by lab member John White, a team of half a dozen scientists and artists worked for 15 years to connect most of the dots. All told, Dr. Brenner and his colleagues produced 132 maps, encompassing about 5,000 chemical synapses, 600 electrical synapses, and 2,000 neuromuscular junctions. In 1984, they delivered their Tolstoyan, 450-page manuscript—subtitled “The Mind of a Worm”—to *Philosophical Transactions of the Royal Society*. It was published two years later as a special one-volume issue of the journal.

The scientific community initially greeted the paper with a collective yawn, perhaps because so few researchers knew what to make of it. One reviewer confined his comments to the introductory discussion, writing “after all, few will read the detail.” But *C. elegans* research eventually flourished, largely because of all those connectome maps. Thousands of laboratories around the world would adopt the roundworm as an essential animal model. “‘The Mind of a Worm’ became their bible,” Dr. Emmons wrote.

The study of Dr. Brenner’s connectome has yielded numerous benefits, including the discoveries of:

- How the roundworm responds to temperature, chemicals, touch, and other stimuli—fundamentals that apply also to the nervous systems of higher organisms;
- Netrins, members of a class of proteins that guide nerve projections called axons to their intended targets. Netrin defects have been linked to human tumors;
- MicroRNAs;
- RNA interference; and
- Programmed cell death.

Since its publication 36 years ago,

Dr. Brenner’s paper has been cited more than 4,000 times—a level of recognition achieved by just a handful of studies. In 2002, Dr. Brenner was honored with a share of the Nobel Prize in Physiology or Medicine for findings related to his work on *C. elegans*. He died in 2019 at age 92.

BUILDING A BETTER CONNECTOME

Voluminous though it was, Dr. Brenner’s roundworm map was incomplete. It skipped large portions of the worm’s body and pertained only to the hermaphrodite (which can self-fertilize and is considered the equivalent of the female of the species), not to the male.

In 1999, Dr. Emmons and his colleagues took on the challenge of finishing Dr. Brenner’s map. Looking back, it seems as though Dr. Emmons’ career had been designed to lead him to this very task.

A native of Sudbury, Massachusetts, Dr. Emmons discovered his love for science and mathematics through his father, a professor of applied engineering at Harvard University. Dr. Emmons earned a B.S. in biology at Harvard, followed by a Ph.D. in biochemistry at Stanford, where he grew interested in gene function and regulation and developmental biology.

Shortly after earning his doctorate in 1974, he heard a lecture on *C. elegans* and quickly realized that this tiny organism could help him in his research.

Geneticists gain insights into how normal genes work by inducing mutations and observing their effects. So they prize animal models that have readily manipulable DNA, short life cycles, and quick reproduction—all of which the roundworm offers.

C. elegans by the NUMBERS

1900

YEAR FIRST
DESCRIBED
AS A SPECIES

1 to 2

worms able to
fit on the head
of a pin

3 DAYS

development
from a fertilized
egg to a fertile
adult

LIFE SPAN

2

to

3

WEEKS

38%

C. elegans genes with
human equivalents

PROTEIN-CODING GENES

20,444 in roundworms

~21,000 in humans

NEURONS

383 in an adult
male

302 in an adult
hermaphrodite

SYNAPSES

~8,000

chemical
& electrical
connections

15,000
to
20,000

ELECTRON-MICROGRAPH

SLICES

NEEDED TO CONSTRUCT
the complete connectome

ROUNDWORM RESEARCHERS
WORLDWIDE

1970



10 to 20

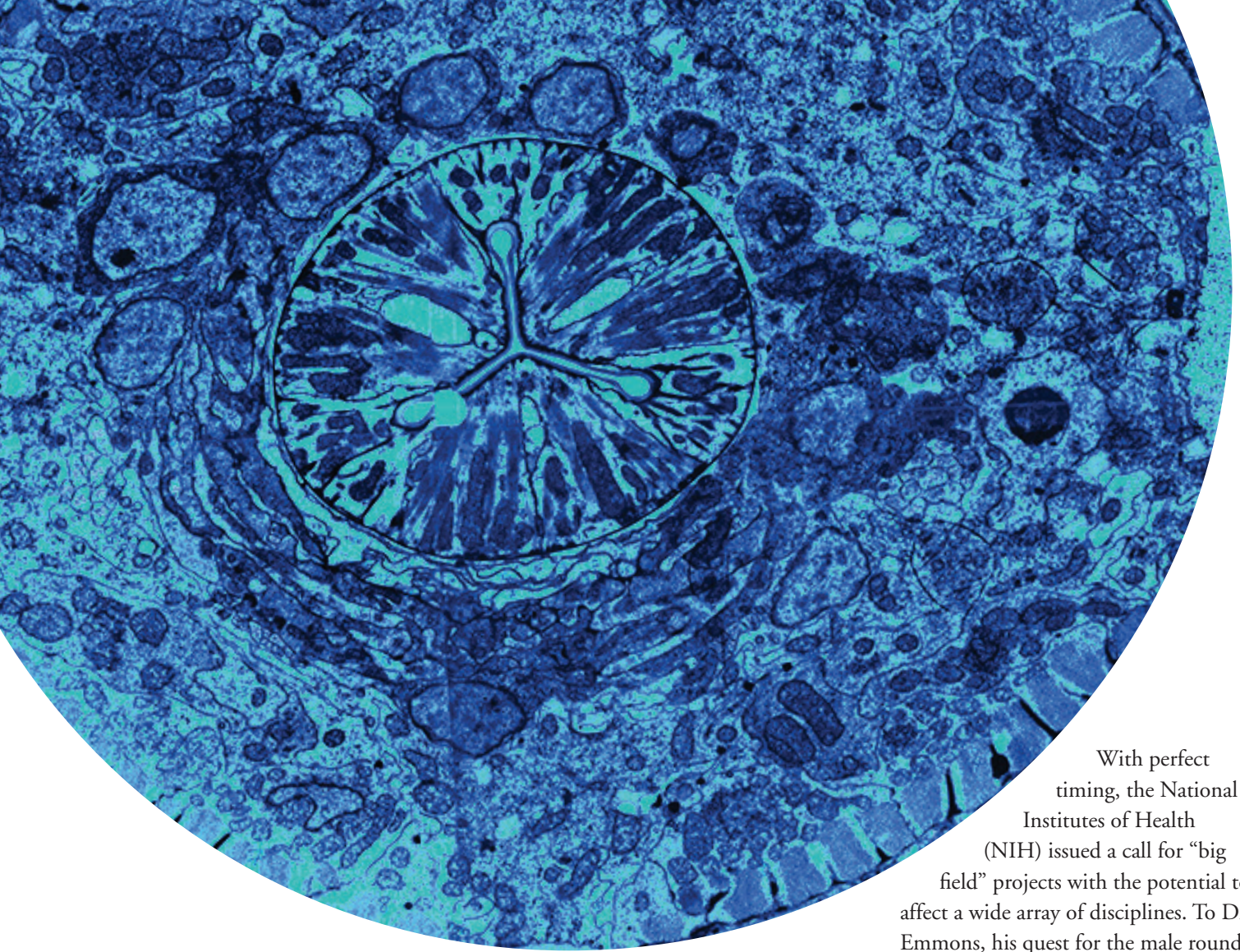
TODAY



4,000 to 5,000

6

NOBEL PRIZES
AWARDED TO
C. ELEGANS
RESEARCHERS
TO DATE



The image above is among thousands of *C. elegans* cross sections curated by electron microscopist David Hall, Ph.D.

Dr. Emmons joined the Einstein faculty in 1979. Several years later he took a sabbatical to do a postdoctoral fellowship at the Medical Research Council, the mecca of *C. elegans* research, studying under Jonathan Hodgkin, Ph.D., one of Dr. Brenner's former students.

Upon returning to Einstein in 1986, Dr. Emmons studied how genes encode roundworm morphology (form and structure), eventually focusing on male mating behavior and the neurons responsible. "It struck me that the male connectome was a big missing piece of *C. elegans* biology. Our field is characterized by completeness. We seek to know all the cells in the organism, all the genes in the genome, and all the connections in the nervous system," Dr. Emmons says.

With perfect timing, the National Institutes of Health (NIH) issued a call for "big field" projects with the potential to affect a wide array of disciplines. To Dr. Emmons, his quest for the male roundworm connectome fit the bill. The NIH agreed, awarding him a pilot project grant to develop the necessary software. The project would ultimately be funded for 10 years by the G. Harold and Leila Y. Mathers Charitable Foundation.

"We thought it could be done with the help of a personal computer, but we really didn't know," Dr. Emmons recalls. "The male is much more complex than the female. Also, it was possible that some of the neurons ran in the plane of the slices rather than across them, which would mean we wouldn't be able to see all the connections using serial electron micrographs."

Dr. Brenner by this time had different research priorities and was pleased that others were continuing work on the *C. elegans* connectome, according to Dr. Emmons.

MEETING THE CHALLENGE

To complete the male connectome, Dr. Emmons would need an electron microscopist with expertise in roundworms. Such specialists were rare at the time, so he was incredibly lucky to find one at Einstein: David Hall, Ph.D., professor in the Dominick P. Purpura Department of Neuroscience.

Dr. Hall began working with *C. elegans* while earning his doctorate at the California Institute of Technology. He came to Einstein in the mid-1970s to study the comparative anatomy of

gap junctions in animals, including fish and snails, but eventually switched back to *C. elegans*.

“I returned to a field that was starving for people to do EM,” Dr. Hall recalls. “When I said I was open for business, researchers from all over started sending me *C. elegans* mutants for imaging.”

Dr. Emmons would come to rely on Dr. Hall’s know-how for his connectome studies. In addition, Dr. Hall provided a priceless resource: the *WormAtlas*, a trove of roundworm data that would

eventually include all of Dr. Brenner’s original connectome maps and images (see “The *WormAtlas*,” page 44).

Constructing the male connectome was possible, but also arduous. In 2012, after a dozen years of work, Dr. Emmons and his colleagues published in *Science* the wiring diagram of the part of the nervous system controlling mating in the male roundworm. Their findings revealed that male mating requires 144 neurons—nearly half the worm’s total number—and described the connections among those 144 neurons and



Electron microscopist Dr. Hall sits between a desk featuring a *C. elegans* electron micrograph cross section and boxes containing many other cross sections of the roundworm.

The WormAtlas: All Things Anatomical in One Place

By the 1990s, connectomics pioneer Sydney Brenner had closed his lab and moved on to other pursuits, his voluminous roundworm research files left to collect dust on shelves at the Medical Research Council in England. But thanks to an Einstein scientist, this invaluable trove of data wouldn't remain untouched for long.

In 1998, David Hall, Ph.D., professor in the Dominick P. Purpura Department of Neuroscience at Einstein and a veteran roundworm researcher and electron microscopist, won a National Institutes of Health grant to establish a center for *C. elegans* anatomy at Einstein. Among the center's goals were to extend the use of electron microscopy (EM) in roundworm research and to create a clearinghouse for all types of anatomical data for *C. elegans*.

Dr. Hall asked Dr. Brenner's permission to move the roundworm files to his fledgling center at

Einstein, for further analysis and safekeeping. "Dr. Brenner and his colleagues agreed, with the stipulation that we devise some way to communicate the data to the roundworm community," Dr. Hall says.

The data would become the centerpiece of the *WormAtlas* (www.wormatlas.org), a leading resource for *C. elegans* researchers. The open-source (i.e., freely available) *WormAtlas* offers tens of thousands of EMs, wiring diagrams, anatomical illustrations, detailed handbooks on both sexes and on worms in every stage of development, links to outside roundworm resources, a compendium of worm-related publications, a community forum, and more.

Dr. Hall, a coauthor of Dr. Emmons' groundbreaking *Science* and *Nature* papers, is constantly expanding the *WormAtlas* with data from his own studies and from researchers the world over.

64 muscles, involving more than 8,000 synapses.

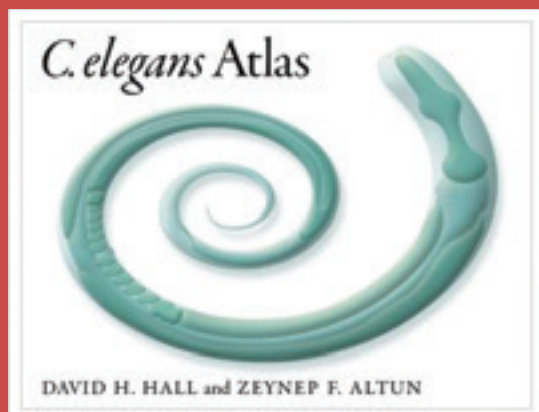
"Our work [on] the underlying function that governs mating behavior in the male roundworm is a step toward identifying how an animal controls seemingly complex movements," Dr. Emmons said at the time. In addition to finding out how the neurons and muscles are connected, the researchers for the first time accurately measured the weights of those connections—in other words, they estimated the strength with which one neuron or muscle communicates with another.

Dr. Emmons' contribution to the roundworm canon was awarded the 2013 Newcomb Cleveland Prize by the American Association for the Advancement of Science (AAAS), recognizing the most outstanding paper published in *Science* from June 2012 to May 2013.

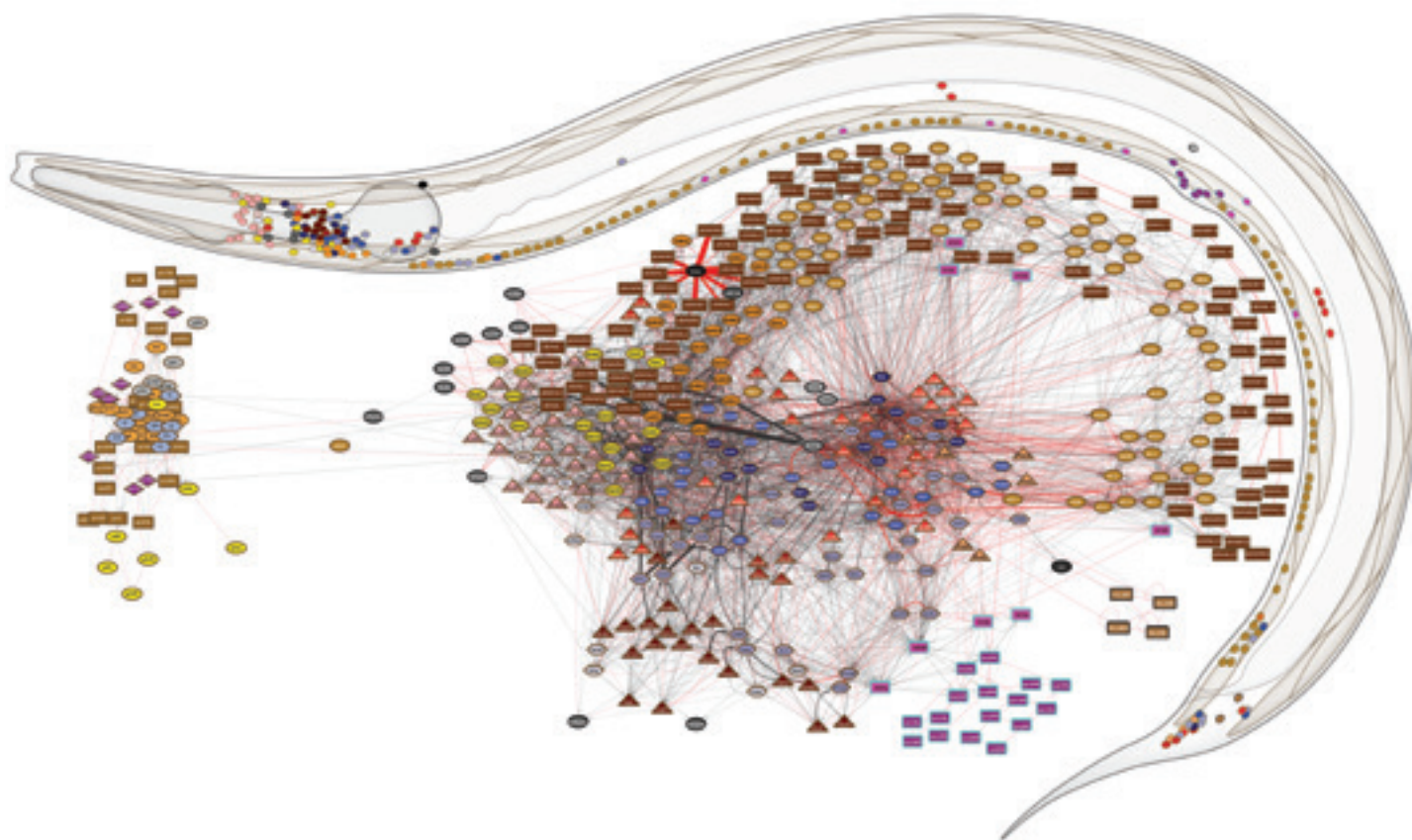
"This one paper emerged as a tour de force from amongst many competitive entries," *Science* editor-in-chief Marcia McNutt remarked at the time. "The robust model system will contribute significantly to our further understanding of the precise mapping between neuron activity and essential behaviors that ensure survival of the species."

Still, there were those who wondered what all the fuss over connectomes was about. At a 2012 debate held at Columbia University just before the publication of the *Science* paper, New York University neuroscientist Anthony Movshon remarked that the connectome "is a sort of a bed on which we can build experiments—and many people have built many elegant experiments on that bed. But that connectome by itself has not explained anything."

It would take further research by



The 348-page *C. elegans Atlas* is derived from the online *WormAtlas*. (Cover illustration by Chris Crocker.)



Dr. Emmons to convince doubters that mapping neural connections was worth the effort.

THE MIND OF A WORM 2.0

Although the AAAS award would have been a fitting capstone to his career, Dr. Emmons had more dots to connect. Using new electron micrographs and Dr. Brenner's old ones, he and his team compiled complete wiring diagrams of the adult male and the hermaphrodite roundworm. They found all the synapses connecting neurons with one another, as well as the synapses connecting nerves to muscles and other tissues, such as the gut and skin, and the connections between the muscle cells—including estimates of the strength of those synapses.

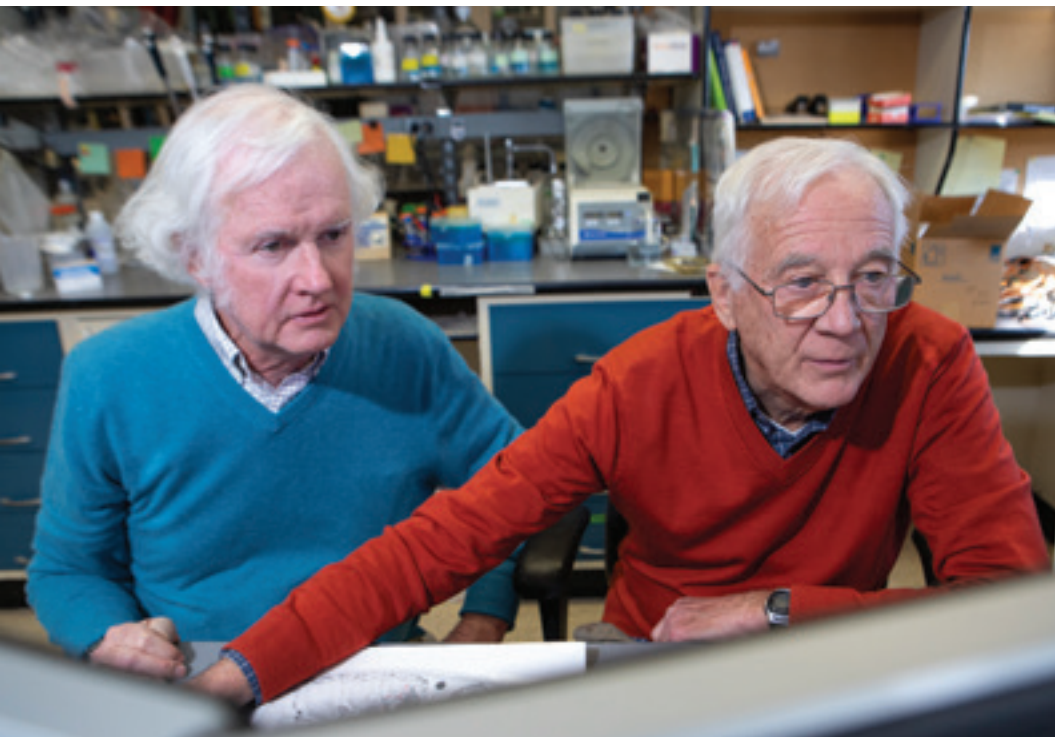
The EM images were digitized and analyzed using the group's homegrown

software, which significantly facilitated the process. Yet it took seven more years of work before Dr. Emmons and his colleagues could complete the two connectomes and publish their maps in July 2019 in *Nature*. By diagramming both the male and female *C. elegans* nervous systems, the researchers were able to make the first comprehensive comparison of the wiring of the sexes.

"While the synaptic pathways in the two sexes are substantially similar, a number of the synapses differ in strength, providing a basis for understanding sex-specific behaviors," Dr. Emmons says.

The primary sex differences pertain to reproductive functions: for the hermaphrodite, it's the vulval and uterine muscles and the motor neurons that control them; for the male, it's the large number of additional neurons, sex

This image, from the 2019 *Nature* paper published by Dr. Emmons and his colleagues, shows the nervous system and nerve connectivity of the adult *C. elegans* hermaphrodite. Triangles equal sensory neurons, ovals or circles equal motor neurons, hexagons equal interneurons (which connect sensory and motor neurons), and rectangles equal muscles. Shades of red equal categories of sensory neurons, shades of yellow and orange equal classes of motor neurons, and shades of blue equal categories of interneurons. Sex-specific neurons are pink or purple.



"Since the roundworm nervous system contains many of the same molecules as the human nervous system, what we learn about the former can help us understand the latter."

— DR. SCOTT EMMONS

muscles, and connections in the tail that generate the circuits for copulation. But beyond those reproductive differences, a surprising percentage—up to 30%—of synapses between neurons in central pathways shared by both sexes also appear to differ considerably in strength.

The *Nature* paper attracted a lot of attention in both the lay and scientific press, including major articles in *The New York Times*, *The Washington Post*, *The Telegraph*, *The Guardian*, and *New Scientist*. The findings mark "a major step forward in the attempt to understand how a brain's function emerges from its form," wrote University of Rochester neuroscientist Douglas S. Portman in a "News & Views" article accompanying Dr. Emmons' paper in *Nature*.

"Depicted graphically, the new connectomes don't obviously resemble artificial neural networks or the wiring

The project to map the *C. elegans* connectome involved the close collaboration of neuroscientist Dr. Hall, left, and geneticist Dr. Emmons.

schematics of simple electronic devices; they look more like the cobwebs that lurk at the back of the broom cupboard," Dr. Portman added. "Although intriguing patterns can be identified, distinct circuits for specific behavioral responses are not readily apparent. As others have pointed out, the connectome is only a map of possibilities."

But those very possibilities are what drive researchers in connectomics. "These connected networks serve as starting points for deciphering the neural control of *C. elegans* behavior," Dr. Emmons says. "Since the roundworm nervous system contains many of the same molecules as the human nervous system, what we learn about the former can help us understand the latter."

Dr. Emmons believes that the combined impact of his two major connectome papers—first in *Science*, then in *Nature*—has largely persuaded skeptics that plotting neural connections is worth the effort. "We not only mapped the connectome, we mapped the first natural neural network," he says. "Using graph theory, we were able to separate the neurons and muscles into groups, and we could say that this group must be doing this and that one must be doing that—linking specific parts of the connectome to specific behaviors."

Researchers have hypothesized that some neurological and psychiatric disorders, such as schizophrenia and autism, are "connectopathies"—that is, problems caused by "faulty wiring."

“This hypothesis is strengthened by the finding that several mental disorders are associated with mutations in genes that are thought to determine connectivity,” Dr. Emmons says. “Connectomics has the potential to help us understand the basis of some mental illnesses,” possibly suggesting new treatment strategies. In concluding his *Nature* “News & Views” article, Dr. Portman wrote: “Once again, Brenner’s tiny worm, occupying its unique sweet spot between simplicity and complexity, finds itself on the front line of biology’s most challenging problems.”

ON TO THE HUMAN CONNECTOME?

Dr. Emmons is now studying how the roundworm’s wiring is encoded in the genome, a challenge as complex and laborious as his connectome studies. Meanwhile, other groups are attempting to draw wiring diagrams of more-complex model organisms, including the fruit fly and the mouse.

If these efforts are successful, connectomics will become even more relevant to the study of human biology. Whether neuroscientists will ever be able to map the human nervous system, with its 100 billion neurons and quadrillions of connections, is the stuff of far-off dreams.

“My imagination isn’t good enough to contemplate the implications of knowing the whole human connectome,” Dr. Emmons says. “It’s a profound thought, though. It could ultimately get to questions about the nature of consciousness.” **E**



WATCH THE VIDEO

See Dr. Emmons explain the worm connectome:

magazine.einstein.yu.edu/worm20

A Sampling of *C. elegans* Researchers at Einstein



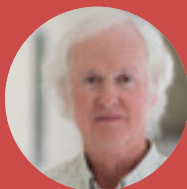
Michael Aschner, Ph.D., professor of molecular pharmacology, in the Dominick P. Purpura Department of Neuroscience, and of pediatrics, and the Harold & Muriel Block Chair in Molecular Pharmacology

Using roundworms, rodents, and tissue cultures as experimental models, Dr. Aschner studies how heavy metals, such as methylmercury and manganese, are transported in the nervous system and cause neurodegeneration.



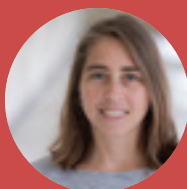
Hannes E. Buelow, Ph.D., professor of genetics and in the Dominick P. Purpura Department of Neuroscience

Dr. Buelow works with roundworms to understand how developing axons and dendrites (which relay signals away from and to neurons, respectively) navigate the extracellular space in order to connect to their partner neurons. Improper neuronal connections have been linked to a range of neurological problems, including Alzheimer’s disease, schizophrenia, and autism spectrum disorders.



David Hall, Ph.D., professor in the Dominick P. Purpura Department of Neuroscience

Dr. Hall, a pioneer in the use of electron microscopy to study the roundworm connectome, currently uses the technique to map neural connections and neural development in both younger and older roundworms and in mutants—work that may improve our understanding of early development and aging. As described in “The WormAtlas: All Things Anatomical in One Place” (page 44), Dr. Hall also serves as director of this premier online resource for *C. elegans* researchers.



Peri Kurshan, Ph.D., assistant professor in the Dominick P. Purpura Department of Neuroscience

A new member of the Einstein faculty, Dr. Kurshan studies synapse formation in *C. elegans*, with the goal of understanding how defects in the development and function of synapses lead to neurodevelopmental disorders, such as autism spectrum disorders and intellectual disability.

PASSIONATE PURSUITS

Finding the Body's Internal Beauty

Medical student Adele Heib honors those who donate themselves to science

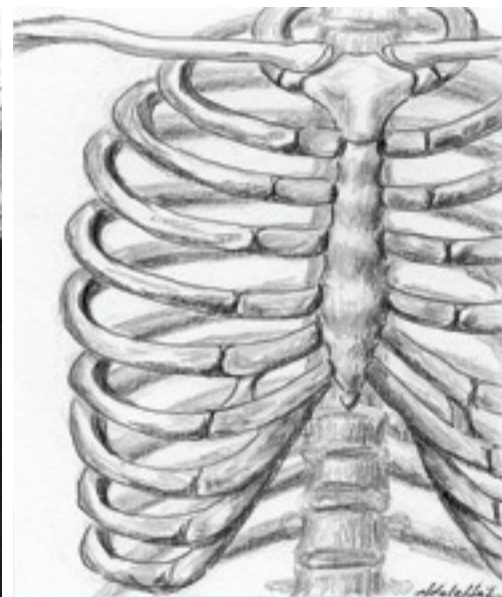
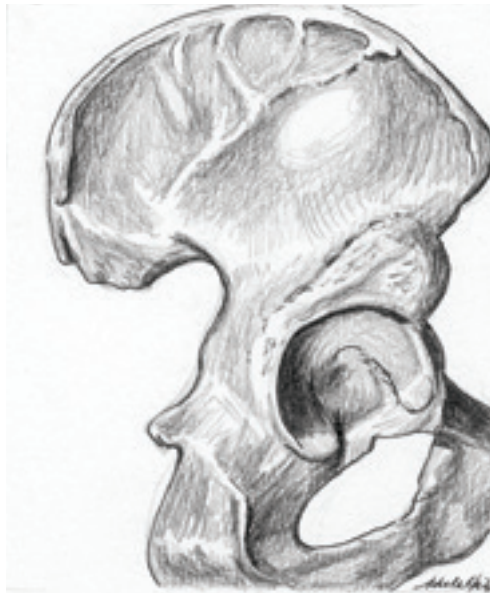
BY WAYNE COFFEY

A striking piece of art, measuring 3½ by 4½ feet, hangs on the corridor wall connecting the Forchheimer and Belfer basements. It comprises 40 drawings of body parts, ranging from the wispiest air sacs to the chunkiest leg bones, each about 5 inches square and drawn by Adele Heib, a third-year Einstein medical student.

Farther down the corridor, near the Belfer elevator, a magazine rack holds copies of *Ad Libitum*, Einstein's annual art and literary magazine. Inside its pages are two more of Ms. Heib's creations, showing a weathered gas station and an inviting arched entryway. "Drawing is a really nice way to escape the rigors of med school and decompress—to kind of lose yourself in the process," she says. "For me it's therapeutic."

THANKING THE DONORS

The opportunity to draw the various parts of the body arose when Ms. Heib took the clinical and developmental anatomy course, in which first-year students dissect cadavers to deepen their understanding of the human structure. After completing the class, Einstein students present a gift to their school during the "Convocation of Thanks" ceremony, which celebrates their achievements and pays homage to the people whose bodies were donated.



Four of the 40 sketches of human body parts that third-year medical student Adele Heib completed include, clockwise from top left: the pelvis (specifically the ilium, ischium, and acetabulum), the diaphragmatic crus, the sternum (rib cage), and the mandible (jaw).



“Drawing is a really nice way to escape the rigors of med school and decompress—to kind of lose yourself in the process. For me it’s therapeutic.”

— ADELE HEIB

The ceremony, one of the first of its kind in the country, was begun by Todd Olson, Ph.D., emeritus professor of anatomy and structural biology. Every March, anatomy students decide on their gift and then present it. New gifts take their place alongside previous ones along the Belfer-Forchheimer corridor, including a mounted and framed blue scrub top, signed by every student in one class, and a surrealist painting of Albert Einstein wearing headphones.

Ms. Heib’s drawings, selected as the class gift for 2018, took three weeks to complete. She worked on the project day and night while studying, painstakingly drawing one body part from each of the 40 cadavers dissected that year. Her favorite mediums—ink and graphite—captured the nuances and contours of structures representing every major organ system in the body. She found it a powerful way to reinforce many of the anatomical intricacies she had learned about in the course.

“The human body is amazing and fundamentally beautiful, and I wanted to represent that,” Ms. Heib says. “There’s so much fluidity, so many patterns and lines. And I like using black and white to make it cohesive.”

Sherry Downie, Ph.D., professor of anatomy and structural biology and in

the Arthur S. Abramson Department of Physical Medicine and Rehabilitation and current director of the anatomy course, regularly walks through the Belfer-Forchheimer corridor and says she continues to be impressed by Ms. Heib’s work. “Adele’s drawings are beautiful, but what strikes me the most about them is the fact that she thought to create one to honor each cadaver.”

LINKING ART AND SURGERY

Ms. Heib says she has loved art for as long as she can remember. Growing up in Rye Brook, New York, she would often draw on her own at home.

As much as she savors every opportunity to take out her sketch pad, Ms. Heib knows that pursuing a career in medicine was the right choice for her. And when she recently did a surgical rotation, she realized that her artistic sensibility might well make her a better physician, too.

“I am a very visual learner, a very tactile, hands-on person,” Ms. Heib says. “During an operation, you have to visualize in your brain how it’s going to go. You have to know your anatomy and be very particular about everything. If I go into surgery, I think my art background will help with that visualization and with mapping out what I have to do.” **E**



Two of Ms. Heib’s ink sketches can be found in recent issues of Einstein’s *Ad Libitum* magazine. At top is “Station #59” and above is “Entryway.”



VIEW MORE

Find additional art by Ms. Heib: magazine.einstein.yu.edu/art20

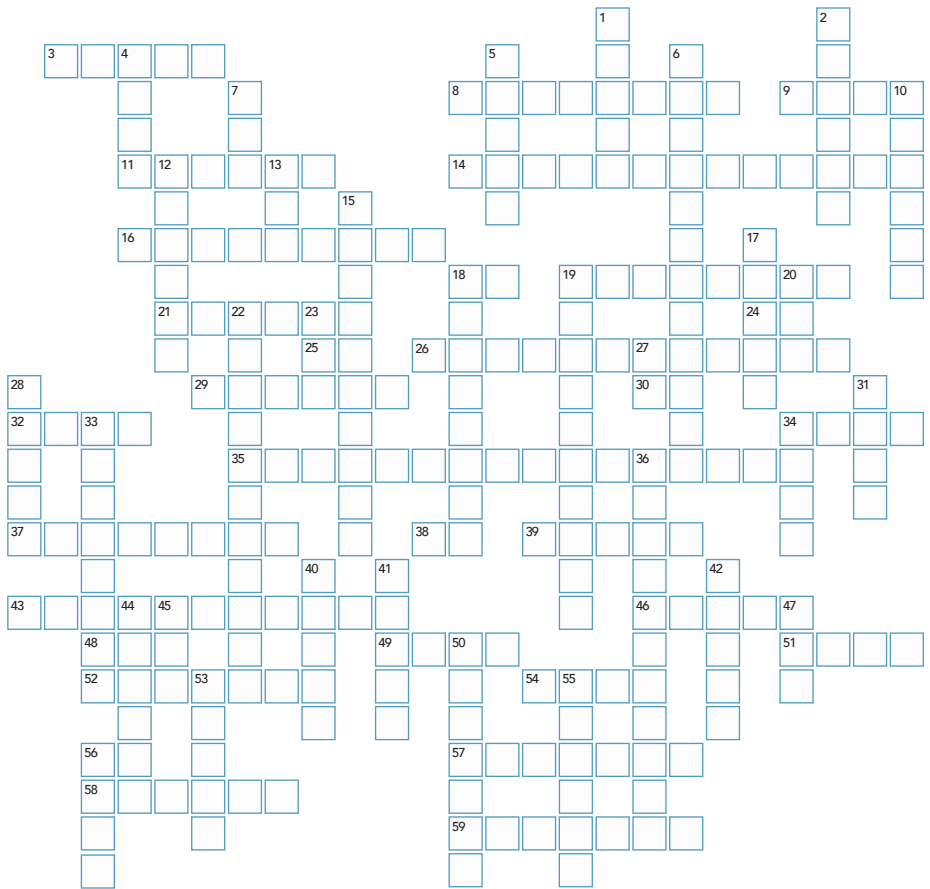
ALBERT'S PUZZLER

BY DEIRDRE BRANLEY

Great and Nobel Deeds (in Physiology or Medicine)*

Across

- 3 Common model organism, and you can bake with it
- 8 2000 Nobel research focused on this neurotransmitter
- 9 Einstein's student-run free clinic
- 11 Petechia, or a mark of shame
- 14 2018 Nobel research led to creation of this cancer-treatment strategy
- 16 Nobel winner who shares name with city in Maryland
- 18 Element named for Glenn Seaborg, winner of 1951 Nobel in Chemistry
- 19 "Guinea-pig doctor" who won the 2005 Nobel
- 21 Unexpected variant of a gene
- 24 Short for silicon
- 25 Calcium's atomic symbol
- 26 Genus of the species implicated in stomach ulcers
- 29 Not cancerous
- 30 How you pronounce @ in an email address
- 32 Syndrome caused by the MeCP2 gene, found only in girls
- 34 Smallest structural and functional unit of an organism
- 35 Bronx-born Nobel winner Rosalyn Yalow co-developed this lab technique
- 37 Invention made by benefactor of the Nobel Prize
- 38 A nurse, or abbreviation of radon
- 39 Main artery from heart
- 43 They won the Nobel for discovering DNA: _____ and _____
- 46 Married couple awarded 2014 Nobel share this last name
- 48 Across Manhattan from the UES
- 49 Reverse the effects or results of
- 51 An established standard or average
- 52 Eric Kandel shared 2000 Nobel for discovering learning process in this animal
- 54 Oldest (age 87) Nobel winner (1966) has a tumor-inducing virus named after him
- 56 English for être or ser
- 57 Bacteria need quorum _____
- 58 Condition characterized by low blood counts
- 59 Owed his 1945 Nobel to an uncovered Petri dish



Down

- 1 One of 2012 Nobel winners who spoke at Einstein as a Lasker winner
- 2 Department of family and _____ medicine
- 4 Disease caused by uncontrolled HIV infection, for short
- 5 *C. elegans*
- 6 Country with the most Nobel laureates
- 7 Common name for ovum
- 10 Winners of 2019 Nobel found how cells "sense and adapt to" this molecule
- 12 A physical injury, or disturbing experience
- 13 2003 Nobel was awarded for development of this imaging technique
- 15 Frenchman who received 2008 Nobel, for the discovery of HIV
- 17 What autophagy rids the cells of
- 18 Only deceased recipient of a Nobel
- 19 Only woman to receive an unshared Nobel, awarded in 1983
- 20 Let sleeping dogs _____
- 22 Albert Einstein won the 1921 Nobel "for his services to" which area of physics?
- 23 NIH's cancer research funder
- 27 Barium's symbol
- 28 Psychoanalyst nominated 32 times but never won a Nobel
- 31 Thinner, longer bone of the forearm
- 33 Perception of noise or ringing in ear
- 34 Sac-like pocket that contains fluid
- 36 2015 Nobel honored Chinese discoverer of this antimalarial drug
- 40 Type of joint at the knee, elbow, and ankle
- 41 Bones of head, known collectively
- 42 These cells are attacked by the body in type 1 diabetes
- 44 Where Nobel Prize is awarded
- 45 Medical acronym for apnea
- 47 Nucleic acid essential in regulating the expression of genes
- 50 Before becoming extinct, a species of animal slowly _____ (2 words)
- 53 Artificial opening made in hollow organ
- 55 Awarded 2016 Nobel for discovery of autophagy
- 56 A soothing ointment

* Note: All references are to the Nobel Prize in Physiology or Medicine unless otherwise indicated.



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puzzler2020](http://magazine.einstein.yu.edu/puzzler2020)

MOTIVATIONS

The Front Line of Philanthropy at Einstein and Montefiore

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- 54 Continued Connection: Dr. Rachel Katz
- 58 Spotlight: Caring for the Littlest Hearts
- 62 Your Impact: Targeting Cancer
- 66 Class Notes
- 68 In Memoriam

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MOTIVATIONS

A Message From Co-Presidents of the Women's Division

TERRI GOLDBERG & TRUDY SCHLACHTER



Terri Goldberg and Trudy Schlachter

In 1953, a group of New York City women came together to help build an inclusive medical school that would conduct world-changing research. Two years later, these pioneering women—later dubbed the Women's Division—took part in the groundbreaking on what became Einstein's campus.

Throughout the Women's Division's storied past, generations of members have raised more than \$100 million to fund investigations into breast cancer, translational medicine, molecular cardiology, and more.

Today, we write with pride as co-presidents of the Women's Division—a group that has since expanded tremendously while staying true to our mission of funding science.

Einstein's history carries a common theme: We can repair the world with enough passion, persistence, and people. We remember one of those leaders with great fondness—Burton P. Resnick, who served on the Einstein Board of Trustees for more than four decades (see opposite page). His clarity of purpose, foresight, and inspiring generosity helped shape Einstein into the research powerhouse it is today.

In this edition of *Motivations*, you'll read about others who share this mindset. Dr. Rachel Katz's family scholarship has helped propel aspiring doctors' careers (page 54) since 2001. The Feinberg family has partnered with Einstein researchers who have made promising strides against an important type of cancer (page 62). And the John H. Gutfreund Fetal Heart Program, launched in 2017 in memory of former Montefiore trustee and father of current trustee J.P. Gutfreund, addresses critical cardiac concerns for hundreds of mothers and infants in the Bronx each year (page 58).

From those stories we learn that the path toward a healthier future is possible, and where there is no path, we can forge one. On behalf of the Women's Division, we appreciate your willingness to join us on this journey.

With gratitude,

A stylized, handwritten signature of Terri Goldberg in white ink.

Terri Goldberg

A stylized, handwritten signature of Trudy Schlachter in white ink.

Trudy Schlachter

REMEMBERING BURTON RESNICK, BOARD CHAIR EMERITUS

The Einstein and Montefiore communities lost a devoted and loyal friend on Dec. 14, 2019. Burton (“Burt”) P. Resnick, chair emeritus of Einstein’s Board of Trustees, whose family legacy includes long-standing support of the College of Medicine dating back to its founding, died peacefully at his home in Rye, New York, at age 83. Burt joined the Einstein board in 1976, serving for more than four decades, including 19 years as chair.

A FAMILY MAN

Burt graduated from the University of Chicago with a B.A. in philosophy in 1956 and then joined Jack Resnick & Sons, Inc., the New York real estate development, construction, ownership, and management business that his father founded in 1928. The company’s holdings include a long list of residential and commercial buildings, many of which helped shape New York City’s real estate industry and its skyline. At the time of his death, Burt was chair and chief executive officer; his son Jonathan has served as president since 2007 and is the third generation to lead the 92-year-old enterprise.

Working closely with Sam Weinberg and other members of Einstein’s board, Burt championed construction of the Michael F. Price Center for Genetic and Translational Medicine/Harold and Muriel Block Research Pavilion.

Burt and his wife of 57 years, Judith, were major supporters of research at Einstein. They partnered with John Condeelis, Ph.D., professor and co-chair of anatomy and structural biology, who is the inaugural holder of



the Judith and Burton P. Resnick Chair in Translational Research.

The Resnicks also funded the Judith and Burton P. Resnick Chair in Cell Biology, currently held by Arthur Skoultschi, Ph.D., and encouraged medical student research through the Burton P. Resnick Medical Student Research Award in Aging, presented annually.

A FAMILY LEGACY

With his sister Marilyn and her husband, Stanley M. Katz, the Resnicks

established the Einstein Montefiore Resnick Gerontology Center in memory of the Resnick family patriarch and matriarch, Jack and Pearl, whose devotion to Einstein is recognized through the naming of Einstein’s Jack and Pearl Resnick Campus.

The Resnick and Katz families also teamed with Burt’s and Marilyn’s brother Ira to honor the memory of their late sister, establishing the Susan Resnick Fisher Chair in Brain Cancer Research. This chair supports the research of Dr. I. David Goldman, director of the National Cancer Institute–designated Albert Einstein Cancer Center. The Katz family’s generous support of the College of Medicine includes the creation of a cancer prevention program and is recognized in the title of Einstein’s dean: the Marilyn and Stanley M. Katz Dean.

Burt is predeceased by his parents and by his sister Susan. He is survived by Judith; their three sons, Jonathan, Scott, and Peter, and their wives; his sister and brother-in-law Marilyn and Stanley M. Katz; his brother and sister-in-law Ira M. and Paula Resnick; and nine grandchildren. **E**

DR. RACHEL KATZ CLASS OF '95

BY RACHEL EDDEY & SEAN MCMAHON

A family's gift eases the burden of medical debt for several Einstein students

Many years before Rachel Katz, M.D. '95, arrived at Einstein, she had a strong connection to the school. Dr. Katz's mother, Monique, is a Vassar graduate and Einstein 1963 alumna, and her father, Mordecai, served on the Yeshiva University Board of Trustees. Both were—and remain—generous philanthropic supporters.

Dr. Katz's connection to Einstein became that much stronger in 2001, six years after her graduation, when her parents created a scholarship in honor of her and her husband. For nearly two decades, the Rachel Katz and Robert Sidlow Scholarship Fund has afforded medical students the financial opportunity to study, discover, and grow at Einstein.

"When I learned that my parents planned this scholarship, I was overwhelmed with pride—but not at all surprised," Dr. Katz says. "They are very modest and never wanted credit for it. They'd just say, 'This is what we're going to do.' My parents have always served as role models for how to help others, and this scholarship joins a long list of examples they have set throughout my life."

Her parents' motivation to support Einstein was the college's commitment to Jewish values, including its belief in diversity and the need to provide a welcoming environment for all. On a personal level, Dr. Monique Katz had chosen to attend Einstein for the opportunity to obtain an outstanding education in an environment that facilitated



Rachel Katz, M.D. '95

her Orthodox religious observance.

Dr. Rachel Katz followed her mother's path to Einstein after earning bachelor's and master's degrees in English and comparative literature at Columbia University. She completed her residency training in pediatrics at Einstein. She is currently the vice chair for undergraduate medical education at the Lewis M. Fraad Department of Pediatrics at Jacobi Medical Center, the site leader for Jacobi's pediatrics clerkship, and a professor of pediatrics at Einstein. She also serves as assistant dean of Einstein at Jacobi Medical Center.

A SHARED PASSION FOR MEDICINE

This year's Rachel Katz and Robert Sidlow Scholarship recipient, Ashley Force, Class of 2022, was similarly inspired by her own mother's path. Born and raised in St. Petersburg,



Monique Katz, M.D., second row, center, is surrounded by her fellow residents from Jacobi Medical Center shortly before giving birth to her daughter, Rachel.

"My parents have always served as role models for how to help others, and this scholarship joins a long list of examples they have set throughout my life."

— DR. RACHEL KATZ

Florida, Ms. Force developed a love of medicine at a young age. Her mother, Estella Martinez, emigrated to the United States from Colombia and worked as a healthcare aide to put herself through nursing school.

Ms. Force would often accompany her mother to nursing homes and assisted-living residences and would help her mother prepare for exams at the dining room table, holding a stack of flash cards and quizzing her. The study sessions launched a mother's career in nursing and sparked a daughter's direction in life.

"I was so enthusiastic about all the things my mother was learning," Ms. Force says. "I found the body to be fascinating and was genuinely moved by the science."

After graduating summa cum laude from the University of Florida, Ms. Force applied to medical schools up and down the East Coast. Her visit to

Einstein made the choice easy. Not only was everyone warm and engaging, but Ms. Force also loved how passionate the professors were about teaching.

A HEAVY DEBT LOAD

With the cost of medical education constantly increasing, philanthropy becomes ever more important. According to the Association of American Medical Colleges (AAMC), the medical school class of 2019 had a four-year cost of attendance of more than \$330,000 for students enrolled in private institutions and more than \$250,000 for those in public medical schools. The median debt load for U.S. medical students is \$194,000, as calculated by the AAMC in October 2018.

The Katz family recognizes the monetary sacrifices required for an Einstein education, and Dr. Katz says she is proud that her parents' scholarship has already assisted several students. As with



Monique Katz, M.D. '63

MOTIVATIONS | CONTINUED CONNECTION



Photo by Jason Torres

Scholarship recipient Ashley Force, second from left, meets with other members of Einstein's chapter of Building the Next Generation of Academic Physicians, all members of the Class of 2022: Alexander Ferrera, left, Juan Pablo Forero, and Kripali Gautam.

all scholarships, an internal leadership committee selects recipients each year.

When Ms. Force learned that she had received the Rachel Katz and Robert Sidlow Scholarship, she says, she “couldn’t have been happier. Einstein is a place where people encourage and nurture medical students of all backgrounds, a place where people do whatever is possible to help those students accomplish their goals. Because of the Katz family, I can focus more on why I came here and less on how I’ll stay.”

LOOKING FORWARD, GIVING BACK

Ms. Force has a particular interest in spinal surgery, though she doesn’t know for sure what her professional future will hold. What she does know is that she will forever appreciate the Katz family for helping her.

“I’m here because someone who came before me cared—and I mean that about my mother, who set such a strong example, as well as the Katz family,” Ms. Force says. “The power of the narrative is not lost on me, especially in the field of compassionate medicine.”

Ms. Force is passing on that generosity of spirit. She is the treasurer of the Einstein chapter of Building the Next Generation of Academic Physicians, an organization that provides medical students and residents from diverse backgrounds with the resources to start careers in academic medicine.

Adds Dr. Katz: “I believe it is our job in life to help each other—across families and across generations. I am proud of my parents, how they have lived their lives, and how they are providing for future generations.” **E**


“Einstein is a place where people encourage and nurture medical students of all backgrounds. Because of the Katz family, I can focus more on why I came here and less on how I’ll stay.”

— ASHLEY FORCE



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"We're using our economic power to fund and inspire support for research that improves human health."

— Trudy F. Schlachter, Co-President,
Albert Einstein College of Medicine, Women's Division

"Women are making a tremendous difference by funding biomedical research through private philanthropy."

— Terri L. Goldberg, Co-President,
Albert Einstein College of Medicine, Women's Division

WOMEN FUNDING SCIENCE

Leading the way at Albert Einstein College of Medicine (clockwise from left): Trudy Schlachter; Ana Maria Cuervo, M.D., Ph.D., Robert and Renée Belfer Chair for the Study of Neurodegenerative Diseases; Terri Goldberg; and Chinazo O. Cunningham, M.D., M.S., Professor, Department of Medicine

The Women's Division of Albert Einstein College of Medicine in New York City has raised millions of dollars to support world-class science at Einstein. More than 1,000 women strong, we are dedicated to elevating research at every level—from the bench to the bedside—through philanthropy. Our extraordinary volunteers are funding science and truly saving lives.

To learn more, visit einstein.yu.edu/womensdivision or call the office of development at 718.430.2411.



Montefiore

MOTIVATIONS | SPOTLIGHT

CARING FOR THE LITTLEST HEARTS

BY AMY O'CONNOR

New fetal cardiac program addresses critical concerns for expectant mothers



The news was a shock: A young expectant mother learned that her soon-to-be-born daughter had a major heart defect. The woman had only recently immigrated to the Bronx from Yemen and wasn't fluent in English. She needed someone to explain what was wrong and tell her whether her baby would survive. But more than anything, she needed someone who could help save her baby's life—and communicate with her in a sensitive way about what that meant.

Fortunately, a contact referred her to the John H. Gutfreund Fetal Heart Program at the Children's Hospital at Montefiore (CHAM), where she met Nadine Choueiter, M.D., associate professor of pediatrics at Einstein and the program's director.

"I speak Arabic, so I could understand her as well as her core values," says Dr. Choueiter, a native of Lebanon. "We cared for her and built a personal relationship with her. We provide medical and genetic counseling to all of our families and make sure they receive the support they need."

Dr. Choueiter (pronounced SHWAY-ter) explained to the young woman that her fetus had a serious condition called transposition of the great arteries (TGA). In TGA, the two main arteries leaving the heart are reversed, so blood pumped from the heart to the rest of the body contains too little oxygen. Fortunately, surgery in the first few weeks of life—a so-called arterial switch—can correct the condition.

Left: Nadine Choueiter, M.D., uses a fetal heart monitor as she talks to maternity patient Tawhida Rahman at the John H. Gutfreund Fetal Heart Program's Montefiore Hutchinson Campus in the Bronx.



From left: Fetal heart nurse coordinator Guytree Keso watches as Dr. Choueiter goes over a model of an infant heart with maternity patient Tawhida Rahman and her husband, Mohammad Zahid Hessain.

"I'm happy to say that the baby received lifesaving surgery successfully," Dr. Choueiter says. "She is now nearly a year old and doing well."

A COMMON BIRTH DEFECT

Such success stories are common in the program, which provides care to an underserved community. The range of services includes expert diagnoses, interventional cardiology, postpartum support, quality-of-life counseling, and, when needed, neonatal cardiac surgery in a state-of-the-art facility. The program team also cares for expectant mothers with diabetes or other conditions that can affect fetal heart development. In keeping with Montefiore's mission, practitioners treat all patients regardless of ability to pay.

Congenital heart problems are relatively rare, affecting 1% of babies, but are the most common of all birth defects. In most cases, there's no known cause for congenital heart disease, and there's nothing the parents could have done differently to prevent the heart

"We provide medical and genetic counseling to all of our families and make sure they receive the support they need."

— DR. NADINE CHOUEITER

MOTIVATIONS | SPOTLIGHT

“We serve a community in the Bronx with so many different cultures and languages and provide excellent care to people who would otherwise not receive it.”

— DR. NADINE CHOEITER

defect from happening. In some cases, it's thought that genetic factors and certain maternal environmental exposures may result in abnormal growth or formation of the heart early in pregnancy.

Each year, the John H. Gutfreund Fetal Heart Program's team of professionals—cardiologists, obstetricians, surgeons, maternal/fetal-medicine specialists, nurses, social workers, and allied health practitioners—provides comprehensive care to more than 1,000 expectant mothers and their families from the Bronx and across the tristate area. Dr. Choueiter and Daphne Hsu, M.D., professor of pediatrics at Einstein and co-director of the Pediatric Heart Center at CHAM, launched the program in 2017.

“It is the most gratifying feeling to save a life,” Dr. Choueiter says. “We serve a community in the Bronx with so many different cultures and languages and provide excellent care to people who would otherwise not receive it. If

we weren't here for these babies with heart problems, or if they had been born in a different place, they would not be alive today.”

The Stavros Niarchos Foundation (SNF) provided the initial funding for the program in memory of John H. Gutfreund, a philanthropist and longtime member of Montefiore Health System's Board of Trustees, who died in 2016. “Supporting the program just made sense,” SNF's co-president Andreas C. Dracopoulos says. “The medical expertise, the vision, the leadership support and, most important, the need to care for these vulnerable children were all there. Dr. Hsu and Dr. Choueiter love what they do, and that feeling is contagious.”

A COMMITMENT TO THE BRONX

J.P. Gutfreund, the son of Mr. Gutfreund, is a current Montefiore trustee and supports the program with his time, passion, and philanthropy.

Daphne Hsu, M.D., listens to a child's heart at the Pediatric Heart Center at the Children's Hospital at Montefiore.



Photo by Jason Torres



Susan Gutfreund, center, cuts the ribbon on the fetal heart center named in honor of her late husband, John Gutfreund, who served Montefiore as a board member for decades. Her son, J.P. Gutfreund, a current Montefiore trustee, is at left; former Montefiore chief executive officer Steven Safyer, M.D. '82, is at right.

“My father was a true New Yorker with a strong sense of civic duty,” the younger Mr. Gutfreund says. “He believed that less-affluent communities deserved quality healthcare. So for more than 50 years, he had an unwavering commitment to Montefiore and the Bronx.” As plans for the program progressed, the younger Mr. Gutfreund and his wife learned they were expecting their first child. “Infant and family health were definitely on my mind,” he says.

In keeping with his family’s tradition of giving back, Mr. Gutfreund and his longtime friend Jon Moskowitz, a member of the Montefiore and Einstein Council (an affinity group designed to help shape the future of the institution), persuaded fellow donors to participate in the 2019 inaugural Heal-a-Heart Golf Tournament at the Bayonne Golf Club in Bayonne, New Jersey—all to benefit the program.

“That these doctors offer top-tier care

to so many families and are saving so many children’s lives is truly John’s legacy,” Mr. Moskowitz says. “It takes the latest technology and the greatest people to make this work. Through Heal-a-Heart and my personal philanthropy, I’m proud to do my part in ensuring that this legacy endures.”

Adds Dr. Choueiter: “We treat very sick children and, after they have gone through a lifesaving surgery, we do everything we can to make sure they will always be well. Every member of the team is deeply committed to serving the community. It is so gratifying for us to make a difference for so many children and their families.”

The baby born to that young Yemeni mother continues to seek care at CHAM. Thanks to the staff at Montefiore—and the commitment of generous donors such as SNF and the Gutfreund and Moskowitz families—the crucial support that began before her birth will continue long into her future. **E**

“That these doctors offer top-tier care to so many families and are saving so many children’s lives is truly John’s legacy. It takes the latest technology and the greatest people to make this work.”

— JON MOSKOWITZ



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MOTIVATIONS | YOUR IMPACT

TARGETING A SURPRISINGLY COMMON CAUSE OF CANCER

Thanks to one family's philanthropy, researchers are moving closer to new treatments for Lynch syndrome

BY GARY GOLDENBERG

In 2009, Lori Feinberg Kany of Short Hills, New Jersey, was diagnosed with breast cancer, joining millions of other women with this dreaded disease. However, her case was different from most.

After learning of her family's medical history, including a brother diagnosed with colorectal cancer at age 29, an astute genetic counselor advised her to get tested for Lynch syndrome, a heritable disorder that raises one's risk for a host of cancers, especially colorectal cancer, typically beginning in middle adulthood. The test came back positive, profoundly changing her life in more ways than one.

Since that fateful day, Lori has undergone a double mastectomy and colon cancer surgery. She has persevered through a series of health crises and would tell you that they have motivated her and her family to commit to promoting Lynch syndrome research, mainly at Montefiore and Einstein.

People with Lynch syndrome inherit a mutation in one member of a pair of genes controlling a vital process called DNA mismatch repair (MMR). During cell replication, MMR corrects any typos in the DNA bases that spell out our genetic code.

For people with Lynch syndrome, their remaining "good" copy of the MMR gene can still handle mismatch errors for a while. But by the time people reach their 30s or 40s, that good copy is likely to suffer damage—allowing DNA errors to go uncorrected. As a result, Lynch syndrome sufferers have up to an 80% risk of developing colorectal cancer during their lifetimes—20 times the usual risk. MMR defects also cause some 20% of



Winfried Edelmann, Ph.D., and Einstein colleague Elena Tosti, Ph.D., study the mechanisms underlying colon cancer development caused by defective DNA mismatch repair.

sporadic (noninherited) colorectal cancers as well as a subset of breast, gynecological, and urological cancers.

SUPPORTING LYNCH SYNDROME RESEARCH

For a decade now, Lori's family—including her mother (Betty Feinberg), her brother (Peter Feinberg), and two sisters (Jami Simons and Randi Feinberg)—has underwritten the research of Winfried Edelmann, Ph.D., professor of cell biology and of genetics and the Joseph and Gertrud Buchler Chair in Transgenic Medicine at Einstein. Dr. Edelmann is a leading authority on MMR. He is best known for creating the first mouse model that closely mimics the key molecular, genetic, and clinical aspects of Lynch syndrome in humans.

Lynch syndrome is a heritable disorder that raises one's risk for a host of cancers, especially colorectal cancer, and typically begins in middle adulthood.

MOTIVATIONS | YOUR IMPACT

Thanks to this advance, the National Institutes of Health recently awarded Dr. Edelmann and his colleagues a five-year, \$3.1 million grant to study how genetic and dietary interactions in their mouse model affect signaling and regulatory pathways in intestinal stem cells, problems which give rise to colorectal cancer. Findings from this research could lead to advances in detecting, preventing, and treating Lynch syndrome in particular and colorectal cancer in general.

“The Feinberg family helped us greatly in our efforts to develop our mouse model,” Dr. Edelmann says. “More importantly,” he adds, “they initiated my collaboration with Dr. Eduardo Vilar-Sanchez,” a physician-scientist and Lynch syndrome specialist at MD Anderson Cancer Center in Houston.

Together, Drs. Edelmann and Vilar-Sanchez discovered that colorectal

cancer cells in Lynch syndrome are highly sensitive to rapamycin, a drug commonly used to prevent organ-transplant rejection and to treat certain cancers. In one mouse study, treatment with rapamycin nearly eliminated Lynch syndrome tumors within two to three weeks—a response that stunned the researchers. They are now working with Sanjay Goel, M.B.B.S., professor of medicine at Einstein and gastrointestinal oncologist at the Montefiore Einstein Center for Cancer Care, to set up a clinical trial to assess rapamycin’s use in Lynch syndrome patients.

Drs. Edelmann and Vilar-Sanchez are also trying to make rapamycin therapy last longer, since the tumor returns once treatments are stopped. “We have since learned that cancer stem cells have a membrane protein called MDR1 (multi-drug resistance 1), which pumps out any toxins (including rapamycin) that get into them,” Dr. Edelmann says.

“When we treated our Lynch syndrome mouse model with rapamycin plus a drug that inhibits MDR1, rapamycin was able to almost completely wipe out one type of cancer stem cell. We don’t know yet if these results will be long-lasting, though this is a promising step toward a new treatment.”

Partial credit for this fruitful collaboration belongs to Peter Feinberg, who knew of Dr. Vilar-Sanchez’s work at MD Anderson and thought it would be beneficial to put the two researchers in touch. “I wanted to do something that could leverage their respective knowledge and bring two renowned institutions together,” he explains. “I pinch myself. It’s a dream turning into a reality.”

“I’m president of the Winfried Edelmann Fan Club,” jokes Lori, a retired lawyer and active philanthropist. “But seriously, I wish I had so much more to give. His brain is limitless, but his funds are not. Our goal is that



“When we treated our Lynch syndrome mouse model with rapamycin plus a drug that inhibits MDR1, rapamycin was able to almost completely wipe out one type of cancer stem cell.”

— DR. WINFRIED EDELMANN

Dr. Edelmann holds a slide containing sections of the liver and spleen of a mouse model of Lynch syndrome.

Photo by Jason Torres



Betty Feinberg, a longtime Einstein trustee, helps fund Einstein's research on Lynch syndrome and hopes to raise awareness of the condition.

"Philanthropy was what we knew growing up. Our parents instilled in us a tremendous sense of obligation to help make the world a better place. We'd like to think we're doing that."

— RANDI FEINBERG

somebody sees this article and they tell a friend about his work, and then they tell a friend."

THE WAY OF THE FEINBERGS

In addition to supporting Lynch syndrome research, the Feinbergs hope to raise awareness of the condition, which affects about 1 in 370 people in the United States. "I'm amazed at how few people know about the syndrome," says Jami Simons, a retired teacher and active community volunteer. "When people hear about breast cancer, they think 'BRCA,' the so-called breast cancer gene. But anyone with a family history of breast or ovarian or colon cancer ought to find out if they have one of the Lynch syndrome genes. All it takes is a simple blood test."

While there's no cure for Lynch syndrome, people who test positive can undergo regular cancer screenings to catch growths before they turn

cancerous or when they're still treatable. "I live by the creed that what I have won't necessarily kill me, but ignoring it might," Lori says.

The siblings' philanthropic work was inspired by their parents: Betty, a longtime Einstein trustee, and her late husband, Sheldon, a prominent business leader in the second half of the 20th century.

"Decades ago, my parents recognized the need to fund brilliant researchers in the embryonic stages of their careers, when money is so tight," says Peter, a former banker whose work now focuses on "impact investments" that help put medical and social innovations into everyday practice.

"Philanthropy was what we knew growing up," Randi Feinberg adds. "Our parents instilled in us a tremendous sense of obligation to help make the world a better place. We'd like to think we're doing that." **E**



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SupportLynchResearch](https://einstein.yu.edu/donors/SupportLynchResearch)

CLASS NOTES

1960s

Joyce Lowinson, M.D. '62, was honored at the “On the Front Lines of the Opioid Epidemic” conference held at Montefiore and Einstein in September 2019 (see page 4). She is the founding director of the division of substance abuse and a professor emerita of psychiatry and behavioral sciences at Einstein.

Anna Chao Pai, Ph.D. '64, recently published her memoir, *From Manchurian Princess to the American Dream*. The book highlights the hardships of immigration, the discrimination that she and her family endured when they moved to the United States from China when she was 4 years old, and her enduring faith in the American dream.

1970s

Harold Pincus, M.D. '75, was named 2019 Mentor of the Year at Columbia University’s Irving Medical Center. He is a professor and the vice chair of psychiatry at Columbia’s Vagelos College of Physicians and Surgeons, and is the co-director of Columbia’s Irving Institute for Clinical and Translational Research. He is also the national program director for the Health and Aging Policy Fellows Program and serves as a senior scientist at the RAND Corporation.

Kathryn (Katy) Stein, Ph.D. '76, is currently a biotechnology consultant (see katystein.com) after having spent

22 years at the U.S. Food and Drug Administration and 14 years in industry. She still loves to work and does not foresee retiring anytime soon. This past spring she was honored to receive the Alumni Association’s Distinguished Ph.D. Alumna Award from Einstein.

Nancy Scattergood Donovan, M.D. '78, was named the 2019 Southwestern Vermont Health Care Foundation’s Health Care Leadership Honoree. She earned a bachelor’s degree in biology from Franklin & Marshall College in Pennsylvania and studied at the College of Medicine and Dentistry at Rutgers University in New Jersey before attending Einstein. Dr. Donovan completed her internship and residency at the University of Wisconsin–Madison. She has been a member of Southwestern Vermont Medical Center since 1983 and staff president since 1996.

1980s

Hasan Bazari, M.D. '83, had first thought an inability to speak fluently after he suffered a stroke four years ago could have ended his career. But with renewed determination, he has continued to be active. Today he teaches, oversees reflection sessions in the cardiac care unit, attends conferences, and is proud to be able to venture outside his comfort zone. At Massachusetts General Hospital, he was the program director of internal medicine from 1994 to 2014. He now serves on the Alumni Association Board of Governors at Einstein.

Joel Cohen, M.D. '83, moved with his four adult children and his wife, Pearl, to Jerusalem, where he has been working in the stroke unit at Shaare Zedek Medical Center. During the past year each of his children has married: Tova to Gil Herrmann, Natan to Sarah Bayer, Meir to Ahuva Ross, and Sara to Chanina Landesman. In October Dr. Cohen welcomed his first grandson, Ariel Yona Landesman.

Joshua Lipsman, M.D. '83, married his partner of five years, Jonathan Sorge, on July 6, 2019. For the past year they have been living in the Hudson Valley in the riverside village of Athens, New York, where Dr. Lipsman is a trustee on the village board. Earlier this year he became the medical director for Humana’s Medicare Advantage product line. He also partnered with associates in June to open his second boutique medical start-up in New York City, Ever/Body, a cosmetic dermatology practice.

Linda Broyde Haramati, M.D. '85, is still happy to be at Einstein after all these years. She leads the cardiothoracic imaging division in radiology at Montefiore. She and her husband, Nogah, enjoy spending time with their three grandchildren; the oldest is 2.

Michael Zelefsky, M.D. '86, is the vice chair of and a professor in the department of radiation oncology, clinical research, and is the chief of the brachytherapy service, at Memorial Sloan Kettering Cancer Center. He was also appointed to the newly established

Greenberg Chair in Prostate Cancer Research. He pioneered the development of MSK Precise, which comprises hypofractionated radiotherapy, real-time image guidance, magnetic resonance imaging planning, and the use of a hydrogel spacer between the rectum and the prostate.

Neal Shipley, M.D. '87, lives on Manhattan's Upper West Side and is married; he has three children and two dogs. He has spent most of the past 20-plus years as an emergency department physician and emergency department director. In 2010 he co-founded an urgent-care business in Manhattan. Dr. Shipley is currently the medical director for Northwell Health GoHealth Urgent Care, which has 51 locations in the metropolitan New York area and treated more than 500,000 patients in 2019.

1990s

Yvette Calderon, M.D. '90, was elected to the board of directors of the American Board of Emergency Medicine. She was also honored with Crain's 2019 Notable Women in Health Award. She is the chair of the department of emergency medicine at Mount Sinai Beth Israel Hospital.

Alan Dayan, M.D. '91, is proud to report that his oldest son began his first year at Einstein in August, and was thrilled to join him for the White Coat Ceremony. Dr. Dayan currently lives in Brooklyn with his wife, Perline. They have five children; the older ones are on their way to making their own nests. He practices orthopedic surgery at New York University, specializing in adult

reconstruction and sports medicine. Although he has not attended many Einstein reunions, he gives a shout-out to the Class of 1991.

Ian Walters, M.D. '93, was recently named chief executive officer of Portage Biotech Inc. As board director, he was instrumental in leading the company's recent acquisition of the drug-development company SalvaRx Limited, which he founded in 2015 and led in its production of cancer immunotherapy drugs. In a career spanning more than 20 years, he has contributed to four significant oncology drug approvals. Before founding SalvaRx he worked at Bristol-Myers Squibb (BMS), where he managed physicians overseeing the international development of oncology compounds as well as biomarker and related diagnostic work. Dr. Walters was a core member of BMS's strategic transactions group, which evaluated and executed licensing agreements, mergers and acquisitions, clinical collaborations, and the company's immune-oncology strategy.

David Markenson, M.D. '94, was recently inaugurated as the president of the Colorado Medical Society. He also became the chief medical officer of the American Red Cross, a position he says he could not, when he was in medical school, have imagined ever holding. As a volunteer for the past 15 years, he has served as the chair of the National Science Council of the American Red Cross. He also co-chaired the evidence group for the International Federation of Red Cross and Red Crescent Societies, which is the parent group of the 192 Red Cross national societies.

STAY IN TOUCH

Keep your classmates up to date by submitting your news to *Einstein* magazine. We look forward to including you. Email us at einsteinalumni@einsteinmed.org.

2000s

Kyle Lapidus, M.D., Ph.D. '09, is the founder of Affective Care, an organization that provides and oversees psychiatric care and treatment throughout New York State. He completed his residency in psychiatry at Mount Sinai Medical Center's Icahn School of Medicine, and is board-certified by the American Board of Psychiatry and Neurology. In addition to his experience with mood and anxiety disorders, Dr. Lapidus has particular clinical expertise in the management of treatment-resistant depression and obsessive-compulsive disorder. His pioneering studies have appeared in many scientific publications related to the treatment and development of ketamine and dTMS, along with other novel approaches to improving patient outcomes. He is dedicated to developing cutting-edge treatments, and he co-created Validose, an intranasal medical device that facilitates the delivery of medication.

2010s

Caitlin McMullen, M.D. '10, gave birth to a baby girl in February and is loving family life in Florida. She reports that her mother retired in 2018 after a rewarding 38-year career as a

MOTIVATIONS | CLASS NOTES

neonatologist and is transitioning to “civilian life” by spending lots of time with her two granddaughters and pets.

Lauren Tannenbaum Roth, M.D. '16, has returned to Einstein as an attending physician in the Comprehensive Family Care Center and as an instructor of pediatrics at Children's Hospital at Montefiore. She recently completed her residency at NewYork–Presbyterian

Hospital/Columbia University Medical Center. She is excited to work with Einstein medical students and plans to focus on expanding the health curriculum for lesbian, gay, bisexual, transgender, and queer patients, particularly within pediatrics.

Evan Tamura, M.D. '16, started the Refugee Health Alliance listserv in November 2018 and completed a family

medicine residency at Harbor-UCLA Medical Center in June 2019.

Alana Warhit, M.D. '18, was married on May 27, 2019. She is a resident in psychiatry at NewYork–Presbyterian Hospital/Weill Cornell Medical Center. Her husband, Kevin Sean Beckoff, is an associate in the real estate group of Kirkland and Ellis LLP in Manhattan. [E](#)

IN MEMORIAM

Perry Eck, M.D. '65, age 79, MASH (mobile army surgical hospital) unit physician in the Vietnam War, in private practice for nearly 40 years; March 24, 2019, Rochester, New York.

Jacob Gerstenfeld, M.D. '60, age 84, retired ophthalmologist and member of Einstein's second graduating class; June 5, 2019, Palm Beach Gardens, Florida.

Asao Hirano, M.D., age 92, professor emeritus of pathology and of neuroscience at Einstein, the former Harry M. Zimmerman Professor of Neuropathology at Montefiore, former associate program director of diagnostic neuropathology (electron microscopy studies), and author of more than 800 articles in medical journals and textbooks translated into several languages; July 25, 2019, Sleepy Hollow, New York.

Ernest Kalman, age 85, former member of the Einstein Board of Overseers for many years, co-founded the Hallenbeck/Kalman Cancer Research Laboratory at Einstein; Jan. 16, 2020, Bedford Hills, New York.

Thomas Kaye, M.D. '78, age 67, neurosurgeon in the Springfield, Massachusetts, area for 30 years; Jan. 27, 2020, Longmeadow, Massachusetts.

John Larkin, M.D. '92, age 57, primary care physician in Tipton County, Tennessee, since 2005, formerly in practice in Manhattan; Dec. 16, 2019, Covington, Tennessee.

Charles Robert Michael, age 82, investor and philanthropist who endowed the Charles Michael Chair in Autoimmune Diseases at Einstein; Dec. 5, 2019, Saddle Brook, New Jersey.

Tim Nelson, age 63, Einstein's telecommunications technician for more than 15 years; Sept. 24, 2019, the Bronx, New York.

Paula Neyman, M.D., age 93, clinical associate professor emerita of pediatrics at Einstein; Oct. 23, 2019, Monroe, New York.

John Robbins, M.D., age 86, former associate professor of pediatrics at Einstein, National Institutes of Health researcher, vaccine pioneer, and winner of the 1996 Albert Lasker Clinical Medical Research Award; Nov. 27, 2019, Manhattan.

Detlef Schlondorff, M.D., age 77, renal investigator for more than five decades and Einstein's former director of nephrology; Oct. 16, 2019, Manhattan.

Jonathan Warner, Ph.D., age 82, professor emeritus and former chair of the department of cell biology; Sept. 5, 2019, Pelham, New York.

A LOOK BACK



Photo by Jason Torres

Lymph Notes, Then and Now

Decades ago, a histology lesson inspired Einstein medical students to call their a cappella group the Lymph Notes—a name that has stuck. Those Lymph Notes, at top, “sang at the slightest provocation,” according to the 1960 yearbook, “and it was hard to keep them shut up for very long.” Their repertoire ranged from folk songs to numbers by Richard Rodgers and Oscar Hammerstein II, and included tunes such as “If I Loved You” from the musical *Carousel*. The songs have changed over the past 60 years, but the Lymph Notes are still harmonizing. Between 12 and 20 medical students practice every week, and the group performs at an annual concert each spring in the Mary and Karl Robbins Auditorium. Organizer and second-year student Sarah Kellner, at bottom far right, says, “It’s a way to keep music in our lives, and art and medicine go hand in hand.” Listen to the Lymph Notes at magazine.einstein.yu.edu/notes20. **E**



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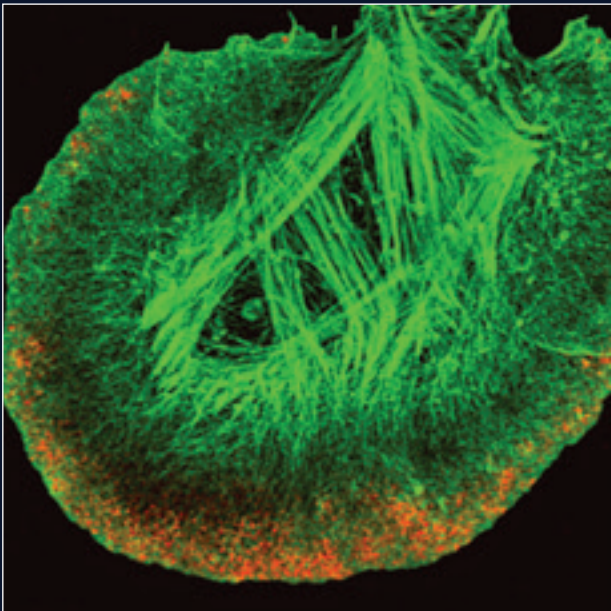
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Science at the Heart of Medicine



EINSTEIN IMAGE

Cell movement is essential for crucial biological processes. It can help heal wounds but also lead to the spread of cancer cells (metastasis). It's triggered when actin protein molecules combine, or polymerize, into actin filaments. Growing actin filaments push the cell membrane outward, forming projections called lamellipodia that propel the cell. Visualizing this highly dynamic activity has proved challenging. To find the stains and preservation techniques that best capture actin polymerization within lamellipodia, researchers in Einstein's Analytic Imaging Facility and the lab of John Condeelis, Ph.D., took motile cells from a rat breast cancer cell line, preserved (fixed) them in five different ways, and labeled the actin with nine different stains. The double-stained image shown here, using structural illumination microscopy, was judged the most accurate and detailed. Phalloidin Alexa-488 (green) revealed most of the cell's actin filament network. Anti-actin antibody AC15 Alexa-555 (red) showed actin staining that was limited to areas closer to the membrane.

Image credit: Vera DesMarais, Ph.D., and Robert Eddy, Ph.D.