UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | SPRING 2019

PITTMED

AFTER KISSING HIS WIFE AND CHILDREN,

THE DOCTOR PUTS ON HIS CAMOUFLAGE UNIFORM AND A BULLETPROOF VEST.

THE TREE OF LIFE RESPONSE

FOLLOW-UP

Join in the conversation **@PittMedMag**. Because you seem like someone interested in healing and discovery.

Pitt Public Health
@PittPubHealth
Following

.@DrDaraDMendez provides great insight into high maternal mortality rates, particularly in African Americans, in this @PittMedMag article.

Pitt Med Magazine @PittMedMag
Our experts tackle #maternalmortality rates and race in this issue's installment of Tough Questions: bit.ly/2ANyGO0 @PittPubHealth, @UPittNursing

Medmagger
@Medmagger
Following

Pitt Medcast on the road! Live at the AAAS meeting in DC. @jeremymberg @aaas @MylyndaM @elainevitone thank you all! @PittMedMag

8:14 AM - 16 Feb 2019

Jeremy Berg
@jeremymberg
Following

Back home after the #AAASmtg. Good talks, lively discussion of open access and Plan S (thanks again @madamscientist), @PittMedMag podcast on promises and perils of personal genomics (thanks @MylyndaM), and awarding @AAAS @sciencemagazine Newcomb-Cleveland Prize.

MAKE TRACKS

'Cause you don't want to miss the latest *Pitt Medcast*, including "Imperfect Pitch," where we separate hype from reality as personal genomics companies ramp up the marketing, and "Labors and Losses," where we probe why new mothers die at an alarming rate in this country. bit.ly/pittmedcast

Wait—are you a podcast newbie? You're not alone. But it's easy-peasy to listen, once you get the hang of it. For our quick guide to get you going, visit bit.ly/pittmedcast_newbie.

RECENT MAGAZINE HONORS

2018 National Association of Science Writers Excellence in Institutional Writing (E. Vitone, "Cut Off")

2018 Carnegie Science Center Honorable Mention Science Communicator (J. Bittel, for contributions to *Pitt Med*)

CORRESPONDENCE

We gladly receive letters (which we may edit for length, style, and clarity).

Pitt Med
400 Craig Hall
University of Pittsburgh
Pittsburgh, PA 15260
Phone: 412-624-4354
Fax: 412-624-1021
E-mail: medmag@pitt.edu
pittmed.health.pitt.edu

For address corrections:

***Pitt Med* address corrections**
ATTN: Melanie Sadarananda
M-200K Scaife Hall
University of Pittsburgh
Pittsburgh, PA 15261
Phone: 412-648-9741
E-mail: mms239@pitt.edu

CONTRIBUTORS

LIBERTY FERDA ["#MeToo in Midlife" and two obituaries] is a nonfiction writer and poet. Ferda has written about race, contributing to the anthology of personal essays, *The Beiging of America*. And in the chapbook *Psalms for Mother Emanuel: An Elegy from Pittsburgh to Charleston*, she reflected on the 2015 massacre at Mother Emanuel AME Church. For this issue, Ferda said she felt heartened while researching Rebecca Thurston's work on the effects of sexual harassment because it "might lead to better solutions for people." Ferda teaches English at Pitt and is a 2010 graduate of the University's nonfiction writing MFA program.

Artist MICHAEL HIRSHON ["Personal Best"] makes his *Pitt Med* debut in this issue, illustrating how researchers are testing and enhancing the limits of the human body. "The assignment was largely guided by the technology," he says. "I had to consider where I could apply subjectivity and where I had to adhere to the reference material." As a kid, Hirshon was inspired by children's books and the covers of his parents' copies of the *New Yorker*. Hirshon's illustrations have appeared in *The New York Times* and *The Washington Post*. His work has been recognized by the Society of Illustrators and American Illustration. He lives in Madison, Wisc.

PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, SPRING 2019 (MARCH/APRIL/MAY)

VOL. 21, ISSUE 1

6

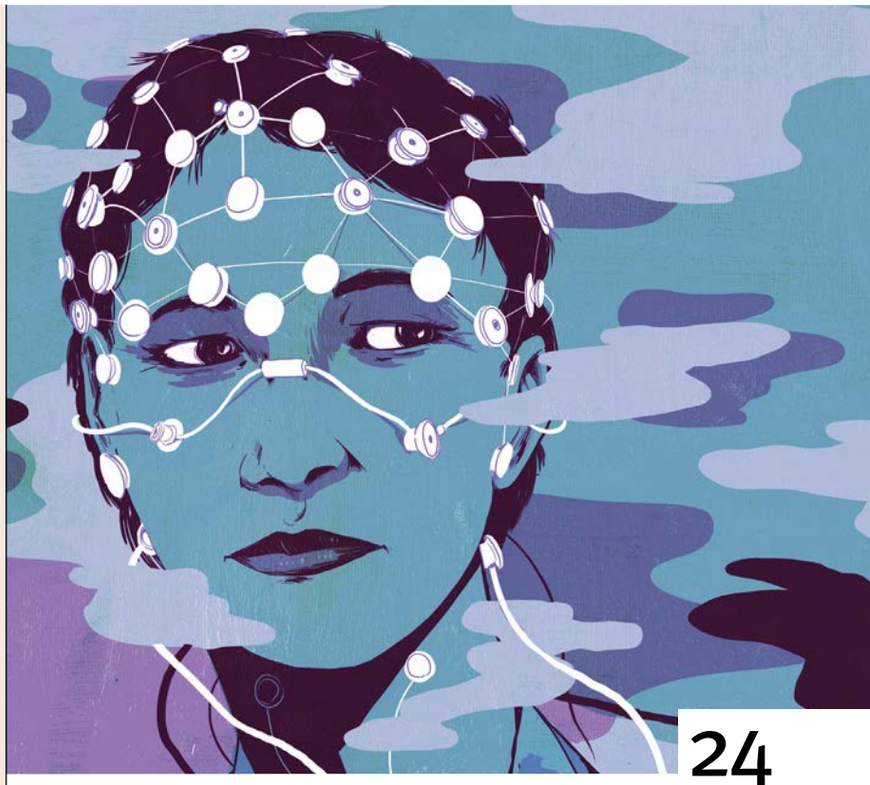
DEPARTMENTS

8

40 1/2

COVER

Pittsburgh's medical response to the Tree of Life massacre. (Cover typography: Elena Gialamas Cerri)



24

FEATURES

PITTMED

PUBLISHER
Arthur S. Levine, MD

EDITOR IN CHIEF
Erica Lloyd

ART DIRECTOR
Elena Gialamas Cerri

SENIOR EDITOR
Elaine Vitone

ASSOCIATE EDITOR
Gavin Jenkins

CONTRIBUTING EDITOR
Cara Masset

PRODUCTION MANAGER
Chuck Dinsmore

CIRCULATION MANAGER
Melanie Sadarananda

INTERNS
Luisa Garbowit, Prachi Patel

EDITORIAL ADVISORS
Lisa Barsom, PhD
Jeremy Berg, PhD
Michelle Broido, PhD
Paula Davis, MA
Robert Ferris, MD/PhD
Joan Harvey, MD
Joshua Levenson, MD '11
David Lewis, MD
Margaret C. McDonald, PhD, MFA
Loren Roth, MD
Steven Shapiro, MD
Peter Strick, PhD
Ann Thompson, MD
Bennett Van Houten, PhD
Simon Watkins, PhD
Marshall Webster, MD, Res '70

VICE CHANCELLOR, STRATEGIC COMMUNICATIONS AND MARKETING
Ellen Moran

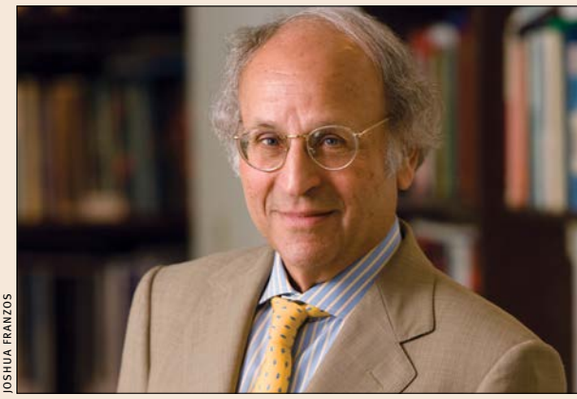
ASSISTANT VICE CHANCELLOR, MARKETING
Kate Ledger

University of Pittsburgh

Pitt Med is published by the Office of the Dean and Senior Vice Chancellor for the Health Sciences in cooperation with the Office of University Communications. It is produced quarterly for alumni, students, staff, faculty, and friends of the School of Medicine. PR 6747

The University of Pittsburgh is an affirmative action, equal opportunity institution. © 2019, University of Pittsburgh

Like people, ideas have social lives. They're one way when they're by themselves, and another when they're surrounded by their peers. Crammed together, they grow more uncertain, more interesting, more surprising. . . . [T]here's a special atmosphere that develops whenever truly different ideas congregate, and, on the whole, it's too rare. —Joshua Rothman



JOSHUA FRANZOS

When I came to Pittsburgh in 1998, I was already part of a community—the community of physician-scientists. And here, I was welcomed into a far broader community of scholars—an extraordinary cohort of artists, writers, engineers, economists, chemists, sociologists, historians, and other thinkers. In many ways, it was a return to my roots. I come from a long line of rabbis; which is to say, my people have always been scholars and academics—philosophers, even. And in my youth, I was a student of literature, an actor, and an aspiring writer. My early explorations of the humanities were anything but a false start. They were not a misguided attempt to find my way. And they did not delay the discovery of a more appropriate path for me through the biomedical sciences. Quite the opposite, literature and theatre, writing and acting, led me straight into a life of the mind, where we investigate what really matters and where truth lies, where we explore the fullness of human potential, and where I was encouraged to interrogate my own *raison d'etre.*

I'm not sure I could have articulated it as an undergraduate, but I know now that the most exciting ideas and intellectual advances often occur in the space where disciplines collide. We all do some of our most important work when we find our way to this space.

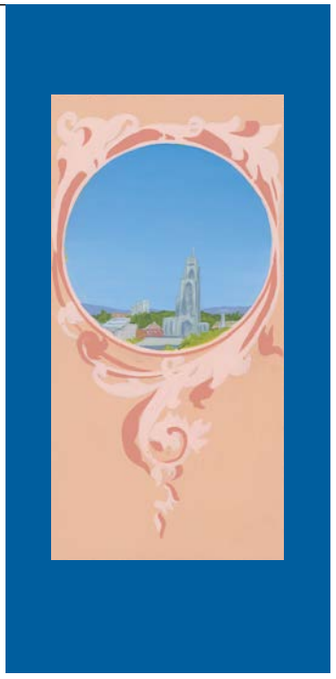
For the past 50 years, in addition to my leadership roles, I've been a physician and molecular biologist, studying, in my more recent history, how DNA becomes damaged and how it repairs itself, especially with respect to cancer. Now, I am turning my attention to the brain, especially to DNA damage and repair therein. If ever there were a space where disciplines needed to collide, this is it! Even with my somewhat naïve, and frankly amateurish, perspective on neurobiology, perhaps I can contribute a bit to what we know about the structure and function of our gray and white matter—the life of the mind and the uniqueness of our species writ large. I plan soon to establish a lab within the new Alzheimer's Disease Basic Research Center, a part of the University's Brain Institute. As our population ages, perhaps the greatest threat to public health and to our health care economy is Alzheimer's disease. It would be deeply rewarding if, in some small way, I could help us take steps toward preventing this terrible disease. As with virtually all chronic diseases, prevention would be far more effective—and certainly more definitive—than treatment.

The mysteries of the brain will become my new focus as a physician-scientist. I will be stepping aside from my roles as senior vice chancellor for the health sciences and Petersen Dean, effective once a search is completed and a successor is in place.

I have very much relished these leadership roles. And I have great pride in what we've collectively accomplished here. By any objective measure, we've raised the academic stature, visibility, and respect of the health sciences programs and, in turn, all of Pitt.

We've recruited and retained many wonderful scholars during my tenure. They are attracted to Pitt and Pittsburgh for many reasons, but especially our collaborative environment and our bench-to-bedside ethos. Pitt's psyche and structure (notably our many centers and institutes) encourage cross-pollination and healthy collisions between disciplines. I expect that my own research will reap these benefits, as well. Wish me luck! (Of course, just as I have never abandoned the humanities, I think it unlikely that I will ever abandon my relishing the whole of medicine and biologic science and the people and structures that lead to their advance.)

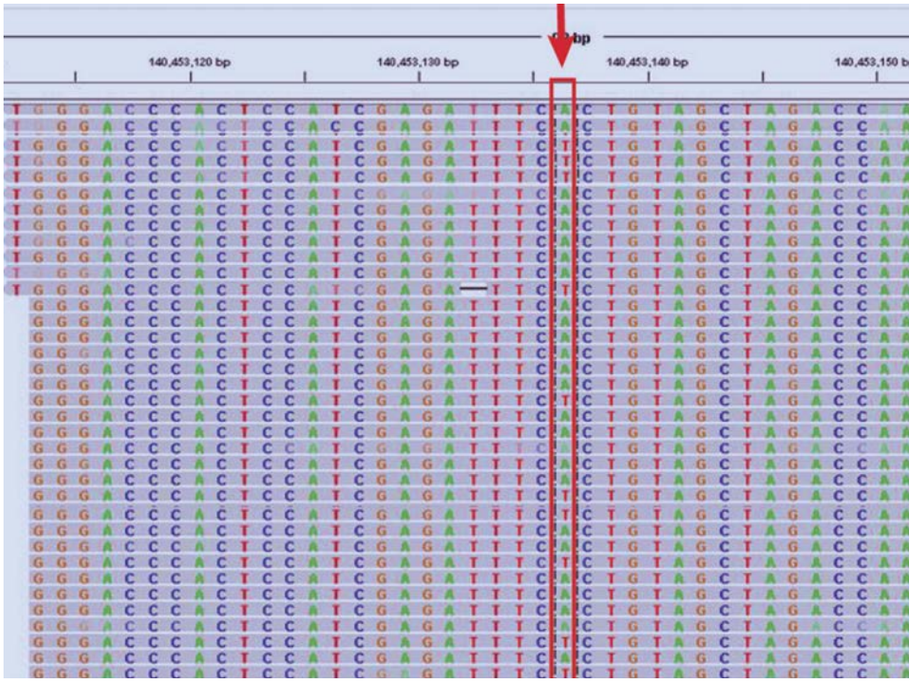
Arthur S. Levine, MD
Senior Vice Chancellor for the Health Sciences
John and Gertrude Petersen Dean, School of Medicine



Devoted to noteworthy happenings

at the medical school

ThyroSeq sifts through 112 genes associated with thyroid malignancy.



MARINA NIKIFOROVA

FLASHBACK

Steven Israel remembers sitting in an exam room in the '80s, distraught. The cornerback for the Pitt Panthers realized he'd hurt his ACL badly and might never play again. His doc, Freddie Fu, reassured him. Not only would he fix his knee, Fu said, he expected Israel would one day play in the pros. At that point, no one but Israel's dad had told him he was good enough for the NFL. Israel did get back on the field and found everyone wanted to talk about his "Freddie Fu knee." Israel went on to play for the Rams, the 49ers, the Patriots, and the Saints.

Israel told his story in November at the official naming of the Freddie Fu Sports Medicine Center, part of the UPMC Rooney Sports Complex on the South Side, which Fu helped conceptualize and design two decades ago. Fu and his team have raised the bar on ACL treatment and care for sports injuries of all kinds. There will be more opportunities to honor Pitt's chair of orthopaedic surgery: September 13 is now Dr. Freddie Fu Day in Pittsburgh.

KANTO NAGAI

Next for Nodules

For about 70 percent of patients with thyroid nodules, doctors can determine whether or not a nodule is malignant with a quick needle biopsy, says Marina Nikiforova, MD professor of pathology and director of the Molecular and Genomic Pathology Laboratory. For the rest, however, that determination must be made with a more extensive procedure that can be risky and costly.

Nikiforova and her husband, Yuri Nikiforov, MD/PhD professor and vice chair of pathology, spent more than a decade creating a new test that determines the malignancy of a nodule without surgery. They call it ThyroSeq; it uses next-generation gene sequencing to comb through 112 genes associated with thyroid malignancy.

Sally Carty, MD chief of the Division of Endocrine Surgery and professor of surgery at Pitt, helped test ThyroSeq's clinical validity and is on board with avoiding the surgery when possible: "Why should patients have to go through a diagnostic operation that produces risks or long-term sequelae?"

The test became available nationwide for patients with Medicare in January.

–Evan Bowen-Gaddy

CAMI MESA

Overheard: Mystery in Havana

In 2016, Americans posted at the U.S. Embassy in Havana heard a high-pitched noise. A high-pressure sensation often accompanied the noise, which they heard in their homes and hotel rooms over the span of several months. The symptoms that followed the noise—severe insomnia, nausea when using a computer, ear pain, vertigo, tinnitus, headaches, and cognitive difficulties—were so intense that dozens of U.S. diplomats eventually fled Cuba. A similar case was reported at the American consulate in Guangzhou, China. Soon after, an international firestorm started over whether this was the result of a deliberate sonic attack or hysteria from a string of coincidental symptoms. Now, a couple of years later, a team of researchers including Carey Balaban, a PhD professor of otolaryngology, confirms that personnel who report having these symptoms indeed suffer from real injuries. The researchers examined 130 American embassy personnel (25 of whom reported experiencing symptoms), as well as 10 roommates of personnel affected. (The roommates did not experience symptoms.) The team, led by a University of Miami faculty member, published its results in a recent issue of *Laryngoscope Investigative Otolaryngology*.

Some say it was an acoustic energy weapon while others suggest it was the obnoxiously loud chirping of a Jamaican field cricket. What was your impression when you first heard about this story and the reported symptoms?

Interested and skeptical. I am well aware of the complexities of symptom attribution with balance disorders and novel experiences. Yet, I was also aware that emissions of acoustic (e.g., infrasound or ultrasound) or electromagnetic energy like radio frequencies or light could not be ruled out. For example, it's been known for decades that radar pulses can be audible, produce neuron discharges in auditory networks in the brain, and result in sound that can be recorded inside the head. Parametric speakers [which beam sound focused at high intensity into a relatively small area] use ultrasound as a carrier for directed sound application. Pest control devices use ultrasound and electromagnetic emissions. Hence, I wanted to know more.

Your team tested several Havana personnel. What were the results?

They showed a previously unencountered set of signs [including injury] and symptoms that suggested a primary inner ear effect.

The idea of an attack like this is unsettling. Are there any precautionary measures that we all need to be taking?

In my opinion, it's unsettling, period, whether deliberate or inadvertent. The bottom line is that possible sources of the medical findings do not have an easy or obvious answer. Extremely capable experts in biological, physical, and engineering sciences are currently investigating possibilities.

—Interview by Kate Benz

Faculty Snapshots

In November, physician Ann Thompson was lauded by the Group on Women in Medicine and Science of the Association of American Medical Colleges for her work advancing the roles of women in both academic medicine and science. Thompson is vice dean for Pitt's School of Medicine and professor of critical care medicine and pediatrics.

Thompson

Neurobiologist Peter Strick received the 2018 National Institutes of Health Director's Transformative Research Award for his project, "The Neural Basis of the Brain-Body Connection." Strick is the founding scientific director of the University of Pittsburgh Brain Institute and the Thomas Detre Professor and chair of the Department of Neurobiology. He is one of nine researchers receiving the award which, according to the NIH, supports "exceptionally innovative research projects in the biomedical field with strong potential to shift current paradigms through trailblazing and transformative methodologies that might otherwise struggle to find support via conventional funding."

Strick

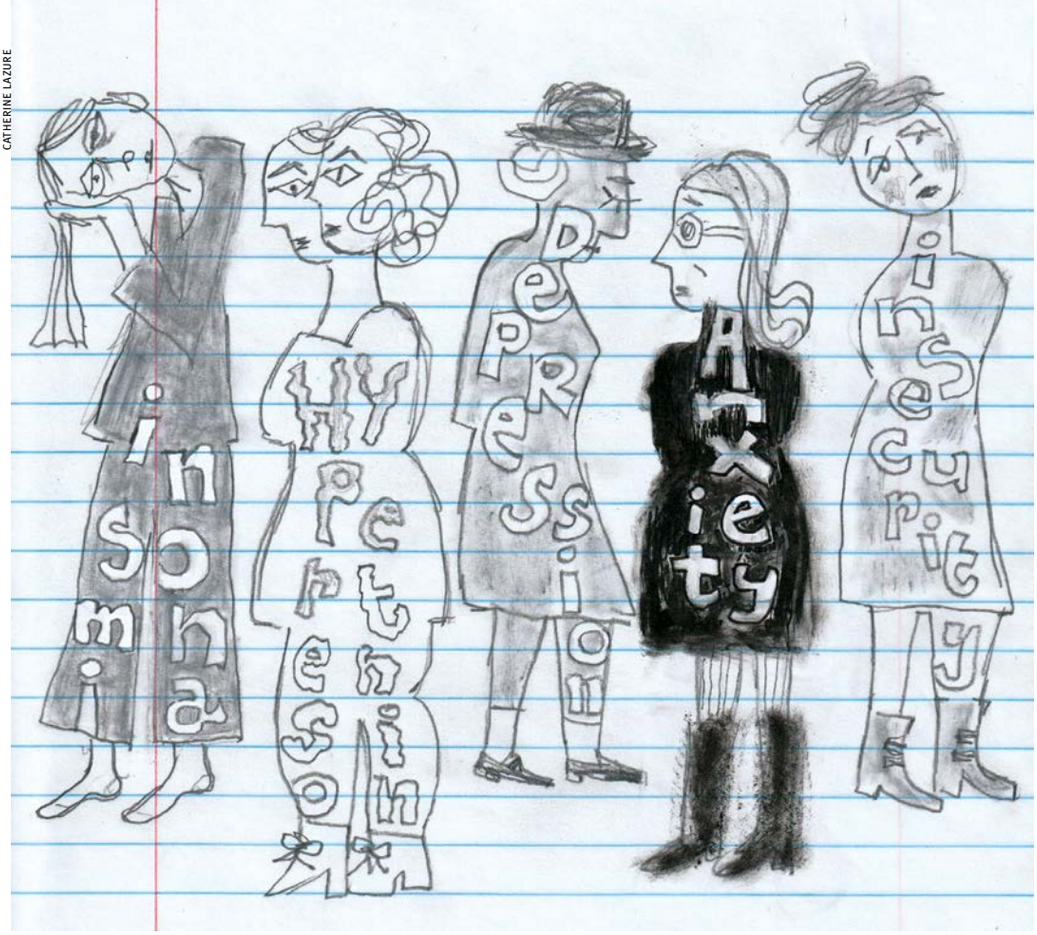
For discovering a connection between low vitamin D and high morbidity and disease severity in patients with inflammatory bowel disease, physician David Binion received the Bruce and Cynthia Sherman Charitable Foundation's 2018 Sherman Prize. Binion, codirector of the IBD Center and director of Translational IBD Research, was one of three recipients to receive the prize, which is given to leaders in the IBD field who focus on patient care and is considered the highest honor awarded to an IBD investigator. Binion and his team made the vitamin D discovery during a five-year study that included 965 IBD patients. "We feel fortunate to have received this validation of our work," he says.

Binion

Bahar

Ivet Bahar will go to Istanbul this March to receive the Kadir Has Outstanding Achievement Award. Bahar, a Distinguished Professor who holds the John K. Vries Chair in the Department of Computational and Systems Biology, was unanimously selected for the award. Named after the founder of Kadir Has University in Turkey, the annual award recognizes a scientist making significant contributions to her field and society. "Complex biomolecular systems dynamics has been my passion for two decades," Bahar says. "It is a nice feeling to receive recognition for the work I love." *–KB*

#METOO IN MIDLIFE



CATHERINE LAZURE

In a study published recently in *JAMA Internal Medicine*, approximately one in five women in midlife reported having been sexually assaulted or harassed. And those incidents can have profound long-term health effects, notes Rebecca Thurston, director of the Women's Biobehavioral Health Laboratory at the University of Pittsburgh.

Thurston is a PhD professor of psychiatry, epidemiology, and psychology. Her team surveyed 304 women ages 40 to 60. Women who'd experienced harassment were nearly four times as likely to have developed hypertension and two times as likely to be dealing with clinically poor sleep than women who did not report a history of harassment. Those who experienced assault had significantly higher odds of elevated depressive symptoms and anxiety in addition to poor sleep. These numbers held true even after adjusting for socioeconomic status, demographics, and medical history.

"We've known for a while that sexual violence is really important for women's mental health broadly, but we haven't focused on measured aspects of their physiology or gone much beyond self-reporting," says Thurston. She notes that sexual assault occurs most often in late adolescence and early adulthood, but there isn't as much nationally representative data on harassment yet.

"We've undergone a transformation as a society and are now more aware of these issues, but our science is just catching up," she says. *—Liberty Ferda*

Serious Stool

You may not think of your intestines this way, but they are, in a certain sense, a shared space; and all of us are landlords, offering residence to a whole slew of actors—gut bacteria. When these tenants aren't helping our health, sometimes it's best to kick them out and invite a new family into our gut microbiome. The best place to find better bacteria? Poop.

Diwakar Davar, UPMC Hillman Cancer Center oncologist/hematologist and assistant professor of medicine at Pitt, is leading a clinical trial to study how fecal transplants could help melanoma patients whose tumors are resistant to immunotherapy. The trial is funded by Merck and the National Cancer Institute.

Davar says the presence of adverse gut bacteria in the intestinal lining can allow cancers to subvert the immune response in patients receiving PD-1 inhibitor therapy. In the trial, he's building a stool bank using samples from patients who have had successful immunotherapies, then transplanting those samples into melanoma patients. "The hope is that this re-energizes the immune system and gets it to work again," says Davar. A team of researchers in Chicago demonstrated in a 2015 *Science* paper that the approach was successful in animal models.

The trial goes hand in hand with the work of cancer immunologist Hassane M. Zarour, who is based at Hillman and is a Pitt professor of medicine, immunology, and dermatology. Zarour studies the mechanism by which cancer cells resist PD-1 inhibitors.

He has been trying to make something like this happen for a while. It wasn't an easy sell. Yet there is now "ample evidence," Zarour says, that certain gut inhabitants can regulate immunity. *–EBG*

FOOTNOTE

Pitt Med leads by example. Literally. Twenty Pitt researchers were named on the 2018 Web of Science report on Highly Cited Researchers. The report spans the past decade and includes 21 fields of science. Highly Cited Papers are defined as those that rank in the top 1 percent for citations for a specific field during a publication year.

DANCING FOR A CAUSE

Classical Indian dance teams from around the country performed at Pitt in February to raise money for the Birmingham Free Clinic in Pittsburgh. The annual dance competition, called Dhirana, was established in 2012 by Pitt students who wanted to celebrate their cultural heritage while supporting a good cause. Since then, they've raised about $79,000 for the clinic, which provides free medical care and social services support to uninsured and medically disenfranchised Pittsburghers. *—LF*

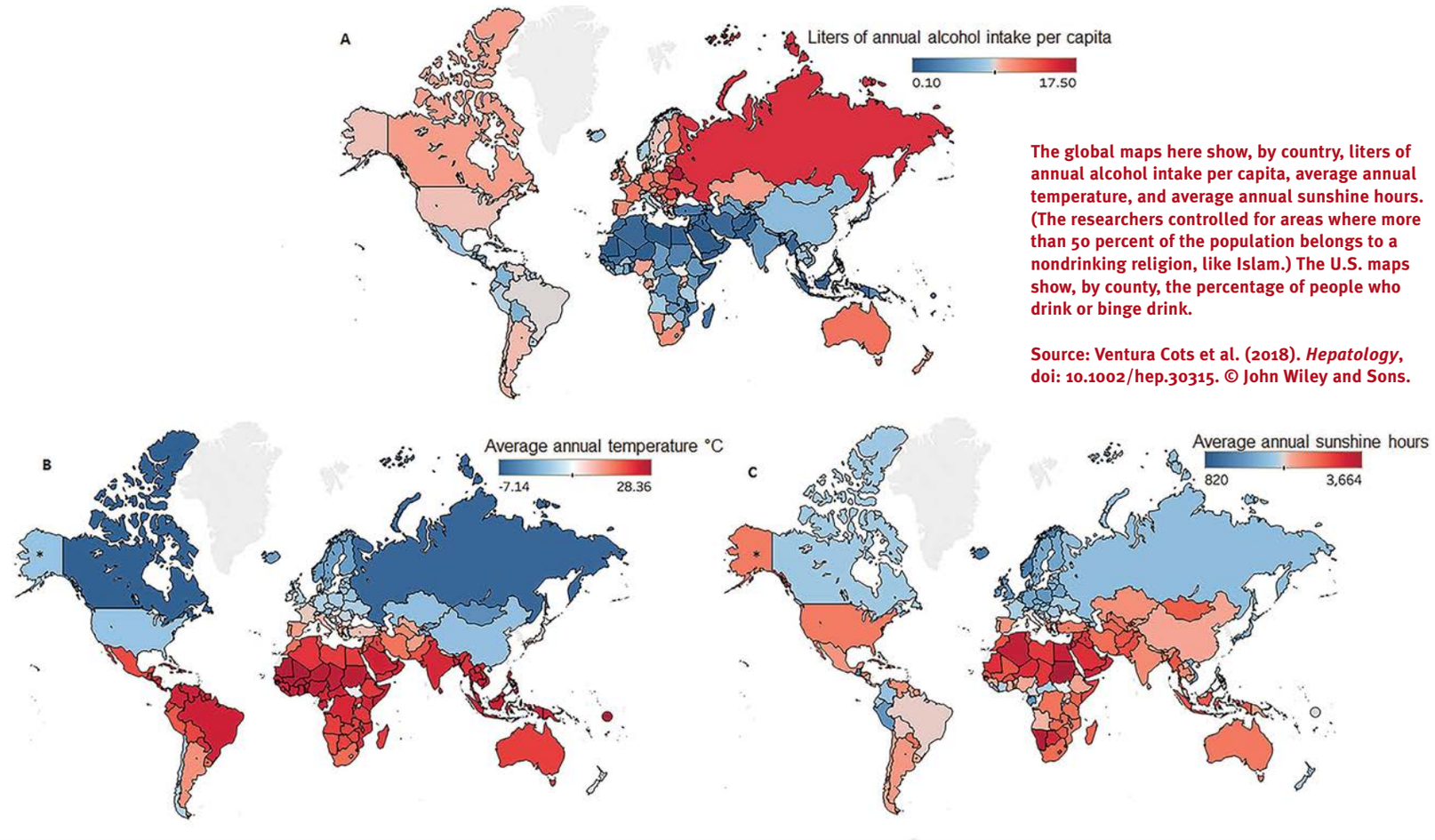
ADERINSOLA POPOOLA/UNIVERSITY OF PITTSBURGH

Pitt and the National Academies

Where does this nation turn for authoritative answers to complex questions about medicine and health? Since 1970, it's been the National Academy of Medicine (which until recently was called the Institute of Medicine). Three physicians from the University of Pittsburgh were recently elected to its membership.

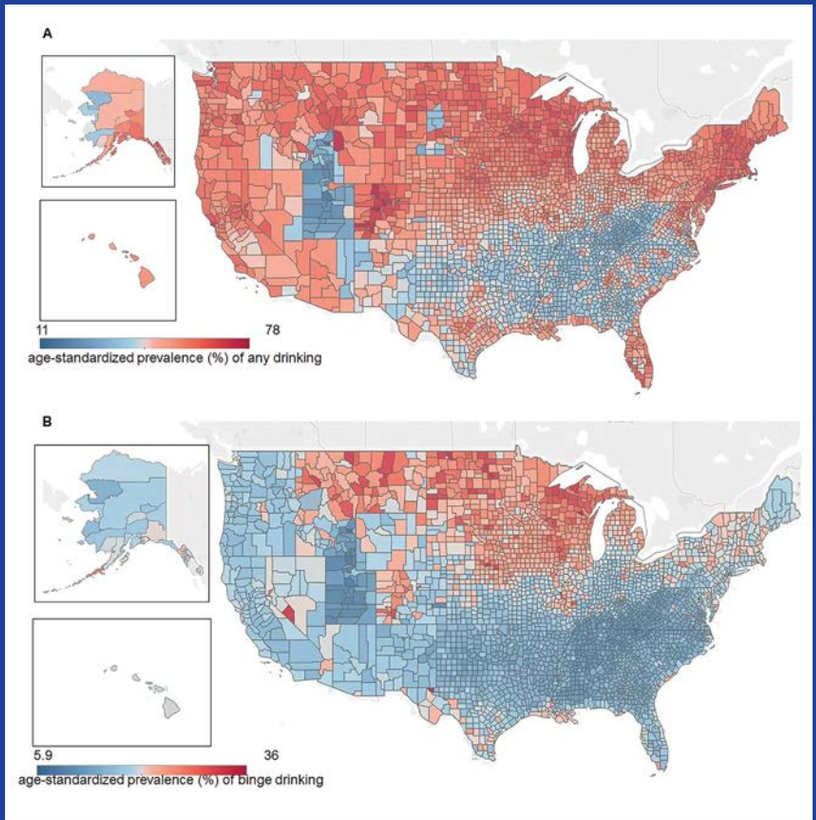
They are Amy Houtrow, MD/MPH/PhD associate professor of physical medicine and rehabilitation as well as pediatrics; Clifton Callaway, MD/PhD professor of emergency medicine, who holds the Ronald D. Stewart Chair; and MD neurological surgery chair Robert Friedlander, the Walter E. Dandy Professor of Neurosurgery and Neurobiology.

Speaking of national academies, Stephen Badylak, DVM/PhD/MD professor of surgery and deputy director of the McGowan Institute for Regenerative Medicine, was elected a 2018 fellow of the National Academy of Inventors. He holds 300 patents worldwide. *—Erica Lloyd*



The global maps here show, by country, liters of annual alcohol intake per capita, average annual temperature, and average annual sunshine hours. (The researchers controlled for areas where more than 50 percent of the population belongs to a nondrinking religion, like Islam.) The U.S. maps show, by county, the percentage of people who drink or binge drink.

Source: Ventura Cots et al. (2018). *Hepatology*, doi: 10.1002/hep.30315. © John Wiley and Sons.



JIM BEAM AND JACK FROST ...

ARE BETTER FRIENDS THAN YOU THINK

At 5 p.m. you leave work, and the sky is already as black as your Honda's snow tires. Crossing the parking lot, you shuffle across patches of ice and tighten a scarf that's losing its battle with the wind. Inside the car, you blow on cupped hands while the engine roars, and you think, *Some bourbon would warm me right up.*

If you can relate to that, you're not alone. People living in regions with lower temperatures and less sunlight consume more alcohol, according to Ramon Bataller, MD/PhD associate director of the Pittsburgh Liver Research Center and a professor of medicine at Pitt. (Bataller is from sunny Valencia, Spain.)

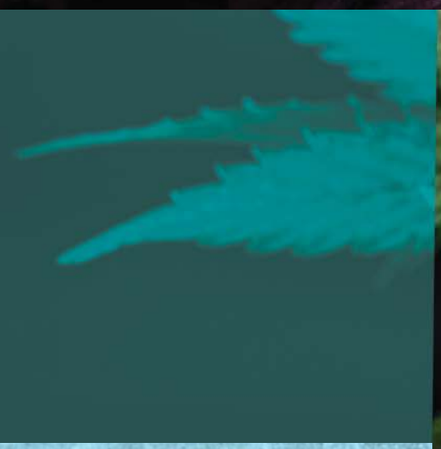
For years, Bataller, who also serves as chief of hepatology at UPMC, had suspected that people residing in cold, grayer regions drink more alcohol than those who live along the equator. To determine whether his hypothesis was correct, Bataller and his team gathered figures on average sunshine, temperature, and alcohol consumption, as well as cases of cirrhosis, from 193 countries and all 50 states. Stretching from the dry heat of America's Southwest to snow-capped Eastern European cities, global and national trends show that cold and cloudy skies correlate with increased alcohol intake and cirrhosis.

The reasons probably vary, according to Bataller. Drinking alcohol in the cold can create temporary sensations of warmth. Low light can also contribute to depression, he says, and increase alcohol use.

Meritxell Ventura-Cots, the principal author of the study and a postdoctoral fellow in Bataller's lab, says while various factors, such as socioeconomic status and religion, also contribute to individual alcohol intake, the research can help policymakers consider climate when targeting alcohol-related issues globally.

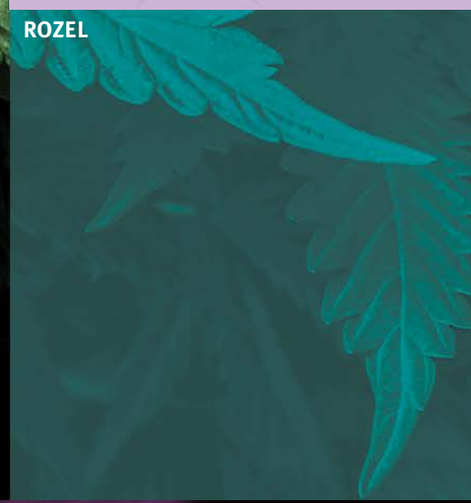
Bataller is investigating whether vitamin D, which we get from sunlight, can help prevent addiction and alcoholism. This may help him treat patients in Pittsburgh, where he's noticed high rates of alcoholism in youth.

—Prachi Patel



ROZEL

MERLIN



DO YOU NEED WEED?

HOW DO PHYSICIANS AND PATIENTS NAVIGATE THE USE OF MEDICAL MARIJUANA?

"I need medical marijuana."
"I use medical marijuana."
"I have medical marijuana on me right now."

If a patient were to enter UPMC resolve Crisis Services in Point Breeze and utter any of these statements to medical director John Rozel, it would create a complicated situation—one Rozel is still trying to figure out three years after Governor Tom Wolf legalized medical marijuana in Pennsylvania.

Rozel, an associate professor of psychiatry at Pitt, notes that it gets tricky for clinics to draft policies when medical marijuana is still banned by federal law. For example, resolve Crisis Services urges patients to bring their medication to visits because the facility doesn't have a large formulary. If a patient were to reveal a bag of marijuana to Rozel, should he inspect the packaging to make sure it was bought at a dispensary? What if a patient has a medical history that would justify having medical marijuana under Pennsylvania law but is carrying the drug in a sandwich bag, as though it was bought off the street? Should Rozel request to see the patient's medical marijuana certification? And if the patient has that, should Rozel question where the marijuana in the unmarked bag was purchased? Rozel says he would need to handle these situations in a way that respects the clinical needs of the patient, as well as the liability needs of resolve.

Cost is another issue, says Rozel. To receive a medical marijuana certification, most patients have to see a specialist who will recommend using the drug. Will insurance cover that visit? Probably not, according to Rozel. That out-of-pocket charge is followed by a $50 bill for the state's certification card. After that, it's off to a dispensary, where the price of medical marijuana is significantly higher than on the street. When the Commonwealth first legalized medical marijuana in 2016, the drug was only sold in heavily processed forms, like pills, tinctures, and vaporizable concentrates. Last year, selling dry-leaf marijuana for medicinal purposes became legal in Pennsylvania. Dry-leaf is cheaper than other forms, but smoking the drug, which is a fast and easy way to feel its effects, remains prohibited.

Medical marijuana creates other issues for practice. We spoke to Rozel and Jessica Merlin, an MD/PhD and associate professor who specializes in chronic pain and addiction, to hash out the dilemmas doctors and patients face.

What do we know about medical marijuana?

MERLIN: The evidence base is really limited. When I tell patients this, they're surprised because there's so much about medical marijuana in the media. On its Web site, the Pennsylvania Department of Health has a list of the conditions for which somebody can be certified to receive medical marijuana. The list includes cancer, chronic pain, spasticity, ALS, and Parkinson's, and it is not based on medical evidence or science. It was developed by legislators with some influence from the medical field. There's a case for chronic pain, and you'll hear anecdotes about people with PTSD being really helped by medical marijuana. And you know, it's not that there aren't people who can't be helped, but there really is little to no high-quality evidence.

ROZEL: When it comes to the use of medical marijuana for psychiatric illnesses, frankly, the evidence isn't fantastic. As an emergency psychiatrist, I see tons of substance use disorders, including with marijuana. So, it creates a very tricky situation. When folks say, "I need medical marijuana," or, "I use medical marijuana for *blank* psychiatric issue," I'm left scratching my head, wondering: *Is this for legitimate use, related to ongoing recreational use, or part of a substance use issue?*

Now, at the end of the day, I don't begrudge someone who has metastatic osteosarcoma with severe pain to have access to something like medical marijuana. The challenge is making sure that it's used appropriately for chronic and severe conditions, while also recognizing this: Is it really appropriate to turn to a largely untested, highly inconsistently produced substance when there are any number of evidence-based, safe, and effective interventions that are available? Have those been tried first?

Why is there a lack of evidence?

MERLIN: A couple of reasons. One is there are hundreds of chemicals in marijuana. THC and CBD, or tetrahydrocannabinol and cannabidiol, are the most commonly studied.

PHOTO OF MARIJUANA: GETTY IMAGES. PORTRAITS: COURTESY MERLIN AND ROZEL. PHOTO ILLUSTRATION: ELENA GIALAMAS CERRI.

We think about medicine as one substance, and we can do trials of that one substance. But, it's more difficult when you're dealing with hundreds, and in addition, there are different modes of administration to take into account. People might inhale it like a cigarette, vape it, eat it in a brownie, or rub it on their skin. So, the studies that have been done are very heterogeneous in terms of the mode of delivery, and that makes them harder to interpret. Another reason studying marijuana is complex: In the United States, it's a Schedule-1 substance, which means it's hard to get. The federal government considers it to have no medical role. As a result, there are logistical barriers on doing a randomized trial. The government will only allow researchers [on federal grants] to get it from one source in Mississippi.

ROZEL: There is actually some interesting research out there looking at CBD, which is one part of medical marijuana that may be effective for some psychological disorders, including possibly schizophrenia. But we have to figure out how to interpret that data knowing that the marijuana plant itself, often much higher in THC, can actually be a significant exacerbator, possibly even a precipitant of, a lot of these same psychological disorders.

CBD has promise, but it needs to be researched, and a lot of the regulations around researching medical marijuana [make it] almost impossible to actually engage in [the research]. One of the things that was really novel and unusual about Pennsylvania's medical marijuana laws is that we created a passage to say, "Hey, look, academic medical centers should be able to do organized research around medical marijuana." Fantastic, wonderful, absolutely. We need to build the evidence base. However, then when Pitt Med and any number of other major reputable academic medical centers put their names in and said, "Hey, we want to apply for this," they were summarily rejected. It makes it really tough. At the federal level, there's a small amount of federally produced medical marijuana that can be used for research. But it's incredibly limited and, quite frankly, the word on the street is their marijuana is not so great. It's not very potent, not very effective for studying.

What are some negative side effects doctors should know about?

MERLIN: Worsening of mood symptoms. Depression, anxiety.

Marijuana is probably not as impairing as alcohol, but it is impairing and is highly associated with motor vehicle accidents. This is especially a problem because people don't necessarily think about it.

Another physical manifestation is marijuana-induced hyperemesis. A lot of people use marijuana extensively for nausea, and then they keep going to their doctor because they can't keep anything down. It can become a chicken-or-the-egg kind of thing. And it can be very hard to persuade people that their vomiting is actually from the marijuana that they're using to help with the vomiting.

ROZEL: We certainly know, clinically, lots of folks living with trauma and the symptoms of PTSD who turn to medical marijuana; and a lot of them do seem to subjectively report that this helps. They say it takes the edge off their anger, the edge off the flashbacks, what have you. But, we also have some observational research that says when you look at people with PTSD who are also using marijuana, they are most likely to be physically violent. Well, that's concerning too. Now, it's a correlation, and we don't know whether or not it's causation. It could simply be a particular patient's PTSD was that bad, they'd blown through all traditional treatment interventions, had turned to medical marijuana, and were going to be violent with or without medical marijuana.

The evidence base is really limited. When I tell patients this, they're surprised because there's so much about medical marijuana in the media.

Now, we do have really good data indicating that if someone's living with a severe mental illness—like schizophrenia or bipolar disorder with psychotic symptoms—and they use recreational marijuana, high THC marijuana, there's a significant increased risk for violence. But that's a small subset of the broad swath of people living with psychiatric illness, so there are a lot of unknowns.

How do doctors navigate this issue with patients?

MERLIN: There are a few ways. I think if clinicians are interested in this, they should call a dispensary and ask for a visit. I've done this. It was incredibly helpful. Now I know what they are likely to experience at a dispensary and whether or not it's something I'd recommend.

When you certify somebody for medical marijuana, you're saying, *Yes, they have a condition that's on this list, and I think marijuana would help.* So, could I say that for some patients? Sure. But the thing that I'm concerned about is what comes next. They go to the dispensary. It's not a pharmacy. Not a health-care facility. It's a business. And I've seen two people who have lost substantial amounts of money at the dispensary.

It varies by state, but to certify patients for medical marijuana in Pennsylvania, you are required to go through a course. From my experience, and from talking to my colleagues, the course is not scientifically rigorous. In the course I took, there was a lot of inaccurate information about the role of marijuana for treating opioid addictions. It was actually stated, "They say there's no evidence for this." The course actually endorsed the use of marijuana as being safer than buprenorphine for the treatment of opioid use disorder, which is a very dangerous approach. I mean buprenorphine is an evidence-based treatment with lots and lots of evidence in terms of mortality and other key outcomes. And here's somebody giving a webinar to people getting certified for medical marijuana saying, "You know, marijuana is better"—despite the fact that there's absolutely no evidence.

To understand this more, clinicians should familiarize themselves with the medical literature. There are excellent conferences that focus on substance use broadly but have a lot of content about marijuana.

Anyone with a medical license can get certified. It takes almost no time at all. But if you really want to learn more about it, I recommend connecting with some of those resources to really understand the implications.

—Interview by Gavin Jenkins

GETTY IMAGES

BABY BURN

A NEW TOOL FOR UTI DETECTION

BY KRISTIN BUNDY

"When adults have a urinary tract infection [UTI], they can tell the doctor it burns when they pee," says Nader Shaikh, MD/MPH associate professor of pediatrics at the University of Pittsburgh and UPMC Children's Hospital of Pittsburgh. "You check their urine, and they're usually right."

With diaper-wearing infants and pre-verbal toddlers who present with a fever in the emergency department (ED), diagnosing UTIs is much more difficult. "You can't ask babies to pee in a cup," says Shaikh, "and they don't talk, so we usually have to do a catheterization to get a clean sample."

But catheterization is upsetting and painful. Children often need to be held down while the genital area is cleaned and the tube is inserted. Then, it's fingers crossed that there even *is* any urine on board to be emitted, sampled, and sent to the lab. When children test positive, then they must also undergo an ultrasound.

The effort might be worth it if a UTI diagnosis is highly likely, but the probability of UTI is just 5 to 10 percent in a baby presenting with a fever in the ED, says Shaikh. "That means you have to test approximately 10 kids to get the child with the UTI." So, which ones do you test, and which ones do you leave alone?

In spring 2018, Shaikh and his colleagues published in *JAMA Pediatrics* a study of UTICalc, a free, Web-based UTI probability calculator they developed at Children's.

In a large data set of children who were 2 years old or younger (and another large data set to validate the first), the investigators demonstrated that UTICalc reduced UTI testing by 8 percent and decreased the number of UTI misdiagnoses to zero.

The first step of UTICalc assesses a child's risk factors. It includes five YES/NO questions on age, temperature, other source of fever, gender, and race. (White children are more likely to contract UTIs.) "Once you put in the child's baseline information, you get the probability of UTI," Shaikh says. Then the physician can decide whether to sample the child's urine.

The second step focuses on interpreting the urine test results. When the labs come back, physicians enter specific data points (like white blood count). UTICalc then provides a more refined probability of UTI.

"If the probability goes down to 1 percent, you might say, *I'm not going to treat; this is probably not a UTI*," says Shaikh. "If it goes up, then you might decide the other way."

By improving diagnostic accuracy, the calculator can help reduce the number of patients who are being overtreated with antibiotics. It can also help kids who should be getting catheterized but aren't.

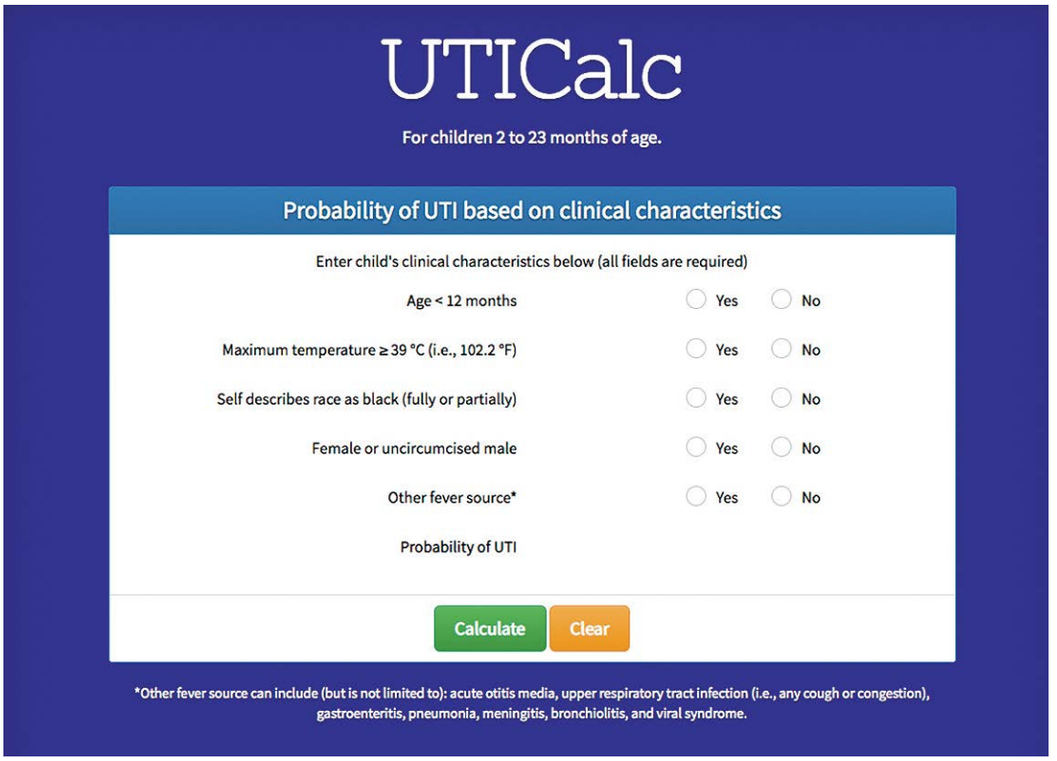
"Both mistakes happen, but it's more common that we overtreat," says Shaikh. "And part of that problem is that the tests we have right now are good but not great. We can't predict well who's going to have a UTI or not, so we tend to be more careful and treat more children than need it."

The UTICalc team put a lot of effort into building an accurate tool that keeps the number of required fields to a minimum, so that it's user-friendly, Shaikh says. Ultimately, the end product's variables were very similar to those of an American Academy of Pediatrics algorithm, he adds, but UTICalc also makes probability cutoffs (the percentage chance of UTI) more transparent to physicians.

In the first six months after the *JAMA Pediatrics* paper, analytic reports showed nearly 16,000 users and more than 45,000 entries. And several clinicians and researchers have contacted Shaikh about presenting UTICalc at a journal club or including it in future study designs.

Shaikh is a member of the UTI Center at Children's, one of the few centers in the country devoted to addressing these elusive childhood infections.

"There are so many mysteries about UTI in babies," Shaikh says. "It's hard to understand why some get a UTI, and some don't. They're *all* sitting in diapers!" ■



In the first six months after the *JAMA Pediatrics* paper, almost 16,000 providers used UTICalc. The tool (pictured here) is available at https://uticalc.pitt.edu.

A red "molecular beacon" highlights LRRK2 activity in brain tissue of a person who died of Parkinson's disease.

FROM "LRRK2 ACTIVATION IN IDIOPATHIC PARKINSON'S DISEASE," DI MAIO ET AL., SCI. TRANSL. MED. 10, EAAR5429 (2018) 25 JULY 2018. REPRINTED WITH PERMISSION FROM AAAS.

WASTE DISPOSAL

AND A BRIGHT SPOT FOR PARKINSON'S

BY ALLA KATSNELSON

Most cases of Parkinson's disease seem to be caused by some murky combination of genetic and environmental influences. In about 1 out of 10 people with the condition, though, genetic glitches are solely at fault. The most common among these glitches is a mutation in a gene called LRRK2, which drives its encoded protein into a frenzy of activity.

Pharmaceutical companies are developing drugs that hobble LRRK2 protein activity to treat the disease in the small subset of patients who carry the mutation. But J. Timothy Greenamyre, professor of neurology at the University of Pittsburgh, thinks meddling with LRRK2 might have a bigger payoff. He and his colleagues report that the protein plays a central role in the disease, even when the gene is not mutated. "Rather than targeting something like 3 percent of Parkinson's patients," he says, drugs that tamp down LRRK2 activity "may help virtually everyone with Parkinson's disease. And that's good news." The team published their findings last summer in *Science Translational Medicine*.

Greenamyre had a hunch that LRRK2 had deeper ties to the disorder than researchers had previously suspected. But studying the protein was a challenge because only a tiny amount of it is present in the cell. So as a first step, he and his colleagues set out to develop a sensitive method to visualize it in action. By creating a so-called molecular beacon, a marker designed to glow red when the protein is mid-task, they could see that LRRK2 tends to sit in a type of nerve cell that gradually atrophies in people with Parkinson's disease.

When they deployed the molecular beacon in tissue taken from people who had died from nongenetic forms of the disease, they found that LRRK2 protein activity was surprisingly high. Further studies suggested that oxidative stress ratchets up LRRK2 activation, which could explain how environmental factors can kick the gene into disease-causing mode, even when it's not mutated.

The researchers then turned to a rat model of Parkinson's. In the model, animals are fed rotenone, a chemical used in pesticides, which causes a real mess—clumps of a protein called alpha-synuclein accumulating over time, much like they do in humans as Parkinson's advances. Again, by deploying their molecular beacon, Greenamyre and his team found that LRRK2 glowed bright with activity within cells.

When the team gave the rats rotenone along with a compound that prevents LRRK2 activation, however, the alpha-synuclein clumps didn't form. Alpha-synuclein is normally cleared away by a cellular waste disposal system called autophagy, but that process was disrupted in rats given rotenone. Their brain cells had an unusually low number of lysosomes—tiny membrane sacs that act as garbage trucks, ferrying detritus out of the cell.

"The basic story, then, is that in Parkinson's disease, LRRK2 gets overactivated by oxidative stress," explains Greenamyre. That interferes with a pathway that regulates autophagy, which in turn causes abnormal proteins such as alpha-synuclein to build up.

At least one company is already beginning to test LRRK2 inhibitors in Parkinson's patients who have mutations in the gene.

In the meantime, Greenamyre's lab wants to better understand the gene's importance. He and his colleagues are working to further define how toxins and oxidative stress can affect autophagy via LRRK2 activity.

And the team has shown that, in rats, the new inhibitors can prevent abnormalities in cellular waste disposal caused by the disease. ■

THE WEST WING

ON 3550 TERRACE STREET

BY ERICA LLOYD

The addition will be built on existing foundational infrastructure.

Plans include a renovated Falk Library of the Health Sciences; the library will have an entrance on Lothrop Street, making it more convenient for all health sciences students.

Bringing Scaife Hall's mid-century physical plant up to snuff would have cost $54 million. Instead, Scaife's new addition will supply high-efficiency HVAC, plumbing, and electrical to the rest of the building, while offering seven floors of contemporary learning space.

Once upon a time, in the summer of 1954, University of Pittsburgh officials came together with civic leaders to break ground for a building devoted to the education of health professionals. The building, Scaife Hall, would be connected to Presbyterian Hospital. Industrialist Alan Scaife led the University's campaign to raise funds for the construction effort. On that summer day, his wife, Sarah Mellon Scaife, stood on the hillside next to the hospital and struck the earth with a gleaming spade. Two years later, a broad, imposing 11-story limestone structure opened its doors to students and scholars.

Scaife Hall's designers envisioned an academic home to some of the country's most promising minds in medicine. The next two decades brought a golden age of sorts, with the likes of Frank Dixon, Jack Myers, Klaus Hofmann, Niels Jerne, Julius Youngner, and Jonas Salk inspiring Pitt Med students.

Sixty-five years after Sarah Scaife wielded that shovel, the human body has not changed, but some of the ways we teach about it and explore its mysteries have. So the School of Medicine is planning an education addition and renovation that capitalizes on how learning happens today. Later this year, pending some approvals, Pittsburgh leaders will again come together for a groundbreaking next to Presbyterian; this time, they'll be celebrating the raising of the School of Medicine's new West Wing.

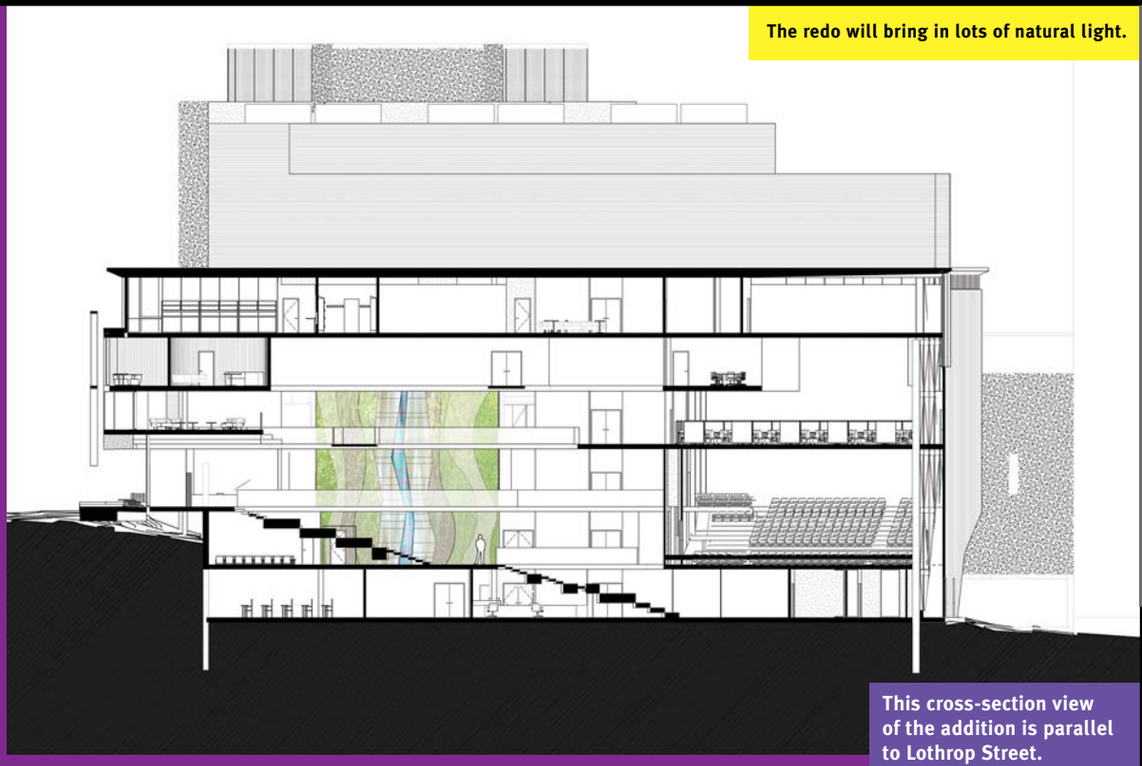
"We've learned a lot about how adults learn, and we understand that many people don't learn from one-hour lectures one right after the other all day every day," says Ann Thompson, vice dean of Pitt's School of Medicine. So before the raising of the new will be the razing of the old: specifically, the two-story structure at the corner of Terrace and Lothrop Streets, where the school's largest lecture halls are currently housed.

RENDERINGS NOT FINAL

Where it makes sense, the school will salvage and reuse existing wood trim and travertine.

In the existing lecture rooms, seats are bolted to the floor in the direction of the stage. The auditoriums and classrooms in the new seven-story wing will make it easier to break into groups and flip lectures (so learners can present from their seats).

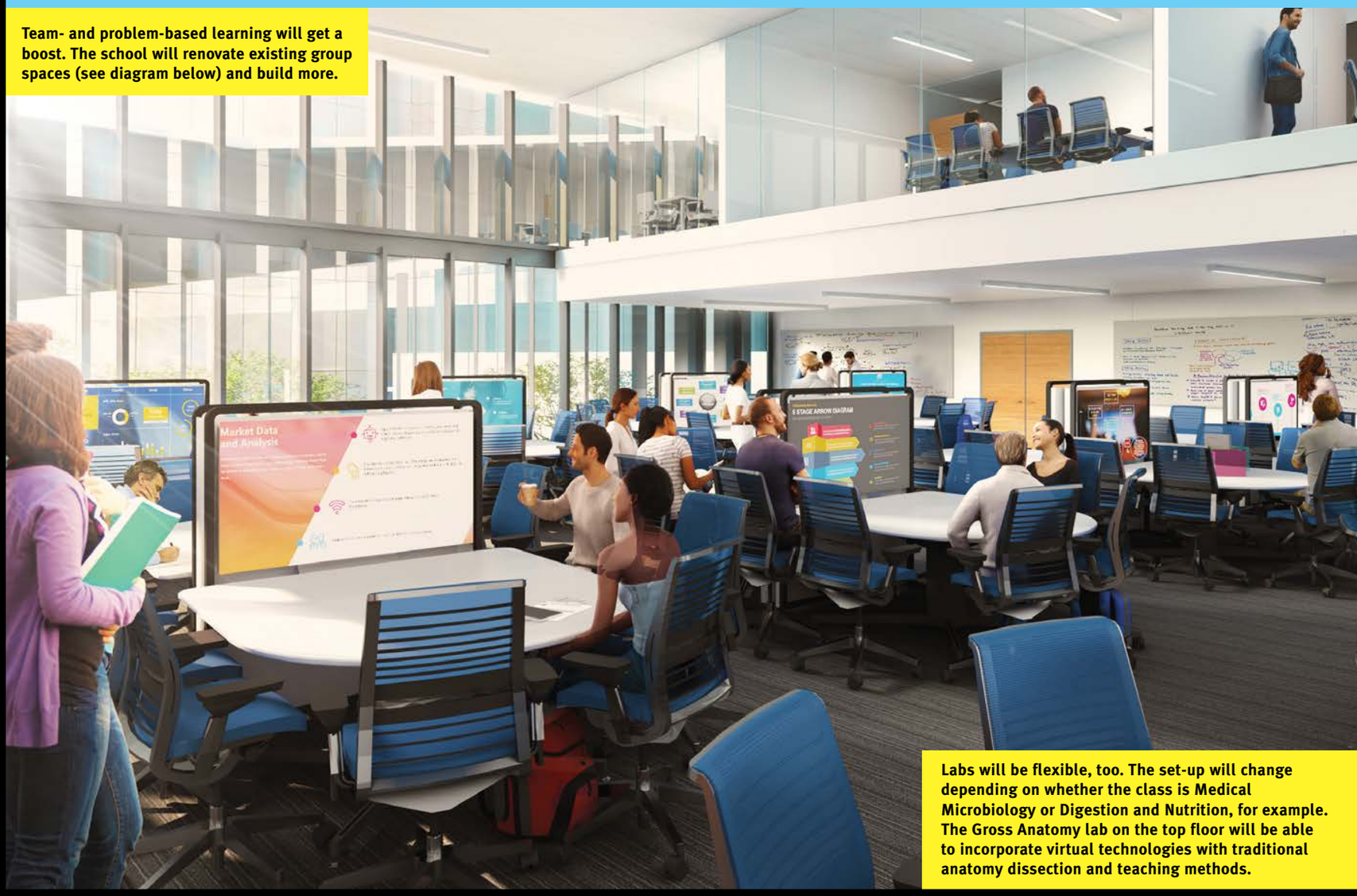
The redo will bring in lots of natural light.



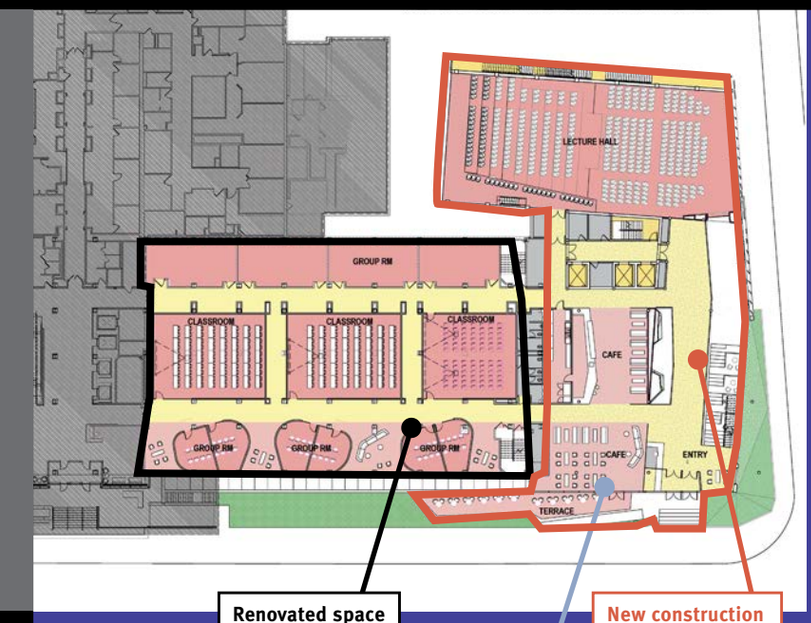
This cross-section view of the addition is parallel to Lothrop Street.

The $129 million project includes 110,000 square feet of new construction and 47,000 square feet of renovations.

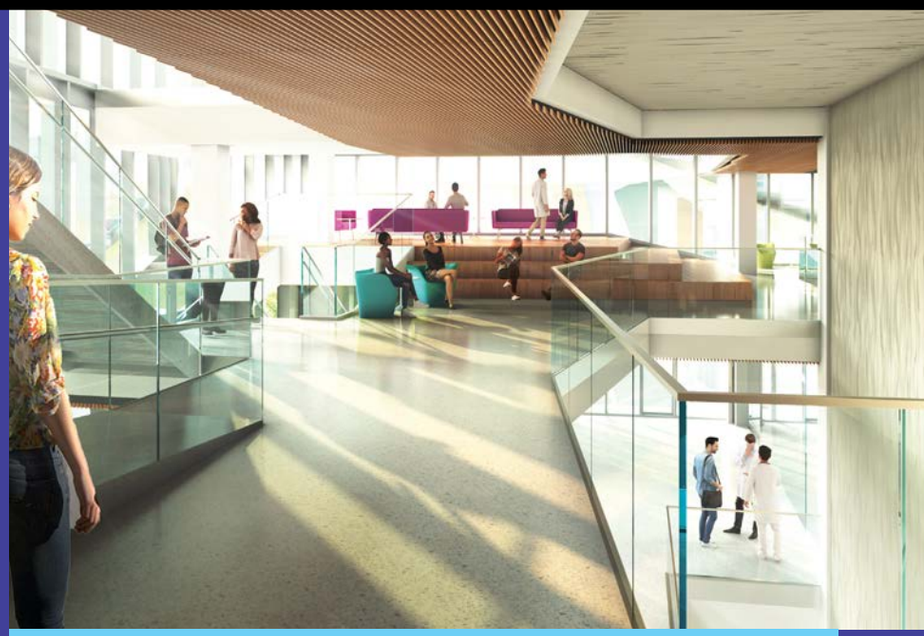
Team- and problem-based learning will get a boost. The school will renovate existing group spaces (see diagram below) and build more.



Labs will be flexible, too. The set-up will change depending on whether the class is Medical Microbiology or Digestion and Nutrition, for example. The Gross Anatomy lab on the top floor will be able to incorporate virtual technologies with traditional anatomy dissection and teaching methods.



A partial main entry level (fourth floor) layout, after renovations and additions.



Lounges. Couches. Cafes. Carrels. Ad hoc meeting and plug-in areas aplenty will accommodate a range of study styles. They'll also offer places to kick back. And we'd be remiss in not mentioning the student-only areas—"where they can snooze, study, hang out, play ping-pong, make a mess," says Vice Dean Thompson with a smile.

OCT. 27, 2018

PITTSBURGH'S DARKEST DAY AND THE MASS CASUALTY RESPONSE

BY GAVIN JENKINS

Pittsburgh's responders were prepared for a national tragedy.
(Photo: Alexandra Wimley/*Pittsburgh Post-Gazette* via AP)

At **9:58 A.M.**, Oct. 27, 2018, Keith Murray is getting his 3-year-old son ready for another preschooler's birthday party when his phone vibrates. Murray, clinical assistant professor of emergency medicine at the University of Pittsburgh and medical director for the Pittsburgh police department's SWAT, reads the following message from the SWAT team:

ACTIVE SHOOTER, MULTIPLE SHOTS FIRED, SERIOUS HEMORRHAGE, TREE OF LIFE SYNAGOGUE, 5898 WILKINS AVENUE, 15217.

As one of a select group of physicians around the country who serves as a member of a special operations unit, Murray keeps his SWAT gear staged in his house for such an emergency. This hybrid practice is so new there is not an agreed upon title for it, yet. But, Murray has gone through basic and advanced SWAT training, including special weapons and tactics exercises. For the past seven years, he has drilled with Pittsburgh's SWAT for 16 hours every month.

After kissing his wife and children, the doctor puts on his camouflage uniform and a bulletproof vest with an attaching radio. He grabs a helmet, headset, and two backpacks filled with medical gear and rushes from his house. He hops in his Ford F-150 and heads toward Tree of Life Synagogue, which is usually a 15 or 20 minute drive from his suburban home.

AFTER KISSING HIS WIFE AND CHILDREN, THE DOCTOR PUTS ON HIS CAMOUFLAGE UNIFORM AND A BULLETPROOF VEST.

SEVERAL MINUTES BEFORE Murray receives the alert, Leonard Weiss wakes up to a clanking noise. A Pitt assistant professor and emergency medicine physician, he didn't get home until 4 a.m. from UPMC Mercy. He assumes the noise is construction work—not unusual for a Saturday morning in Squirrel Hill—and rolls back over. But moments later, the clanking wakes him up again. This time it's more rhythmic, and it's followed by screaming.

"Just a terrible screaming," he says. "So loud and angry that I never would have expected to hear it in this neighborhood."

Weiss, who serves as EMS medical director and assistant medical director for STAT MedEvac, lives adjacent to Tree of Life Synagogue. A man armed with an AR-15-style semi-automatic rifle and three Glock .357 handguns had just entered the synagogue and begun firing on worshippers. Tree of Life is home to three congregations: Tree of Life, New Light, and Dor Hadash. New Light and Tree of Life had started separate Shabbat morning services; Dor Hadash was set to begin a Torah study session.

Guessing that the rhythmic sound is some kind of automatic rifle, Weiss scrambles out of bed, turns on his EMS radio, and looks out the window. The dispatcher names the streets around his house and confirms what Weiss feared when he heard the screams: There is an active shooter at the synagogue.

Worried about stray bullets, Weiss gathers the radio, his phone, and his clothes and heads to the basement. While he dresses, he listens as the police organize a response over the radio. His heart is racing; the shooting is right outside his front door. But, with years of EMS experience, he's also used to snapping into action.

Weiss (Res '15, Fel '16) feels robotic tying the laces on his boots and throwing on a shirt. The only thing he is thinking: *I need to go outside.*

Dressed, he calls in to the dispatch, identifies himself, and is told the location of Tactical Command's staging area, which is where the police response is being overseen. He climbs the basement stairs to the first floor of his house and calls his mentor, Ronald Roth, professor of emergency medicine, chief of EMS Division in the Department of Emergency Medicine, and the medical director for Pittsburgh's Department of Public Safety. Roth lives in Point Breeze (which borders Squirrel Hill), but he's in Carnegie. He received the same alert as Murray and is in his car, heading to the staging area.

"I'm hearing the gunshots," Weiss tells Roth. "And I see teams forming outside. I'm gonna head out; I'll update you."

On his way to Squirrel Hill, Murray listens to the police scanner and goes through a medical threat assessment in his head. He envisions the geography surrounding the synagogue and considers where it is located in comparison to the level-one adult and children's trauma centers in Pittsburgh. He thinks to himself: *UPMC Presbyterian and UPMC Children's Hospital are both over two miles away; UPMC Mercy is about four; and, if there are a lot of victims, there's Allegheny General Hospital, which is almost six.*

With one hand on the steering wheel, he texts two of SWAT's four Tactical EMS team leaders. (The city has a cadre of 16 Tactical EMS personnel divided into four teams.) Murray checks to see if they know everything he knows—the synagogue's surroundings, the assessment of closest hospitals—and then he asks if they have heard any new details, specifically regarding the number of possible victims or shooters. He wants to know exactly what he's driving into, but there's no new information.

He's about to call his close friend, Matthew Neal, when Neal calls him. (Murray's son was getting ready to go to Neal's daughter's party.) Neal, trauma surgeon and Roberta G. Simmons assistant professor of surgery at Pitt, specializes in hemorrhagic shock. He also receives SWAT alerts in case of situations

like this. He tells Murray that he's skipping the birthday party and heading to UPMC Presbyterian's emergency department to help with the response. As the two talk, Neal (MD '06, Res' 14, Fel '15) follows several police cars on the Parkway North, speeding toward the Veterans Bridge as other motorists pull over.

While Murray and Neal drive, two Pittsburgh police officers exchange gunfire with the shooter. An officer is shot in the hand and the other's ear is grazed by either shrapnel from broken glass or a bullet. The man retreats into the building.

Driving up Shady Avenue in Squirrel Hill, Murray sees that the police have blocked the intersection with Wilkins Avenue. He wants to get as close to the synagogue as possible, but the road is already lined with ambulances and patrol cars. Police dispatchers have called every available officer to the area. Murray drives up to the blockade, turns left into a driveway, and parks in someone's front yard.

Murray jumps out of his truck, checks his radio, puts on his helmet, and runs toward Tree of Life. On the way, he meets a SWAT officer who also just parked, and they do a quick "buddy check" to make sure each has the right equipment.

When they reach the corner of the synagogue, they join about eight other SWAT officers. They form what is called an Emergency Entry Team (EET) and wait for permission from Tactical Command to storm into the synagogue. Another EET has formed at the other end of the building, and police are setting up a perimeter.

SOMETIME AROUND 10:30 A.M., a SWAT officer announces on the police radio, "We're about to make entry." The other team punches into the synagogue from another location shortly after.

SWAT team members find a couple hiding.

"We've got to evacuate some of these hostages," an officer reports on the radio. Officers rush them outside and up the street beyond the barricade.

SWAT confirms by radio, "Be advised … trauma surgeon is with the team."

As they search the building, they find several dead.

SWAT finds an injured worshipper. The person has been shot, and Murray works with a Tactical EMS medic. They announce over

STOP THE BLEED

In 2017 Matthew Neal and his 9-year-old son, Cameron, stood in front of a crowded room at Rodef Shalom Congregation. Neal, a Pitt trauma surgeon who specializes in hemorrhagic shock, demonstrated to the community members how to perform emergency medicine tactics, such as how to pack a wound and apply a tourniquet. The session was part of a training initiative called Stop the Bleed.

A person can bleed to death in less than five minutes. Neal and his son coached the attendees (a number of Pittsburgh synagogues were represented at the session) on skills that can save a life after a car crash, a kitchen accident, or a mass shooting.

The SWAT team members and Tree of Life survivors who suffered gunshot wounds during the massacre would not have lived without the techniques police officers and EMS used from their Stop the Bleed training, says Neal.

The idea for Stop the Bleed came about after the Sandy Hook Elementary School shooting in December 2012. A few months after the shooting, Lenworth Jacobs Jr., a surgeon at Connecticut Children's Medical Center, and the American College of Surgeons assembled experts from government and the medical and security communities to draw up the Hartford Consensus, a set of national guidelines to help people survive mass shooting events.

In the spring of 2016, Neal joined a steering committee to implement a Stop the Bleed program in Western Pennsylvania. The committee included nurse David Bertoty, clinical director of emergency and trauma services at UPMC Presbyterian; surgical PA Benjamin Reynolds, clinical assistant professor of surgery; surgeon Raquel Forsythe, assistant professor of surgery and critical care medicine, who is director of education for trauma surgery at Pitt; and surgeon Andrew Peitzman (MD '76, Res '83), a Distinguished Professor of Surgery who holds the Mark M. Ravitch Chair in surgery here.

The committee's goal was to combat the threat of mass shootings by creating a training program that would be accessible to everyone in the region. "We went to UPMC and said, 'This is the public health crisis of our time,'" notes Neal. "'We don't know when the next event will be, but we know there will be one.'"

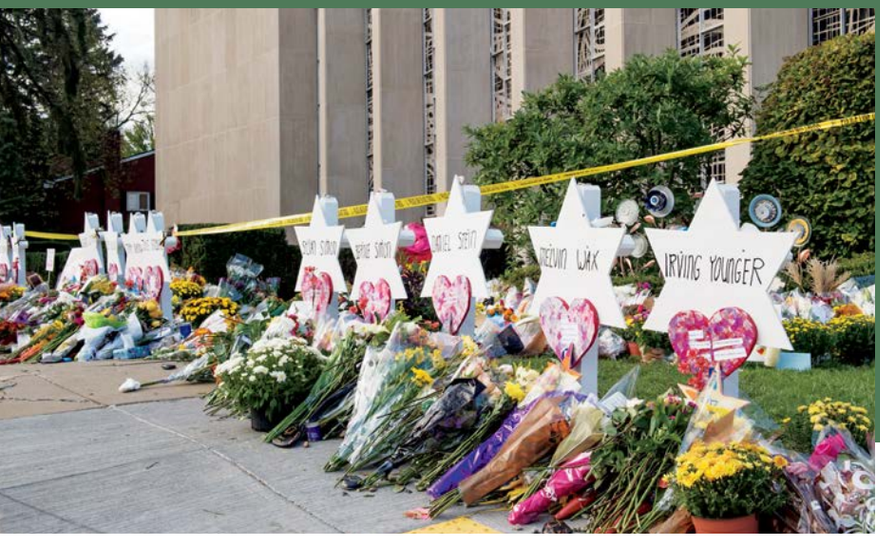
TOM ALTANY / UNIVERSITY OF PITTSBURGH

Med students participate in a Stop the Bleed training.

UPMC provided $1.3 million to fund Stop the Bleed; and with its first step, the committee designed a "train the trainers" program. The committee began by teaching first responders, who could then spread the program into communities. Stop the Bleed trainers have taught faculty of entire school districts, Boy and Girl Scouts groups, and 4-H clubs. When Neal taught members of Pittsburgh's synagogues in 2017, the Jewish Healthcare Foundation bought tourniquet kits for each congregation in the city.

Neal would like to see Stop the Bleed skills become as commonly understood as CPR. However, he knows that the idea of packing a wound and applying a tourniquet can seem overwhelming for some.

"That's why I bring Cameron along," he says. "I say, 'If a 9-year-old can do it, so can you.'" *—GJ*



On Oct. 27, 2018, a gunman entered Pittsburgh's Tree of Life Synagogue and killed 11 people: Joyce Fienberg, 75, Richard Gottfried, 65, Rose Mallinger, 97, Jerry Rabinowitz, 66, Cecil Rosenthal, 59, David Rosenthal, 54, Bernice Simon, 84, Sylvan Simon, 86, Daniel Stein, 71, Melvin Wax, 87, and Irving Younger, 69. A memorial was erected outside the synagogue.

the radio, "Applying tourniquet at this time."

Tactical EMS rush the congregant from the building and to the hospital.

A team locates another wounded victim, whom they rush to the hospital.

At one point, a police officer enters a room and is met by gunfire. He sustains gunshot wounds, and soon after, SWAT team members manage to pull him from the room. They remove the officer's body armor and helmet and cut off most of his clothes. Tactical EMS, with Murray, perform a full-body search for life-threatening hemorrhage, airway issues, and head wounds. They pack his wounds, apply five tourniquets, and roll him onto his back. They place him on a MegaMover and then a stretcher. Moments later, an ambulance carries the officer to UPMC Presbyterian; Murray and two Tactical EMS medics remain alongside him.

AROUND 11:15 A.M., Murray returns to Tree of Life. By now, another wounded officer and the alleged shooter, who has surrendered and is wounded, are receiving treatment from Tactical EMS.

A total of 11 people were found dead inside the synagogue. And now, the terror is over.

The Tree of Life attack has been called the deadliest ever on a Jewish community in the United States. At a press conference later that Saturday, Pittsburgh Mayor Bill Peduto described it as the "darkest day of Pittsburgh's history."

Tactical EMS transported seven people, including four police officers and the alleged shooter, from Tree of Life to three level-one trauma centers—UPMC Presbyterian, UPMC Mercy, and Allegheny General.

All seven live, thanks to what Murray calls "the chain of survival."

The chain of survival begins with the SWAT team members who are trained to pack wounds and apply tourniquets. Murray says that the officers who were shot inside the synagogue likely would have bled to death if they hadn't received immediate medical attention from fellow officers and Tactical EMS. Neal adds that one of the worshippers probably would have died, as well, if not for immediate medical attention at Tree of Life.

When Neal gets out of his car at UPMC Presbyterian, he sees colleagues parking. Dozens of off-duty physicians, surgeons, nurses, and residents had rushed to help.

Driving into the city, Neal was anxious. He wondered how many people had been injured, and he was worried about Murray and other friends who had gone to Tree of Life. The moment he steps inside the hospital, his anxiety diminishes.

He hurries to the back of the emergency department and joins one of six surgical teams, each staffed with eight to 10 medical professionals. Neal adds: "The teams had assembled; and I looked around at all these incredible professionals, and I said, 'We got this.'"

Don Yealy, emergency medicine physician who serves as chair of Pitt's emergency medicine department, senior medical director for UPMC Health Services Division, and vice president of emergency and urgent care for UPMC Physician Services, says that planning and practicing for such a tragedy took countless hours. The emergency department drills for how to handle mass shootings, infectious pathogens, and radiologic threats. Sometimes they do tabletop walk-throughs, and other times they hold exercises with mock patients.

"[On October 27], it was actually fairly

easy to know what needed to be done and know that it was going to happen fairly seamlessly," Yealy says.

A mass casualty response has multiple components, including gathering information to verify the tragedy, calling additional personnel to help, clearing hospital space, and preparing for several hours of care as an unknown number of patients arrive.

When Roth (MD '82, Res '85) reaches the command post around the corner from Tree of Life, he acts as the point person for the medical response. He updates Yealy (Res '88), who remains in contact with the emergency departments.

SHORTLY AFTER 10 A.M., UPMC Presbyterian confirms a mass shooting is in progress. Stephanie Gonzalez, assistant professor of emergency medicine, reads the attending trauma physician responsibility card.

Each UPMC emergency department has a binder filled with folders of instructions for multiple types of possible tragedies. The folders consist of laminated cards that outline the responsibilities of each staff position.

Following her card's instructions, Gonzalez makes sure that each of the emergency department's three trauma bays is properly staffed with an attending trauma physician, an attending surgeon, nurses, a patient care technician, at least two residents, and an anesthesiologist. Gonzalez's card also warns her not to get too involved with patient care. She has to continue to oversee the emergency department as patients arrive.

As the staff read their respective cards and started preparing, Gonzalez describes the mood as calm and organized.

"It was very quiet," she says. "There were no people shouting. There was no sense of panic. There was just this nice, regimented approach. I don't think it's anything that you would expect if you were thinking of a department preparing for a potential onslaught of patients."

When the first victim arrives from Tree of Life (the officer who was shot in the hand), the emergency department staff manage the trauma patient as they always would: They assess his breathing and circulation. They address his bleeding.

"You kick into doctor mode," Gonzalez says. "This is what you do."

Gonzalez recalls a sense of unity and a feeling of teamwork among the staff. She credits the laminated cards with helping to promote organization. "It was very helpful for each person to look at their card and know: *Okay, now I know what I need to do next.*"

"IT WAS EERIE," ROTH SAYS OF BEING AT THE COMMAND POST. "WE HAD JUST DONE THIS [IN A DRILL]."

Adam Tobias, assistant professor of emergency medicine, assistant residency program director, and a member of UPMC Presbyterian's disaster committee, wrote most of the disaster response plan, and he oversees the scheduled drills for Pitt and UPMC.

Tobias (MD '06, Res '09, MPH '11) realized the importance of implementing a simple approach in 2010, following a trip to Israel to learn how hospitals there prepare for mass casualty situations. The trip was sponsored by the Jewish Healthcare Foundation.

Roth, who grew up in Squirrel Hill and was bar mitzvahed at Tree of Life, says that when Pitt's emergency medicine department, UPMC, and Pittsburgh's first responders began an active shooting training program several years ago, Jewish community groups were some of the first to participate in drills. Nine months before the Tree of Life shooting, the Jewish Community Center (JCC) in Squirrel Hill hosted an exercise for police and EMS.

"It was eerie," Roth says of being at the command post. "We had just done this [in a drill]. Two or three people came up to me afterwards and said, 'Wow, I got inside and the training from the JCC kicked in.' To the credit of the Bureau of Public Safety, they had trained for this."

"I preface every commentary with saying that any kind of congratulatory speak is appropriately attenuated and blunted by the severity of what happened," Neal says. "But I am so immensely proud of this team and this community."

Yealy speaks with pride of the response, as well. He notes the Tree of Life shooting also showed ways they can improve, particularly in terms of communication. Tobias agrees: "You have 1,000 things running through your head, and my phone was ringing off the hook."

Murray says he learned that SWAT officers need more tourniquets and updates to individual first-aid kits.

After a while on **SATURDAY NIGHT**, Gonzalez and a few colleagues are finally able to sit down to rest. That's when it starts to sink in that the episode had been driven by hate. "There was this sense of us pulling together to stand against the trauma, if that makes any sense," Gonzalez says.

That evening, Tobias, Roth, and Weiss gather at Weiss's house to debrief and process what happened while Neal heads home to his family.

Tobias, who grew up in Squirrel Hill and lives there with his wife, says the shooting was difficult to absorb.

His parents had attended Tree of Life the night before the massacre.

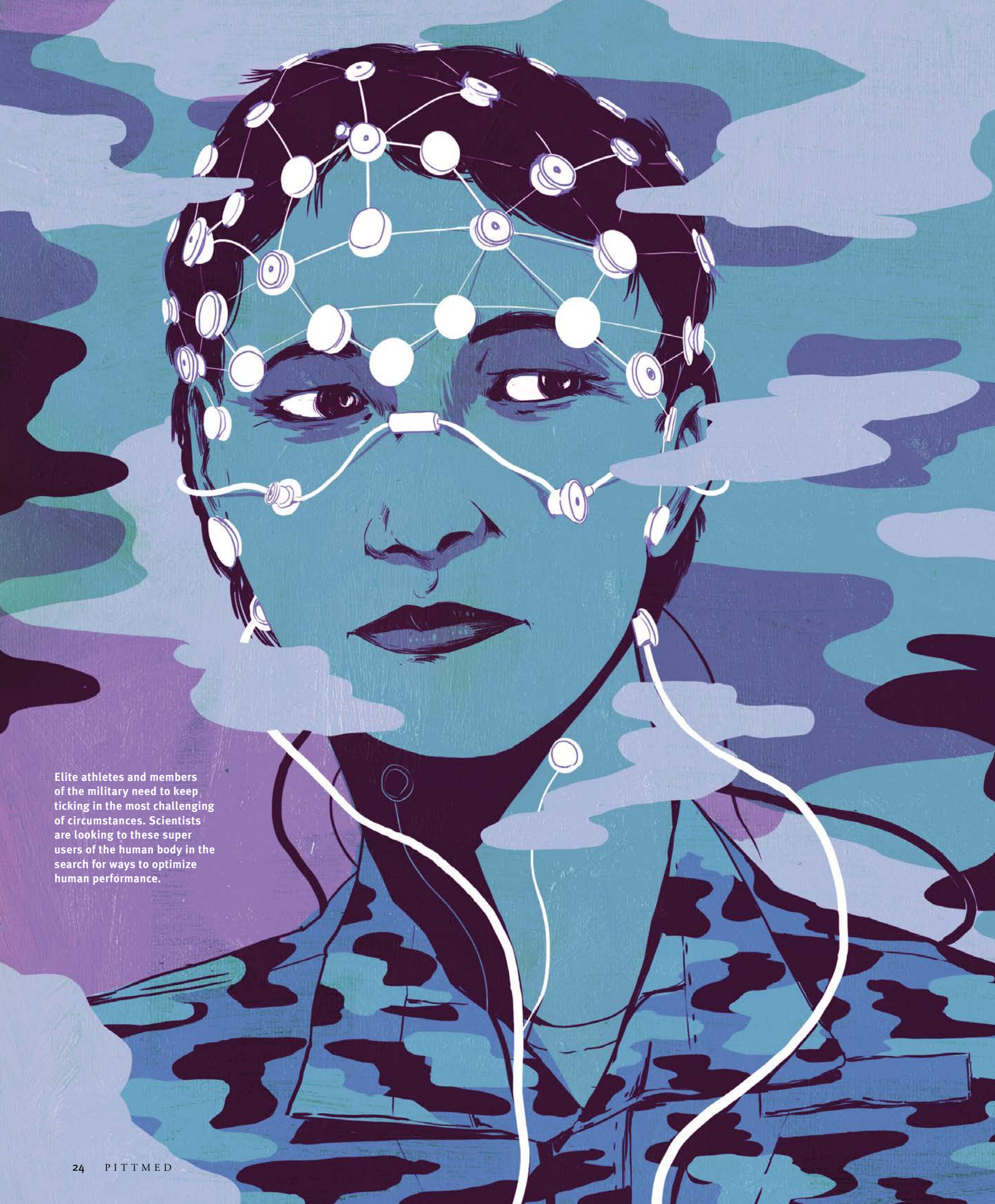
The bullet holes in the synagogue door, being part of the mass casualty response, it all felt surreal to the physicians whose lives are intertwined with the community attacked.

"It's very personal," Tobias says. "I drive by the synagogue every day. It's still hard to believe it happened."

EARLIER THAT DAY, AROUND 4 P.M., Murray returned to his truck; he was met by a couple. It was on their front yard that his Ford was parked.

Murray, whose SWAT uniform was covered in blood, began to apologize for driving onto their lawn, but the couple stopped him.

"They thanked me for what I do," Murray says. "It was really nice of them." ■



Elite athletes and members of the military need to keep ticking in the most challenging of circumstances. Scientists are looking to these super users of the human body in the search for ways to optimize human performance.

PITTSBURGH AS A HUMAN PERFORMANCE CITY

BY ELAINE VITONE

PERSONAL BEST

For U.S. Army truck drivers on major supply routes in Afghanistan, a daily commute amounts to several anxious hours in a convoy of dozens of vehicles. Every morning, they wake up knowing they will be attacked on that road to Bagram Airfield. They know because it's happened to them before—30, 40, even 50 times.

A truck might be hit by an IED, says the University of Pittsburgh's Ronald Poropatich. Or, just as dangerous is when a driver falls asleep at the wheel. "That happens a lot," says Poropatich. So the soldiers get hurt or die because of a simple thing we all take for granted: sleep.

Other service members commute via "HALO" jump—high altitude (maybe 30,000 feet, to evade radar), low opening (at 1,500 feet, *BAM!*, open chute). They hurl themselves out of a jet to certain danger behind enemy lines, hooked up to an oxygen mask. Because the air is thin those miles above the Earth.

Dangerous doesn't even begin to cover it.

ILLUSTRATIONS | MICHAEL HIRSHON

But as it turns out, the most common reasons for American soldiers to be medically evacuated from combat theatre today are not injuries from jumping from planes or taking enemy fire. They're musculoskeletal injuries, but largely from training and carrying around a rucksack.

Everyday wear and tear on the joints. Sleep, or lack thereof. Both the mundane and the obviously death-defying can do us in.

How do we keep ticking? Researchers in a growing field known as human performance optimization want to know how we can function at our best even when our circumstances aren't. Human performance is a crucial concern for the American military, says Poropatich, director of Pitt's Center for Military Medicine Research (CMMR), which works closely with the Veterans Affairs and the Department of Defense (DOD) research arms to solve military medical problems.

But improving performance isn't just in the interest of service members, of course. "There are lots of people at Pitt" chasing down this goal, says Rory Cooper, "whether it's post-transplant, or post–spinal cord injury, or amputation, or our own Division I athletes, or special operations forces." Cooper himself, founder of the Human Engineering Research Laboratories (HERL) and Distinguished Professor in the Department of Rehabilitation Science and Technology in Pitt's School of Health and Rehabilitation Sciences, has garnered numerous awards for his contributions to assistive technology, a field that enhances daily living for persons with disabilities. He's also an elite athlete, medaling in the Paralympics and National Veterans Wheelchair Games year after year. (He's racked up 150 Wheelchair Games medals.)

In June, Pitt will host a national conference on human performance optimization, organized by collaborators across the health sciences. In September, the DOD will join in on a two-day meeting with Poropatich and others at Pitt to discuss how academia can fill in gaps in the DOD's own efforts. "To open their eyes to areas of human performance optimization that they're not currently thinking about," says Poropatich.

Across campus, with full support from university leadership—notably, Chancellor Patrick Gallagher—a movement is afoot to plant a flag here and unify disparate and complementary human performance efforts more formally. In October 2018, Pitt released a 30-year master plan that includes a massive redevelopment of the athletic campus; a Human Performance Center features prominently in a new area dubbed Victory Heights.

When scientists study a disease, they often start with the most extreme cases and work their way back. In the study of our physicality and its limits, soldiers and elite athletes are super users. And at Pitt, both are in abundance: Service members and veterans have been volunteering for Pitt studies for years. A number of national sports franchises are expressing interest in partnering with the University. And NCAA Division I athletes are just outside the doors of Pitt scientists.

Pitt, it seems, is uniquely positioned to anchor Pittsburgh as a Human Performance City. ■

Right Time, Right Place

When Freddie Fu became head physician for Pitt Athletics in 1986, there was a regular fixture on the sidelines of seemingly every college and pro football game: an oxygen tank. Throughout the '70s and '80s, coaches had their players inhaling 100 percent oxygen between plays—to speed up recovery, beat fatigue, and enhance their performance, the thinking went.

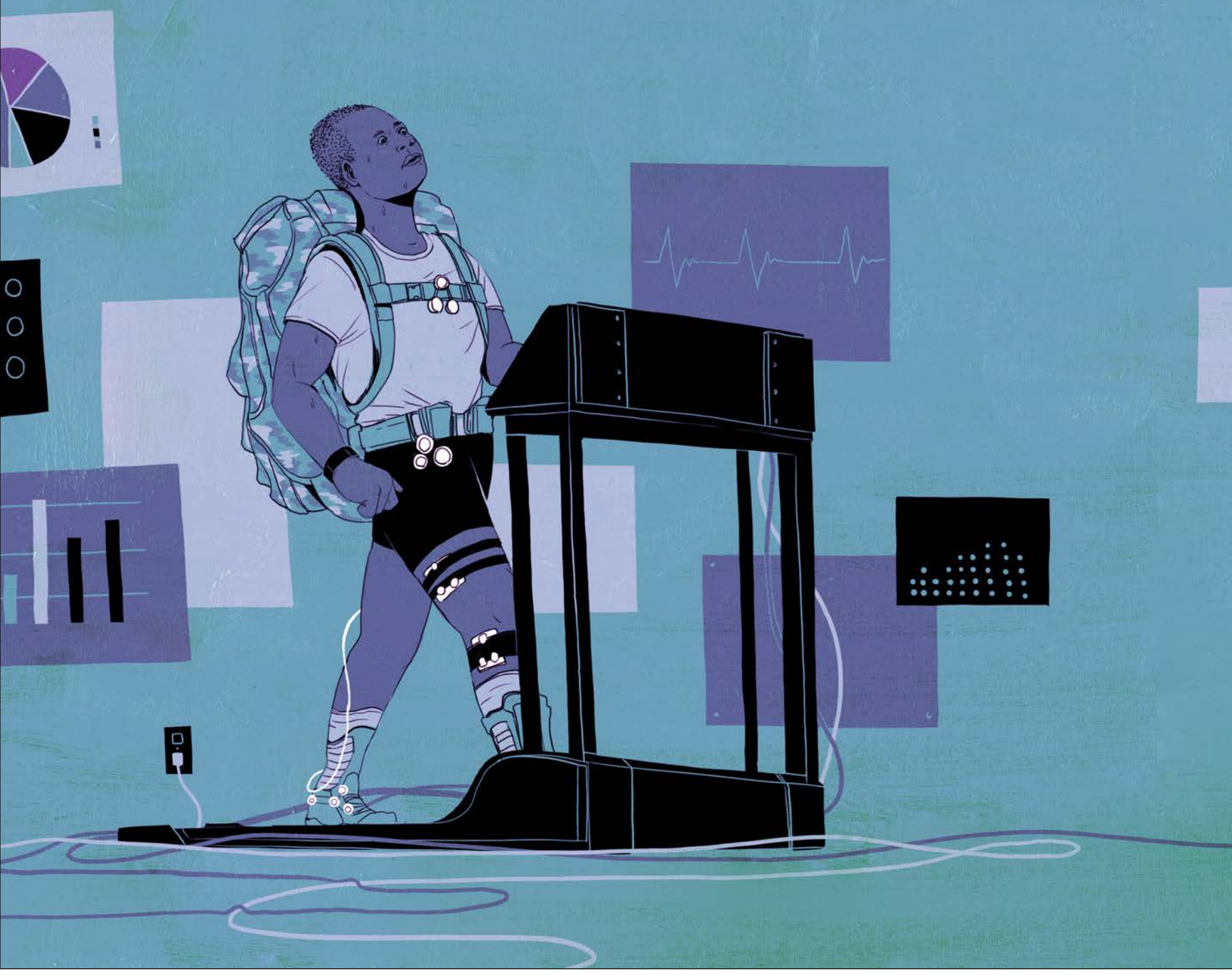
"It was a placebo," recalls Fu. "Just hocus-pocus." And he told everyone so, over and over, for years. (The *Journal of the American Medical Association* published a study with the same conclusion in '89.) Still, it took a decade to get the tanks rolled away, and not without plenty of complaints from fans. "It's so hard to change the mentality of people," says Fu, chair of orthopaedic surgery at Pitt.

Sports medicine has not been immune to the haste to find the Best New Thing to gain a competitive edge, he says. Through the years, a number of surgical and medical approaches, high on hype and low on hard science, have done more harm than good for patients. For example, pain pumps, once all the rage for post-op pain, proved damaging to joint linings and turned the rare unfortunate patient arthritic.

Fu, world renowned for innovating and evaluating surgical fixes for injured athletes' knees, has made Pitt a powerhouse in probing the biomechanics of sports injuries. He helped conceptualize the UPMC Rooney Sports Complex, which opened in 2000 on the South Side. (It's where the Steelers and Panthers do indoor training.) The sports medicine center there was just named for Fu. And in 2015 the UPMC Lemieux Sports Complex, a comprehensive outpatient sports medicine facility and training site for the Pittsburgh Penguins, opened in Cranberry. ("Nobody else has *two* sports centers," Fu says.)

Fu oversees one of the largest, most comprehensive sports medicine clinical and research operations in the world. And he has worked to bring human performance optimization from the realm of the hocus-pocus to solid, replicable, peer-reviewed science.

Ten years ago, his department opened the Orthopaedic



Biodynamics Laboratory, equipped with technology that illuminates previously unseen details of joint function before and after surgery. "We call it EKG of the knee," he says.

In 1990, with an investment of $5,000 and half a classroom in Trees Hall, Fu founded the Neuromuscular Research Laboratory (NMRL). Slowly and steadily, NMRL grew, encompassing studies of a variety of athletes, as well as military service members. Three years ago, an entirely new facility dubbed the Neuromuscular Research Laboratory/Warrior Human Performance Research Center (NMRL/WHPRC) opened on Pittsburgh's South Side.

Today, in the 11,600-square-foot space where lab meets gym, NMRL researchers study just about every physiological aspect of the human form *in medias res*: proprioception, postural stability, strength, range of motion, flexibility, bone and mineral density, you name it. There's an on-site biochemistry lab, a suite of motion-capture cameras, a transcranial magnetic stimulator. (TMS is a noninvasive way of stimulating specific areas of the brain.) It even has a swimming flume and an underwater treadmill.

NMRL, which is part of Pitt's School of Health and Rehabilitation Sciences (SHRS), is interdisciplinary to the hilt. Current collaborators include mathematicians, physiologists, and engineers, as well as School of Medicine faculty. And the list continues to grow.

The lab studies both physical and cognitive performance, how various stressors affect performance, and what can be done to counteract the impact of stressors.

Brad Nindl, an SHRS professor of sports medicine and nutrition, came on board as director when the new facility opened. He calls it his dream job, and this physiology PhD does seem every bit the part. He's a military guy—a reservist who served for 20 years as an Army Medical Department government scientist, primarily studying biomarkers for fitness and health outcomes.

"And I grew up a coach's kid—very motivated to be the best athlete I can be," he says.

In his dad's day, exercise physiology was central to the study of

human performance. By the '80s, the field had gone "very molecular," he says, a trend that continued into this century. Throughout the past 15 years, the brain has been increasingly, well, on the brain in terms of the military's priorities—cognitive readiness and resilience are front-and-center priorities now. And in the past five years, exercise physiology research is complementing our expanding knowledge of health at the micro level, from head to toe. Human performance optimization is now more of a hybrid of both basic and applied science, Nindl says.

In 2015, the United States lifted the ban on women in close ground combat; a year later, the United Kingdom followed. A better understanding of physiological differences between the sexes, particularly in upper-body strength, immediately became crucial to both countries' militaries and the new crop of service women who wished to join them. Nindl is a coprincipal investigator on a three-year study funded by the U.K. Ministry of Defence. SPARTA, which stands for Soldier Performance and Readiness as Tactical Athletes, will evaluate the efficacy of a variety of physical training regimens in preparing women for what's required on the job. "I've done a lot of work looking at both men and women and how they adapt," says Nindl, "and I know that with optimal proper training you can significantly [close physical performance] gaps."

Taking me on a tour of the NMRL, he stops each of the colleagues in his path for briefings. Like Nindl, they are all PhD faculty members in the Department of Sports Medicine and Nutrition within SHRS.

Shawn Flanagan, an assistant professor, tells me about a project that was just funded by the Department of Defense (DOD). He's collaborating with Nathan Yates, an associate professor of cell biology and scientific director of Pitt's Biomedical Mass Spectrometry Center. Working with an army lab near Boston, they'll be collecting urine samples of enlisted soldiers, in hopes of finding a molecular signature of physiological resilience. They want to learn to identify who is more likely to experience a musculoskeletal injury.

"Urine is interesting. Quantity is not an issue," Flanagan says. "You [urinate] every day. It's noninvasive. And it's naturally integrative, right? I mean, 30 percent of proteins in urine are from plasma, not from the kidney, so you can detect brain-specific proteins, muscle-specific proteins, bone-specific proteins. It's not just garbage."

Kim Beals, an SHRS associate professor who studies diet as a means of injury prevention and performance optimization, has worked with every branch of Special Operations forces in the U.S. military. She studies nutrition (the given fuel demands of, say, walking, in snowshoes, up the side of a mountain, through a foot of snow, for x number of miles) and determines appropriate recommendations, given on-the-job constraints, which, of course, are many.

"These guys carry what they need on their backs," she says. "They have to make choices between carrying food or carrying ammunition or carrying water or other supplies that they need. It's a compromise."

Beals is writing a proposal with Alison Morris and Michael Morowitz—director and associate director, respectively, of the School of Medicine's Center for Medicine and the Microbiome. They want to examine whether probiotic supplements might help undo some of the negative effects of operational stress—or even increase cognitive performance.

Before Chris Connaboy—assistant professor in SHRS, former U.K. military infantry soldier, and Nindl's coprincipal investigator on the SPARTA study—came to Pitt three years ago, he was in Houston developing a behavioral metric for NASA. The metric measures how human movement is affected by microgravity, stress, changing physiological states, and anything else you might encounter on a mission to Mars. He realized concussions, and what they do to human performance, were an important next frontier for him; but he had zero background in this area.

Once you've had a concussion, you're more than twice as likely to have another. You're also twice as likely to have a lower-limb musculoskeletal injury.

He wanted to learn from the best.

"And it's Pitt. It's just fantastic," he says.

From discussions with his new Pitt colleagues (notably, Anthony Kontos and Michael "Micky" Collins, PhDs who are, respectively, research director and director of the Sports Medicine Concussion Program), Connaboy learned that once you've had a concussion, you're more than twice as likely to have another. Further, you're twice as likely to have a lower-limb musculoskeletal injury.

Using his newly developed behavioral metric, Connaboy and NMRL doctoral student Shawn Eagle looked at dozens of people with a history of concussion and compared them to controls. He found that the former had trouble with what is called perception-action coupling.

"It's the ability to accurately assess your action boundaries," he explains, to successfully coordinate and time your actions even as your environment changes. It's putting yourself in the right place at the right time.

He adds that there are ways to retrain for and rehabilitate this skill. "But we need to know it's compromised first"—preferably, before the person goes back on the job, onto the field, or into combat theatre and winds up with a musculoskeletal injury, another concussion, or worse. ■

Sleepless Fights

Anyone who's ever pulled an all-nighter knows that, come morning, flying off the handle is pretty much your new default mode. Sleep and emotional well-being are inexorably linked—and often, so are sleep disorders and mood disorders. Interestingly, in studies of people who have both, researchers consistently find that when the treatment plan starts with fixing the sleep problems first, the severity of the mood disorder lessens all on its own, whether it be PTSD, depression, anxiety, or suicidality. Even cravings for alcohol decrease when sleep improves.

Anne Germain, PhD professor of psychiatry, psychology, and clinical and translational science, is among the scientists who've shown this robust and remarkable phenomenon. Working with service members and veterans for more than a decade, she's found that sleep therapy is a solid step toward symptom relief.

And now, Germain hopes to convince much broader scientific circles that sleep is integral not just to what we feel but to everything we do.

It's well documented that if you assign a sleep-deprived person a computer-based task day after drowsy day, performance suffers. The first to go is vigilance, the ability to detect and attend to cues in the environment. Motor performance and working memory follow, as well as emotional reaction. The latter can err either on the snappy and overreactive side, or the blunted and numbed. And when emotional reaction is off base, that, in turn, messes up a person's decision-making.

Good luck explaining this to the chronically sleepless, though.

Across the board, Germain says, people quickly develop a perception that they're adjusting to sleeplessness and are doing just fine, thankyouverymuch. We've all been there, "and effectively, we are completely wrong," she says. "Even after a night or two of insufficient sleep, you see this pattern come up. Performance is decreased." That effect doesn't go away as your sleep drought drags on.

And, she adds, all this self-delusion can be terribly risky.

"We're no longer a good judge of our behavior. What we [in sleep medicine] tell people is that if you've been awake for 24 hours, it's the equivalent of being over the limit for blood alcohol when you're driving."

So what saves our military service members, essentially out in harm's way and drunk from sleeplessness? In a word, Germain says: training. They know what to do when a given threat befalls them because practice makes perfect. In her experience, soldiers might tend to get a bit slower at performing various tasks in the throes of sleep deprivation, but not significantly less accurate. This is probably because they sacrifice speed to maintain accuracy, she says, and the patterns of brain circuitry that support the best course of action are deeply ingrained.

Sleep is replete with million-dollar questions for the military. At the top of the list: Is there a way to make five hours of sleep as restorative and beneficial as eight?

Germain and colleagues are exploring this and other questions. She and the Neuromuscular Research Laboratory's (NMRL) Brad Nindl are coprincipal investigators in a large, multi-institutional, multifaceted study of neurocognitive and physical performance in simulated military tasks, complete with the typical stressors of the job: caloric restriction, physical exertion, and sleep loss. The study, which launched in January with funding from the Department of Defense, will follow 80 service members for six-day stretches through marksmanship exercises at a reserve center in Coraopolis, tactical mobility exercises in the UPMC Lemieux Sports Complex in Cranberry, and sleep studies in Germain's Oakland lab.

Amy Haufler, a coinvestigator at the Johns Hopkins Applied Physics Laboratory, will apply an adaptive decision-making test of her own design. The NMRL's Chris Connaboy will apply his NASA–tested, NASA–approved behavioral metric, which Germain calls "an amazing, testable model" for deciphering exactly what abilities loss of sleep degrades first.

One of the study's aims is to identify biomarkers of how well individuals tolerate stress, using predictive analytics, bioinformatics, and machine learning. And in the sleep lab, Germain will look for predictors of performance, as well: brain signatures like wave patterns or duration times for sleep's distinct phases. If she can find such signatures, it might be possible to augment them, she notes, in one of two ways:

There's "the messier approach," as she calls it. "Very short-acting medications that could be used to optimize the efficiency of sleep, in terms of its restorative power. Currently we don't have medications like that," so they would have to be developed.

Then there's the neater approach: Labs across the country (including that of Pitt's Fabio Ferrarelli) are beginning to show success in influencing the sleeping brain using transcranial magnetic stimulation. TMS is currently used to diagnose conditions like stroke, and to treat major depressive disorder.

And then, there are approaches that are neater still: sound and light stimulation during sleep. "Even when your eyes are closed, [you] can still detect light," says Germain. Best of all, these nonmedication approaches are rapidly reversible, do not cause grogginess, and have no known side effects. ■

Your Move

Scientists have long known of a correlation between slowing gait and cognitive decline. In 2017, Andrea Rosso, assistant professor of epidemiology in the Graduate School of Public Health, published a study finally identifying losses in a particular brain region—the right hippocampus—as a common link to both. For 14 years, she had a cohort of 70-somethings volunteer for imaging studies, mental acuity tests, and a timed 18-foot stroll down the hallway.

Rosso found that the simplest and most low-tech test—just a stopwatch, some tape on the floor, and a few minutes every year or so—was enough to flag the earliest sign of trouble.

Our movements tell a story.

And there are more ways of capturing and quantifying our movements all the time. Wearable technology offers real-time monitoring in granular detail that was never before possible, explains Nathan Urban, Pitt's vice provost for Graduate Studies and Strategic Initiatives, codirector of the Center for the Neural Basis of Cognition, and professor and vice chair of neurobiology. (The new Apple Watch, released in December, can even take your EKG, he notes.)

Pitt scientists can ask questions like: Do they have a trick? Are elite performers doing something different—mechanically, molecularly, whatever—that makes them run farther or faster or with less fatigue? What should the Panthers be doing on the day before the game? Is it better to prep and practice more or to sleep longer?

There's lab-based tech, too, like in all those behind-the-scenes reels you've seen of actors covered in dots as they defend Middle-earth. (Pitt's Neuromuscular Research Laboratory has a similar setup, minus the green screen.) Urban points out that emerging camera-based motion technologies—no dots required—are on the market as well, and Pitt's new Center for Research Computing has hardware that's the perfect fit. He notes that two years ago, Pitt made substantial investments in integrating data and technology into academic pursuits across disciplines, just as it opened a new School of Computing and Information.

Urban is hatching plans to make these technologies widely available to researchers throughout the University. While Pitt raises funds to bring its new Human Performance Center from master plan to reality, he's talking to potential partners and funders, building up resources, and launching pilot projects, some of which bring in machine-learning and robotics expertise from Carnegie Mellon University (Urban's former academic home). His vision: Space for both human- and animal-motion models. Space for data analysis. Whole fleets of wearables that are widely available to researchers studying disease screening, disease progression, how well a given treatment is aiding in disease or injury recovery, and more.

And all of this will be right in the big fat middle of hundreds of college athletes, bodily "super users" whose everyday doings present a potential firehose of data. Pitt scientists can ask questions like: Do they have a trick? Are elite performers doing something different—mechanically, molecularly, whatever—that makes them run farther or faster or with less fatigue? What should the Panthers be doing on the day before the game? Is it better to prep and practice more or to sleep longer?

Urban acknowledges that wearable tech presents a number of ethical questions. (For starters: Who can access the data? How will the data be used?) He and his colleagues are in discussions with bioethics experts to prepare for what lies ahead.

This won't be a one-way street, though. The researchers will have something to give back to their study volunteers, right then, in the moment: data. And those data can have real dividends for health.

Here's what I mean. Urban, for example, tells me he's been prescribed physical therapy for back pain.

"I will say that continuing to do your exercises when the pain is no longer quite as severe is hard," he says.

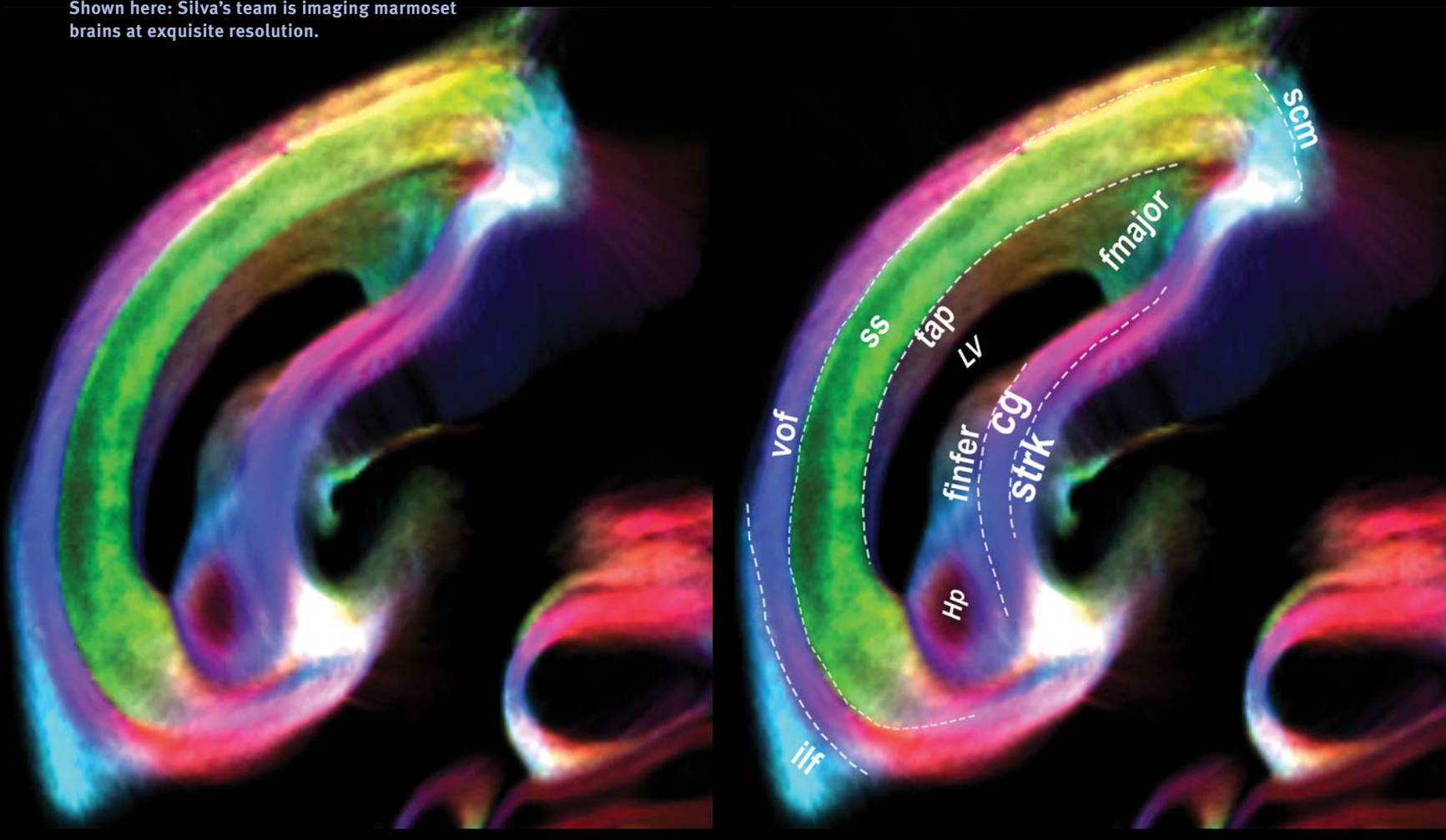
"But, if you have a way of assessing whether someone is doing exercises correctly, and providing feedback, I think it would be much more likely that someone would continue," he says. If you can tell them their range of motion is improving, or they're getting stronger, or performing better than they did last week, "that exact kind of feedback could be very, very important for ensuring that people are compliant."

You do something, you get something, which influences your behavior. This is basic psychology-textbook reinforcement.

And there you are, invested and encouraged by your own self-efficacy. Working as your own personal agent of change. Controlling your own behavior and outcomes.

Bettering your own personal best. ■

Afonso Silva believes scientists need a new model for neurodegenerative diseases. Shown here: Silva's team is imaging marmoset brains at exquisite resolution.



ALL THE WRONG PLACES

PICTURE THIS

BY JASON BITTEL

CIRONG LIU, JOHN NEWMAN, FRANK YE, CECIL YEN, DANIEL GLEN, DIEGO SZCZUPAK, PIOTR MAJKA, JOSEPH GUY, SEUNG KWON HA, MARCELLO ROSA, DAVID LEOPOLD, AND AFONSO SILVA

All across your brain, blood vessels are snugly wrapped in a quilt of tightly knit cells known as the blood-brain barrier. But these cells aren't here to keep your brain warm. Instead, they act like gatekeepers, guarding the brain against intrusion by toxins and other pathogens that would do it harm, all the while granting access to certain other molecules we need, such as oxygen and glucose. The skull gets all the credit for protecting our most precious organ, but we wouldn't last a day without the blood-brain barrier.

Interestingly, some of the worst neurodegenerative diseases seem to be associated with failures of this structure. This year, 800,000 Americans will suffer a stroke, accounting for a death every four minutes. More than 1 million people in the United States will struggle with some form of multiple sclerosis. In 2018, it was estimated that 5.7 million Americans were living with Alzheimer's disease.

These are complex diseases, with many molecular actors at play. Yet, Afonso Silva, a neuroscientist and bioengineer who's spent the past 20 years working at the National Institutes of Health (NIH), also believes: "There might be a common mechanism by which many of these brain diseases work. And one way or another they're associated with a local inflammation of the blood-brain barrier."

Silva's team is offering astonishing new views of compromised brains. He hopes this information will offer some clarity for how to approach neurodegeneration. Despite four decades of research dedicated to studying Alzheimer's, Parkinson's, multiple sclerosis, and other neurodegenerative diseases, scientists have yet to come up with a way to do much about any of them.

Part of the problem, says Silva, is that when patients go to the doctor because of symptoms associated with a neurological disorder, the disease is already at a well-developed stage.

At that point, we can diagnose various neurodegenerative diseases. We can track them as they progress. But we are powerless to stop them. And some believe this is because we've been looking for clues in all the wrong places.

"The species that is most widely used in biomedical research nowadays is the mouse," says Silva. "And wonderful things are being learned about the biology of the brain and even about some basic mechanisms of disease."

Yet, while rodent models have led to innumerable medical insights, many things about them still don't match up.

For example, to study stroke, many researchers have looked to a human condition known as CADASIL, or cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy. Up to 80 percent of people with CADASIL will experience a stroke by the age of 50. And because the condition is created by the mutation of a single gene, scientists have discovered that it's relatively easy to produce in rodent models. This should make the disease a home run for stroke research. However, rodents don't seem to be as affected by CADASIL as humans.

Either the mice don't stroke spontaneously, says Silva, or the strokes are too small to cause meaningful damage that we can study.

And it's not just stroke. Scientists have come up with more than 20 different compounds that treat amyotrophic lateral sclerosis, otherwise known as ALS or Lou Gehrig's disease, in rodents. But none of them have worked in humans.

"A lot of findings in the mouse brain just do not translate to the human brain," says Silva.

But he has a hunch about some animals that might help us fill that gap. They're called common marmosets, or *Callithrix jacchus*—pip-squeak-sized primates with brains remarkably similar to our own.

You see, Silva is a virtuoso in the world of magnetic resonance imaging, or MRI. And for the last decade and a half, he and his team at the NIH have been peering into the brains of marmosets at increasingly mesmerizing resolutions. At the same time, the scientists are learning how to tweak the primate's genome to create models for human conditions. And as of this winter, Silva and seven of his closest colleagues have taken up posts in the Department of Neurobiology at the University of Pittsburgh in an attempt to push this body of work further.

In the next four years, Silva hopes to breed enough working marmoset models of CADASIL to begin to unravel its origins. What's more, through a partnership with Peter Strick, Distinguished Professor and chair of neurobiology at Pitt, he aims to create the world's first marmoset model of Alzheimer's disease. With any luck, the animals will help scientists crack the neurodegenerative disease game wide open.

As a kid growing up in Brazil, Silva remembers marmosets as always being nearby. "All you needed to do was look up at the trees, and they would be there," he says.

In fact, he likens the primates to the squirrels that dominate parks here in the United States. Small, clever, and not above a bit of thievery.

"They are incredibly adaptable animals, so they live really well in civilization. They are experts in identifying food opportunities—and that includes the lunchboxes of unaware students," says Silva.

To be honest, he never considered that these same rascally creatures might hold secrets in the fight against Alzheimer's disease, multiple sclerosis, and stroke in humans. Back in those days, practically nobody was looking at marmosets as models for human disease. The animals were thought to be somewhat unintelligent by scientists, says Silva, because they wouldn't sit for hours on end in a lab and complete repetitive tasks like larger primates, such as macaques. Researchers also preferred macaques because they were seen as being hardier, less susceptible to stress, and capable of more refined hand movements. Of course, rodents were more desired still, because of their small size and cost, rapid reproduction, and ease of manipulation. For many years, Silva's gaze had settled there, too.

"I had already established a track record of studying the anatomy and function of the rodent brain. But I was getting to a plateau where I wasn't really learning much more," he says.

But then, a serendipitous event changed Silva's course. In 1999 he joined the NIH,

Yet, while rodents have led to innumerable medical insights, many things about them still don't match up.

Silva (standing, hand on chin) at the Asia-Pacific Symposium on Advances in Ultra-High-Field MRI in China in 2017. Among the field heavyweights in attendance—Seong-Gi Kim, formerly in radiology at Pitt, who took the photo.

where he inherited a colony of marmosets. The researcher who previously had been working with the animals had taken a position in Germany, and the colony was sitting idle.

"I think it was the best thing that happened to me," says Silva.

While others had shied away from the animals, Silva found them to be surprisingly good study subjects. As adults, marmosets weigh about half as much as a box of dry spaghetti, which makes them easy to handle. They also don't carry any diseases known to infect humans. In contrast, Silva says, you fear for your life if a macaque sinks its teeth into you, because the animals can carry herpes B, which can lead to meningitis, and simian immunodeficiency virus, which is comparable to HIV/AIDS.

But even more notable is the fact that the brains of marmosets are much more similar to our own than are rodent brains.

"There are many areas of the brain that primates have that rodents don't. For example, the prefrontal cortex, which [includes more than a dozen] areas that are very important for decision-making and emotions," says Silva. "These areas are much more developed and more complex in primates than in rodents.

What's more, the ratio of gray to white matter found in the marmoset is also very similar to that of a human. This is important, because what we refer to as "white matter" is actually the long, reaching arms of the neurons, called axons. Brain cells use axons to trade electrical impulses with one another, and in some cases, axons can be found snaking their way across entire sections of the brain, allowing for one part of the organ to communicate with another. But to conduct electricity across such wide expanses, axons have to insulate themselves with a white layer of fat called myelin.

Rodent brains don't have much white matter though, because they're so small. This is fine for the mice and rats, of course, but it makes the animals less than ideal for studying human diseases that manifest in white matter, like multiple sclerosis.

The other interesting thing about marmoset brains is that they lack the wrinkles most people picture when thinking of a human brain. But this difference in appearance is actually a boon, because wrinkles can get in the way of good imaging.

"The main advantage of having a smooth brain is that I can easily locate on the surface of their brain any functional area that I want. So if I want to study the somatosensory system, the sensation of touch, it's right there; or the visual cortex, it's right there. The prefrontal areas also are very easy to access just because I don't need to deal with the convolution of the cortex," says Silva.

The proof is in the pudding. Throughout the past several years, Silva and his colleagues have pushed MRI technology to new limits by creating images of marmoset brains at resolutions down to 80 micrometers isotropic, which means that the images created at this resolution can be three-dimensional.

To put this into perspective, that's a resolution about 60 times better than what is possible in macaques, says CiRong Liu, one of the neuroscientists Silva is bringing with him from the NIH. And it's 4,000 times better than what's being used in the Human Connectome Project, which is a collabora-

tive effort to map the human brain at high resolution.

Put another way, not only can the team see nerve fibers, but they can also see the direction in which the fibers are arranged. It's sort of like looking at a map of the United States and being able to zoom in and note the flow of traffic on a highway.

"In the white matter, we're seeing structures we were never able to see previously in human data or macaque data," says Liu.

In 2017, Liu and Silva published their work in the journal *NeuroImage*, providing a high-resolution, three-dimensional atlas of the marmoset brain. Such an atlas had not existed before. In all, they mapped 54 cortical areas and 16 subcortical regions, which gives them and other research teams a road map that can be used to pinpoint areas of importance.

Even to a layman's eyes, the atlas is gorgeous—like looking at the neon greens, pinks, and yellows of a soap bubble. And the crispness with which you can make out structures compared to similar images taken in macaques and humans is plain to see.

In part, images like these are only possible because marmosets are extremely small, as primates go. Not including its skull, a marmoset brain is only about as big as a shelled pecan, and it weighs less than a AAA battery. Even still, it took one of the most powerful MRI machines on the market nearly one week to record brain structures in that kind of detail.

But the marmoset brain atlas becomes even more useful when you add in the work of JungEun Park. "She's the one who has eyes in her fingertips," says Silva.

Unlike Silva and Liu, who specialize in imaging, Park is an expert in genetic engineering. Using a variety of techniques, she can add to, delete from, or otherwise annotate an animal's genome to make it more relevant for study.

It's a slow, painstaking process laden with disappointment. After Park performs her manipulations, she surgically implants the transgenic embryos back into a surrogate mother. Then, she must wait for nature to take its course, which in common marmosets is about five months. Unfortunately, the odds of survival are not good.

"Marmosets naturally have a high percentage of early stage miscarries. We don't know why," says Park, who will join Silva and Liu at Pitt this summer.

Out of every 10 transfers, just two to three will result in pregnancies. Then the team must wait another 18 months for the animals to become mature so that the marmosets can participate in studies or contribute to the next generation of transgenic models. It's a long time compared to mice, which take only around two months to reproduce and reach sexual maturity. But as far as primates go, marmoset reproduction is about as quick as it gets. Depending on the species, macaques require three to seven years from conception to sexual maturity, for instance.

The good news, says Silva, is that female marmosets can produce two litters each year and most often give birth to twins. Triplets even happen on occasion. All of which makes marmosets sort of like the rodents of the primate world.

At the NIH, Park, Silva, and colleagues used these techniques to not only create a marmoset model of multiple sclerosis, but also to track that animal with MRI scanning as it developed a lesion in its white matter.

"You don't know where to look before the lesion is there," says Silva, "but once the lesion forms, and you have those coordinates, you can go back in time and say, 'Aha!'"

In fact, in a study published in 2014, the scientists were able to use this retrospective approach to find evidence that the blood-brain barrier had been compromised two to three weeks before there was any other visual evidence of the lesion in the scans.

"It was allowing things that should not cross the blood vessels to cross the blood vessels," Silva explains.

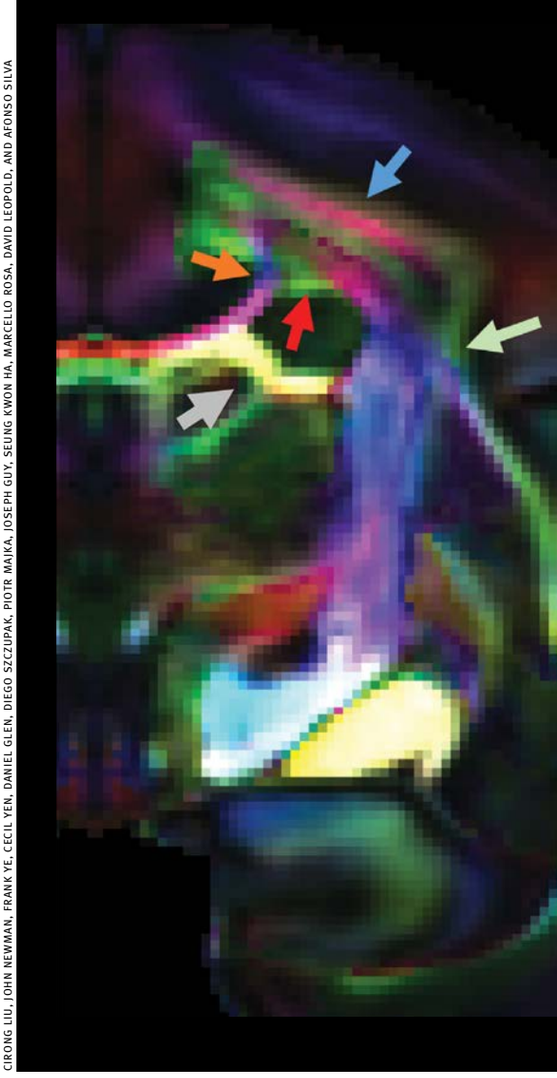
All of which leads the team to hypothesize that if scientists could develop a technique that's super sensitive to permeability of the blood-brain barrier, they might be able to predict where and when a lesion will appear. Then doctors might use steroids or other drugs to slow it down, and with it, the progression of multiple sclerosis.

In a similar fashion, Silva is confident his team will be able to study the development of Alzheimer's disease in marmosets. Despite being small and reproducing relatively quickly, the animals can live well beyond 10 years of age. There's also evidence that later in life they start to develop amyloid plaques and neurofibrillary tangles—irregularities that are hallmarks of Alzheimer's in humans. What we don't have evidence of just yet is that these lesions affect the marmosets in any meaningful way. However, researchers might be able to accelerate this aging process by engineering a transgenic line of marmosets that expresses mutant presenilin, a protein scientists have connected to early onset Alzheimer's disease.

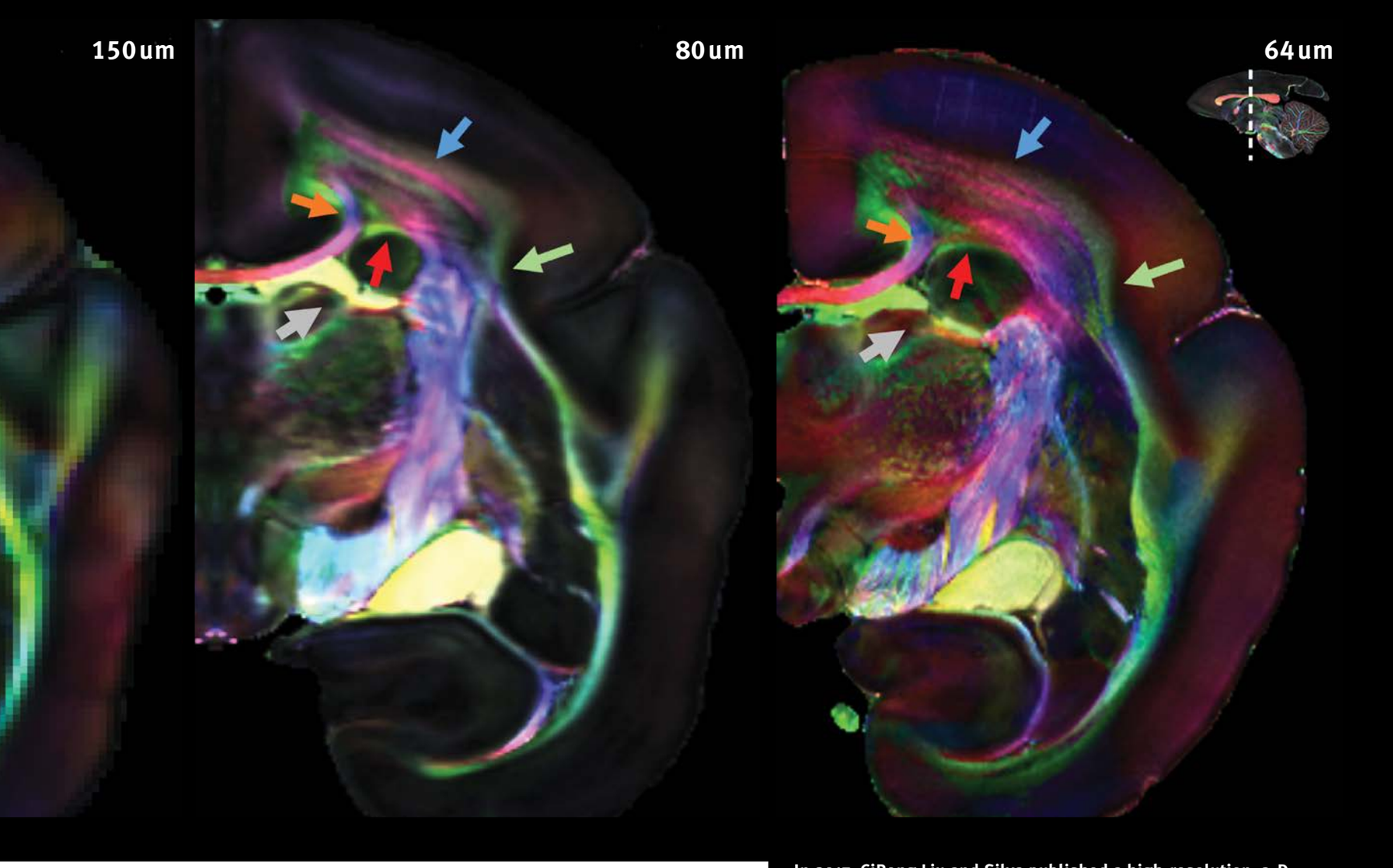
As exciting and promising as marmoset models are, it's important to note they are not perfect.

For instance, just as presenilin is linked to early onset Alzheimer's, a protein known as A53T alpha-synuclein has become associated with the rise of early onset Parkinson's disease. You might think that by adding such a protein to the marmoset genome you could reliably create a model in which to study Parkinson's.

But this isn't the case, says Marina Emborg, director of the Preclinical Parkinson's Research Program at the Wisconsin National Primate Research Center, because marmosets already express this protein naturally.



CIRONG LIU, JOHN NEWMAN, FRANK YE, CECIL YEN, DANIEL GLEN, DIEGO SZCZUPAK, PIOTR MAJKA, JOSEPH GUY, SEUNG KWON HA, MARCELLO ROSA, DAVID LEOPOLD, AND AFONSO SILVA



In 2017, CiRong Liu and Silva published a high-resolution, 3-D atlas of the marmoset brain. Such an atlas had not existed before. In their new work, Liu and Silva are focusing on white matter. Shown here are the axonal white matter highways of the marmoset brain through which nerve impulses travel to relay information from one area of the brain to another. Green axons transport impulses front to back, red axons transport left to right, and blue axons transport up to down. The higher-resolution images show more complexity at the intersections.

"It's not a mutation for them, and they don't have Parkinson's," Emborg explained at a meeting of the National Academies of Sciences, Engineering, and Medicine in October.

All models are wrong, goes the oft-repeated aphorism in statistics, but some are useful.

"When Dr. Silva first started combining MRI and molecular genetics in the marmoset, it was a bit of a gamble because very few people in the world worked in either MRI or genetics of the marmoset," says Alan Koretsky, chief of the Laboratory of Functional and Molecular Imaging at the National Institute of Neurological Disorders and Stroke and Silva's former boss. But it was a risk that's paid off. Koretsky notes that many groups are moving ahead with these approaches.

"I think progress in biomedical research really has relied on asking the right question, in the right model, at the right time, and with the right tools," says Koretsky.

Given where things now stand with advances in imaging and genetic analysis, Koretsky believes Silva and others in the field are on the cusp of breakthroughs in understanding neurodegenerative disease. "I think there's a sense everywhere that we have been making rapid progress," he says, "and that progress is going to translate to an impact sooner or later."

It may be that no one is more eager about the addition of Silva's team than Arthur S. Levine, Pitt's senior vice chancellor for the health sciences and Petersen Dean of the School of Medicine. He will be opening a lab that studies Alzheimer's. Once a successor is found to fill Levine's sizable shoes, he plans to step down from his administrative responsibilities, after 20 years, and work alongside Silva and Strick in the search for clues to neurodegeneration. (More about Levine's new career as a neuroscientist in a future issue.)

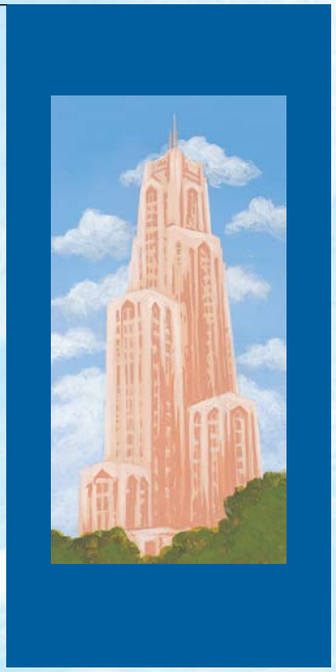
Peter Strick is also more than delighted to have Silva on board. "Afonso has got incredible imaging skills," says Strick. "What he's able to do in terms of resolving the brain structure is just remarkable."

Now, Strick wants to use Silva's skill set to complement his own work mapping unexpected neural connections throughout the body, such as those between cells in the retina and regions of the brain associated with depression and others in the liver involved with metabolism.

He compares these kinds of collaborations to the parable of the blind men and the elephant. "You can look at things from different perspectives, and it's when you combine those perspectives that you get powerful insight," says Strick. "[Silva] started [in December], and we had a grant in on January 25. I can't wait. He's already changed some of the direction of my research, and I've already changed some of the direction of his."

For Silva, who completed his PhD in biomedical engineering at Carnegie Mellon University in 1996, the return to Pittsburgh feels like his whole career is coming full circle.

"It started here. It will likely end here." ■



CLASS NOTES

'70s

Nocturia, or frequent waking at night to void the bladder, is extremely common, can be very disruptive to sleep, and, in the case of older patients, is a likely cause of many falls and fractures. **Jeffrey Weiss** (MD '78), who authored the first textbook on the subject, devised a now widely used classification scheme for this often-multifactorial condition to help physicians tailor treatments more effectively. Most recently, he's studied the nexus between nocturia and hypertension, finding that when blood pressure does not dip as it should during sleep, it's considered "a malignant form of hypertension," he says, and is associated with nocturia as the kidneys secrete extra sodium into the urine. "We are looking at sodium-restricted diets as treatment for both non-dipping hypertension and nocturia, as well as the use of certain diuretics to treat both problems." Weiss, who's chaired urology at SUNY Downstate College of Medicine since 2010, just stepped down from that position and is now pursuing a PhD from Ghent University in Belgium.

'90s

William Gregory Feero (PhD '96, MD '98) is the research director of the Maine-Dartmouth family medicine residency program and associate professor of community and family medicine at the Geisel School of Medicine at Dartmouth College. He developed a program that identifies patients at high risk for common hereditary syndromes associated with cancers and provides them with precision care using a genetics-based risk assessment. Since starting in 2015, the program has tripled the number of referrals for cancer genetics services from clinics. Though precision medicine has yet to enter mainstream health care, Feero believes "it is absolutely inevitable we will move closer to using this approach to care for patients."

Working with economists and outcomes researchers, **Jodi Beth Segal** (MD '94), Johns Hopkins professor of medicine and associate director of the Center for Health Services and Outcomes Research, recently developed a new tool to measure the overuse of health-care resources like cancer screening or emergency department imaging. Segal hopes that the Overuse Index will reveal drivers of overuse and, ultimately, suggest appropriate points for intervention. Codirector of the Center for Drug Safety and Effectiveness at Hopkins, Segal leads a new program for predoctoral and postdoctoral trainees studying pharmacoepidemiology. When asked about the most important outcome of the program, Segal responds like a true teacher: "Helping our students to have impact."

Segal

Clifford Eskey (MD '93) is the director of neuroradiology and the vice chair for radiology research at Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire. Eskey's practice primarily focuses on interventional neuroradiology, treating aneurysm and stroke patients (among others) with image-guided surgery. "Saving someone from major disability by restoring flow to a blocked cerebral artery is one of the most gratifying things that I get to do," he says. He's also been trying out new hobbies: "I'm gradually gaining expertise as an amateur pinball repairman," he says.

'00s

Timothy Witham (Neurological Surgery Resident '01) is professor of neurosurgery and orthopaedic surgery at Johns Hopkins University and the associate program director for its neurosurgery residency. He also directs the spinal medicine program at Johns Hopkins Bayview Medical Center. Witham's current research interests focus on improving spinal fusion outcomes by developing new methods using tissue engineering—research that allows him to work alongside biomechanical engineers. He's also interested in work-life balance as it applies to neurosurgeons. He will serve as the scientific program director for the Lumbar Spine Research Society's annual meeting in April.

William Dale (Internal Medicine Resident '02, Geriatric Medicine Fellow '03) is a geriatrician and palliative medicine physician who joined the City of Hope National Medical Center, Los Angeles, in 2017. He serves as the Arthur M. Coppola Family Chair of the Department of Supportive Care Medicine. Previously, at the University of Chicago (where he earned his MD as well as a PhD in health policy), Dale founded the Specialized Oncology Care & Research in the Elderly (SOCARE) Clinic, which he recently expanded to City of Hope. And his devotion to medicine reaches beyond the hospital: He and his wife are coproducers of *The Elephant in the Room*, a forthcoming film about a palliative care team working with terminally ill patients.

Michael Boland (MD '01) is an associate professor of ophthalmology at the Johns Hopkins Wilmer Eye Institute, where he was appointed residency program director in 2016. "It has been a distinct privilege," he says, "to be responsible for a program that trains the future leaders of our field." Boland is also the institute's information technology director, overseeing a

From left: Mario Ferretti, Rory Cooper, Rosemarie Cooper, and Eliana Ferretti.

system that hundreds of department faculty and staff use to track 250,000-plus patient visits annually. In a related role, he serves on the American Academy of Ophthalmology's Medical Information Technology Committee, where he has been able to help navigate the transition to electronic health records.

Some Einsteins of the rehabilitation world hung out at the Albert Einstein Hospital in São Paulo, Brazil, last fall. Pitt's **Rory Cooper**, whose titles include director of the Human Engineering Research Laboratories, was a keynote speaker at the Sixth International Brazilian Paralympic Conference. He and **Rosemarie Cooper**, Pitt assistant professor of rehabilitation science and technology, reunited with Pitt alumni **Mario Ferretti** (Sports Medicine Fellow '05), chair and professor of orthopedic surgery at Albert Einstein Hospital, and **Eliana Ferretti**, professor of occupational therapy at the Federal University of São Paulo, who earned her MS and PhD degrees in rehabilitation science under Rory Cooper's tutelage.

In October 2017, **Kirsten Lin** (MD '06) founded Family Matters Direct Primary Care, Pittsburgh's first direct primary care practice—meaning, among other things, patients typically pay physicians directly. "After some soul-searching and logistical preparation," says Lin, Family Matters was born—and alongside it, Direct Care Physicians of Pittsburgh, an organization that links prospective patients to such physicians in the area. Her new role grants Lin the opportunity to build closer relationships with her patients than modern primary care settings typically allow. She charges patients a flat monthly fee, ranging from $38 to $68, that allows her to bypass insurance and grants patients access to her by phone and e-mail in addition to in-person visits, seven days a week.

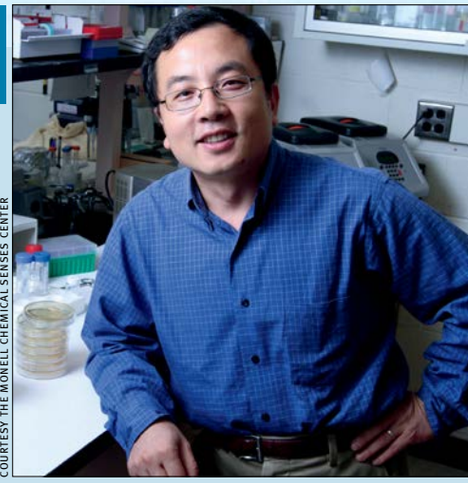
'10s

Patricio Polanco (Surgery Resident '12, Surgical Oncology Fellow '14) is an assistant professor in the Division of Surgical Oncology at UT Southwestern Medical Center focusing on gastrointestinal cancers. Over the last five years Polanco's research team has published several peer-reviewed papers supporting the use of perioperative chemo-radiation treatments in patients with pancreatic, stomach, and rectal cancers. Many of these treatments have been shown to improve the chances of survival in patients with these tumors. Polanco travels to his home country of Peru once a year with the Peruvian American Medical Society on its annual medical mission to the city of Ayacucho, where he provides surgery to low-income Peruvian patients and surgical training to local surgeons.

—Cara Masset, Rachel Mennies, Jon Kunitsky, Kelsey Sadlek, and Elaine Vitone

BITTER BLOCKER

PEIHUA JIANG



COURTESY THE MONELL CHEMICAL SENSES CENTER

Jiang

Mary Poppins knows how to sweeten a raw deal. "Just a spoonful of sugar," she trills as she spins across the stage.

Molecular neurobiologist Peihua Jiang (Neurobiology PhD '01, Neurology Fellow '02) intends to best that umbrella-twirling nanny. Since 2016, Jiang has studied the perception of bitter flavors, intent on short-circuiting the sensation. "There are a lot of very effective drugs, but because of the awful taste, children will refuse to take those pills," he says. "If we can eliminate or reduce the bitter taste from pharmaceutical active ingredients—anti-malaria and anti-HIV drugs, for example—we may be able to help pediatric populations to take their life-saving pills more rapidly."

Now an associate member of the Monell Chemical Senses Center in Philadelphia, Jiang got his start in gustation—the study of taste—as a postdoc at Mount Sinai, working in the lab of Robert Margolskee. He was drawn toward the field because taste is the sense least studied. So far, he has untangled the structure and function of taste receptor proteins and genes. And he discovered the identity and function of certain adult taste stem cells; an ongoing five-year, $1 million NIH-funded grant supports that work.

Jiang has also tackled the causal relationships among taste receptor structure, dietary choice, and metabolism. Modern humans may have been spared the imperative to experiment with novel—and potentially toxic—fare, but other species aren't so lucky. In a 2018 paper in *Molecular Ecology* on the array of bitter taste receptors found among Myotis bats, which live on every continent except Antarctica, he notes the hazard of overconsuming potentially toxic insects.

The giant panda's sweet tooth was the subject of a 2014 report in *PLOS ONE*. "We tried to compare the panda receptor to the human receptor," he explains. "If we understand [the human sweet tooth], perhaps we can develop a way to reduce sugar intake."

More recently, Jiang has looked beyond the tongue, to chemosensors in the throat, sinuses, and even the gut, where they seem to detect parasitic infections and mediate inflammatory disorders. "If we identify these extra-oral receptors," he says, "we could target them to improve treatment of those diseases."

—Sharon Tregaskis

SHELDON ADLER

JULY 13, 1934–NOV. 15, 2018

Adler

On the first day of class, a roomful of Pitt medical students waited for their professor, a renowned kidney expert, to start lecturing. Instead, the expert, physician Sheldon Adler, handed out a case study involving a patient suffering from an allergic reaction following a kidney transplant. Their tasks? In small groups, determine learning objectives, consult medical librarians, share research, and collaborate to make a diagnosis and design treatments. He'd provide some guidance, but mostly it was up to them.

Adler was embracing a new trend in medical education in the 1980s called problem-based learning, which focused on self-directed learning, critical thinking, and teamwork—not the typical rote memorization and competition for grades that med students expected.

"Students were no longer passively fed information, and they could understand material better," says Charles Reynolds III, geriatric psychiatrist and Pitt professor emeritus who worked with Adler to champion the pedagogy. Adler, then senior associate dean, spearheaded full implementation of the curriculum by 1992. Well liked among the professors, he still met resistance to change—from faculty and students. He responded with grace and humor; he would crack jokes about needing a hearse to haul away outdated ideas.

"We experienced a profound culture change thanks to Shelly's efforts," says Reynolds.

Adler also knew when to take a break from the tension for a stroll in the park, where he could name all the birds and trees.

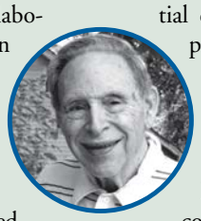
Adler died in November, but his legacy continues. Since 2002, the Sheldon Adler Award for Innovation in Medical Education has recognized other teaching pioneers at Pitt Med. —*Liberty Ferda*

ROBERT CONNAMACHER

DEC. 20, 1933–NOV. 28, 2018

A prof would stitch a cut on a frog's belly to demonstrate suturing techniques for a group of local high school students. Next, he would pass the needle to one of them, saying, *Imagine you're a surgeon. This is your patient.*

This was a typical moment in Robert Connamacher's time at Pitt from 1967 until his retirement in 2016. The PhD associate professor of family medicine wanted these teens—mostly African Americans—to see themselves as potential doctors. There weren't many health professionals who looked like them, and he was dedicated to changing that. He ran the after-school Medical Explorers program (now Health Professions Prep), in which high schoolers took mini science courses and attended lectures by faculty of various ethnic backgrounds.



Connamacher

Connamacher supported a similar program for college graduates, the Summer Pre-medical Academic Enrichment Program (SPAEP).

"I had some doubts in college, but his encouragement solidified for me that I was on the right path," says Yunuen Valenzuela (MD '02), who attended SPAEP in 1995, landed admission to Pitt Med, and now practices in Florida, where fluent Spanish speakers like Valenzuela are invaluable.

Also active with the Student National Medical Association (SNMA), Connamacher showed support for that group by attending conferences all over the country—but only by train. He hated to fly, and sometimes uncertain rail schedules had him arriving a week early. He was eventually inducted into the national organization's Hall of Heroes.

J. Nadine Gracia (MD '02), a first-generation Haitian American and SNMA national president emeritus, met him when she was a first-year Pitt Med student and an officer in the med school's chapter of SNMA. Together they mentored Pitt undergrads through the Pre-Medical Organization for Minority Students. She fondly remembers walking across campus for meetings as he inquired about her studies and her life.

"You knew he was invested in your success," recalls Gracia, who later became deputy assistant secretary for minority health during the Obama administration. "He cared for students and considered them part of his extended family." —*LF*

HENRY MANKIN

OCT. 9, 1928–DEC. 22, 2018

Mankin

Whether instructing a classroom of fidgety elementary schoolers or Harvard medical students, Henry Mankin (MD '53) taught bone physiology the same way—assigning each cell type a theme from Sergei Prokofiev's *Peter and the Wolf.* "Every time you see this cell, you sing it this way," his son Keith Mankin (MD '88) remembers his father saying. Before long, the room would be in chorus.

Mankin, who died in December at age 90, was a world-renowned orthopaedic surgeon and chair of orthopaedic surgery at Massachusetts General Hospital and Harvard Medical School.

Kurt Weiss (Res '08) recalls being treated by Mankin for osteosarcoma as a kid. "When you were in the room with him as his patient, you were his whole universe," Weiss says. After Weiss pursued orthopaedics himself, he learned of his doctor and mentor's significant contributions to the field. "I remember thinking, *Holy mackerel. This guy is brilliant.*"

Those contributions included research on Gaucher disease and spinal disorders, as well as the active, dynamic nature of cartilage. Mankin also cofounded the Musculoskeletal Tumor Society and was a champion for women and underrepresented groups in medicine, winning the 2004 Diversity Award from the American Academy of Orthopaedic Surgeons.

Freddie Fu (MD '77) remembers his friend and mentor Mankin, who grew up in Squirrel Hill, as "really a true, blue-collar, down-to-earth, funny Pittsburgh person" who loved to teach.

"You teach someone, they continue to teach what you say, and you never disappear," Keith Mankin recalls his father saying. "You live forever."

—*Prachi Patel*

IN MEMORIAM

'40s

RALPH F. WALDO
MD '48
OCT. 31, 2018

'50s

DONALD G. BIRRELL
RES '51, RES '55
DEC. 6, 2018

GILBERT L. ASHOR
MD '54
FEB. 6, 2018

DAVID A. VERMEIRE
MD '54
OCT. 18, 2018

DONALD R. KOEHLER
MD '55
DEC. 29, 2018

CHARLES A. COLTMAN JR.
MD '56
NOV. 28, 2018

WILLIAM T. FOLLETTE
RES '56
JAN. 31, 2018

JOHN W. LOFTIS
MD '56
NOV. 12, 2018

HERBERT F. CRONIN
MD '57
AUG. 17, 2018

HAROLD GLICK
MD '57
JAN. 9, 2018

F. GENE BRAUN
MD '58
OCT. 28, 2018

BRET RUDY: A HIGHER BAR

BY SHARON TREGASKIS

COURTESY NYU LANGONE HEALTH

Rudy started out as a pediatrician dedicated to kids infected with HIV. He now can help even more people as executive director of NYU Langone Hospital–Brooklyn.

In the early 1990s, many pediatricians figured kids whose symptoms pointed to HIV lacked the emotional maturity and resilience to cope with a fatal diagnosis—so they opted not to even test for the disease.

Bret Rudy (MD '85) thought otherwise. As a fellow in pediatrics at the University of Pennsylvania, he launched a dedicated clinic at Children's Hospital of Philadelphia (CHOP).

"Being quite frank, there was a juxtaposition of the kids who were infected through transfusions and perinatal exposure and an emerging group of teens who acquired HIV through sexual transmission," says Rudy, now a professor of pediatrics at New York University. "There were still people talking about 'innocent' and 'noninnocent' victims."

Funding was nonexistent, so Rudy recruited volunteers—including social workers, nurses, psychologists, and fellow physicians—to stay after hours to staff the clinic a few evenings each week. Rudy was intent on providing comprehensive care in a setting where every kid felt safe and dignified—including those counting on survival sex to secure such necessities as food or housing and those whose outlook had been profoundly altered by their experiences as survivors of violent crime. "Our job was to find resources so that we could help them break down the social barriers that would prevent them from taking care of their health and looking forward to their future," says Rudy. "We never gave up on anyone, no matter how bad the situation."

Rudy later joined the Centers for AIDS Research, served on the Ryan White Title IV Strategic Planning Committee, and joined the White House Advisory Committee on Adolescents for the Office of National AIDS Policy. As chair of Project ACCESS, he led development of a national social marketing campaign promoting HIV counseling and testing in teens. And, all the while, he ran clinical trials to develop treatment protocols tailored to teens and young adults. Recent papers he's coauthored include a comparative analysis of partner notification programs for youth living with HIV, an overview of the continuum of care available to them, and a report on the biomarkers that distinguish effective viral suppression among young people.

Now executive hospital director and senior vice president for NYU Langone Hospital–Brooklyn, Rudy credits his early experiences launching CHOP's Adolescent HIV Initiative, which is celebrating its 25th year, with propelling him into other leadership roles. "You start to see the bigger picture to impact more lives and give other people opportunity."

Since 2016, Rudy has overseen a transformation of operations at NYU's Brooklyn outpost, intent on matching quality of care in the borough with what patients receive from NYU's flagship medical center in Manhattan. "By 2020, Brooklyn will be the third largest city in the country," he says, "about the same size as Houston." Already, the hospital has added ambulatory pediatric and surgical oncology services as well as trauma and stroke centers; it has also implemented an electronic health records system that unites the hospital with the Family Health Centers at NYU Langone's 35 school-based clinics and affiliated homeless health-care centers. "It's amazing to see some of the young physicians and nurses who are really committed to what we're doing in Brooklyn," says Rudy, "who really love the diversity of patients we serve, who bring so much energy and creativity to their jobs."

Rudy traces his own leadership style to the example set by the late, beloved Pitt professor Charles Watson. "When he walked … through a hospital, his whole emphasis was on how you're respectful to the patient, the staff, the aides. That's something I've taken with me: Set the bar high for yourself, so everyone around you sets their bar a little higher." ■

NORMAN N. KRESH
MD '58, RES '59, RES '63
OCT. 27, 2018

'60s

CHESTER M. BERSCHLING
RES '60, '62, '64
DEC. 29, 2018

GERALD I. KAUFER
MD '63
OCT. 22, 2018

JOHN WHITAKER EWING
MD '64
NOV. 27, 2018

'70s

GILMORE M. SANES JR.
MD '70
OCT. 13, 2018

KENNETH M. STANKO
MD '77, FEL '83
OCT. 25, 2018

'80s

DIANNA L. BOURKE
PHD '85
OCT. 28, 2018

EDWARD E. LONGABAUGH
MD '89
OCT. 12, 2018

FACULTY

ANTHONY M. HARRISON
RES '65
JAN. 28, 2019

Emergency medicine attending Brian Malley (in scrubs) spies his peripheral veins in their 15 minutes of fame as the vessels are scanned by SonoGames contestants (from left) Vi Nguyen, Neha Hafeez, and Keelin Moehl, aka Team Buena Onda (Spanish for "Good Vibes").

YES WE SCAN! YES WE SCAN!

First-year Pitt Med student Alex Zhang dabs clear gel on the skin of a 30-something-year-old actor (or "standardized patient") and slides the ultrasound probe to the left of his sternum while Desireé Neville (Fel '16), assistant professor of pediatrics, looks on. Turning the probe, Zhang peeks between the man's ribs, revealing what, to the untrained eye, seems to be a hazy, two-toned maze on the screen above.

But it's textbook: a parasternal long-axis view of the heart.

"Beautiful," says Neville—and a point for Team 50 Shades of Grayscale!

In February, nine student teams competed in Pitt's second annual SonoGames, a test of knowledge and skills in ultrasound. The event, sponsored by the Office of Medical Education, was organized by Caelie Kern, Ellen Ribar, and Harmony Yourish—students in the Ultrasound in Medicine Interest Group. Emily Lovallo, assistant professor of emergency medicine and assistant director of ultrasound services for the Department of Emergency Medicine, serves as the group's faculty advisor.

Andy Henderson, a second-year student who competed last year as well, says that the group's hands-on practice and one-on-one instruction panned out for him recently as a volunteer at the Birmingham Free Clinic. "A couple months ago, someone came in and needed a renal scan. No one there felt comfortable doing it. And I was like, *Okay, I'll give it a shot*." Successfully completing the scan was "really affirming," says Henderson—who, by the way, took second place in this year's SonoGames, along with Wesley Ramirez and Vu Dinh (their team name, WAVIN, is a portmanteau of their first names).

In the final *Jeopardy!* (style) round, the Acoustic Shadows—first-year students Elaina Anglin, Insiyah Campwala, and Anjana Murali—clinched the championship.

—Elaine Vitone

—Photograph by Martha Rial

CALENDAR

FOR ALUMNI & FRIENDS

Unless otherwise noted, for information:
Melanie Sadarananda at 412-648-9741
or mms239@pitt.edu

MEDICAL ALUMNI ASSOCIATION EXECUTIVE COMMITTEE BOARD MEETING
MARCH 21, 6 P.M.
University Club

THIRD-YEAR MEDICAL STUDENT PINNING CEREMONY
MAY 3, 3 P.M.
Scaife Hall, Lecture Rooms 5 & 6

GRADUATING CLASS LUNCHEON & AWARDS CEREMONY
MAY 17, 11 A.M.
Twentieth Century Club

SCOPE AND SCALPEL
MAY 17, 7 P.M.
MAY 19, 2 P.M.
Central Catholic High School
McGonigle Theater
For information:
scopeandscalpelsociety@gmail.com
or engage.pitt.edu/project/15051

SCHOOL OF MEDICINE COMMENCEMENT
MAY 20, 3 P.M.
Soldiers & Sailors Memorial Hall & Museum

WHITE COAT CEREMONY
AUGUST 11, 11 A.M.
Carnegie Music Hall

To find out what else is happening at the medical school, visit health.pitt.edu and maa.pitt.edu.

GETTY IMAGES

FOR REAL! TWEEN SCIENCE

Have you ever seen a dog bury its nose in a patch of grass and thought: *What could it possibly be sniffing?* It turns out, a lot.

Of the thousands of genes embedded in our DNA, about 400, when untangled and expressed, produce proteins that let us humans detect the scent of flowers and freshly cut grass when we go for a walk. And pups? They have 800 genes to help them smell. When they sniff the grass, they glean a lot more intel, like which poodle already marked that plot.

You've probably heard that canines, with their superior snouts, are trained to find victims in disasters, identify explosives, and hunt down drugs. But did you know they can also detect disease?

Dog owners with diabetes have noticed their dogs will lick, nudge, or jump up on them when their sugar levels dip low, reminding them to eat. And studies have shown dogs are also able to identify when samples of human blood, sweat, or clothing carry traces of other diseases, including ovarian cancer, lung cancer, and malaria.

Unlike Labradors or beagles, we can't rely on our noses to tell us when someone's sick. But what if we could build a better nose? Sounds like a project for Marvel tech genius Tony Stark (aka Iron Man), right? Well, Pitt researchers are on it.

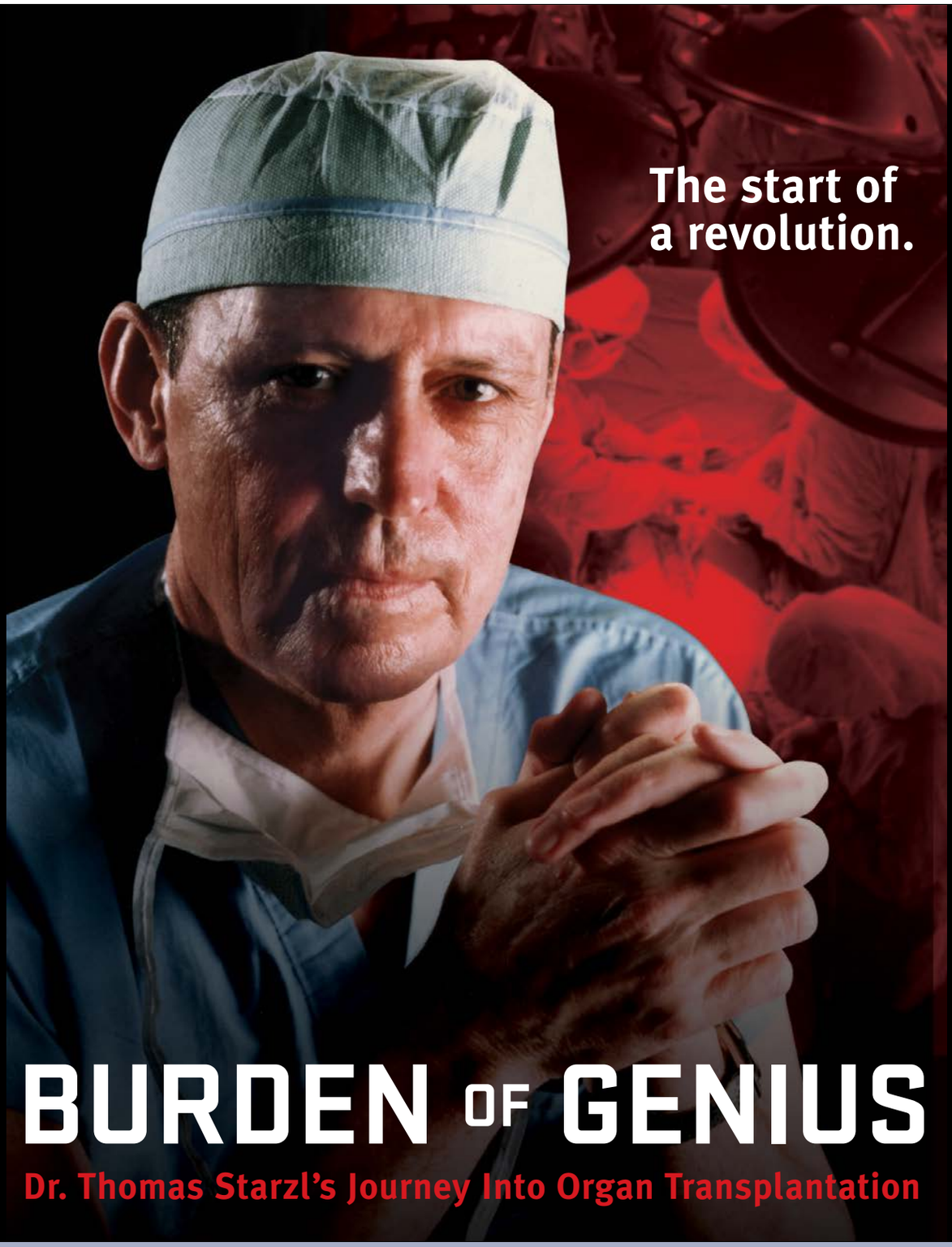
Nathan Urban's lab is tracking how animals like mice (they have a whopping 1,200 genes for scent in their DNA!) identify where a smell, perhaps a waft of stale cheese, is coming from. And Christopher Wilmer's lab, just down the street, has been testing how spongy synthetic materials can filter gases and differentiate scents. Both labs' ultimate goal is to contribute toward nose-like technology that's better than the schnoz of *Homo sapiens* and more reliable than Rufus's. Until then, the next time a pooch wiggles its cold, wet nose in your face, we can only wonder what it's sniffing! *—Prachi Patel*

Is there a topic you'd like us to explore? Drop us a line at medmag@pitt.edu.

UNIVERSITY OF PITTSBURGH
SCHOOL OF MEDICINE
SUITE 401 SCAIFE HALL
PITTSBURGH, PA 15261

CHANGE SERVICE REQUESTED

NONPROFIT ORG.
U.S. POSTAGE
PAID
PITTSBURGH, PA
PERMIT NO. 511



BURDEN OF GENIUS

Dr. Thomas Starzl's Journey Into Organ Transplantation

Giant leaps forward in science are not made by wimps. The film ***Burden of Genius*** shows what it takes to revolutionize medicine—and the price paid by some who do.

This University of Pittsburgh production has been winning awards at film festivals and captivating audiences around the world, from London to New Delhi. Now it's coming home to Pittsburgh, where Dr. Starzl made history.

April 12–18, 2019
Rangos Giant Cinema
Carnegie Science Center
Featuring special guest speakers.

For tickets or to learn more about the film and find out about future screenings, visit: **starzlfilm.com.**

official selection GLOBAL HEALTH FILM FESTIVAL 2018 films to inspire change

CLEVELAND INTERNATIONAL FILM FESTIVAL GLOBAL HEALTH COMPETITION WINNER

Official Selection CINEQUEST FILM FESTIVAL

2018 HEARTLAND INTERNATIONAL FILM FESTIVAL OFFICIAL SELECTION

5th ANNUAL RAW SCIENCE FILM FESTIVAL OFFICIAL SELECTION