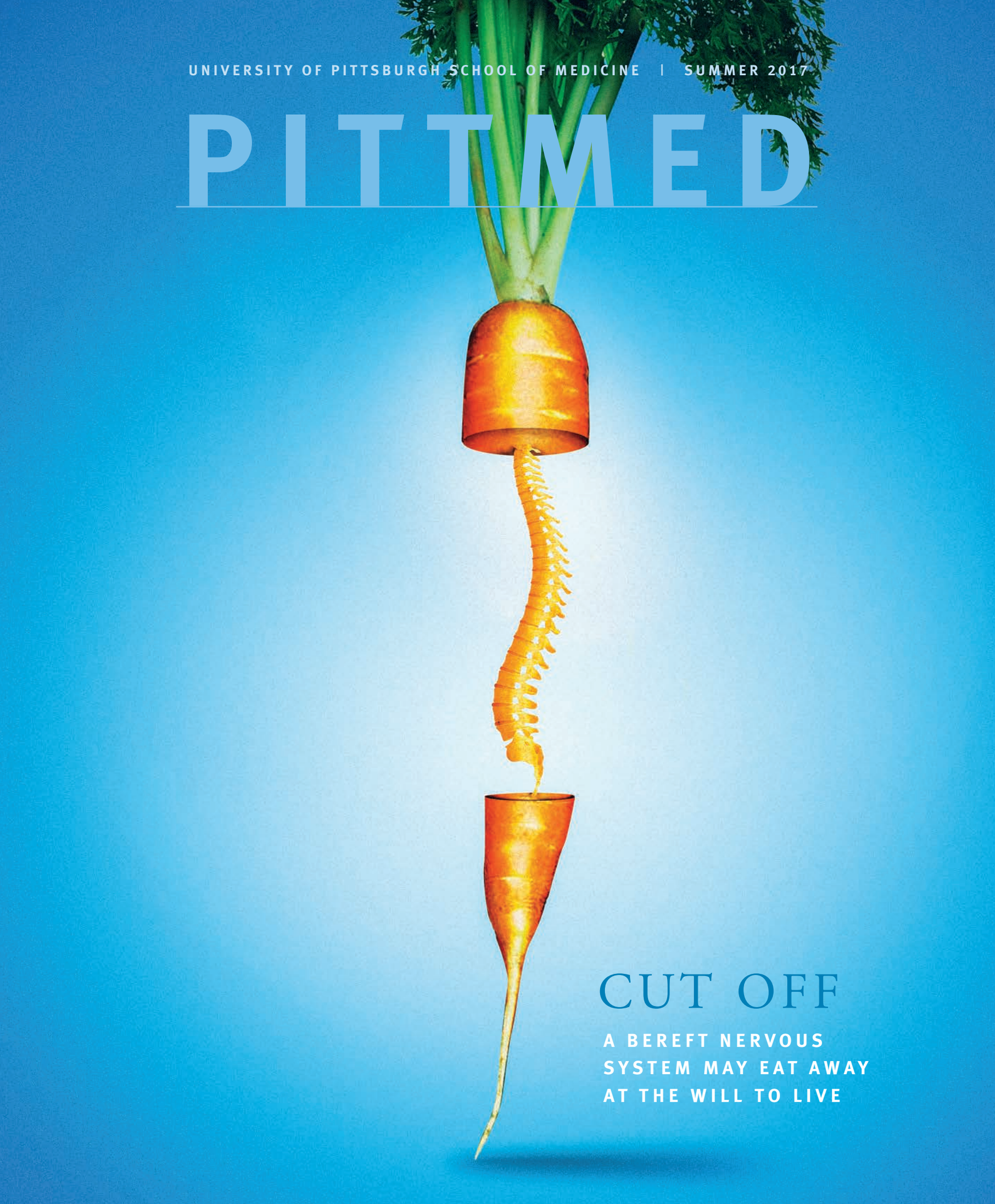
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | SUMMER 2017

PITTMED



CUT OFF

A BEREFT NERVOUS SYSTEM MAY EAT AWAY AT THE WILL TO LIVE

EXTRA MINDFUL

I loved your articles on mind-body unity ("Mind is Matter," Fall 2016, and "The Big Picture," Spring 2017, by Elaine Vitone). I have seen the side effects and benefits of treatments patients *thought* they were receiving—but because of errors were not—including chemotherapy and radiation. I have written about my experience as a surgeon working with children and adult cancer patients. [*Editor's note: What follows is an excerpt of an essay submitted by Dr. Siegel.*]

I began to pay more attention to what was said in the operating room—simple things, like changing an injection from feeling like a "bee sting" to a "mosquito bite." Before patients awakened from a procedure, I would say, "You will wake up comfortable, thirsty, and hungry." I had to start adding, "But you won't finish what is on your plate" when my patients began to gain weight.

To reassure children that they would not be in pain while they were undergoing surgery, I would tell them, "You will go to sleep when you go into the operating room." I was shocked to have children fall asleep as they were being wheeled into the O.R.

Once, a woman I was about to operate on was in a total panic. I spent a long time trying to calm her down, but nothing worked. With a look of fear on her face, she said, "Thank God all these wonderful people will be taking care of me." I knew agreeing with her wouldn't accomplish anything, so I said, "I know these people. I have worked with them for years. They are not wonderful people." For a second she looked bewildered but then burst out laughing, as did everyone in the O.R., and we all became family. Fear cannot exist in the presence of love and laughter.

Bernie Siegel (Res '62)
Woodbridge, Conn.

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

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As a writer for *National Geographic News*, *The Washington Post*, and *Smithsonian.com*, **JASON BITTEL** ["Cancer's Lifelines"] has made a career reporting on animals; recent topics include the enemies of chickens, vigilante whales, rodents on the lam, and drunk Groundhog Day revelers. While covering a story on telomeres for *Pitt Med*, he became in awe of researchers and their willingness to tweak lab tests "about 10,000 times until something gives." Bittel and his family are putting the finishing touches on a new house in Murrysville, Pa. The woodsy acreage will give him the opportunity to capture photos of foxes and opossums with a trail-cam.

GAVIN JENKINS ["Strike a Connection" and other stories] became *Pitt Med*'s associate editor in February. It's all at once brand new yet nostalgic: Since arriving, he's used a landline, operated a fax machine, and taken in some vogue dancing—the latter was while on assignment for this magazine. Jenkins, who was once a sports writer, was impressed by the athleticism of the dancers; watching them was his favorite part of researching his story on eradicating AIDS. He is writing a book about working at a gas station, a job Jenkins took while pursuing his MFA at Pitt. His stories have been published online by *The Atlantic*, *VICE*, and *Narratively*.

PITTMED

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VOL. 19, ISSUE 2

7

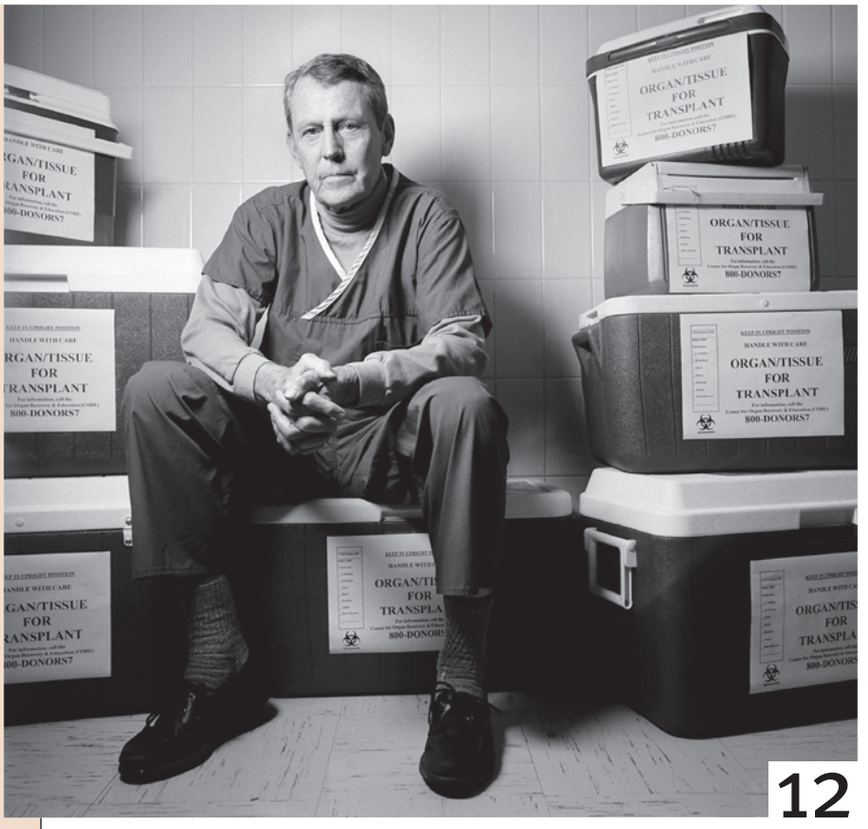
DEPARTMENTS

34

40 1/2

COVER

Pitt's Lisa Pan has linked malnourished nervous systems to life-threatening depression in adolescents. (Cover illustration: Jesse Lenz © 2017.)



12

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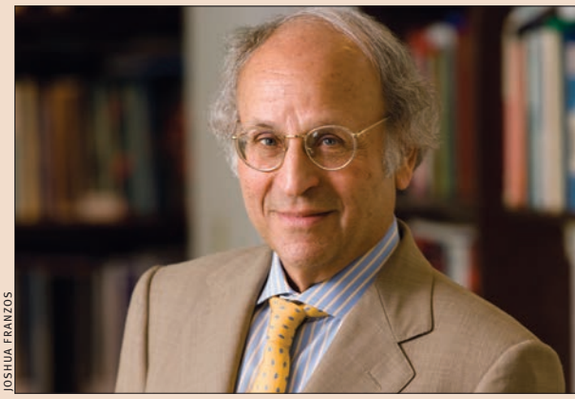


JOSHUA FRANZOS

Until I began to learn to draw, I was never much interested in looking at art.
—Richard Feynman

Support for the liberal arts is dwindling at many U.S. universities in favor of technology-related skills training courses.

There was a time when there was no distinction between the humanities and the sciences. They were seamless. Think of Aristotle, Da Vinci, Descartes. Indeed, the humanities and sciences inform each other in important, although often ineffable, ways. Where they intersect is often a crucial nexus.

Ada Lovelace, poet Lord Byron's daughter, is often described as the first computer programmer. She was encouraged by her mother to study math to tame her restless spirit—the thinking was that algebra might serve as a prophylactic to ward against the mental afflictions that tortured her celebrity father. Lovelace came to view mathematics as a beautiful, poetic language, which empowered her to explore "unseen relations between things," as she put it. I imagine many mathematicians feel the same way.

The composer Alexander Borodin, the poet William Carlos Williams, and the authors W. Somerset Maugham and Anton Chekhov were all physicians. It's not surprising that a doctor would examine what it means to be human on more than one plane. As the existentialists asked, how do we find meaning when life's impermanence presents itself so vividly to us daily? We must be taught to think with complexity if we are to answer such complex questions.

For most of Western history, the poor, people of color, and women were discouraged or excluded from pursuing a liberal education. Even within the aristocracy, the contributions of women were suppressed. Lady Lovelace had the potential for eminence in math, yet delving deeper into her studies was likely to injure her, her mentor Augustus DeMorgan believed. The intensity would have required "all the strength of a man's constitution to bear," he wrote. Such "tension of mind" was for the men who would run things; the rest of the crowd was welcome to build specific skill sets to keep the machine going—though their voices would be "all but absent from history," as Emily Dickinson put it.

The critic Francine Prose has considered whether the humanities are under attack now precisely because they enable students to think in more complex ways than the simplifications of our current political and corporate discourse.

Middle and low income families are being priced out of higher education altogether. Our current situation, of flat wages and rising education costs, must be addressed. But let's not sell each other short. Imagine if our civic leaders were to adopt the scientific method—a template for civil, disciplined, evidence-based, and sound discourse—to probe this problem.

Are we about to pedal backward so that a mere sliver of the population is privy to the pleasures and rigors of literature, language, philosophy, art, music, and history? Or of mathematics, physics, and biology? These pursuits allow us to create, imagine, and engineer great works. They help us to perceive and understand nature and its abstractions. And they help us understand each other. We can't afford to be frugal of spirit. I'd make a similar argument regarding access to health care. A civilized society has its foundation in the liberal arts *and* sciences, and also in the wellness of all of its people. These are investments that enrich us and make the world a better place.

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

THINK BEFORE YOU INK

Say a guy wants a tattoo that would cover a suspicious-looking mole on his arm. A recent Pitt survey in *JAMA Dermatology* noted that there isn't a standard protocol for tattoo artists in this situation.

Yet any dermatologist will say tattooed skin is hard to screen for skin cancer. The Pitt survey suggests a potential teaching moment on this front.

"Tattoos are a big part of culture," says first author Westley Mori, a fourth-year Pitt med student who will do his dermatology residency at the University of Minnesota. Considering the documented rise in melanoma among young people—a prime demographic for tattoos—the artist is uniquely positioned to help.

Mori says he hopes to team up with other dermatologists at tattoo conventions throughout the country to educate artists on recognizing skin cancer and referring clients to doctors. Similar initiatives to train hairstylists to look for signs of scalp melanoma have seen success. *—Micaela Fox Corn*

CAMI MESA

Tattoos might cover skin growths.

Duo Doubly Honored

Patrick Moore, leader of the Cancer Virology Program at the University of Pittsburgh Cancer Institute and a Distinguished Professor of Microbiology and Molecular Genetics, and Yuan Chang, an American Cancer Society Research Professor and a Distinguished Professor of Pathology, were presented with the 2017 Paul Ehrlich and Ludwig Darmstaedter Prize on March 14 in Frankfurt. One of the most prestigious awards in medicine, the prize is given annually to researchers who have made significant contributions in the fields of immunology, cancer research, microbiology, or chemotherapy.

The duo discovered two of the seven known human viruses that directly cause cancer; and this year, they also received a Passano Award, which is given to medical and scientific researchers who have advanced their field.

"It's a tremendous honor," Moore says of the recognition. In 1994, Chang and Moore discovered the Kaposi's sarcoma-associated herpesvirus, or human herpesvirus 8 (also known as KSHV or HH-V8), and in 2008, they identified Merkel cell polyomavirus (MCV). "We're just *really* interested in viruses that cause human cancers," Chang says. *—Gavin Jenkins*

PHOTO ILLUSTRATION BY STACY INNERST

Moore and Chang were honored in Frankfurt.

COURTESY RICHARD PAN

Pan

Overheard

Shot in the Arm for Communities

Before becoming a California state senator, Richard Pan (MD '91), a pediatrician, was on the faculty at the UC Davis Children's Hospital and helped establish organizations to build healthier communities. (One of those organizations resulted in 65,000 Sacramento-area children gaining access to health, vision, and dental care.) Two years ago, *TIME* called Pan, 51, a hero after he authored Senate Bill 277, which eliminated the personal belief exemption that many parents had used to prevent getting their children vaccinated. This spring, Pan gives the commencement address to the University of Pittsburgh School of Medicine's Class of 2017.

Why was your vaccine legislation important?

[People were] worried that [their kids were] going to catch a deadly disease at school because some other parents decided not to vaccinate their children. Their schools were unsafe. And so, SB277 is about [restoring] community immunity to neighborhoods in California.

What problems will Pitt med graduates face?

In the late 1800s, early 1900s, . . . there were very few truly effective drugs, a handful. So a lot of physicians became leaders in the community—creating hospitals and so forth—because they realized that that's where they could make the most difference; because what they had in their black bags back then was pretty limited.

After World War II, we made tremendous strides in developing the kind of science and technology to be able to help individual patients. We developed new medications, new techniques, new procedures, devices. . . . But we also realized that the problems facing [many of] our patients, like obesity, addiction, behavioral issues, are not ones we can solve [by] going to the pharmacy or the O.R. We need to understand the social determinants of health. [Doctors] were more integrated in [community wellness 100 years ago]. We sort of became dis-integrated [as we acquired] more tools, . . . and public health became more of a government function. Somewhere, we've got to bring those two [roles] back together again. And I think that's the challenge. Even when we think about health care costs—we spend 70, 80 percent of a health care dollar on managing chronic diseases. That's where all the money is going. *—Interview by Gavin Jenkins*

FLASHBACK

When David Shulkin (Res '89, Fel '90) was training at Pitt, he asked to study care costs. It was an unusual request, but Shulkin's curiosity paid off. He discovered that most doctors drastically underestimated prices of tests they ordered—that was at a time when health care costs were about to skyrocket. His findings were published in the *Annals of Internal Medicine* and reported on by the *Pittsburgh Post-Gazette*. Now the nation will benefit from this prescient physician. In February, he was sworn in as secretary of the U.S. Department of Veterans Affairs. He served as the VA's undersecretary for health for 18 months under President Obama before President Trump nominated him.

TYPOGRAPHY: ELENA GIALAMAS CERRI

Brain Teaser Team

Mental health is getting raised to the power of two. The University of Pittsburgh and Pfizer have teamed up to use computer modeling to determine whether certain genetic markers and anatomical variations can predict brain disorders.

Kayhan Batmanghelich, an assistant professor in Pitt's Department of Biomedical Informatics, is leading the effort. Batmanghelich's team will use brain imaging measurements, like cortical thickness and subcortical structure volumes, and then relate those measurements to the genetic markers of the disease. They'll start with schizophrenia, mining datasets that include these factors as well as clinical cognitive measurements.

Pitt works on the method, algorithm, and software development for the project. Afterward, Pfizer will access the software Batmanghelich's team is creating to apply to its own datasets. Batmanghelich says the complex project will probably take more than a year.

"We hope there will be more collaboration between academia and industry," Batmanghelich says. *—Elaina Zachos*

Competitive Advantage

Jennifer Bomberger, PhD assistant professor of microbiology and molecular genetics, studies bacteria and the vicious things they do. Looking specifically at bacteria in immune-compromised hosts—like patients with cystic fibrosis—Bomberger says *Pseudomonas aeruginosa* has a competitive advantage over other bacteria.

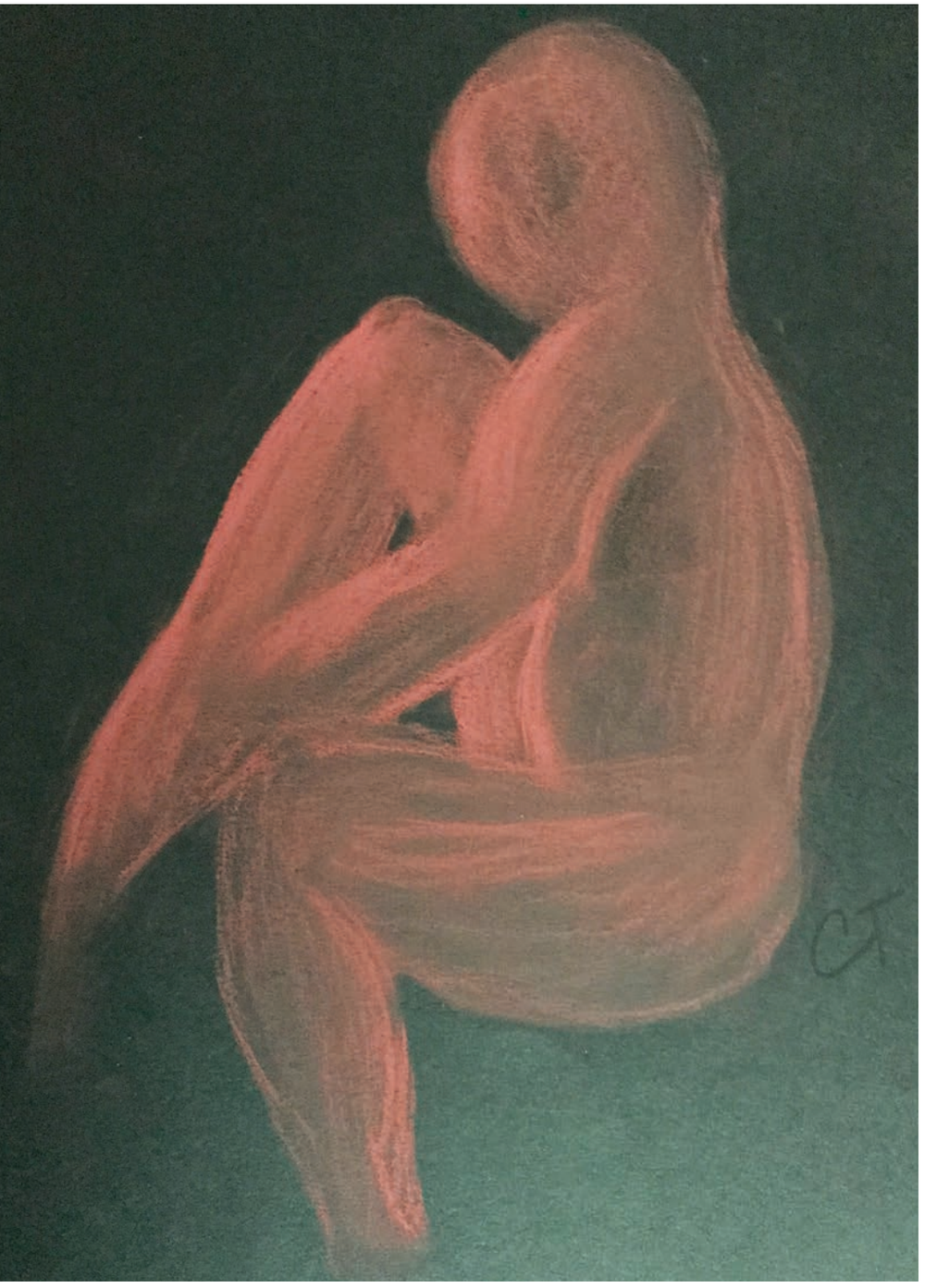
In a recent paper published in *Proceedings of the National Academy of Sciences*, Bomberger and her team reported that *P. aeruginosa* manipulates a host's immune response to survive. Many microbes actually fight to reduce lung inflammation, but *P. aeruginosa* encourages it. In fact, Bomberger says, "the bacterium thrives in an inflammatory environment." Patients with cystic fibrosis often battle many kinds of infections from a young age, but chronic *P. aeruginosa* infection typically dominates by the time a patient becomes an adult.

The team also identified biological changes that happen in cells infected by *P. aeruginosa*. Now that Bomberger understands how the bacterium functions, she and her team, which includes collaborators at Dartmouth and Harvard universities, are looking into new therapeutic targets. *—Evan Bowen-Gaddy*

FOOTNOTE

Twenty days and 120,000 hands of Heads-up, No-Limit Texas Hold'em ended Jan. 30, when an artificial intelligence program developed at Carnegie Mellon stomped four world champions during a man vs. machine tournament at Rivers Casino in Pittsburgh. The bot that called the humans' bluffs ran on the Pitt/CMU Pittsburgh Supercomputing Center's Bridges machine.

"We were halfway through and knew there were about 130 hours of losing ahead of us," says player Jason Les, laughing. The bot learned from its mistakes and got better as the days progressed. No hard feelings. Les considers it a benchmark, proving technology has the power to improve people's lives in ways far more significant than a poker game. But a rematch? "There's no reason to think that humans could ever overtake it," he says.



DETAIL OF LIFE

The School of Medicine and Carnegie Museum of Art have partnered to give med students a new appreciation for the human form and humanity itself, through the lens of an artist. The drawing class, a minielective, helped Christy Taylor (Class of '20, who happens to be featured on the opposite page) home in on details: like the structural difference in leg muscles between men and women models or the story told by a work on display at the museum.

Taylor says she found the class soothing. "I was most surprised by how calm I felt during the course," she says. Taylor's drawing shown here, done in 30 minutes, portrays a male nude who posed in the museum studio for the class. *—Gavin Jenkins*

Next Generation

Nolan Priedigkeit, an MD/PhD student in the University of Pittsburgh and Carnegie Mellon Medical Scientist Training Program (MSTP), has been gaining national news attention for recent breast cancer research findings published in *JAMA Oncology*. As a member of Adrian Lee's lab here at Pitt, he has helped identify genes that allow breast cancer to spread to the brain. (Lee directs Pitt's Precision Medicine Institute.) A few of the now known genes are targeted by already existing drugs, making for a smooth transition to clinical trials.

After the news coverage, the lab received messages from clinicians that a few advanced breast cancers responded to the proposed therapies. "Starting this dialogue, and sometimes debate, with other clinicians, researchers, and patients fuels the responsible translation of these discoveries into clinical practice," says Priedigkeit. "And we're fortunate that a few news articles nurtured this conversation."

Shinjini Kundu, another MSTP standout, was named a "40 under 40" honoree by *Pittsburgh Magazine* last fall. Kundu graduated from high school at the age of 16; and before she was old enough to legally purchase alcohol, she'd earned bachelor's and master's degrees in electrical engineering from Stanford University. Last spring, she completed her PhD in biomedical engineering at Carnegie Mellon, and she is currently working on her MD at Pitt. After graduation, Kundu hopes to work at the intersection of engineering technology and the medical community. "It is incredibly humbling to realize the immensity of how much is still left to discover," she says. "And it is truly exciting to think that I might be able to chip away at some of that unknown in some way."

Luka Pocivavsak, an MD/PhD, has codesigned a surgical graft for coronary bypass surgery. The bypass tube, called TopoGraft 2.0, mimics a healthy artery—it wrinkles and unwrinkles to the rhythm of a human heartbeat. The invention earned a seed grant from the Center for Medical Innovation (CMI) in Pitt's Swanson School of Engineering. "Blood is very sticky," says Pocivavsak, adding that the TopoGraft 2.0 will help it flow through the body smoothly.

Pocivavsak is a fourth-year general surgery resident interested in natural geometries and topologies in the human body. His codesigners were Robert Kormos, MD professor of surgery and bioengineering; chemical engineer Sachin Velankar at the Swanson School of Engineering; and his mentor, Edith Tzeng, an MD professor of surgery.

Philip Carullo, a second-year anesthesiology resident, is the cocreator of the Esophocclude. The device—a swallowable, self-expanding tube—prevents the flow of gastric acid into the lungs. Carullo created the device with Youngjae Chun, a PhD assistant professor of industrial engineering, for patients receiving breathing tubes. The Esophocclude has earned the inventors two consecutive grants from Pitt's CMI to continue to develop the product. *—Evan Bowen-Gaddy and Kylie Wolfe*

TEAM TWINS

Identical twins Crystal (left) and Christy Taylor (both of the Class of '20) didn't get competitive when it came to applying to medical school. But when it comes to video games?

"*Mortal Kombat, Street Fighter* . . . We are very avid players," says Christy, laughing.

The Taylors were raised in Florida, and each earned a bachelor's degree in biology and master's degree in public health from the University of Miami. While in grad school, Crystal taught biostatistics, and Christy epidemiology. Christy notes that their public health training will help them address the social determinants of health as they provide care.

Their grandmother, a nursing assistant, piqued their interest in medicine.

"She'd always explain the importance of a profession that allows you to help people make life-changing decisions," says Christy.

The twins endured some difficult life changes themselves before entering the University of Pittsburgh School of Medicine. When they were in high school, one of their parents struggled with a debilitating condition. Christy and Crystal eventually moved in with their grandmother; and after college, they struck out on their own. They say it was the kindness of people here that drew them to Pittsburgh, 1,200 miles from their grandmother.

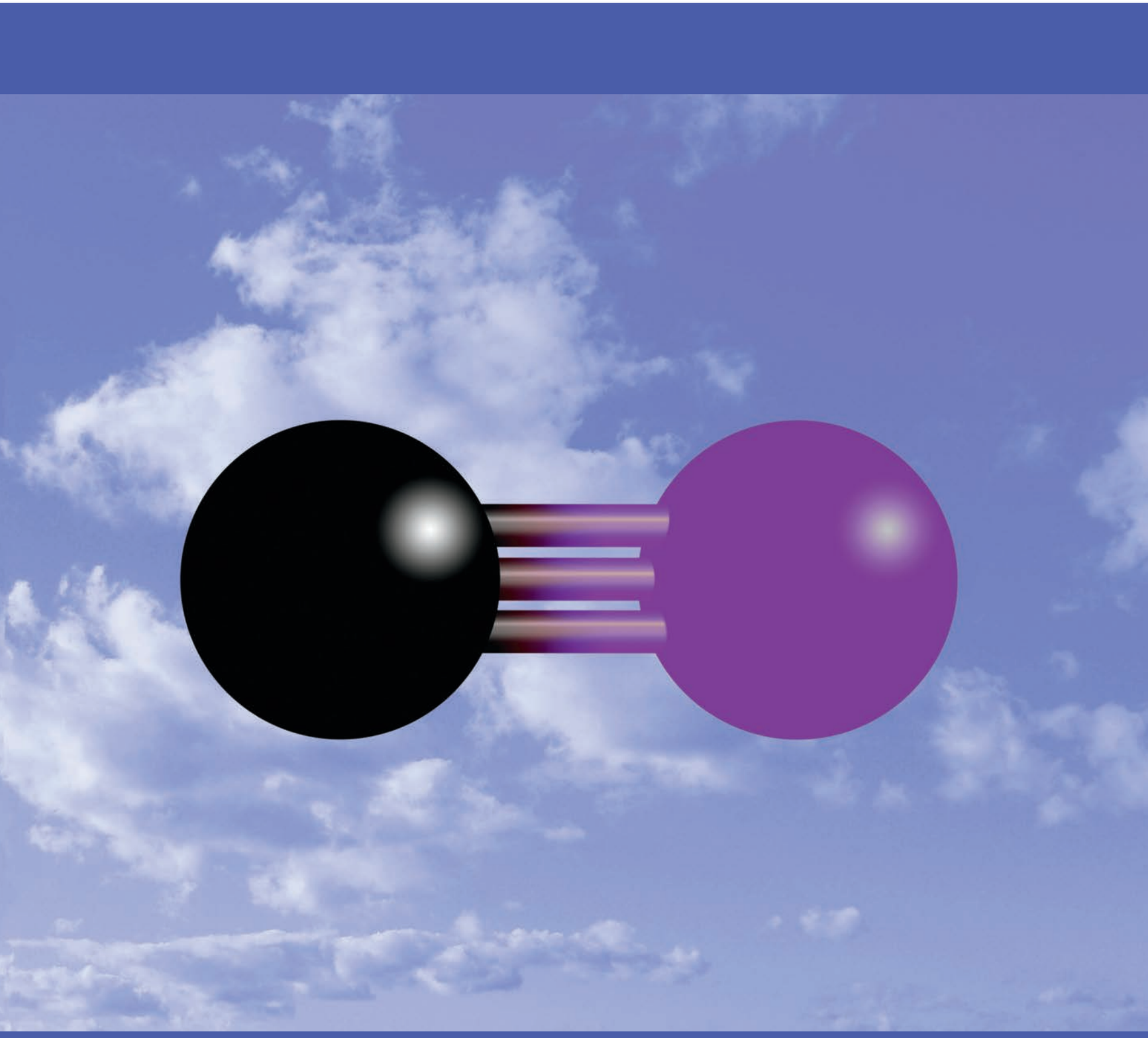
They attend many of the same classes, and both light up when asked what specialty they'll pursue.

"I hate dressing up," says Crystal, who is interested in surgery. "I remember watching TV like, 'Oh my gosh, doctors get to wear scrubs and sneakers? Sign me up!'"

"I hate dressing up, too," says Christy. "But I'm leaning towards cardiology."

And they'll continue supporting one another. "We really balance each other out. We don't really have anybody except each other," says Crystal. *—Kate Benz*

—Photography by John Altdorfer



Normally, carbon monoxide (shown here) has a half-life of 320 minutes. An engineered form of neuroglobin brings the half-life down to 35 seconds.

ANTIDOTE ANECDOTE

POTENTIAL NEW THERAPY FOR CARBON MONOXIDE POISONING

BY ALLA KATSNELSON

ILLUSTRATION BY STACY INNERST

Mark Gladwin was at his family's Oregon summer house almost four years ago when a visiting colleague posed a vexing question. "Just out of the blue, he asked me if there was an antidote to carbon monoxide poisoning," recalls Gladwin, a critical care physician and chair of medicine at the University of Pittsburgh.

The answer was no. Each year, some 50,000 Americans find themselves in the emergency department after inhaling the noxious gas. Gladwin recalled a recent incident in which a man and his 17-year-old son had been brought into the emergency department, unconscious, after working with power tools and a generator in their home when the power had gone out. Neither survived.

Each year, some 50,000 Americans find themselves in the emergency department after inhaling the noxious gas.

As he puzzled through possibilities after his colleague's departure, inspiration struck. Gladwin's team had been working on a genetically engineered version of a molecule called neuroglobin, a form of hemoglobin naturally produced in the brain. They had hoped to put the molecule to work ferrying oxygen to brain tissue starved of it after a stroke but encountered a snag: The altered neuroglobin, called H64Q, bound oxygen too tightly.

That clinging property, Gladwin realized, could be a boon in this alternative context: If the molecule also bound carbon monoxide, it might be able to mop up the poison from the blood and deliver it to the kidneys for excretion.

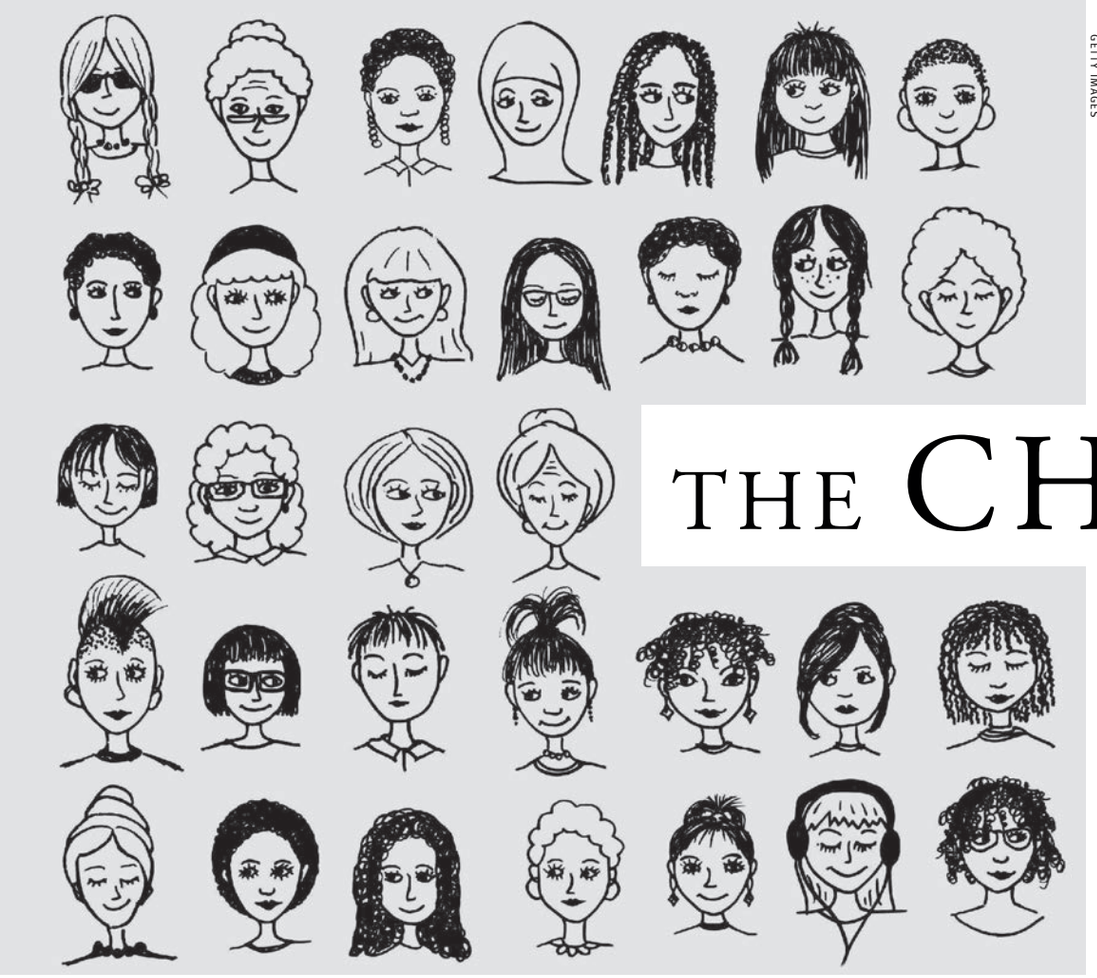
To his delight, the strategy worked. "The concept of the therapy is quite simple," he says. "It binds carbon monoxide with almost irreversibly high affinity." Normally, carbon monoxide's half-life—the amount of time needed for it to clear the body—is 320 minutes. In hyperbaric oxygen therapy, the standard treatment for carbon monoxide poisoning, the half-life is 20 minutes. Meanwhile, animal studies show that the gas's half-life in the presence of H64Q is just 35 seconds. Mice would normally die a little over 4 minutes after exposure to lethal doses of carbon monoxide. In the studies, H64Q worked universally, saving the animals' lives. "When we give our antidote at the end, we really pull them back from the edge," says Gladwin, who is Pitt's Jack D. Myers Professor.

Despite crystal-clear results in animal studies, Gladwin foresees some hurdles in bringing H64Q to the clinic. First, he and his colleagues are currently producing the tweaked protein by inserting the DNA coding for it into the genome of the bacterium *Escherichia coli*. Poisoned patients will probably require 50–100 grams of H64Q. "One major issue is, can we make enough of it?" he says. The lab is working with a company that believes it can.

Another challenge is safety. "We know that if we give it to a mouse that has carbon monoxide poisoning, it's safe," Gladwin says. "What we don't know yet is, what if we give it to someone who doesn't have carbon monoxide on board?" The molecule's hungry binding site could cause trouble by reacting with another substance in the body, such as nitric oxide. "It could be toxic, particularly in the kidneys," he says. That makes it risky to test the treatment in healthy volunteers, a necessary step for gaining approval from the Food and Drug Administration. It also raises concerns for situations when the antidote might be given by mistake to people who appear to be suffering from carbon monoxide poisoning but are misdiagnosed.

Gladwin and his colleagues are actively testing H64Q, and they are also developing backup versions of the molecule that might not have these drawbacks. But even if neither the original nor the knockoffs pan out, he believes that their efforts have forged a clear way forward.

"We've introduced a new paradigm—that you can design a high-affinity carbon monoxide scavenger," Gladwin says. "So while we hope our molecule will be the molecule that becomes the antidote, we are also satisfied that we've shown proof of principle—that this approach can work." ■



GETTY IMAGES

SHIFTING WOMEN'S HEALTH IN THE RIGHT DIRECTION

BY ELAINE VITONE

THE CHANGE

TYPOGRAPHY: ELENA GIALAMAS CERRI

Pitt/UPMC scientists recruited premenopausal women across the city for a multi-institutional study in 1996. They were asking a lot: an extra doctor's visit once a year, forever. Yet about 400 from Pittsburgh volunteered, and at last count, 90 percent were still in. "They have been wonderful," says Karen Matthews, Distinguished Professor of Psychiatry and principal investigator for the Pittsburgh arm of the study. "It's quite a testament to their commitment to helping to figure out what is going on during these transitional years."

Though most women now live at least a third of their lives after menopause, its long-term effects on women's health are just beginning to come into focus, thanks in large part to the study, known as SWAN, or Study of Women's Health Across the Nation. SWAN was funded in part by the National Institute on Aging (NIA). The study, which recruited more than 3,000 women in seven sites, has yielded more than 400 papers to date, including several recent findings from Pitt investigators.

Matthews has long been intrigued by changes she's observed in women's cholesterol levels around the time of the final menstrual period. In January, she published in *Stroke* a paper outlining her findings that the extent of these changes can be used to predict the extent of plaque buildup in coronary arteries about six years later. Interestingly, the women's lipid levels were still well below what would trigger a physician to prescribe a drug or recommend a behavioral change, per current guidelines. This paper suggests that doctors should be aware of not just the absolute cholesterol levels, but also a sizeable uptick therein.

Among Matthews' collaborators is Graduate School of Public Health colleague Samar El Khoudary, the first author on a paper published this January in the *Journal of the American Heart Association*. The study found that high levels of pericardial fat—a type of fat surrounding the heart—may signal a higher risk of heart disease in women who are postmenopausal. This risk is most pronounced at lower levels of estrogen, supporting a potential role of the hormone in explaining this association.

Last fall, Rebecca Thurston, a PhD professor of psychiatry, clinical and translational science, epidemiology, and psychology, published in *Menopause* a SWAN study showing that hot flashes and night sweats are not just a fleeting nuisance, lasting around three to five years, as everyone has always assumed. They last upwards of a decade on average. And hot flashes can point to serious health problems for some women. As detailed in *Stroke* in January, SWAN data revealed four distinct trajectories in menopausal women's cardiovascular health, each with its own outcome pattern. Women with early onset menopausal symptoms were especially at risk, she found. And the unfortunate "super flashers," who have these symptoms for some 15 years, are also at heightened risk for cardiovascular disease.

Now, with a $3.7 million grant from NIA, Thurston's team is connecting menopausal symptoms and cardiovascular health to sleep disturbances, mood, and changes in the cerebral vasculature and other markers of brain aging. This comes after a series of papers from her group linking loneliness, anxiety, depression, and history of physical and sexual abuse in childhood to cardiovascular events down the road.

Thurston—a member of the board of trustees for the North American Menopause Society and recipient of the International Menopause Society's Henry Burger Prize—is a psychologist at the Midlife Health Center at Magee-Womens Hospital of UPMC, one of the few clinics in the country devoted exclusively to the menopause transition. "We try to take this mind-body approach," she says of her MD colleagues Amy Imro, Director Mary Elizabeth Peterson, Kathy Scruggs, and Judith Volkar, each of whom is trained and credentialed in menopause management. At the center, clinical practice is directly informed by the university's robust menopause research efforts.

SWAN participants often tell Matthews they hope for a change for the better in women's health, having grown up at a time when even less was known about menopause, and their mothers wouldn't talk about it. Says Matthews, "A number of them will say that they're doing this [study] so that there can be more information for their daughters." ■

SHARPEN YOUR FACULTIES

SUPPORT FOR NEW PROFESSORS

BY JENNIE DORRIS

Iain Scott, an assistant professor of medicine at the University of Pittsburgh, pauses while appetizers are shared around a table at Soba, a restaurant in Shadyside.

"Did you always think you were going to end up in a position of leadership, or did you fall into it?" he asks, addressing Mark Gladwin, chair of the Department of Medicine, who is sitting at the head of the table. (See p. 8 for a story about his recent work.)

Assistant professors Nathaniel Weathington and Cynthia St. Hilaire nod with interest.

Gladwin laughs and describes the anxiety he used to experience making presentations during his first leadership role as chief resident at Oregon Health and Science University.

"Over time, as confidence grows, it gets easier. You do have to like leadership. You fill vacuums. You fix things," Gladwin says.

Setting up the informal get together was actually an "assignment" for the University of Pittsburgh School of Medicine's Career Mentoring Program (CaMP), which creates contemplative space for junior faculty. The assistant profs were charged with meeting their department chairs to ask burning questions, like: How do they delegate? What happens when they have to discipline a team member? And how do they balance their personal and professional lives?

Ora Weisz, associate dean for faculty development at Pitt med and assistant vice chancellor for faculty excellence in the health sciences, notes that no one even uttered the word "mentor" when she was a junior faculty member. So four years ago, Weisz started CaMP with professors Ann Thompson, vice dean; Jennifer Woodward, associate provost; and Doris Rubio, director of the Data Center at the Center for Research on Health Care. (The organizing committee has since added Gabriella Gosman, vice chair for education for obstetrics, gynecology, and reproductive sciences, and Lori Shutter, vice chair of education for critical care medicine.) CaMP is for faculty members in their second year.

The long-term, in-house approach has received praise from outside consultants, who note that faculty from other universities often have to travel to off-site conferences to learn similar skills. They end up not developing relationships allowing for casual, open conversations that can help smooth their transitions.

Most scientists didn't learn how to run a lab while they were grad students or fellows. But once they are hired as faculty, in addition to pursuing research, teaching, and perhaps seeing patients, they are expected to write grants, balance budgets, and manage employees.

Gladwin compares it to suddenly becoming a small-business owner. "You have venture capital in your program, and you have to be self-sustainable," he says. The series helps junior faculty prepare themselves for these challenges.

It's a juggling act, says Weisz: "It takes about three years to figure out how you should be spending your time. When I was working on my lecture, I felt like I should be in the lab. When I was in the lab, I felt like I should be writing a grant."

Regular meetings also help the new faculty members bond outside of work. At the beginning of the night at Soba, Weathington, who arrived on his bike, was teased by Scott and St. Hilaire for pedaling in the November cold.

Weathington said the CaMP program helped him meet others while doing what can be an isolating job. As he took off his bike helmet, he gestured to Scott and said that without these monthly meetings he would have talked with him only "once or twice in the hall" in the two and a half years they've worked together.

St. Hilaire agreed, noting she can feel detached from colleagues as she works on the top floor of the Biomedical Science Tower, which houses six principal investigators and their labs. "In lab science it's very easy to silo yourself," Weathington says.

With the series, organizers have strived to create a sense of community and involvement, which can be particularly important for the retention of women and faculty from underrepresented groups.

And, Weisz notes, "breaking down barriers is really critical to maintaining innovation in research. Those people who can cross boundaries can make the new sparks that lead research forward." ■

Thomas Starzl at a party that liver transplant recipients threw for him in 1983.

THANK YOU, DR. STARZL

MARCH 11, 1926–MARCH 4, 2017

BY CHUCK STARESINIC

Thomas E. Starzl performed the world's first successful liver transplant in 1967. It's impossible to overstate the difficulty of accomplishing this. Half the blood in the body can flow through the liver in a single minute, and these procedures went on for many hours and through innumerable units of blood. If the patient survived the risky operation, she ran the risk that her immune system would reject the organ. A significant portion of the medical establishment thought that even attempting liver transplantation was wrong and that those suffering from liver disease deserved to die with more dignity.

Yet the seven children (all of Starzl's first liver transplantation patients in 1967 were children) were dying when they came to the O.R. And because of Starzl's bold attempts, in 1968, three were still alive. The other four had lived two to six months, long enough to offer hope for thousands in need. And since 1988, nearly 149,000 people in the United States alone have had liver transplants. The procedure typically adds years, and more often decades, to a patient's life.

Had it not been for Starzl, organ transplantation simply would not be what it is today. Starzl, who died on March 4, was a giant in the field of medicine. He remains an iconic Pittsburgher, akin to Rachel Carson, Fred Rogers, and Roberto Clemente—individuals known for their uncommon combination of skill, determination, courage, and humanity.

"His ability to draw talented individuals into the orbit of his mission, to teach them, to empower them, to grow them, to harden them against fear, doubt, and complacency. To cause them to transcend their own limitations repeatedly. This is beyond leadership. This was his superpower." ***—Ravi Starzl***

Starzl, an MD/PhD and Distinguished University Professor of Surgery, possessed extraordinary qualities required to overcome the obstacles to liver transplantation. First, he had rare surgical skills. ("The best I've ever seen," said longtime colleague Andreas Tzakis. "Where others took two or three moves to get from A to B, Starzl would make a simple acrobatic maneuver that only he could perform.") Second, he devised a way to combine the experimental drug cyclosporine with steroids to better control suppression of the immune system. (This is just one of Starzl's many innovations and discoveries in immunosuppression and enabling a body's immune system to accept a donated organ, also known as achieving "tolerance.") And, he had relentless drive—necessary because success in this endeavor required enduring more failure than most people could stomach.

Starzl's professional accomplishments are celebrated worldwide. On what would have been his 91st birthday this March, several of those who knew and loved him best shared poignant tales that also captured his personal qualities at a "Homegoing Celebration" at Heinz Memorial Chapel on the University of Pittsburgh campus. Joy Starzl, his wife of 35 years, spoke of her husband's private struggles as he worked very publicly to make liver transplantation a reality.

"I heard all those stories when he came home," she said. "When he was angry, when he failed or didn't fail, and how he felt. He shared them with me, and he cried when it was difficult for him. I was there for him, and I'm so grateful I was there for him."

John Fung, founding director of the University of Chicago Transplantation Institute, said that he and others who trained under Starzl were in awe of his genius, tenacity, and humanity. "No one accomplished more, contributed more, or sacrificed more for his profession than Tom," said Fung.

Hollis Hurd spoke as a patient who benefitted from Starzl's career-long investigation of the immunology of organ transplantation and the quest for its holy grail—the induction of tolerance. Before his kidney transplant in 2006, Hurd volunteered to undergo a novel pretreatment designed to spare him the problems associated with lifelong, high-dose immunosuppression. When Hurd asked questions about it, Starzl would grow animated, draw pictures of organ systems on the exam table paper; he once gave Hurd a reading list of scientific papers. "It was just sensational," Hurd recalled. "I was dealing with a real human being who had wonderful ideas and really cared about me. It was the best experience you could imagine."

After Starzl's death, Pitt Chancellor Patrick Gallagher said, "He will be remembered for many things, but perhaps most importantly for the countless lives he saved through his pioneering work."

Mark Nordenberg, Pitt's chancellor emeritus, noted, "We felt privileged to share this campus home with him, and when he said, as he often did, that there was no other place on Earth where he could have advanced his trailblazing work as successfully, it filled our hearts with a special sense of pride."

Renee Williams, 33, who received a liver transplant when she was 14 months old, was interviewed by KDKA, the local CBS affiliate, in March. She said of her doctor, "For a long time, I wanted to make him proud of everything I did. There are no words. I tried to several times, to say thank you." ■

FROM TOP: 1) Starzl on a break skateboarding with his mentor, Henry Bahnson. 2) Starzl (center) talks to Adrian Casavilla (left) and Andreas Tzakis (right) in Pittsburgh in the early 1980s. When Tzakis left Pitt in 1994 to become professor of surgery at the University of Miami, he wrote to Starzl: "Alexander the Great once said of his teacher: 'To my father I owe my life..., to my teacher I owe my good life...' I am in eternal debt to you." 3) Starzl high-fives a young patient. 4) In September 1980, (from left) Denver organ retrieval team members Shunzaburo Iwatsuki, Starzl, and Richard Rubenstein with Sioux City's Gerald Jurkovich. 5) The animal lover typically had a few dogs in his office.

SUPERPOWER SHORT LIST

Professional highlights from a transformative career:

Despite worldwide pessimism regarding the ability to transplant genetically different (allogeneic) human kidneys, Thomas E. Starzl did so at the University of Colorado in 1962 and 1963. His method successfully combined azathioprine and corticosteroids to quell the immune response; that approach invigorated clinical attempts throughout the world.

Starzl's early work helped pave the way to allow donated organs to be viable after being transported long distances.

Starzl performed the world's first liver transplant in 1963 and the first successful liver transplant in 1967, both while at the Univesity of Colorado.

Starzl joined the University of Pittsburgh in 1981 as professor of surgery and led the team of surgeons who performed Pittsburgh's first liver transplant. Thirty liver transplants were performed that year, launching the liver transplant program—the only one in the nation at the time.

Starzl also introduced antilymphocyte globulin and cyclosporine to prevent organ rejection. It was this development in 1980 that advanced transplantation from an experimental procedure to an accepted form of treatment for patients with end-stage liver, kidney, and heart disease. The advance also allowed surgeons to explore the feasibility of transplanting other organs, such as the pancreas and lung.

Human islet transplantation (to cure diabetes) was accomplished successfully for the first time by Starzl's team at Pitt.

In 1989, Starzl announced the first-time use of FK506 (tacrolimus) as a more effective antirejection agent. FK506 greatly improved patient and graft survival rates for liver and other organ transplants and made intestinal transplantation possible. Five years later, FK506 was approved for clinical use by the U.S. Food and Drug Administration.

A major focus of Starzl's later research was transplant tolerance and chimerism (the coexistence of cells from both the donor and recipient). This work offered significant contributions to the understanding of transplant immunology, particularly with respect to how and why organs are accepted.

Starzl was the recipient of more than 200 honors, including the Lasker-DeBakey Clinical Medical Research Award, the Presidential National Medal of Science, and 26 honorary doctorates from universities around the world.

He authored or coauthored more than 2,200 scientific articles, four books, and 300 book chapters. From 1985 to 1999, Starzl averaged one paper every 3.5 days.

In 1999, the Institute for Scientific Information identified him as the most cited scientist in the field of clinical medicine. His citation frequency exceeded 2,000 per year for the period 1989-2007, with a peak of 4,224 citations in the year 1996. That's one citation every 30 minutes.

The book, *1,000 Years, 1,000 People: Ranking the Men and Women Who Shaped the Millennium*, placed Starzl 213th on its list of those having the greatest influence on the world in the past millennium.

Sources: The Official Dr. Thomas E. Starzl Web site and the University of Pittsburgh.
To learn more about this giant of medicine, read our two-part series: www.pittmed.health.pitt.edu/story/only-starzl-dared

PP. 14–15 PHOTOS: UNIVERSITY OF PITTSBURGH

Starzl, c. 1990.

CUT OFF

A BEREFT NERVOUS SYSTEM MAY EAT AWAY AT THE WILL TO LIVE

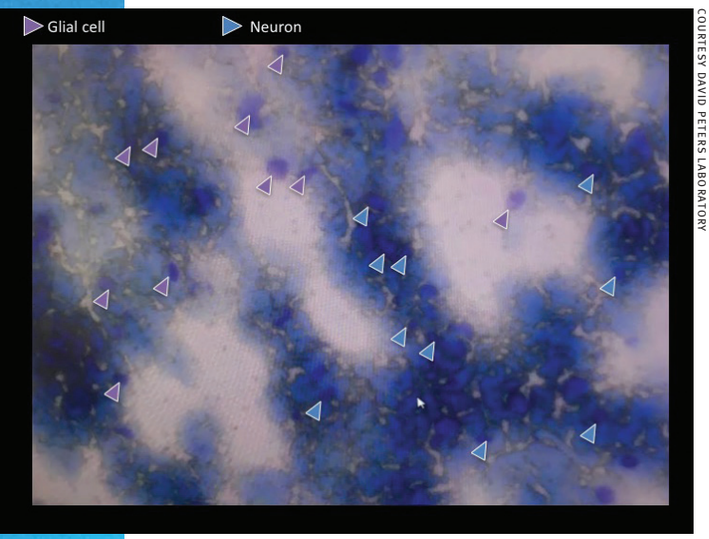
BY ELAINE VITONE

Eve was 12 when she first started thinking about suicide. By the time she was a senior in high school, she'd tried several times. Then one morning, alone at home, she downed a lethal dose of pills. The only reason Eve lived to graduation day was that her parents unexpectedly doubled back that morning. She wound up in the ICU and barely survived.

As her classmates were moving on to start college, pick roommates and majors, and fall in and out of love, Eve (not the patient's real name) and her medical team were trying everything under the sun for her severe and unrelenting depression: SSRIs, mood stabilizers, antipsychotics, even experimental medications typically prescribed to ALS patients. She had dozens of electroconvulsive therapy treatments, and for a few days she seemed to improve. Then she crashed again, suddenly and horribly. At this point, Eve was hospitalized and on 17 medicines, and she was still trying to end her life.

Certain vitamins and other supplements have turned around severe, previously intractable depression in some adolescents.

ILLUSTRATIONS | JESSE LENZ



COURTESY DAVID PETERS LABORATORY

David Peters is examining post-mortem neurons like these from individuals diagnosed with treatment-refractory major depression to identify novel biomarkers. Earlier identification of such individuals may provide alternative treatment plans and thus relieve the depressive symptoms sooner.

"I went up to see her," recalls her doctor, Lisa Pan, years later, "and there was *nothing*. No side effects. No response. *Nothing*. … And I thought, *I have never seen anything like this. What* is *this*?"

The University of Pittsburgh's Pan (Res '03, Res '05, Fel '08) began her research career studying neuroimaging markers of suicide risk in young people. In the clinic, she trained under the wing of David Brent (Res '82, Fel '85), a professor of psychiatry and pediatrics who holds Pitt's Endowed Chair in Suicide Studies and is arguably among the world's foremost experts on treatment-resistant depression (also called treatment-refractory depression) and suicidal behavior in teens. Thirty years ago, Brent envisioned and cofounded Services for Teens at Risk, or STAR, at Western Psychiatric Institute and Clinic. STAR remains one of only a handful of clinics in the country that specialize in this population. Over the years, the crosstalk between research and care at STAR has helped to elucidate suicide epidemiology, risk factors, and treatments, and to establish national guidelines for the management of adolescent depression and suicidal behavior. Brent is a member of the National Academy of Medicine (formerly the Institute of Medicine).

It was on this fertile ground for discovery that Pan, an up-and-coming physician-scientist, found the inspiration to take a way-out-of-the-box approach, with Brent's support.

Pan went to another mentor, David Finegold, a professor of human genetics in Pitt's Graduate School of Public Health. She asked what he thought of examining a lumbar-puncture test (a sampling of cerebrospinal fluid, or CSF) for clues of what was circulating in Eve's central nervous system. Could they check her neurotransmitters, look for any new leads at all? Finegold's answer: Absolutely. In fact, why not do a bigger workup, the kind that is standard when a child presents with signs of a neurological disorder?

As it turned out, Eve's CSF level of biopterin, a chemical the body uses to synthesize several neurotransmitters, was through the floor. Pan and Brent started her on a replacement-therapy regimen, and over the next few months, the team observed the gradual return of this long-absent chemical so crucial to the production of serotonin, dopamine, norepinephrine, pain modulators, and melatonin. And it had a profound effect on Eve.

Within the first week, her affect changed dramatically. She landscaped the family's entire yard in a day. At week three, she became more emotional. Suddenly she was crying over TV commercials and falling in love with the stranger on the line when she phoned in her order for a pizza.

And then, on day 31, a calm after the storm.

Her mood was low at first, but it gradually improved. She had bouts of shaking, insomnia, and trouble finding the right words, but as Pan adjusted Eve's medication dosage and frequency, the side effects subsided. Ten weeks in, she was feeling what psychiatrists call euthymia—medicalspeak for normal.

Six years later, with continued treatment for her biochemical disorder, Eve has a college degree and a job, says Pan, who, with Eve's permission, published her case in the *British Medical Journal* in 2011 and has discussed it at several well-received talks. Eve herself declines interviews about those lightless days. She's more interested in moving on, at last feeling like other young people—and finally having an adulthood and a tomorrow to plan for.

Pan and her team were skeptical at first. This must be a fluke, the scientists told themselves, an incredibly lucky break. Then they tried the same screening on three more patients suffering from treatment-resistant depression, figuring they were long shots, as well.

But all three turned out to have similar metabolic disorders, all of which improved once their systems were regularly "fed" with pills, powders, or IVs—special, highly absorbable forms of what were essentially vitamins.

In most of these patients, the trouble was folate metabolism.

Psychiatrists routinely order blood tests for this vitamin because its depletion is known to affect mood. But these patients' blood levels checked out fine. "So either something was happening with the body's ability to break down the folate enough to have it cross the blood-brain barrier or [with] the body's ability to move it across the blood-brain barrier," Pan says.

The scientists' disbelief sharpened to questions: How did these biochemical anomalies happen to these young people in the first place? Could there be others who are one lumbar-puncture test away from finding their own paths to recovery? And what if the team could do one better—build a cheaper and easier test? Could even more patients be spared years of suffering, or even death?

Practically overnight, these investigations became the new focus of Pan's career. Their first phase culminated this past August in a study in the *American Journal of Psychiatry*, and that was one of the most lauded psychiatry papers of 2016. Though the study was small—just 33 patients—the results were striking. Of these young people with treatment-resistant depression, 64 percent had some form of metabolic deficiency of the central nervous system; controls had

absolutely none. And once the patients' deficiencies were treated, the majority of their symptoms improved. For two of them, depression vanished altogether.

With each press hit, public interest in the work has surged. For Pan's team, it's been like drinking from a fire hose, e-mails and calls from all over the country continuing to flood in: *Can you see my son? Where can I get tested?*

"We spoke with 42 people yesterday," Pan told me the day after the story made *Forbes* last summer. Pan, a professor of psychiatry and of clinical and translational science, practically bubbles over with enthusiasm when she talks about this work. She talks *fast* ("I'm from Philadelphia," she says, by way of explanation), is extremely attached to her phone, and knows scores of patients' phone numbers by heart.

Pan now divides her time between seeing patients at STAR, many of whom travel from out of state; overseeing a small yet mighty testing-referral and care-coordination service for those calling and writing in from around the country; and conducting her research with an ever-expanding list of collaborators both inside and outside the University of Pittsburgh.

ity. But almost all of the patients who enrolled had at least thought about ending their lives.

For all we know about risk factors, says Pan, the problem is that we still can't tell which young adults with depression will die of suicide. Solving this puzzle is her life's work.

Soon after making their discovery about Eve, the team contacted Jerry Vockley for guidance.

An MD/PhD and chief of medical genetics at Children's Hospital of Pittsburgh of UPMC and professor of pediatrics at Pitt, Vockley directs a research program on inherited disorders of energy and protein metabolism. In recent years, he has identified the molecular basis of three.

JOSHUA FRANZOS

Lisa Pan

Vockley explains that the body is a highly efficient factory, churning away ceaselessly in chemical reactions that beget chemical reactions to turn one thing into another into another. This factory's products are our very life, growth, and health. But a flaw in the DNA that is foreman to the entire factory floor can gum up the works in curious ways.

And the same may be true for depression.

With Vockley, the team developed a panel of neurometabolic tests to aid in their search for other known disorders that might be underlying cases of life-threatening depression.

In 2014, Pan's team won a Pitt Innovation Challenge Award from the Clinical and Translational Science Institute to launch their

Once, someone told Eve her trouble was that she just wasn't working hard enough in therapy. Then her doctor learned that she may not be able to make neurotransmitters.

Once, someone told Eve her trouble was that she just wasn't working hard enough in therapy. "And then, you find out she may not be able to make neurotransmitters," says Pan.

In psychiatry, she says, "we're not so far along yet that we know exactly what we're treating. . . . When we approach mental illness, we need to keep an open mind about what might be occurring that we don't understand."

Of the 15 million American adults with major depression, 15 percent do not respond to any available treatments. When Pan first launched her studies, this was the main criterion—treatment-resistant depression, not suicidal-

At that point, it's like a clogged pipe, says Vockley. You'll have one of two problems: either a deficit—no water coming out of the faucet—"or you have a backup of things that shouldn't be there going to places they shouldn't be, like a flood in your basement. That can be toxic to the body. So the body is literally poisoning itself."

Medical genetics is a specialty of last resort, the place patients and their families turn to when their doctors diagnose them with mysterious and troubling conditions like "failure to thrive." But these are symptoms—basement floods, water outages—not diseases. The disease is the cause. For a symptom like intellectual disability, for example, there are literally hundreds of genetic causes to consider.

headlining study. (More funding followed from the American Foundation for Suicide Prevention, the Brain and Behavior Research Foundation, two anonymous donors of Children's Hospital of Pittsburgh Foundation, Joe and Louise Lohman, and The Fine Foundation.) The support allowed Vockley to develop a new panel casting a wider net in the search for patient subsets.

Though Vockley was intrigued by the possibilities, even he had his doubts as the first several patients began to recover.

"I'm no longer skeptical," he says, recalling, among many young people with similar stories, a woman who tried to hide in a corner on the floor. "She couldn't even face me. I examined her under the exam table.

"I couldn't believe she was still alive. This had been going on for years." But the team identified a metabolic deficiency in this young woman's nervous system and treated it. The patient continues to struggle but is no longer suicidal.

The team is hard at work on a multifront research effort: validating their findings in a larger patient sample; examining possible genetic and environmental factors in these deficiencies; widening their scope to include more metabolites; and developing a bigger, better test.

This is not a treatment study, Pan is careful to note. And it's certainly not a double-blind comparison of an experimental treatment versus placebo. It is an effort to understand some of the molecular mechanics of treatment-resistant depression and suicidal behavior, to begin to characterize the biological bases of the many diseases we now lump together under the same umbrella.

"And *then*, moving forward, potentially with help, we may later consider treatment studies," Pan says. (Colleagues at Harvard, Northwestern, and McGill are already lining up to collaborate.)

At STAR, counselors on Pan's team, who are trained in suicide risk assessment, evaluate and enroll study participants. Patients' CSF and blood samples are collected and tested, and if a CSF test reveals a metabolic disorder, Pan's team refers the patient to biochemical genetics for treatment.

The patient returns to STAR six months later for follow-up.

"The lab result actually directly informs the treatment," says Brent. "It's much closer to precision medicine than many things we're doing in psychiatry."

Meanwhile, Robert Naviaux, a colleague in the genetics division at UC San Diego, runs a broad-spectrum analysis on the plasma samples, examining some 600 different metabolites for potential new markers of the disorders the team is finding. And in Pittsburgh, postdoctoral fellow Lora McClain mines the patients' genetic data for variants that might be culprits. This enormous task, at 150,000 data points per study participant, is her sole focus.

Mental illness has always been a difficult challenge from a geneticist's standpoint because there are still woefully few biological measures for psychiatric diagnoses. So even zeroing in on the right patient population to study—the phenotype, as this is called—has been a problem. "But what Lisa has done is filtered it down to depression in the most extreme phenotype," says Finegold.

From the original 33 participants, the study has quickly expanded to 140. And at last count, the finding was still holding up: 57 percent of those tested have a metabolic disorder of the nervous system, all of which are treatable.

Thus far, the team has identified five distinct metabolic deficiencies. (Cerebral-folate deficiency accounts for the lion's share, affecting about a third of the patients enrolled in the study overall.) And for each deficiency, the team is beginning to identify multiple gene variants that are likely implicated.

Interestingly, the study is not just illuminating depression; it's also adding new wrinkles to the science of several other neurological diseases.

Cerebral-folate deficiency, for example, has long been known to cause neurological disorders, sometimes with mood changes as well. But the folate-deficient patients in Pan's study, who present with depression as their only symptom, are believed to be the first of their kind ever documented. And for another metabolic deficiency the team has found in this patient population, an extremely rare disease called lamin B1 deficiency, depression had not been known to be a presenting symptom. Yet another patient subgroup appears to have a mitochondrial disorder—cellular-energy metabolism gone awry—which Pitt postdoc Kaitlyn Bloom is working to get to the bottom of.

The human brain doesn't exactly lend itself to biopsy, notes David Peters, a collaborator with the team for going on two years now. The next best thing, cerebrospinal fluid testing, is kind of like tapping a sewer line.

"It likely reflects the molecular physiological nature of the entire brain," says Peters. So, how do you take this mixed sample, sift through it, and figure out what it's telling you? And how does that translate to an even more distant cousin, the blood?

Peters, an associate professor of obstetrics, gynecology, and reproductive sciences, has in the works a new technology that may help. Funded by the Children's Hospital of Pittsburgh Foundation, a "stethoscope for the brain" will aid the scientists as they comb through samples for clues.

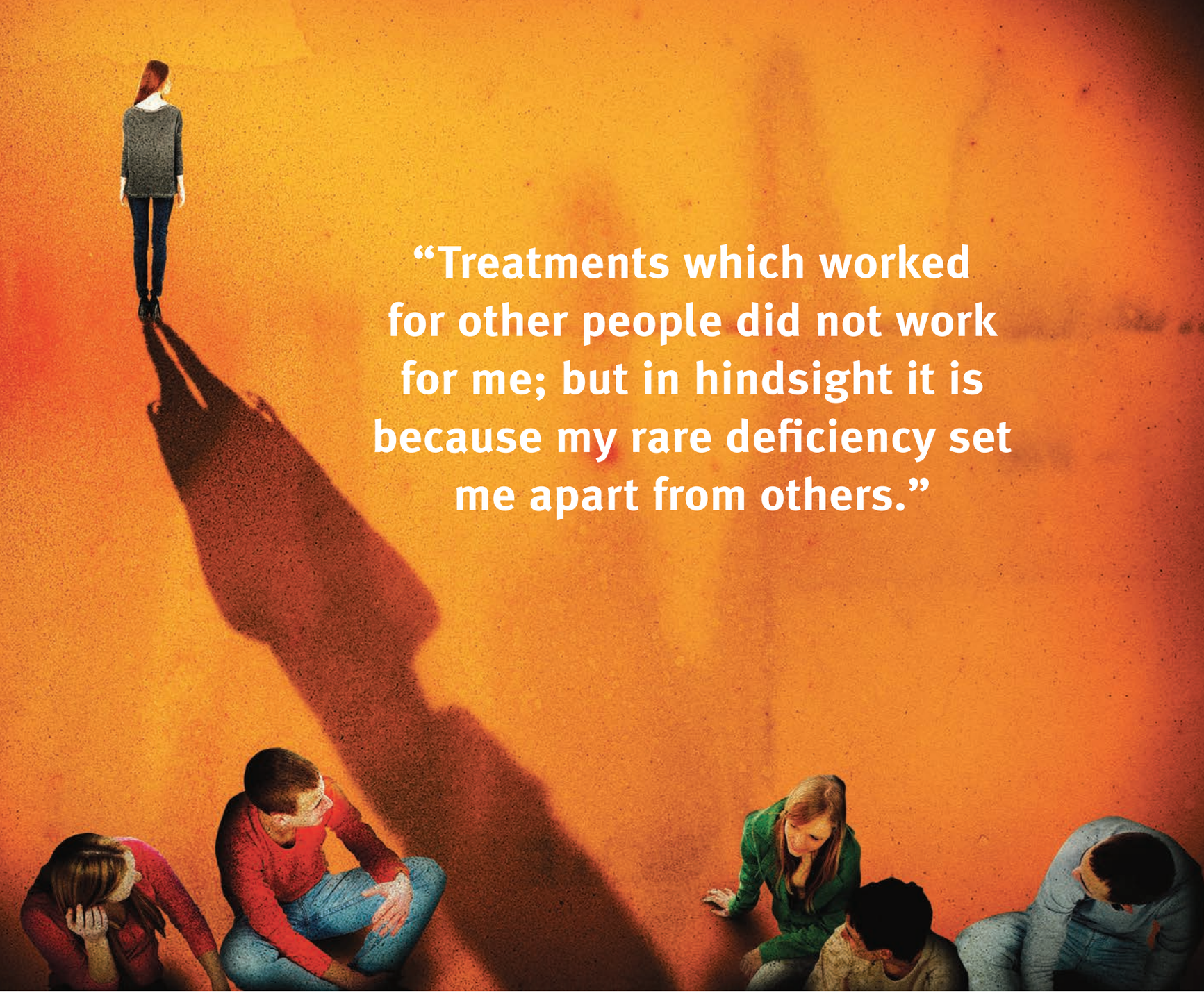
Another investigation led by Peters draws from Pan's expertise in imaging-based markers of suicidality. Previously, using functional neuroimaging, she identified areas in the brain that are associated with a past suicide attempt. Now the team is examining brains donated by people who've died of suicide, with particular focus on these areas.

Finegold, who can't say enough glowing things about Pan ("She understands genetics really well; I'm essentially superfluous"), is optimistic that Pan's findings are not only the tip of the iceberg in treatment-resistant depression, but also a possible starting point for much more. For example, how much of this metabolic-disease framework would transfer over to schizophrenia? If you can develop a new paradigm, he says, sometimes it will work elsewhere, and you can expand it, and sometimes it won't. "But if it doesn't fit, you learn a lot about *why* it doesn't fit."

Pan notes that for many patients, depression and suicidal behavior begin in times of physiologic stress. Which makes her wonder if there are parallels in postpartum depression. A possible multi-institutional collaboration along these lines is in its early stages. "Are these maybe people who have some of these metabolic disorders, and there's been a physiologic change that sets it off?"

Brent, famously rigorous in his approaches, notes that causality is something the team must continue to question. By the time patients walk through STAR's door, they've been suffering from their symptoms for more than a decade. "We don't know whether these [metabolic disorders] cause depression, or whether they emerge secondary to depression," says Brent.

Hence, Pan plans to also study patients who have less severe cases of depression that *do* respond to treatment, in hopes of discovering what sets them apart.



Pan has “a frighteningly good memory,” says Peters, just after one of the team’s Skype meetings that connect the investigators from their offices across Oakland and Lawrenceville several times a week. As they discuss what the data are telling them, Pan computes it all in her head and churns out lists on the spot. *Oh no, absolutely, this is patient X, patient Y, and patient Z,* she says, describing their cases with clarity and detail that are downright “scary,” Peters notes, laughing.

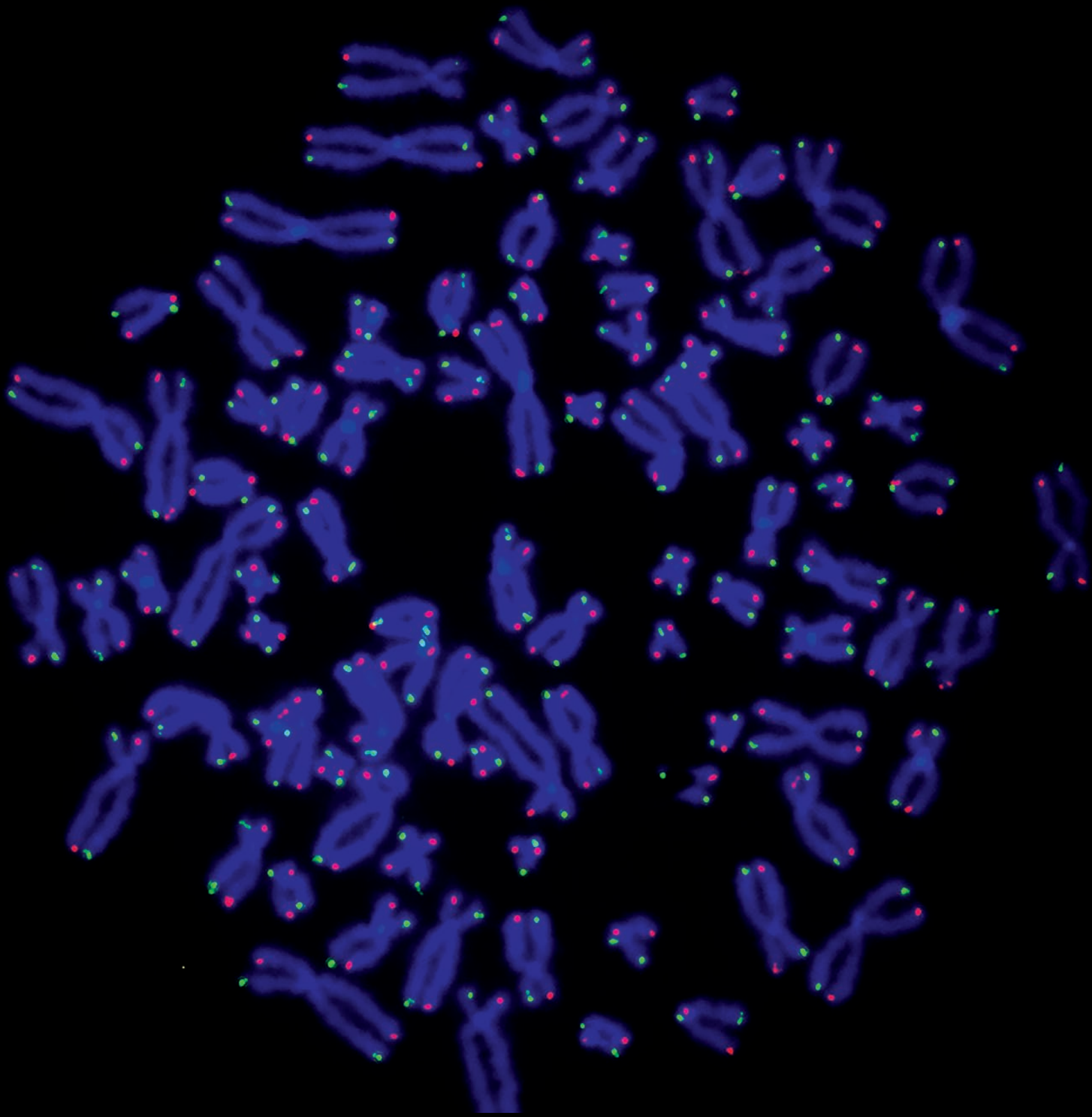
And as the team sketches out the blueprints for what they will build next, these kids are never far from her mind. Pan doesn’t necessarily want the study design that will ensure the quickest way to a grant proposal, says Peters. “She’ll say, ‘I just want to do this because I want to know why such and such is happening.’”

“She’s not distracted by the beauty of the science. It’s: How do we help these poor souls?” he adds.

A growing number of young people are getting their lives back, and that’s happening in a place where care informs science and science informs care.

Recently, the first of them, the archetypal Eve for this potential new paradigm in psychiatry, wrote as much in an e-mail to her former doctor (who still recalls Eve’s phone number six years later):

I owe my life to the successful diagnosis of my biopterin deficiency. Trial after medical trial, there came a point when living what I thought to be a normal life was unfathomable. Treatments which worked for other people did not work for me; but in hindsight it is because my rare deficiency set me apart from others. Were it not for the identification and treatment of this illness, my current success as both a double major and dean’s list student would not be possible. Diagnosis of this medical illness undoubtedly gave me the opportunity to live a life of my own: one with a future. ■



CANCER'S LIFELINES

THE LONG AND THE SHORT OF TELOMERES

BY JASON BITTEL

Like us, our cells are mortal. Each time they divide, the tiny, protective caps at the ends of our chromosomes—our telomeres—get shorter and shorter, sort of like a fuse. When enough of the fuses burn out, the body senses that the cell has run its course and moves into self-destruct protocol. This is the cellular circle of life, a perfectly natural event that happens innumerable times within your body each day. It's probably happening right now.

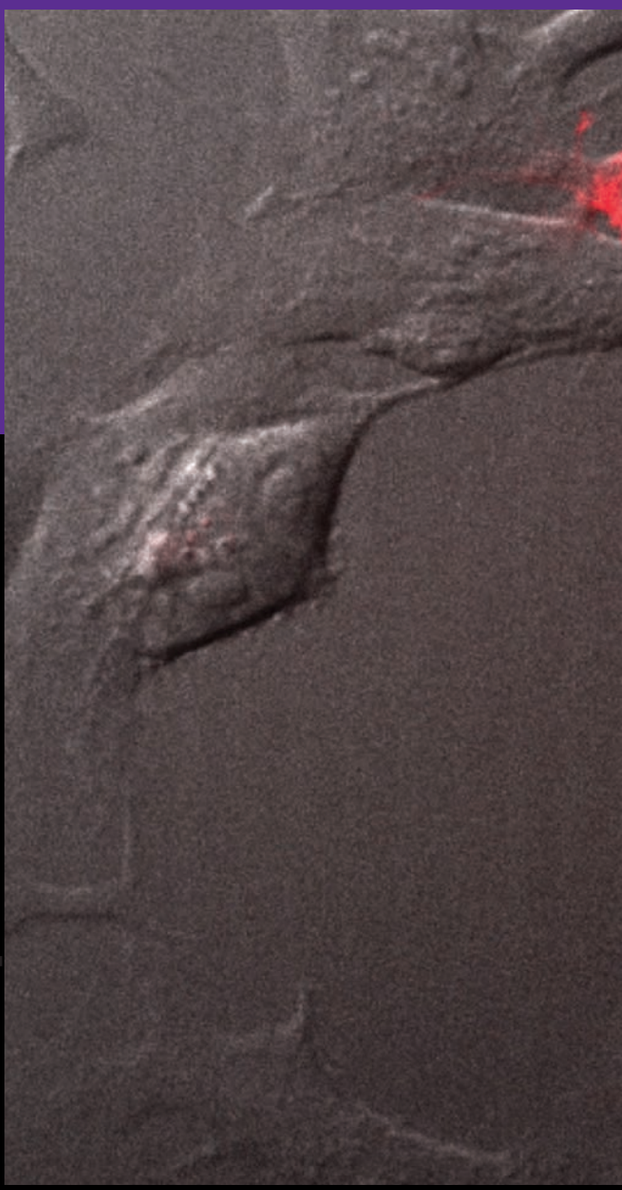
For cancer cells, however, mortality is often sidestepped; they are masters at gaming the body's built-in self-destruct apparatus. One way that cancer cells (about 85 percent of them) do this is by producing telomerase, an enzyme used in our own stem cells to rebuild telomeres.

"Once the cell is able to maintain its chromosomes on its own, then it becomes quite dangerous," says Patricia Opresko, a molecular biologist and associate professor of environmental and occupational health in the Graduate School of Public Health and in the University of Pittsburgh Cancer Institute (UPCI). This is because the cancer cell can now live through things normal cells can't. And as it does so, it gets stronger.

IMMORTALITY UNDONE: Telomeres, often described as the shoelace-cap-like structures on the ends of our chromosomes, have been eyed by some as the key to human longevity. A crew of Pitt scientists and their colleagues are more immediately interested in the job telomeres do for tumors, i.e., serving as infuriatingly effective lifelines for cancer cells.

The key to killing cancer probably means aiming at targets much, much smaller than the width of a cell. And for that we need to peer deeper. In this image, prepared by Pitt's Roderick O'Sullivan, you can see actual, individual chromosomes; it looks like a petri dish of blue bowties. On the ends of each chromosome, notice the tiny, glowing dots. Each dot represents one telomere. We can even tell the lagging strand (green) apart from the leading strand (red).

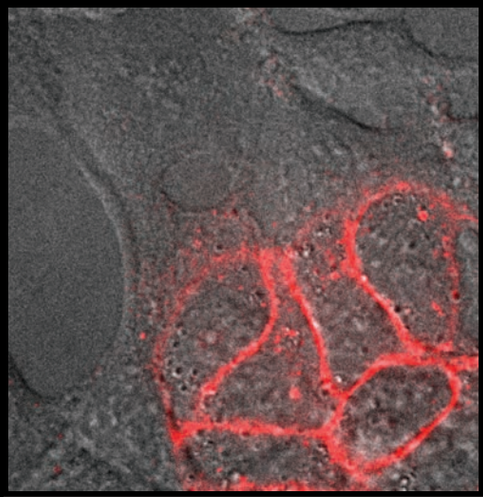
IMAGE COURTESY RODERICK O'SULLIVAN LAB

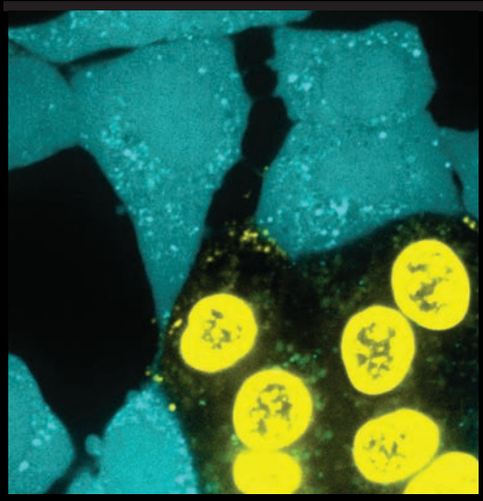


SEARCH AND DESTROY: At 1 to 2 micrometers in length, chromosomes are about 50 times tinier than a dust speck. And telomeres, the coatings that protect the chromosome's tips, are, of course, even smaller. According to one popular analogy, if a chromosome were the length of a car, then the telomere would be about the width of its license plate.

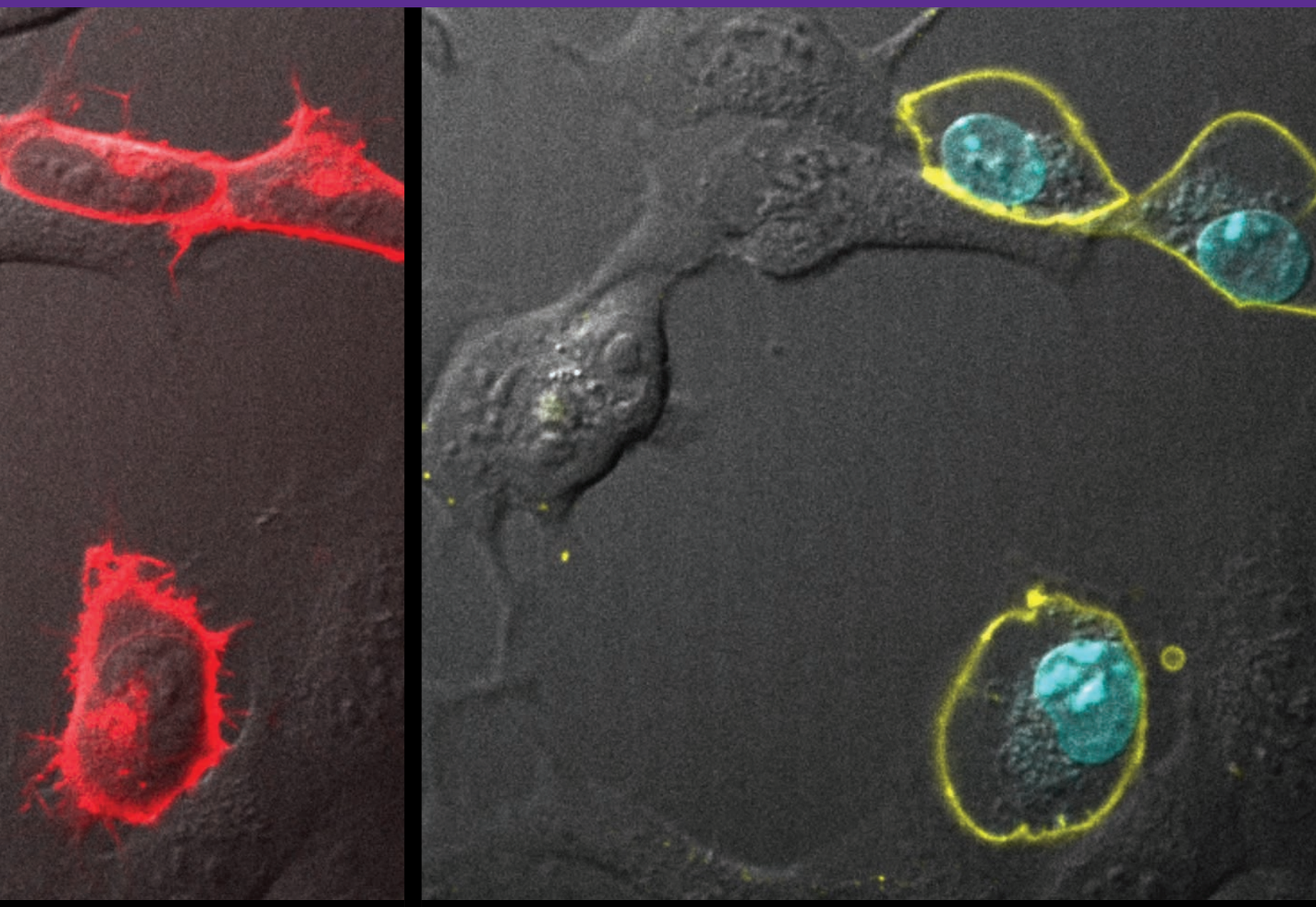
This gives you some idea how difficult it is for scientists not only to see the structures, but also to target them in any precise way. This is where Marcel Bruchez, a member of the Molecular and Cancer Biology program at UPCI and chemical biologist at Carnegie Mellon, comes in. "My goal is to figure out how to measure things that happen in biological systems," says Bruchez. "But the problem with biological systems is they all look the same from a distance. Everything's basically just bags of water, protein, and nucleic acids, and there's not a lot of specific contrast you can get out of that unless you add something to it."

To overcome this, Bruchez has rigged up 14 pairings of proteins and fluorescent dyes (engineered bits of human antibodies) that allow us to label bewilderingly small targets. What's more, when these fluorogen-activating proteins, or FAPs, are exposed to even short bursts of light, they generate higher energy oxygen molecules (singlet oxygen), which cause oxidative damage. In the top images to the right, we can see cancer cells, and only cancer cells, labeled in red. Then, in the next image, we see these same cells exposed to light and destroyed with precision (yellow), while neighboring cells (blue) are left completely unharmed.





IMAGES COURTESY MARCEL BRUCHEZ LAB



"Cancer cells accumulate all these chromosomal changes and rearrangements that they can potentially take advantage of to evade the things we throw at them, like chemotherapeutics and ionizing radiation," says Opresko.

What's interesting is that cancer cells don't typically use telomerase to create long, youthful telomere fuses. Instead, they create short, stubby telomeres just long enough to keep the Bureau of Programmed Cell Death off their backs. And it's this weakness scientists hope to exploit. Remember, shorter telomeres are just a breath away from self-destruction. So if researchers could figure out a way to inhibit telomerase production in cancer cells, it shouldn't take long for those fuses to burn out on their own.

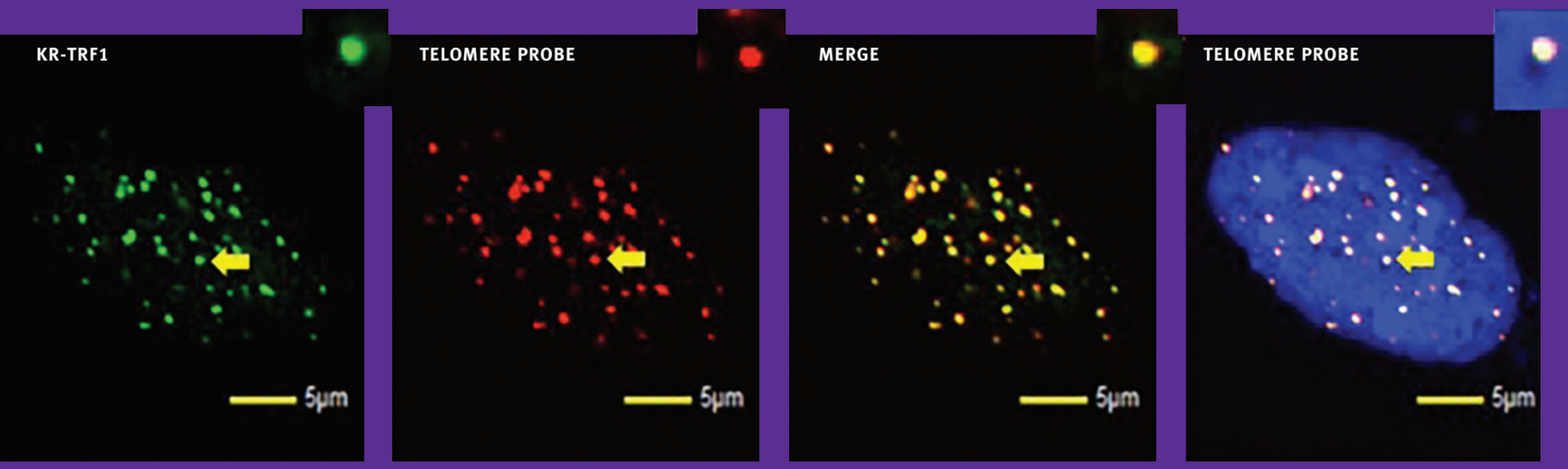
Unfortunately, telomerase is only one pathway to tumor immortality.

In just the past two decades, scientists have discovered that some cancers can perform a sort of chromosomal alley-oop, where a short telomere can actually fix itself by copying and pasting what it needs from a long telomere found elsewhere in the cell. This is what's known as homologous recombination. Homologous recombination is crucial for conjuring up new sperm and egg cells, by the way. It's also employed by the 15 percent of cancers that use what's known as the alternative lengthening of telomeres, or ALT.

"A lot of these cancers are the really, really bad ones," says Roderick O'Sullivan, a Pitt assistant professor of pharmacology and chemical biology, who specializes in ALT. "They tend to be resistant to chemotherapy. And usually, by the time you identify them, [it's] too late."

What's particularly frustrating is that while some cancers are typically telomerase-based and others are ALT-based, the two can also work in tandem. A patient suffering from pancreatic cancer can

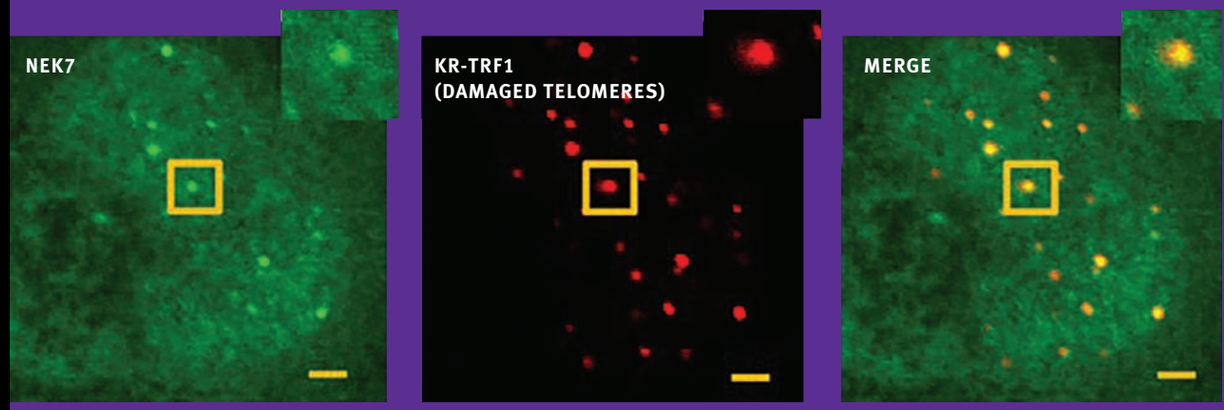
ZOOMING IN: The larger images show the same scenario portrayed on the preceding page but in more detail. The cells are first targeted with FAP (red), then exposed to 15 seconds of light at the extreme red end of the visible spectrum. Unlike ultraviolet light, wavelengths on this end of the spectrum are usually innocuous, which means the scientists can use them to trigger oxidative damage where they need it, without worrying about doing harm elsewhere in the cell. An hour after exposure, we can see that the targeted cells are already starting to self-destruct (yellow).



LASER TARGETED MICROBIOLOGY: In this first row of images, Pitt's Li Lan shows how the KillerRed dye (stained green) can be attached to sites of individual telomeres (marked by a telomere probe with red dots). Blue staining is an individual nucleus. By breaking these components down in highly specific ways, Lan says, we can better understand how cancer cells build themselves back up.

KEYS TO IMMORTALITY: One way cancer cells repair damage is with an enzyme, a kinase called Nek7. In the second row of images, you can see the tiny dots of Nek7 glowing green, then the telomere-targeted damage caused by KillerRed (in red), and finally an overlay showing that Nek7 comes in to stabilize the telomere once it's been damaged. No one knew this interaction existed until Lan brought it to light in a paper published by *Molecular Cell* in March.

THIS PAGE: IMAGES COURTESY LI LAN LAB



have some cells wielding telomerase and some using ALT. Even in a single tumor, both pathways can exist. And what's worse, O'Sullivan says, is that if you inhibit telomerase production in some cancer cells, you can actually activate ALT.

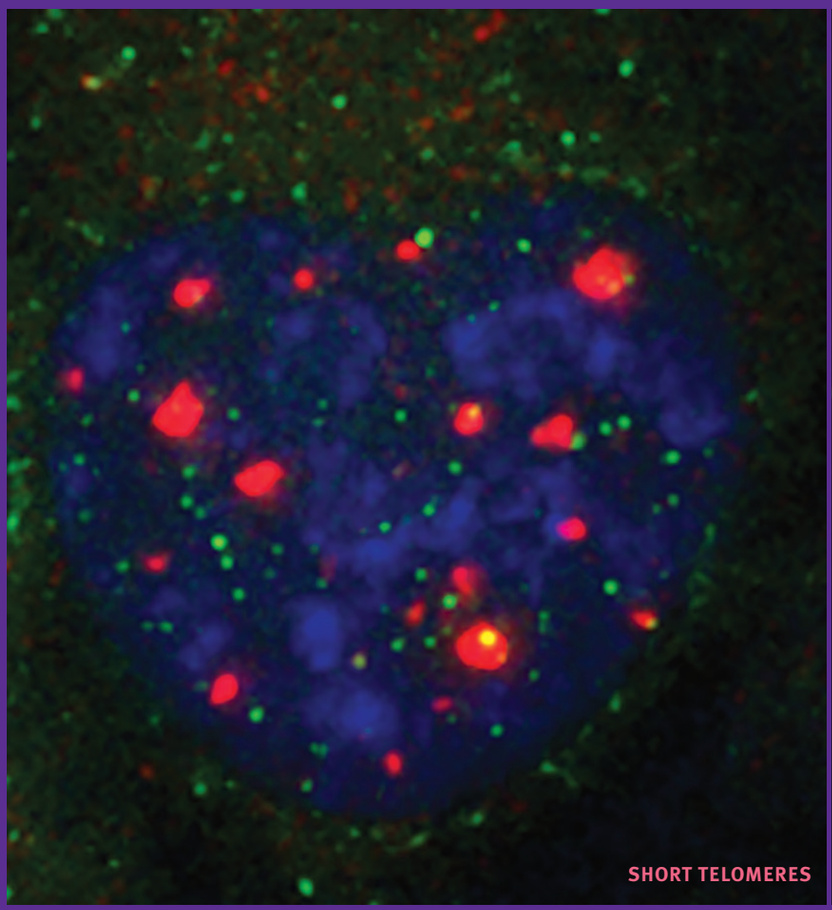
But even immortal cells have weaknesses. And thanks to Opresko, O'Sullivan, and other Pitt people, we're learning more about these vulnerabilities every day. In fact, one way to hamstring these little nasties may be to hit them with a weapon as ancient as life itself—oxidation.

You see, life has been battling with oxidative stress and its constant, caustic bombardments to cellular machinery for perhaps 4 billion years. In fact, the advent of oxygen in the atomosphere is considered one of Earth's first major polluting events.

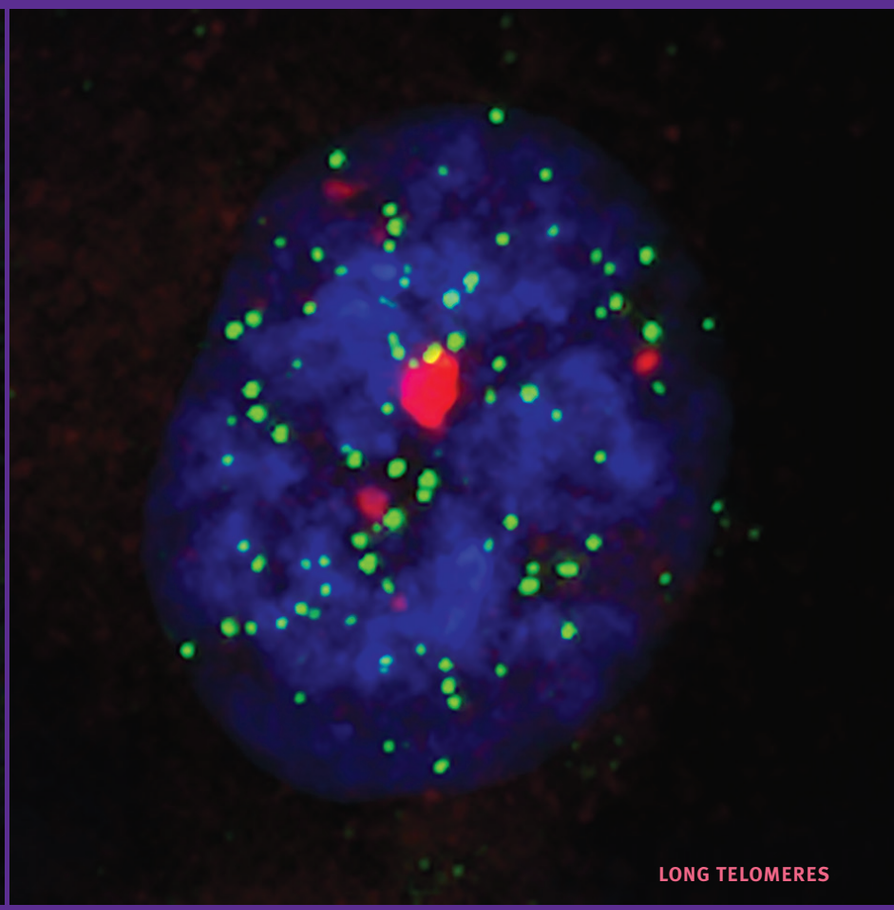
"It's no coincidence that life didn't crawl out of the muck until it had evolved strong pathways for limiting oxidative damage," says Ben Van Houten, Richard M. Cyert Professor of Molecular Oncology in the Department of Pharmacology and Chemical Biology.

What's more, organisms developed ways to take the lemons of oxidative damage known as free radicals and turn them into lemonade. "Our bodies are bathed in DNA damage," says Van Houten. "And actually, a little bit of damage is good for you."

Despite their reputation for contributing to disease and aging, free radicals help us digest our food, kill microbes, and power our muscles and brains. Opresko has even found that, under certain con-



SHORT TELOMERES



LONG TELOMERES

ditions, free radicals can help lengthen telomeres. But too many free radicals scratch away at our cells' internal workings like trillions of tiny, raspy dogs at the back door.

It appears as though cancer cells have even more free radicals bouncing around inside them than regular cells. Cancer cells are really good at processing free radicals before they can cause too much oxidative damage. But if we could inhibit the cancer cell's ability to do so, oxidative damage would theoretically build up to such levels that the cell could not survive.

The Opresko lab has adapted Marcel Bruchez's fluorogen-activating protein technology (see caption p. 24) to constantly bombard the telomeres of cancer cells with targeted oxidative damage to see how they hold up. Preliminary results: not well. "If you continually hammer away at those telomeres, they start to become really unhappy," she says.

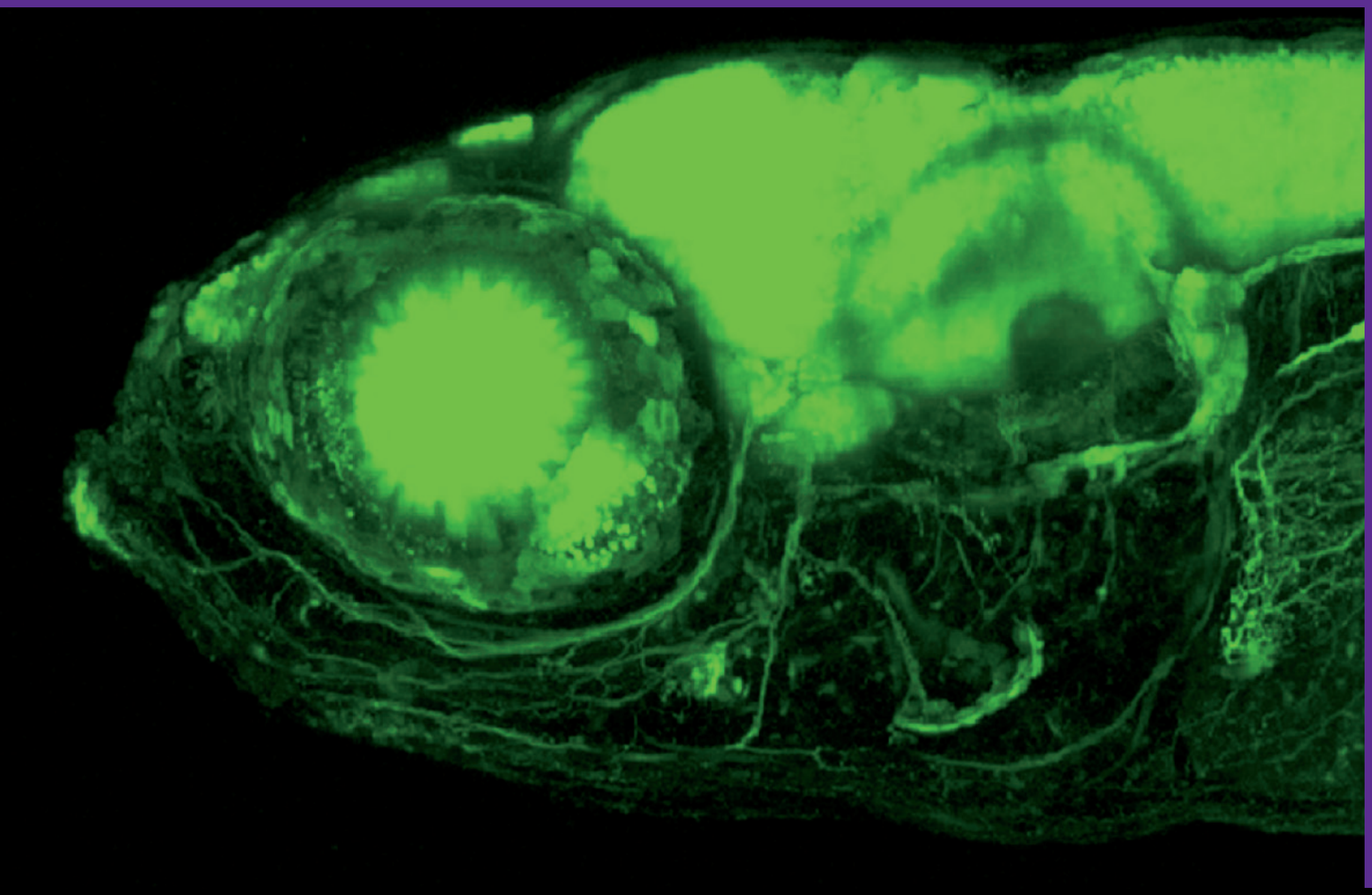
Another researcher, Pitt's Li Lan, MD/PhD assistant professor of microbiology and molecular genetics, has been using a fluorescent protein from jellyfish called KillerRed to inflict oxidative damage at the sections of DNA that produce genes. Similarly, Van Houten wants to understand how oxidative damage mangles mitochondrial DNA and what role that might play in bringing down the beast that is cancer.

These scientists are in search of cancer's Achilles' heel (or heels). And though Van Houten stresses that what they are doing is basic science and not developing any immediate new treatments, he can't help but be optimistic about the armory of techniques he and his colleagues have assembled to probe an adversary known for its ability to duck what medicine throws at it. "This work could change cancer therapy as we know it," Van Houten says. ■

LONG LIVED: With this image set, Patricia Opresko aimed to find out how a cancer line with traditionally short telomeres performed in comparison to a cancer line with uncharacteristically long telomeres when each was treated with inhibitors that prevented the cells from cleaning out telomere building blocks that had been damaged by free radicals. As predicted, both cells endured a great deal of oxidative damage, but the cells with the short telomeres (shown left) appeared to suffer a great deal more than their long-telomered cousins (right). "Every red spot is marking some sort of damage, either a chromosome break or a telomere that can't form its nice structure," says Opresko. The work was published in *Nature Structural and Molecular Biology* in December.

Studies like this tell us that cancer cells with short telomeres are extremely vulnerable to manipulation of their antioxidant mechanism. If doctors can develop therapies aimed at this mechanism, then they may be able to make cancer see red not just in a petri dish, but wherever it crops up in the human body.

THIS PAGE: IMAGES BY ELISE FOUQUEREL, OPRESKO LAB



JUST KEEP SWIMMING: To really understand what oxidative damage does to telomeres, we also need methods for taking what we learn in petri dishes and applying that to living systems. This is why Pitt's Edward Burton (an MD/DPhil) is teaming up with Opresko and others. Burton, a neurologist, doesn't study cancer, but oxidative stress is also associated with neurodegeneration. And he has enabled scientists to witness previously unknown aspects of cellular machinations of neurodegeneration as they happen. Now Burton is helping UPCI colleagues port Bruchez's ingenious FAP tags into zebra fish—which actually have telomeres pretty close in size to those in humans. (Mice have really, really long telomeres, says Opresko.) Although the data for this project are still too preliminary for publication, Burton offered this image of a live, larval zebra fish that's had its retina, brain, and peripheral nerves labeled with a green-fluorescent protein expressed with an approach that's very similar to how his team is labeling telomeres with FAP. Working in model animals, of course, is an important step toward working in humans.

Chinese general Sun Tzu wrote in *The Art of War*: "If you know the enemy and know yourself, you need not fear the result of a hundred battles." Burton and colleagues are poised to show us aspects of disease, and of ourselves, that we've never before recognized.

IMAGE BY EDWARD A. BURTON

Roi Johnson is a youth advisory board member at Project Silk.

STRIKE A CONNECTION

LOCAL ORGS UNITE AIMING FOR NO NEW AIDS CASES BY 2020

BY GAVIN JENKINS

PHOTOGRAPHY BY MARTHA RIAL

Tyreese Taylor and Roi Johnson sit on the hardwood floor in front of their vogue class in downtown Pittsburgh. Vogue is a dance form defined by poses that a fashion model might strike, combined with confined, yet athletic, movement. It's as though a catwalk has been crossed with a dance floor. At Project Silk, where the class is held, vogue is a favorite pastime.

Taylor and Johnson are 22-year-old Pittsburghers who came out as gay to each other in middle school and have frequented Project Silk since they were teenagers. Taylor says he can tell Johnson anything without fear of judgment, and Johnson admires Taylor for his courage. The best friends have grown into leadership roles at the center. Run by Community Human Services, Project Silk is a nonclinical health space that provides support for LGBT people of color ages 13-29, as they learn about housing, employment, education, and wellness.

Each Tuesday evening, Taylor is the vogue instructor, and Johnson leads the warm-up. On this night, Johnson spreads out his legs and leans over toward his left foot, instructing the 14 dancers facing him to do the same.

Behind them is the entrance to a computer room. A television, stereo, futon, and black couch are on the other end of the space. The rest of the décor seems to reinforce the tragic reality of Centers for Disease Control and Prevention (CDC) statistics: In the United States, young, homosexual African Americans are more vulnerable to contracting HIV than any other demographic. For all of medicine's advances in taking on HIV and AIDS, these young people are slipping through the cracks.

Here at Project Silk, a condom dispenser has been affixed to a closet door. Someone has hung on the wall a drawing of an AIDS ribbon wearing boots; posters proclaiming TESTING MAKES US STRONGER and BORN BRAVE drape walls and doors.

In 2015, African Americans made up 13 percent of the nation's population and 45 percent of new HIV cases. And, of the latter number, 67 percent were men who have sex with men (MSM). Allegheny County's HIV statistics reflect what's happening nationally among MSM. According to the county health department, men constitute the majority of new infections, and the "risk factor attributed to the greatest number of new HIV cases" is MSM. And here, infection rates among African Americans are almost seven times higher than among people of European descent.

As he stretches to the left, Johnson begins telling the class about the importance of staying limber before dancing, but he stops midsentence when he notices a friend in the front row.

"I said left," Johnson says. "You went to the right."

"That is exactly why I failed gym," the friend says.

The class erupts in laughter, and after a minute, the warm-up continues. In conversation later, Taylor and Johnson say they joined Project Silk to meet other LGBT people. Before Project Silk, Johnson says Taylor was the only gay person he knew.

"[Project Silk] opened up a whole bunch of doors to a whole bunch of other things," says Johnson, who wants to be a music producer or a nurse someday. (For now, he's doing a lot of babysitting for family.) "I've met new people, found jobs." Taylor, who aspires to be a journalist, says that frequenting Project Silk also has helped him understand the importance of getting tested for HIV.

Grassroots organizations like Project Silk are integral to AIDS Free Pittsburgh, a public health movement that aims to eliminate new AIDS cases and cut the rate of new HIV cases

LEFT: Salim Snyder looks on as Tyreese Taylor dances during a vogue class at Project Silk. RIGHT: Roi Johnson teaches Snyder a move.

by 75 percent in Allegheny County by 2020.

Inspired by similar collective impact initiatives in New York and San Francisco, AIDS Free Pittsburgh is made up of 23 groups—government, social service, and health care organizations, as well as the University of Pittsburgh.

Between 2011 and 2014, Allegheny County averaged 128 new HIV infections per year. The highest number of cases during those years, 132, was in 2014.

By 2015, 2,830 people were living with HIV in the county. That year, 57 new cases of AIDS developed, as well as 145 new HIV cases.

"It was headed in the wrong direction," says John Mellors, chief of the Division of Infectious Diseases at the University of Pittsburgh.

Mellors believes that the epidemic had slipped out of the public's consciousness. And it's not just the general public that's disengaged from the conversation; those at high risk are detached from the reality of the epidemic, as well. "Minority MSM are not connected to major health care institutions."

So how do you get people's attention?

"You can't do it from Scaife 8, overlooking [Petersen Event Center]," says Mellors. "You have to have a grassroots movement. And that's what AIDS Free Pittsburgh is all about."

Fortunately, Pittsburgh is not among the 25 U.S. cities with the highest rates of HIV contraction, yet that 2015 spike in new HIV cases was cause for concern. And it motivated Pitt and UPMC faculty to reach out to other Pittsburgh organizations to start the collective.

AIDS Free Pittsburgh launched in late 2015, when UPMC and Allegheny Health Network (AHN) pledged a combined $1.5 million to end the epidemic in the region.

A similar statewide initiative in Washington aims to cut new HIV cases in that state in half by 2020. A global partnership involving the United Nations, called Fast-Track Cities, focuses on eradicating AIDS in certain major metropolises worldwide by 2030.

But AIDS Free Pittsburgh appears to be the only AIDS eradication movement in a city of this size. Organizers believe Pittsburgh can serve as a proof of concept for Rustbelt and Midwestern cities.

Before AIDS Free Pittsburgh, community organizations taking on the epidemic were not always communicating. "And they certainly didn't want direction from the major health care organizations," Mellors says. "They're filling in gaps that aren't covered by those health care organizations. So, I was pleased with the willingness of people [to join the effort].

"As soon as one institution or entity begins to drive it, it's not going to work," Mellors says.

Now the organizations know more about what the others are doing and are aligning their efforts. Julia Och, AIDS Free Pittsburgh project manager at the Jewish Healthcare Foundation, says partnering enables the organizations to build off of what the others are doing: "For example, we know that Pittsburgh AIDS Task Force, Planned Parenthood, and Prevention Point [Pittsburgh] already each have a really robust volunteer base."

"You have to have a grassroots movement. And that's what AIDS Free Pittsburgh is all about."

The partners are taking a three-pronged approach to ending AIDS in Allegheny County: HIV testing, treatment, and prevention. HIV testing will be the "fulcrum" for AIDS Free Pittsburgh's success, says Mellors.

Several entities within the initiative offer free testing. But to normalize testing, you must first end stigma.

When the AIDS epidemic hit America in the 1980s, many were afraid to share a drink with, or even hug, people living with HIV. That fear seems etched into our nation's psyche.

"There's even stigma within my generation in 2017," says Taylor.

According to the CDC, sexually active gay and bisexual men should get tested every three to six months. However, several people interviewed for this article claimed to know of others who were afraid to be seen walking into a clinic.

Physicians can make the problem worse

Johnson and Taylor have been involved with Project Silk since high school.

without realizing it, Och points out.

A physician might say, *Oh, you don't need an HIV test, do you?* or not offer one at all, Och says. "Yet the routine testing recommendations are for everyone 13 to 64. That's been a CDC guideline for 10 years. By not following that, health professionals are contributing to stigma."

Macedonia Family and Community Enrichment Center (FACE), a nonprofit outreach program, is working to end shame around HIV and AIDS throughout the wider African American community here.

Located in the Hill District, Macedonia FACE uses its relationship with the Macedonia Church of Pittsburgh to educate and promote wellness. The organization also takes on other issues like truancy and bullying.

AIDS Free Pittsburgh is a collaborative initiative made up of 23 groups dedicated to ending the AIDS epidemic in Allegheny County by 2020. Involved in the initiative are . . .

Allegheny County Health Department
Allegheny Health Network
ALPHA Pittsburgh
City of Pittsburgh HIV Commission
Community Human Services
Community Liver Alliance
Gateway Health Plan
Health Care for the Homeless
Jewish Healthcare Foundation
Macedonia Family and Community Enrichment Center
Metro Community Health Center
MidAtlantic AETC
The Open Door
PERSAD Center
Pittsburgh AIDS Task Force
Planned Parenthood of Western Pa.
Prevention Point Pittsburgh
Project Silk
Regional HIV Strategic Collaborative
SeniorCare Management Assistance Funds
Shepherd Wellness Community
University of Pittsburgh
UPMC

Jane Eastman (not her real name) has been a client of the organization's support services for years.

In 2006, she moved from New York to a borough outside of Pittsburgh after a bad breakup. Lonely and still reeling from the end of the relationship, Eastman had a one-night stand with an acquaintance. Six months later, after donating to the Blood Bank, she received a call from the Health Department. She thought it was strange that they wanted her to come in and talk.

Learning that she had HIV depressed her for a couple years. "I thought it was the end of the world," Eastman says. It took her more than a year before she gathered the courage to tell her mother and daughter. It didn't get any easier when more people found out. "The whispers," she says. "That's pretty hard to deal with."

While struggling with depression, Eastman began taking antiretroviral drugs: four in the morning and three at night. And then she sought counseling at Macedonia FACE. Through one-on-one sessions and group meetings, her confidence grew. She became friends with other people living with HIV and slowly realized that, with antiretroviral medication, being HIV-positive is no longer a death sentence.

Mellors, who holds Pitt's endowed Chair for Global Elimination of HIV and AIDS, calls antiretroviral therapy "a miracle in itself." And he says the goal of no new AIDS cases by 2020 is feasible.

"If you're infected, you should not develop AIDS," he says. "You should get treatment long before you develop AIDS." Some patients have viral loads so low that HIV can't even be detected unless they stop taking medication. Eastman now takes three pills a day and might be able to drop down to just one soon. She's in a relationship and expects to watch her granddaughter grow up.

Sometimes people still accuse her of having AIDS. One time, at a party, the host demanded she drink out of a paper cup and eat off a paper plate.

"The stigma is still there because young kids need educated on it," she says.

Ushers and pastors at Macedonia Church wear AIDS ribbons, and earlier this year, for National Black HIV/AIDS Awareness Day, Macedonia FACE produced a short video featuring leaders from African American churches throughout the region. The production, which was shown to more than 20 congregations, urged people to "Get educated. Get tested. Get involved. Get treated. Get talking," to normalize the conversation around HIV/AIDS.

Reverend Richard Wingfield, of Unity Baptist Church in Braddock, Pa., was featured in the video, and he says his congregation's reaction to viewing it was positive. "The stigma is a reality in this area," Wingfield says. "[The video] helped. I think what also would help is . . . watching it every couple of months, just as a reminder."

Infectious disease highlights how intricately humans are linked, yet building connections seems to be one of AIDS Free Pittsburgh's biggest challenges.

Doctors, for example, may want to intervene, but they might not be clued in to what some young LGBT people are experiencing in their day-to-day lives. Consider this: between 20 and 40 percent of homeless youth are members of the LGBT community.

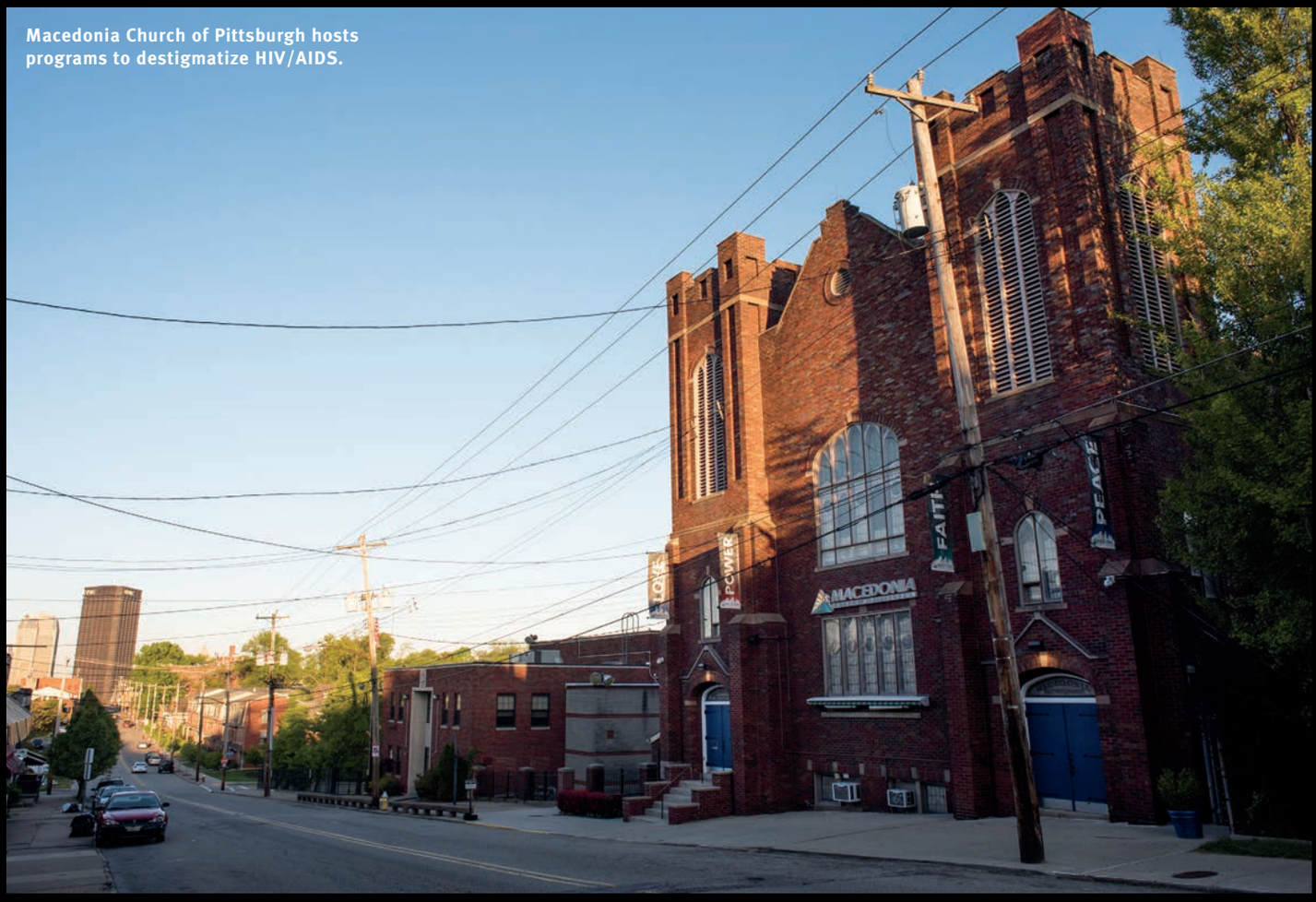
"People are literally couch-surfing through transactional sex. Or any kind of transactional service they need to provide to get basic needs, like housing and food. And that's happening every night," says Project Silk's director of youth programs, Jess Netto.

As Netto sees it, part of her job is bridging a chasm between two worlds—health care institutions and young LGBT people. Project Silk has a youth advisory board, and Netto schedules meetings involving its members, including Taylor and Johnson, and health care providers from AIDS Free Pittsburgh. Taylor says these are productive meetings. A doctor might talk to them about health insurance, and Taylor and his friends might share ideas about how to reach LGBT youth.

"It's good to have your voice heard," Taylor says.

Ken Ho, a physician and assistant professor of medicine at Pitt, is Project Silk's medical director. He has attended Project Silk events, and he says speaking to its members has helped him understand why some young people don't go to a doctor.

"It can be something as simple as, for example, *I don't like it because I'm a transgender woman, and I'm called by the wrong name*



Macedonia Church of Pittsburgh hosts programs to destigmatize HIV/AIDS.

in the waiting room," says Ho.

"That's really important. It may seem like a small thing, but it can send a strong message to someone experiencing health care for the first time."

Note that transgender people carry a disproportionate burden of new HIV cases—in 2013, the number of new infections in that population was three times the national average. Transgender women—i.e., people who were assigned male gender at birth but identify as women—are included as part of the CDC's MSM statistics. This is controversial, and the CDC has recommendations for changing data-collection methods to better serve this group.

There is a pill you can take to stave off HIV. It's called PrEP (pre-exposure prophylaxis).

AIDS Free Pittsburgh offers Ho, who is on the organization's board, a broader platform to build awareness about PrEP and other methods of prevention.

According to the CDC, taking PrEP once a day can reduce the chances of contracting HIV through sex by more than 90 percent. Ho started a PrEP clinic at UPMC in 2013, and he is conducting clinical trials evaluating long-acting injectable PrEP, as well as topical PrEP. (For five years, Ho has also been medical director of the Pitt Men's Study—part of a larger study funded by the National Institutes of Health—that has been following 3,000 men to track the epidemiology, virology, immunology, and pathology of HIV since 1984.)

PrEP is meant for anyone at a high risk for contracting HIV. Yet it's controversial because of concerns that people will stop using condoms while taking PrEP. Also, the cost—$1,300 a month—is steep.

Mellors says that PrEP is highly effective. He's adamant that people who are at risk need to take it: "By highly effective, I mean 90 percent. If we had a vaccine that was 90 percent effective, [the epidemic] would be over."

An AIDS Free partner program headquartered at the Graduate School of Public Health trains health care providers throughout the Mid Atlantic on HIV related issues, including prevention strategies like PrEP.

Yet, "A lot of the people who are at risk don't have insurance," Ho says. AIDS Free Pittsburgh has set aside funds to provide PrEP to people who are uninsured.

Gilead, the company that makes Truvada—the brand name for PrEP—helps fill this gap, as well, with a program that delivers three-month's worth of pills to those who apply. "You can fill out paperwork and renew it and get it again," Ho says. "But it doesn't cover the cost of the doctor visits and the lab work that you need." AIDS Free Pittsburgh is building a program so that clinics can bill the initiative for these costs too.

Taylor calls PrEP a "game-changer," and he predicts AIDS Free Pittsburgh will be successful if it "just keeps doing what it's doing."

He says that most of his friends at Project Silk take PrEP. And Johnson is such a fan of the drug that he posed for an ad promoting its use that ran on the side of area buses. Taylor and Johnson have stable living situations, though. Not everyone they know is so lucky.

"Taking a pill daily is difficult if you don't have a place to store your things," Netto says.

The professionals at Macedonia FACE would agree with Netto. In a recent gathering of the FACE team, heads nod as a program manager describes how stigma around HIV/AIDS and the high infection rate inside the African American community are pieces of a larger problem:

"Socioeconomic situations." ■

MATCH RESULTS
CLASS OF 2017

ANESTHESIOLOGY
Cardi, Alessandra
Hospital of the University of Pennsylvania
Gupta, Ragini
Hospital of the University of Pennsylvania
Manmohan, Rajan
Arizona Health Sciences Center/ University of Arizona, Tucson
Seely, John
University of Virginia Hospital

DERMATOLOGY
Houston, Neil
University of Colorado Affiliated Hospitals
Matsumoto, Martha
UPMC/University of Pittsburgh, Pa.
Mori, Westley
University of Minnesota Affiliated Hospitals

EMERGENCY MEDICINE
Barton, David
UPMC/University of Pittsburgh, Pa.
Bush, Brian
University of Chicago Affiliated Hospitals, Ill.
Chu, Alan
Ohio State University Wexner Medical Center
Cipullo, Jennifer
UPMC/University of Pittsburgh, Pa.
Doyal, Mark
Henry Ford Hospital, Mich.
Kwon, Matthew
Jackson Memorial Hospital/University of Miami, Fla.
Parker-Pitts, Kendra
San Antonio Military Medical Center, Texas
Peifly, Michelle
Thomas Jefferson University Hospital, Pa.
Prabhu, Arjun
Mount Sinai Hospital/Icahn School of Medicine at Mount Sinai, N.Y.
Saltzman, Laura
Stony Brook Hospital, N.Y.
Taren, Adrienne
Hillcrest Medical Center/University of Oklahoma
Teoli, Dac
Riverside Community Hospital/University of California, Riverside

FAMILY MEDICINE
Bruehlman, Alyssa
University of Wisconsin Affiliated Hospitals
Maduka, Sobie
Wright State University Affiliated Hospitals, Ohio
Mirzakazemi, Tahereh
Sutter Medical Center of Santa Rosa/University of California, San Francisco
Paduano, Claire
Boston Medical Center/Boston University, Mass.
Schenk, William
Swedish Medical Center, Wash.
Slowey, Daniel
Oregon Health & Science University Hospital
Wang, Sicong
Madigan Army Medical Center, Wash.
Webber, Molly
Providence Sacred Heart Medical Center, Wash.

FAMILY MEDICINE & PSYCHIATRY
Hedayati, Daniel
UPMC St. Margaret's Hospital/University of Pittsburgh, Pa.

INTERNAL MEDICINE
Baptiste, Julian
Johns Hopkins Hospital, Md.
Bui, John
NewYork—Presbyterian Hospital/Weill Cornell Medical Center
Bullock, Andrew
Vanderbilt University Medical Center, Tenn.
Chai, Andrea
Oakland Medical Center, Calif.
Davis-Maxwell, Anthony
UPMC/University of Pittsburgh, Pa.
Demko, John
University of California, San Francisco
Doerfler, Sean
Duke University Medical Center, N.C.
Doerfler, William
UPMC/University of Pittsburgh, Pa.
Dubique, Jordan
Emory University Affiliated Hospitals, Ga.
Goyal, Akash
Duke University Medical Center, N.C.
Hapak, Sophie
University of Minnesota Affiliated Hospitals
Hartke, Vance
UPMC/University of Pittsburgh, Pa.
Heffner, Danielle
UPMC/University of Pittsburgh, Pa.
Hodzic, Zerina
UPMC/University of Pittsburgh, Pa.
Jang, Sae
Mayo Clinic, Minn.
Kelly, Neil
UPMC/University of Pittsburgh, Pa.
Lahti, Steven
Johns Hopkins Hospital, Md.
Lamm, Vladimir
Emory University Affiliated Hospitals, Ga.
Lin, Elizabeth
University of Michigan Affiliated Hospitals
Martin, Petra
University Hospitals Cleveland Medical Center/ Case Western Reserve University, Ohio
Milne, Megan
University of Texas Southwestern Medical Center
Nguyen, Don
University of Iowa Hospitals and Clinics
Nohar, Ravendra
Saint Mary's Hospital/Yale University, Conn.
Oczypok, Elizabeth
UPMC/University of Pittsburgh, Pa.
Osnard, Michael
University Hospitals Cleveland Medical Center/ Case Western Reserve University, Ohio
Scarlotta, Matthew
Johns Hopkins Hospital, Md.
Sincebaugh, James
Mayo Clinic, Minn.
Siyakurima, Edgar
Jackson Memorial Hospital/University of Miami, Fla.
Toirac, Alexander
Jackson Memorial Hospital/University of Miami, Fla.
Wu, Bryan
University of Texas Southwestern Medical Center
Xu, Zeyu
University of Cincinnati Medical Center, Ohio
York, Zachary
University of Wisconsin Hospital and Clinics
Zhou, Tianhua
University of Wisconsin Hospital and Clinics

INTERNAL MEDICINE & PEDIATRICS
Corbin, Bethany
Strong Memorial Hospital/University of Rochester, N.Y.
Waterman, Lauren
UPMC/University of Pittsburgh, Pa.

INTERNAL MEDICINE—PRIMARY
Devanath, Sudipta
Yale New Haven Hospital, Conn.
Jonnalagadda, Amruth
University of Virginia Health System
Kendrick, Karla
Johns Hopkins Bayview Medical Center/ Johns Hopkins University, Md.
Ware, Benjamin
New York University Affiliated Hospitals

INTERNAL MEDICINE—WOMEN'S HEALTH
Zamanian, Maryam
UPMC/University of Pittsburgh, Pa.

NEURODEVELOPMENTAL DISABILITIES
Bone, Megan
University of Texas Southwestern Medical Center
Simmonds, Daniel
Johns Hopkins Hospital/Johns Hopkins University, Md.

NEUROLOGY
Becker, Christopher
University Hospital/University of Michigan
Kola, Sushma
Mayo Clinic, Minn.
Tay, Justin
Mount Sinai Hospital/Icahn School of Medicine at Mount Sinai, N.Y.
Yau, Wai-Ying
Brigham & Women's Hospital/Harvard University, Mass.

NEUROLOGY—PEDIATRIC
Zhang, Jessie
Stony Brook Hospital, N.Y.

OBSTETRICS/GYNECOLOGY
Bell, Kimberly
Western Pennsylvania Hospital
Evans, Mark
UC Davis Medical Center/University of California, Davis
He, Siping
Emory University Affiliated Hospitals, Ga.
Hong, Christopher
Hospital of the University of Pennsylvania
Slocum, Breonna
MedStar Washington Hospital Center/Georgetown University, D.C.
Swanzy, Leah
Walter Reed National Military Medical Center, Md.
Zachor, Hadas
University of Chicago Medical Center, Ill.

OPHTHALMOLOGY
Nadimpalli, Sameera
McGaw Medical Center/Northwestern University, Ill.
To, Lillian
UPMC/University of Pittsburgh, Pa.
Umfrey, Leah
MedStar Washington Hospital Center/Georgetown University, D.C.
Weed, Jared
UPMC/University of Pittsburgh, Pa.

ORTHOPAEDIC SURGERY
Hankins, Margaret
UPMC/University of Pittsburgh, Pa.
Kaplan, Danie
NYU Langone Medical Center/New York University

JOSH FRANZOS

Neal Godse (MD '17) pins his picture to Pittsburgh after matching with UPMC. The Class of 2017's newly minted Pitt MDs are off to 30 states in all, as well as D.C.

Langhans, Mark
Hospital for Special Surgery/Weill Cornell Medical College, N.Y.
Patel, Stuti
UPMC/University of Pittsburgh, Pa.
Shaikh, Humza
UPMC/University of Pittsburgh, Pa.
Tisherman, Robert
UPMC/University of Pittsburgh, Pa.
Wang, William
Thomas Jefferson University Affiliated Hospitals, Pa.

OTOLARYNGOLOGY

Godse, Neal
UPMC/University of Pittsburgh, Pa.
Kaffenberger, Thomas
UPMC/University of Pittsburgh, Pa.
Sturm, Joshua
NewYork—Presbyterian Hospital/Columbia University Medical Center

PATHOLOGY

Hedberg, Matthew
Barnes-Jewish Hospital/Washington University, Mo.
Dong, Zachary
University of Utah Affiliated Hospitals
Gonzalez, Daniel
Jackson Memorial Hospital/University of Miami, Fla.
Jones, Terrell
UPMC/University of Pittsburgh, Pa.
Milito, Chelsea
Strong Memorial Hospital/University of Rochester, N.Y.
Skvarca, Lauren
UPMC/University of Pittsburgh, Pa.

PEDIATRICS

Bruno, Michael
Children's Hospital of Philadelphia/University of Pennsylvania
Guedes, Brian
UF Health Shands Children's Hospital/University of Florida
Hazen, Benjamin
Children's Hospital of Pittsburgh of UPMC/University of Pittsburgh, Pa.
Kho, Terry
Doernbecher Children's Hospital/Oregon Health & Science University
Levine, Anne
Rhode Island Hospital/Brown University
Loeb, Daniel
Children's Hospital of Pittsburgh of UPMC/University of Pittsburgh, Pa.
Mike, Thomas
Akron Children's Hospital/Northeast Ohio Medical University
Ni, Jennifer
Children's Medical Center of Dallas/University of Texas Southwestern Medical Center
Ohlsen, Timothy
University of Utah Affiliated Hospitals
Radparvar, Melina
UCLA Mattel Children's Hospital/University of California, Los Angeles
Suh, Philip
University of California, Irvine Medical Center
Taft, Maia
Children's Hospital of Pittsburgh of UPMC/University of Pittsburgh, Pa.
West, Caroline
C.S. Mott Children's Hospital/University of Michigan
Yen, Kevin
UCSF Benioff Children's Hospital Oakland/University of California, San Francisco

PEDIATRICS & ANESTHESIOLOGY

Polsunas, Lilinete
UPMC/University of Pittsburgh, Pa.

PEDIATRICS, PSYCHIATRY & CHILD PSYCHIATRY

Pham, Steven
Cincinnati Children's Medical Center/University of Cincinnati, Ohio

PHYSICAL MEDICINE & REHABILITATION

Echebiri, Nnaemeka
University of Texas Southwestern Medical Center
Polsunas, Patrick
UPMC/University of Pittsburgh, Pa.
Yih, Erika
Spaulding Rehabilitation Network/Harvard University, Mass.

PLASTIC SURGERY

Thadikonda, Kishan
University of Wisconsin Hospital and Clinics

PSYCHIATRY

Brooks, Derrick
Thomas Jefferson University Hospital, Pa.
Lindner, Samuel
University of North Carolina Hospitals
McLaughlin, Michael
Brigham & Women's Hospital/Harvard University, Mass.
Mirvish, Judah
University of Maryland Medical Center
Smith, Emily
UPMC/University of Pittsburgh, Pa.
Steele, Marshall
Naval Medical Center San Diego, Calif.

RADIATION ONCOLOGY

Richman, Adam
UPMC/University of Pittsburgh, Pa.

RADIOLOGY—DIAGNOSTIC

Rasmussen, Robert
Parkland Hospital/University of Texas Southwestern Medical Center
Sevco, Tyler
University of Michigan Hospitals
Shin, Donghoon
Boston University Medical Center, Mass.
Smith, Daniel
University Hospitals Cleveland Medical Center/Case Western Reserve University, Ohio
Vasireddi, Anil
UPMC/University of Pittsburgh, Pa.

RADIOLOGY—INTERVENTIONAL

Al-Khafaji, Ahmed
UPMC/University of Pittsburgh, Pa.

SURGERY—GENERAL

Attaar, Mikhail
University of Chicago Medical Center, Ill.
Chidi, Alexis
Johns Hopkins Hospital/Johns Hopkins University, Md.
Dasari, Mohini
University of Washington Affiliated Hospitals
Urrechaga, Eva
Jackson Memorial Hospital/University of Miami, Fla.
Welko, Nicholas
University of Louisville Hospital, Ky.

SURGERY—MAXILLOFACIAL

Moore, Christian
UPMC/University of Pittsburgh, Pa.
Omlie, James
UPMC/University of Pittsburgh, Pa.

SURGERY—NEUROLOGICAL

Karnati, Tejas
UC Davis Medical Center/University of California, Davis
Kondylis, Efstathios
Cleveland Clinic, Ohio
Lawrence, Jesse
West Virginia University Hospital
Trybula, Joy
Northwestern Memorial Hospital/Northwestern University, Ill.
Zhou, James
Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Ariz.

SURGERY—PRELIMINARY

Brynien, Daniel
UPMC Mercy/University of Pittsburgh, Pa.
Byrd, Catherine
Loyola University Medical Center, Ill.
Miller, Matthew
Rhode Island Hospital/Brown University, R.I.

SURGERY—THORACIC

Hess, Nicholas
UPMC/University of Pittsburgh, Pa.

SURGERY—VASCULAR

Mehta, Kunal
Dartmouth-Hitchcock Medical Center/Dartmouth College, N.H.
Zhao, Yin
Montefiore Medical Center/Albert Einstein College of Medicine, N.Y.

CLASS NOTES

'70s

Bleeding is personal, too. **Ernest Moore** (MD '72), a vice chair for research at the University of Colorado's department of surgery, is taking personalized medicine into the realm of critical care. "Ten years ago, everyone's bleeding got the same treatment. We think the treatment has to be tailored to their unique coagulation abnormality," says Moore, who's studying personalized blood coagulation treatments with Pitt med's Jason Sperry, assistant professor of surgery and critical care medicine. Moore spent much of his 40-year career in Colorado as chief of surgery and trauma at Denver Health Medical Center and training for ultramarathons with his coworkers. Today, life has hardly slowed down. He only runs regular marathons now, but he's taken on a new gig as editor of the journal *Trauma*.

Botkin

Jeffrey R. Botkin (MD '79) came to Pitt following in the footsteps of three generations of Botkin physicians. He is now professor of pediatrics and associate vice president for research integrity at the University of Utah, overseeing the university's institutional review board and research ethics education. In his studies, he examines ethical and legal challenges of newborn and prenatal screenings, as well as issues of patient education and informed consent. He is chair of the NIH's Embryonic Stem Cell Working Group and member of the FDA's Pediatric Ethics Advisory Committee.

'90s

"I went from being a cancer doctor," says **Naoto Tada Ueno**, "to a cancer patient." As a result, Ueno (Internal Medicine Resident '93), a medical oncologist, has seen the cancer community from three different sides: patient, doctor, and researcher. This gives Ueno unique insight into his work at the University of Texas MD Anderson Cancer Center. As executive director of the center's Morgan Welch Inflammatory Breast Cancer (IBC) Research Program and Clinic, "the world's largest IBC-specific research program," his work focuses on the development of IBC drugs "from scratch to the clinic." Ueno, who is "passionate about creating the next generation of oncology leaders," was honored with an Outstanding Teaching Award from the UT Health System in 2013.

Ueno

When **Lara Kunschner Ronan** (MD '94), an academic neurologist and neuro-oncologist, worked at Allegheny General Hospital in 2012, using Botox to treat migraines was an emerging practice newly approved by the FDA. Trained by a colleague, "I was an early adopter despite initial skepticism," Ronan notes. Botox allowed Ronan's patients to decrease their dependence on daily medications, helping patients to feel "less sedated," without "bothersome side effects." Today, Ronan directs the Dartmouth-Hitchcock neurology residency program and serves as an associate professor of neurology and medicine at Dartmouth. Botox remains part of her patient-treatment arsenal for migraines; Ronan also cares for patients who have primary or metastatic tumors of the nervous system, in addition to neurological illnesses related to cancer, paraneoplastic disease, and various autoimmune conditions.

Constantin Aliferis (PhD '98), professor of medicine and data science at the University of Minnesota and director of its Institute for Health Informatics, is "very, very excited" about how rapidly his field is growing. His work to shape informatics infrastructure in precision medicine training has resulted in new educational programs across the United States, including 18 new in-house courses. Aliferis is interested in solving long-perplexing problems in his own research. One recent grant proposal examines ways to predict and prevent suicide—"one of the hardest things to do," Aliferis says, in terms of predictive modeling. He hopes his work, alongside that of colleagues at New York University, will pave the way for new treatments and prevention.

'00s

When we last met **Nima Sharifi** (MD '01) in 2014, he was busy accepting the American Association for Cancer Research Award for Outstanding Achievement in Cancer Research, given in part for his work on abiraterone metabolites' ability to block androgen promotion in tumors of the prostate. Now Sharifi and his team at the Cleveland Clinic have discovered that some of these metabolites do quite the opposite: Through a clinical trial, Sharifi's team verified that, "beyond that first metabolized form, abiraterone actually becomes a bad metabolite [5-alpha-abi] that promotes tumor progression," he says. They then realized that by "giving another drug [dutasteride] along with it, you can actually reverse the production of that bad metabolite that promotes tumor progression." Recently, Sharifi accepted the 2017 Richard E. Weitzman Outstanding Early Career Investigator Award from the Endocrine Society, presented yearly to an early career doctor with exceptional research accomplishments.

Uspal with Alex Trebek this January.

COURTESY JEOPARDY PRODUCTIONS

The what: He is a two-time *Jeopardy* winner who earned more than $25,000 in three episodes earlier this year. The answer: Who is **Neil Uspal** (MD '03), assistant professor in the pediatric emergency department at Seattle Children's? "I watch enough that I thought I could do it," says Uspal, who typically catches *Jeopardy* over dinner with his partner. Following an online tryout, Uspal was invited to audition. Then, nothing, not even a letter. Two years later, he was called to appear on the show and faced a medical category. "There was one where I said, 'cortisol,' and the answer was 'cortisone,'" he says. "So that was mildly embarrassing."

'10s

As a recent college graduate, **Laura Goodman** (MD '12) taught English in Mongolia. One day in a friend's *ger*—a Mongolian tent—she reflected on her life and how she could help the people around her. "I had a clear moment," she says, "where I realized medicine was the way to give back." Goodman, who's now a general surgery resident at the University of California, Davis, has returned to Mongolia, this time as a Harvard T.H. Chan School of Public Health research fellow. She's studying birth defects specific to

the Mongolian region as well as Mongolia's surgical infrastructure and capacity. Goodman says in the public health sphere, "global surgery has always been neglected... up until now." Before her return to the States in May, Goodman plans to present her team's findings to Mongolia's minister of health. "I hope that through painting this picture, we can recommend some changes," she says.


Grady

As an undergraduate, **Cynthia Grady** (MD '15) didn't have a mentor to lead her toward medical school acceptance. At her small, historically black university, she noticed too many students were starting out as pre-med and not enough were ending up in medical school. "I had to pave the way myself, in terms of figuring out what I needed to do to get to med school," she says. Today, Grady is a cofounder of the PavedPath (pavedpath.musc.edu), a Web site launched last year that serves as a portal for pre-med students, particularly those in underrepresented groups, to connect with admissions officers, successful medical students, and their peers. Grady, an obstetrics and gynecology resident at Louisiana State University, says though free time to run the site can be hard to come by, "if it's something you feel is worthwhile, you'll put forth the time and effort." *—Evan Bowen-Gaddy, Gavin Jenkins, Rachel Mennies, Susan Wiedel, Kylie Wolfe*

ROBIN WEST

TURNING ATHLETES RIGHT SIDE UP

After more than a decade as an orthopaedic surgeon and sports doc, Robin West (Fel '03) figured she had the hang of her work. Then a bicycle accident left the amateur triathlete with a concussion, multiple broken ribs, and a shattered shoulder.

"I have a totally newfound respect for the medical and psychological aspects of recovery," says the 45-year-old, who underwent two shoulder repair operations and was sidelined from triathlete training, as well as her appointment as chair and medical director for Inova Sports Medicine in the Washington, D.C., suburbs. "It's not just the pain of surgery, but your whole life is turned upside down. I understand how scary it is wanting to get back to where you were before," adds West, who serves as head team physician for the Washington Redskins as well as lead team physician for the Washington Nationals.


COURTESY REDSKINS BROADCASTING NETWORK

West (right) says prevention is an athlete's best defense.

While not all injuries can be avoided, West has made prevention a cornerstone of her practice. In 2015, she led an overhaul of the Nationals' medical program, instituting data-based analytics to monitor the overall health of players and detect issues before they become full-blown injuries. She credits mentor Freddie Fu, chair of Pitt's Department of Orthopaedic Surgery, with spurring her commitment to making herself available to patients. "Any time a Pitt athlete was injured, they were seen immediately," says West, who worked with Fu as a fellow and garnered two Super Bowl rings during her decade as assistant team physician for the Pittsburgh Steelers.

Availability is challenging in the sprawling D.C. metropolitan area, says West, who earned licensure in D.C., Maryland, and Virginia so that she can treat players whether they're at a training site, on the playing field, or in her office. At Inova, she's hired athletic trainers, physical therapists, concussion experts, and a neuropsychologist, in addition to fellow surgeons and primary care docs. "We're a one-stop shop for players and everyday athletes." *—Sharon Tregaskis*

MAA SAYS, "PUT SKIN IN THE GAME"


Kano

Plantains—those starchier cousins of bananas—have skins that are similar to the human epidermis, making them useful for practicing suturing techniques. **Daiji Kano** (MD '16) learned this tip while he was in Ecuador last year for an independent clinical and research elective. He joined Ecuadorian medical students in practicing "simple interrupted" and "horizontal mattress" stitches on plantains. Using the widely available fruit for suturing practice was just one insight into how medical teams in Ecuador are ultra-efficient with their resources. During his three-week experience, he researched acute care surgery outcomes at Hospital Vicente Corral Moscoso and found that its outcomes are comparable to those of hospitals in the United States. Efficiency and solid clinical judgments make up for fewer technological resources, he found.

Kano, now a surgery resident at NewYork-Presbyterian/Queens, recently blogged about his experience in Ecuador on the Pitt Medical Alumni Association's Web site. (MAA's virtual home at maa.pitt.edu got an upgrade this spring, including a student blog!) Kano's trip was supported by MAA's Student Resource Fund. The fund chips in for research-related travel for about a dozen Pitt meders each year. If you find the Student Resource Fund, er, appealing, consider a gift. MAA's Assistant Director **Kelsey Thayer (kelsey.thayer@pitt.edu)** will go bananas over your contribution. You might just set students like Kano onto something good.

The best part of suturing practice in Ecuador? Afterwards, they cooked up the plantains for lunch. *—Cara Masset*

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M. MICHAEL BARMADA
NOV. 14, 1969—DEC. 2, 2016

Michael Barmada (PhD '99) took the notion of "self-help" to a whole new level.

When diagnosed with a rare form of gastroesophageal cancer, the computational geneticist considered himself "lucky" to have the expertise necessary to search for a targeted therapy. His quest included DNA and RNA sequencing of his own tumor and normal esophageal tissue—as well as the creation of a mouse model on which to test potential chemotherapy regimens. He wasn't doing this just for himself, he wrote, but for other scientists and the patients of tomorrow.


Barmada

That can-do optimism and generosity characterized the Detroit native, who is widely remembered as being unstinting with his knowledge and time, not only mentoring numerous graduate students over the years but also training his colleagues in next-generation sequencing. Barmada was associate director of the Center for Simulation and Modeling and codirector of the Bioinformatics Resource Center in the Institute for Precision Medicine. He was an associate professor of human genetics in the Graduate School of Public Health with a secondary appointment at the med school in biomedical informatics.

Uma Chandran, codirector of Cancer Bioinformatics Services at UPCI and a research associate professor of biomedical informatics, calls his contribution to high-throughput computing "invaluable."

In 2012, she says, "Mike single-handedly introduced the entire University community of biologists to high-performance computing by offering two-week, hands-on workshops" to standing-room-only crowds in the Graduate School of Public Health auditorium.

"Our world is full of divas," says colleague Rebecca Jacobson, also a professor in biomedical informatics and a collaborator of Barmada's. "Mike was not a diva. He wanted to get these advances into the hands of grad students and postdocs. He believed in the future.

"Science goes on without any of us. We perish; the field advances," Jacobson says. "I measure this loss in more human kinds of ways. It's the loss of Mike as a person, a colleague, a friend." —*Sarah C. Baldwin*

RICHARD L. WECHSLER
APRIL 22, 1923—JAN. 13, 2017

Walking into the waiting room of physician Richard Wechsler (MD '47) was more like walking into a living room, says Wechsler's son, Lawrence Wechsler (Res '80), Pitt's chair of neurology. With its ornate chairs and abstract and African art, the waiting room distinguished itself from a common doctor's office. "It was his feeling that, if patients have to sit and wait, they ought to be in a stimulating environment that has some beauty to it."

Richard Wechsler, a gastroenterologist and the second in a line of four Wechslers to train or practice medicine at Pitt hospitals, died Jan. 13.

Born in Squirrel Hill, Richard Wechsler attended Harvard College and then Pitt med. After earning his medical degree, Wechsler began practicing with his father, an internist.

At the time, Pittsburgh was not yet the trailblazing medical hotspot that it is today, but Wechsler was determined to help make it so, says his stepson, Carl Kurlander. Wechsler would say, "When this town gets behind something, they do amazing things, like tackle polio." Then he would laugh in hindsight about turning down a job in Jonas Salk's lab, thinking that the research "wasn't going anywhere."


Wechsler

Nevertheless, Wechsler left his own mark. He was one of the first doctors in the region to perform endoscopies, colonoscopies, and cancer screenings. He also served as editor of the *American Journal of Digestive Diseases*, which published much of the early research of Thomas Starzl (see our remembrance of the beloved transplant surgeon on p. 12).

Wechsler "was not afraid of being different," says Kurlander. In fact, even Wechsler's sleeping patterns were different. Lawrence Wechsler says he'd come home from work, sleep from 7 to 9 p.m., then call patients from bed and look at x-rays until midnight. All of these idiosyncrasies—the ultra-comfortable waiting room, the in-office treatments, the late nights with x-rays—his son says, emerged from Wechsler's care for others. "He was doing it, thinking of his patients."

—*Evan Bowen-Gaddy*

IN MEMORIAM

'40s

MILTON L. CAPLAN
MD '40
MARCH 7, 2017

GEORGE F. EDMONSTON JR.
MD '43
JAN. 12, 2017

EUGENE EMERSON
MD '43
MAY 28, 2016

RALPH KNISELEY
MD '43
MARCH 1, 2017

RICHARD N. MCGARVEY
MD '48
JAN. 09, 2017

'50s

GERTRUDE BLUMENSCHEIN
MD '50
FEB. 10, 2017

SAMUEL B. CHALLINOR JR.
MD '52
JAN. 23, 2017

EDWARD D. RADASKY
MD '53
JAN. 18, 2017

JOSEPH JAMES SCARLET
MD '53
JAN. 19, 2017

ROBERT L. EISLER
MD '55, RES '56, '59
JULY 15, 2016

GLENN G. GRIFFITH
MD '56
JAN. 27, 2017

ANTHONY PAUL FENELLO
MD '59
FEB. 15, 2017

HUGH H. HARKINS
MD '59
DEC. 27, 2016

'60s

RICHARD H. KUHN
MD '61
JAN. 31, 2017

JAMES R. SMOLKO
MD '61
MARCH 19, 2017

DWIGHT M. STRUM
MD '62
FEB. 10, 2017

FRANCIS DONALD COONEY
MD '63
JUNE 26, 2016

JOHN H. KNUTZEN
RES '69
NOV. 5, 2016

'80s

HARRY W. WATERS JR.
MD '83, RES '87
DEC. 1, 2016

DONALD L. POWELL
RES '84
SEPT. 22, 2016

'90s

SHERILYN GORDON-BURROUGHS
FEL '95
MARCH 19, 2017

FACULTY

THOMAS E. STARZL
MARCH 4, 2017

JULIUS S. YOUNGNER
APRIL 27, 2017

BRIAN D'CRUZ

POLITICAL HOTSPOT TRAUMA DOC

BY KRISTIN BUNDY

COURTESY GABRIELE FRANÇOIS CASINI

D'Cruz at the the Donka Ebola treatment center in Conakry, Guinea, in January 2015.

Wounded men, women, and children arrived by the truckload at the makeshift emergency bay of the chicken farm-turned-hospital. Brian D'Cruz and a dozen other Doctors Without Borders health care workers—all of whom volunteered to work in northern Syria—rushed to their aid. Scores of civilians had been targets of bombings that day in the lush, mountainous region near the Turkish border. D'Cruz remembers that three people died. Had the hospital not been there, he says, there would have been at least 20 more. "That was my best day in Syria."

D'Cruz

When Doctors Without Borders (aka Médecins Sans Frontières, or MSF) first approached D'Cruz (MD '04, Res '07) about a project in Syria, he said no. Although he had been a part of prior missions in Chad, the Republic of the Congo, and the Central African Republic, he was especially worried about security in the Middle East.

After a few months, he had a change of heart. "Essentially, the more I read about it, the more I was seeing that people there just had no access to care," recalls D'Cruz. "I'm an ER doctor, I work in a trauma center, I'm capable of doing that kind of work, and there's a desperate need for people who are able to do it." So, in August 2013, D'Cruz flew to Syria's Idlib province for a two-month assignment.

The hospital where he worked, which originally began in a cave, had moved to the converted chicken farm (an industrial building fortified with concrete) because its location was relatively safe and the structure was solid. Generators provided power. "At the time, we were the most advanced hospital in the area," D'Cruz remembers.

There, MSF served as a lifeline for people to receive the quality of medical attention they once had. Prior to the bombings, medical care in Syria was sophisticated and readily available. "Patients would carry copies of their MRIs and CTs and all the information they had before the war," D'Cruz says. "That's the first place I've ever worked with MSF where the medical care had been that advanced and then had essentially been taken away." Soon after D'Cruz finished his assignment, MSF was forced to close the hospital. It could no longer guarantee the safety of the staff.

D'Cruz speaks fondly of the Syrian people he met, their beautiful countryside, and their persistence in offering homemade meals as a gesture of appreciation. "They were just regular people like us. It was nice to see how different it *wasn't*—even in the middle of a war."

Since Syria, D'Cruz has participated in three other MSF projects—two in conflict-ridden African countries and one in Guinea serving as the supervising medical doctor for a 90-bed Ebola treatment center.

In between his trips overseas, he works as an attending physician in the emergency department at Inova Fairfax Hospital outside Washington, D.C. He says the hospital and his colleagues fully support his volunteer work. "They trade and cover shifts for me so I'm able to go. A lot of them have told me, 'I'm not able to do what you're doing, so I'll make it possible for you to do it. I'll work in your place so that you can go.'"

D'Cruz has always been drawn to providing medical care during a crisis—something he calls limited-resource disaster response. When he was a Pitt resident, he helped medical teams in New Orleans and Baton Rouge after Hurricane Katrina. In 2011, he went to Haiti after the earthquake. It was in Haiti, while working for another organization, where he first saw MSF in action and applied to be part of their volunteer team.

A labor of love for D'Cruz, providing trauma relief drives his practice forward. "That's part of the reason why I went into medicine—to take care of lots of sick people who don't have anywhere else to go. Even though it's horrible that those things happen, it's very satisfying to do the work as a doctor." ■

TOP: COURTESY SKLOOT. BOTTOM: QUANTRELL COLBERT/HBO.

LARGE PHOTO (FROM LEFT): Selfie shows Rebecca Skloot with Henrietta Lacks's great-granddaughter JaBrea, daughter-in-law Shirley, and granddaughter Jeri pointing to a movie poster featuring Carnegie Mellon grad Renée Elise Goldsberry as Henrietta Lacks. **SMALL PHOTOS:** The relationship between Skloot (played by Rose Byrne) and Henrietta Lacks's daughter Deborah Lacks (Oprah Winfrey) is a major narrative thread in the HBO adaptation of Skloot's book.

Did you notice? Both *Pitt Med* (our very first issue) and Skloot herself make cameos in the film.

IMMORTAL EVER AFTER

Once upon a time, April 2000 to be exact, this contributor note appeared in our pages: *Rebecca Skloot was the assistant editor of* Pitt Med *until this spring, when the call of her book in progress became too loud to ignore. . . . She will continue to contribute to* Pitt Med *as our favorite freelancer until Oprah steals her away.*

That book in progress was *The Immortal Life of Henrietta Lacks*, which has spent more than six years on the *New York Times* bestseller list since it was published in 2010. (The manuscript was also Skloot's thesis for her MFA from Pitt.) The book title refers to HeLa cells, named for their progenitor, Henrietta Lacks, an African American woman who lived outside of Baltimore and died at age 31 of cervical cancer. Her extraordinarily durable cancer cells have been omnipresent in labs for decades, because Pitt grad George Gey (A&S 1921) figured out how to keep them alive while he was on the faculty at Johns Hopkins. HeLa cells made hundreds of medical breakthroughs possible, including the polio vaccine. Yet for decades, Henrietta Lacks's family didn't know they lived on after their mother's death, nor that they were being used for medical research. Skloot's book weaves the family story with larger issues of genetic ownership.

Winfrey not only endorsed the book but took it on as a movie project. The HBO production, which Winfrey executive-produced and starred in, aired this spring. During a publicity tour in Manhattan in April, Skloot and members of the Lacks family were wowed by ads promoting the movie's release seemingly around every corner. Skloot posted on Instagram: *#HeLaFilm posters filling the city. They are everywhere, just like #HeLa. This is too much joy to not share.* —*Erica Lloyd*

CALENDAR

FOR ALUMNI & FRIENDS

Unless otherwise noted, for information:
Ashley Knoch at 412-648-9059 or akk57@pitt.edu

CLASS OF 2017 GRADUATION CEREMONY
MAY 22, 4 P.M.
Soldiers & Sailors Memorial Hall & Museum
For information:
Rhonda Matthews at 412-648-9674 or rmatthews@medschool.pitt.edu

PITT IS IT IN PHILADELPHIA
JUNE 1, 6 P.M.
Kimpton Hotel Monaco Philadelphia
For information:
Sue George at 412-624-4658 or sgg7@pitt.edu

WHITE COAT CEREMONY
AUGUST 13, 3 P.M.
Scaife Hall, Auditoriums 5 & 6
Reception immediately following in the Petersen Events Center Lobby

ORIENTATION LUNCHEON FOR THE INCOMING CLASS
AUGUST 18, 11:30 A.M.
Location TBD

MEDICAL ALUMNI ASSOCIATION REUNION WEEKEND
SEPTEMBER 15–16
Reunion Classes:
1957, 1962, 1967, 1972, 1977, 1982, 1987, 1992, 1997, 2002, 2007, 2012

HEALTH SCIENCES ALUMNI & FRIENDS RECEPTION
SEPTEMBER 2017
Los Angeles, Calif.
For Information:
Rachel Edman at 412-864-1957 or rge6@pitt.edu

HOMECOMING TAILGATE
OCTOBER 14 (three hours before kick-off)
Location TBD

PITT MED ALUMNI & FRIENDS RECEPTION
NOVEMBER 4
Boston, Mass.

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

Think fast! **If a baseball is headed for your head, your brain must process that and respond appropriately, and all this happens in a fraction of a second.**

The time it takes for neural circuitry to do its part depends on a few things: the number of neurons in the brain message pathway (travel distance), the length of the neurons, and the neuron's degree of myelination (sort of a turbo boost). Myelin acts as a blanket of insulation that wraps around segments of neurons for faster relay of information. In between each section of myelin are uncovered sections called nodes of Ranvier. (No, that's not a mountain chain from a Tolkien novel.) As brain signals are transmitted, they jump from node to node along the long, thread-like part of the neuron called the axon. And that allows messages to arrive faster, sometimes at speeds of up to 268 miles per hour.

In our teens and 20s, our bodies enter the big leagues. They are pruning and myelinating brain connections into extra innings. All that revamping allows the brain to work many times faster than when we're little kids.

Ever notice that some elite hitters are at the top of their game just before they retire? That's because of another key player: prediction. From the mound, things happen so fast that a hitter only has the first few milliseconds of the pitcher's release to judge what's coming next. Experience teaches hitters how to read pitchers' cues. That's why some of the best batters get better with age. ***—Kylie Wolfe***

Thank you to Alan Sved, professor and chair of neuroscience, who helped his student and our intern, Kylie Wolfe, think about all of this.

Is there a topic you'd like For Real! to explore? Drop us a line: medmag@pitt.edu

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THINK AGAIN.

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