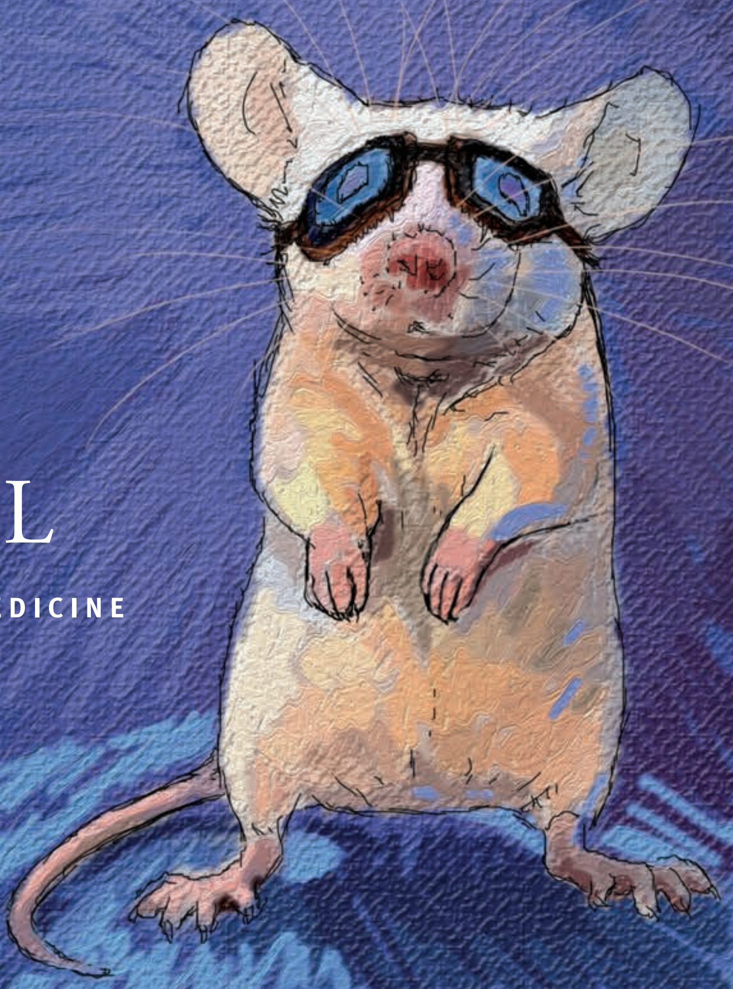
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | SPRING 2017

PITTMED



BLUE LIGHT SPECIAL

PHOTON-TASTIC MEDICINE

NALOXONE AWARENESS

The article “Stepping off the Path to Hell” (Fall 2016) was a timely description of the opioid over-prescribing and overdose epidemic in our country. In your coverage of the many efforts that University of Pittsburgh clinicians and researchers are making to turn the tide of this epidemic, there was one stark omission: providing access to the lifesaving drug naloxone.

Recent legislation and efforts by public health departments across the country are facilitating naloxone distribution, decreasing overdose and death, and improving awareness. Our own Southwestern Pennsylvania leader in overdose prevention, Prevention Point Pittsburgh, has collaborated with Pitt physicians and pharmacists to educate health care professionals on naloxone’s lifesaving capabilities, getting it to people who are at high risk of overdose. Efforts such as these reduce the stigma of addiction and substance abuse as they give many people a second chance.

Jonathan Han, MD
UPMC St. Margaret New Kensington
Family Health Center

Alice Bell
Prevention Point Pittsburgh

Thank you for pointing out our omission. Our writer did originally include mention of naxolone in her draft to us. It was deleted because of an editorial oversight.

MOST POPULAR

James Hawkins Jr. (MD ’81), son of James Hawkins (MD ’52), wrote to tell us *that’s his mom*, Janet Hawkins, on p. 7 of the Fall 2016 issue (see left). His family loves the picture and so do we. (Illustration by Michael Lotenero, based on a photo by Mervin Stewart, MD ’53.)

RECENT MAGAZINE HONORS

Carnegie Science Center
2016 Science Communicator
Honorable Mention, Robyn K. Coggins

2016 Press Club of Western Pennsylvania Golden Quill Award for Education Feature &
Ray Sprigle Memorial Award for Magazines
Cara Masset, “Inside the World of OCD”

2016 Press Club of Western Pennsylvania Golden Quill Award Finalist, Health/Science/Environment Story, Online
Cami Mesa and Elaine Vitone,
“Second Lives: A Pitt Medcast”

CORRESPONDENCE

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

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

For address corrections:

Pitt Med Address Correction
ATTN: Ashley Knoch
M-200K Scaife Hall
University of Pittsburgh
Pittsburgh, PA 15261
Phone: 412-648-9059
E-mail: medalum@medschool.pitt.edu

HEY, MACARENA.

How are you and your funky bunch? We don’t enjoy the silence. Straight up, now, tell us about your doings—or those of a classmate who’s 2 legit 2 quit.

Send us news that makes you go “hmmmm.” (We are especially interested in learning about national honors and unusual community service.) If you have a big scoop, do the running man over your phone and give us a ring—or better, send an e-mail to the address below. Just don’t forget to plug in your modem . . . *As if!*

Pitt Med
412-624-4354
E-mail: medmag@pitt.edu

CONTRIBUTORS

MICAELA FOX CORN [“Students of Valor”] started with *Pitt Med* as an intern in 2015 and never fully left. After getting degrees in psychology and English writing, she decided, “I like learning about science more than I like *doing* science.” When working on her first feature for *Pitt Med*, she was able to learn about something foreign to her life experience—the military. While reporting on veterans who work in medicine, she was awed by how driven all her interviewees were. It seems, she says, “when someone goes to the military and comes back, they do whatever they do with a lot of intention.”

SALLY ANN FLECKER [“The Soul of Psychiatry”] is awfully good at writing profiles that uncover how people shape themselves. In this issue, Flecker tells the story of Chip Reynolds and how his career unfolded following the death of his grandfather. Flecker’s depiction of Reynolds pops from the page as she explores his research and clinical interests related to depression. “I’m continually humbled,” she says of writing. “You’re always talking to people who are passionate about their subject areas, so if you can start to see the world through their eyes, you get to share their fascinations.” Previously the editor of *Pitt Magazine*, Flecker now works as a freelance writer and consultant for various university magazines.

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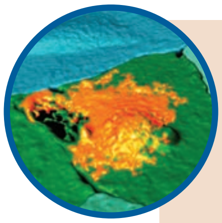

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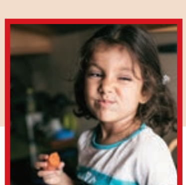

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A Pitt researcher may have found an intriguing way to quell inflammation and control the immune response: blue-light exposure. (Cover illustration: Michelle Leveille © 2017.)

PITTMED

PUBLISHER
Arthur S. Levine, MD

EDITOR IN CHIEF
Erica Lloyd

ART DIRECTOR
Elena Gialamas Cerri

SENIOR EDITOR
Elaine Vitone

GUEST CONTRIBUTING EDITOR
Micaela Fox Corn

INTERNS
Christine Schauer, James Evan Bowen-Gaddy, Kylie Wolfe, Elaina Zachos

PRODUCTION MANAGER
Chuck Dinsmore

CIRCULATION MANAGER
Ashley Knoch

EDITORIAL ADVISORS
Lisa Barsom, PhD
Jeremy Berg, PhD
Michelle Broido, PhD
Paula Davis, MA
Joan Harvey, MD
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Joshua Levenson, MD '11
David Lewis, MD
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Bennett Van Houten, PhD
Simon Watkins, PhD
Marshall Webster, MD, Res '70

VICE CHANCELLOR FOR COMMUNICATIONS
Susan Rogers

SENIOR PERIODICALS EDITOR
Cindy Gill

University of Pittsburgh

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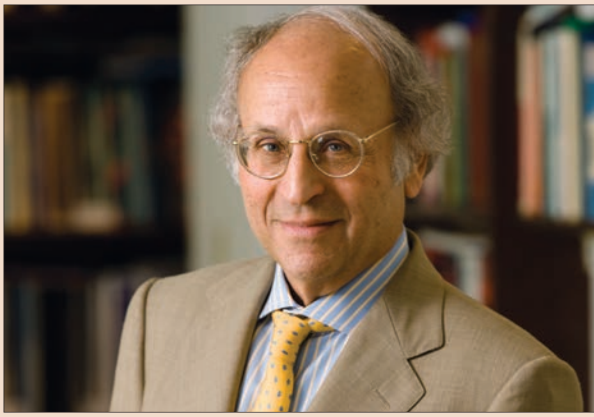


JOSHUA FRANZOS

When I was 12 years old, my parents dropped me off at an eight-week summer camp in Michigan. I had loved my previous camp, but it had closed; the Michigan camp was new to me. I hated it, and after the first day, called my mother asking to come home to Cleveland. I didn't want to stay another minute. But my parents had already paid for the camp; and besides that, the new camp was to make an athlete of me—the previous one, an aesthete. So my mother entreated my older cousin, Donald, to help: *Go get Arthur and talk some sense into him.* Don was a starting assistant professor of physics at close by Ann Arbor.

I don't remember exactly what he said to me, but I do remember that hot summer afternoon. Donald made the roundtrip to fetch and bring me back to his laboratory, which was in a dingy, dusty basement. I'd never been on a college campus before. From the lab fridge, Donald grabbed a beer for himself and a Coke for me. He shook the beer, and when he opened it, foam sprayed into the air. We could see newly bathed dust in the air, backlit from the sunbeam pouring through a transom window. I like to think of that playful instance as the moment when ideas began percolating for Donald's invention, less than two years later, of the bubble chamber. His instrument allowed physicists for the first time to track and visualize subatomic particles.

My mom picked the right person to set me straight. Donald was like a big brother to me. For some time, we shared a two-family house in Cleveland; he was my first science "teacher." How could I not look up to him? Besides being a brilliant physicist (who later switched to molecular biology—like all good physicists of that time!—and then to neurobiology), he was a talented musician (he once played viola with the Cleveland Orchestra). He was bold (drove a Harley, was an accomplished scuba diver, and cofounded the first biotech company). And he was a wonderfully gracious and warm person. The qualities Donald embodied are what I like to call "Levine's six unlinked genes for success": intelligence, creativity, fire in the belly, social adroitness, curiosity, and the ethic of hard work.

These are qualities we look for in student applicants to the medical school, and what I hope to see in department chairs, in others holding positions of leadership, and especially in the best clinicians and scientists. The "genes" (each is undoubtedly a constellation of many genomic influences) I speak of are unlinked, because you can have one without the other, of course. Yet for great success in medicine, science, and most walks of life, they all come into play. For instance, you may be brilliant, creative, curious, passionate, and hardworking, but if you can't collaborate, you won't get far.

Still, even when junior faculty have these raw ingredients for success, they usually need some help. We recruit promising young investigators and academic physicians. However, they've probably not been trained in "grantsmanship," i.e., how to write a successful application that will bring in the very substantial monies needed to run a laboratory. Or in how to recruit patients who are apprehensive about enrolling in a clinical trial. Or to manage a staff. Or to ensure that institutional policies for research compliance are followed. The skills needed for academic medicine are a lot like those needed for running a business, as Mark Gladwin, our chair of medicine, suggests in an upcoming *Pitt Med* story.

I am indebted to Pitt's Darlene Zellers and Ora Weisz, who have created a novel three-year-long series to help young academic physicians and scientists envision and build paths to success, including getting a handle on the quotidian challenges junior faculty are likely to face. The six unlinked genes may be the ideal genotype, but Darlene and Ora's course comprises the value-added phenotype. (I did stay in the camp, but I still only aspire to be an athlete.)

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

VECTORIG/GETTY IMAGES

Global Connector

Timothy Billiar (Fel ’90, Res ’92) won’t soon forget accepting the People’s Republic of China Friendship Award in Beijing in the fall. With his wife, University of Pittsburgh Professor of Surgery Edith Tzeng, at his side, he was celebrated at a 3,000-person banquet and a medal ceremony with Chinese Premier Li Keqiang. Billiar holds Pitt’s George Vance Foster Chair of Surgery.

Billiar was nominated for his work establishing a medical student research and clinical training program at Pitt for students of Central South University Xiangya School of Medicine in Changsha, Hunan Province. The program’s goal is for students to return to China with increased knowledge and enthusiasm to fulfill their institution’s clinical and scientific objectives.

“Health care advances really don’t know borders,” Billiar says.

Billiar is the second Pitt faculty member to receive this award, considered the highest honor China bestows on a foreign expert. Pitt med’s Thomas Kensler received it in 2011; it’s given annually to 50 people who make “an outstanding contribution to China’s economic and social progress,” according to Chinese officials.

—Rachel Wilkinson

FOOTNOTE

Pitt has come a long way since its log cabin days—it’s now the top public university in the Northeast, according to the *Wall Street Journal/Times Higher Education* College Rankings. The honor was secured with the highest scores in three categories: student outcomes, academic resources, and student engagement. (A fourth area was environment.) MIT was ranked as the Northeast’s top private university.

HOLDING THE HELPING HANDS

It’s not unusual for generations to care for one another. But often, family members are overlooked as integral parts of a person’s care team. Throughout the next two years, Pitt’s Health Policy Institute and University Center for Social and Urban Research will join with RAND Health to address this issue. The effort will be known as the Caregiver Project.

The project team plans to identify caregivers and care recipients who are particularly likely to experience health and economic troubles. “Part of our efforts will focus on identifying major risk factors for all of these adverse outcomes,” says Richard Schulz, PhD professor of psychiatry and director of gerontology at Pitt.

The Caregiver Project will be guided by recommendations outlined in a landmark National Academies of Sciences, Engineering, and Medicine report chaired by Schulz, *Families Caring for an Aging America*. Its team will analyze national data sets and conduct literature reviews and surveys in Southwestern Pennsylvania. Information collected in the Pittsburgh region will be used to develop new models of care throughout the United States. *—Kristin Bundy*

Copeland checks out a virtual reality simulation (unrelated to the brain-computer interface he's testing).

UNIVERSITY OF PITTSBURGH

Overheard

Frontiersman for Science

In spring 2015, more than 10 years after a car accident left him paralyzed from the shoulders down, Nathan Copeland had electrodes surgically implanted in the sensory cortex of his brain. Their purpose? To connect Copeland to a brain-computer interface developed by University of Pittsburgh researchers, based on science by Andrew Schwartz, Distinguished Professor of Neurobiology. The technology allows Copeland to control a robotic arm with his mind; it also allowed him to experience sensation through the robotic hand—a first for science. (You might have seen his fist bump with President Obama flashing across news screens in October.) A year and a half into his five-year role in the study led by Pitt's Robert Gaunt and Jennifer Collinger (both of the Department of Physical Medicine and Rehabilitation), we asked Copeland, now 30, for his thoughts on participating in groundbreaking research.

You put yourself on Pitt's research participant registry right after your accident. Did you worry about what a potential study might entail?

From the beginning I thought that the registry was my best chance of improving my life—or someone else's. When the researchers ran through the risks, I'd be like, *Okay, those are possible risks for any surgery, not likelihoods.* My mom was worried about it, though, and she boycotted taking me to my appointments at first. Now she's figured out this is going fine, and it's something meaningful to the world.

You've described the sensation from the robotic hand as being "electrical," sometimes "a sort of pressure." Does it meet expectations?

This is literally the first step in sensation microstimulation, so I wasn't expecting a perfectly normal sensation. What we got is pretty good, [though] I can't compare it to anything I've experienced in the real world.

You've been working with the research team about three times a week. How will you cope with losing sensation after five years, when your study time is up?

Beyond the fact that I've been doing this cool stuff and meeting cool people, it will be like losing function all over again. Ever since the beginning I've realized that's going to be rough, and pretty sad.

What advice would you give study participants coming after you?

Even if the next step isn't miles ahead of where I am now, the next person is still going to be able to do amazing things. To them I'd say, *Just do it if you can.* —*Interview by Lela Nargi*

Faculty Snapshots

With a five-year, $12.5 million grant from the National Institute on Aging, Benjamin Handen, PhD professor of psychiatry, will lead a new multicenter effort exploring biomarkers of Alzheimer's disease in adults with Down syndrome. This population tends to show Alzheimer's symptoms in their 40s. People with Down syndrome are also likely to have a copy, in each of their three chromosome 21s, of a gene that has been associated with the precursor for beta-amyloid, a substance found in excess in the brains of patients with Alzheimer's.

Handen

When and how some key players—like long-lived plasma and memory B cells—develop as part of the secondary immune response has long been up for debate. Earlier this year, Mark Shlomchik, MD/PhD and Pitt's chair of immunology; Florian Weisel, a PhD research assistant professor; and colleagues elucidated the process in an *Immunity* paper that was later highlighted in *Nature Reviews Immunology*. The scientific "tour de force" (as cited by one Faculty of 1000 commentator) has implications for vaccine development as well as for understanding autoimmunity. Shlomchik is one of Pitt's latest to receive a MERIT Award from the National Institutes of Health; the $3.8 million grant will allow him to continue long-term studies on autoimmunity. (Nine other Pitt med faculty also have MERIT Awards.)

Shlomchik

Weisel

Schenker

JOHN ALTDORFER

Supported by a Research Project Grant from the National Institutes of Health, Yael Schenker, an MD, is embarking on trials of the palliative care intervention she designed for patients with advanced cancer. For this and other projects, Schenker, an assistant professor of medicine, received an Early Career Investigator Award from the American Academy of Hospice and Palliative Medicine. —*Kristin Bundy, Elizabeth Hoover, and Erica Lloyd*

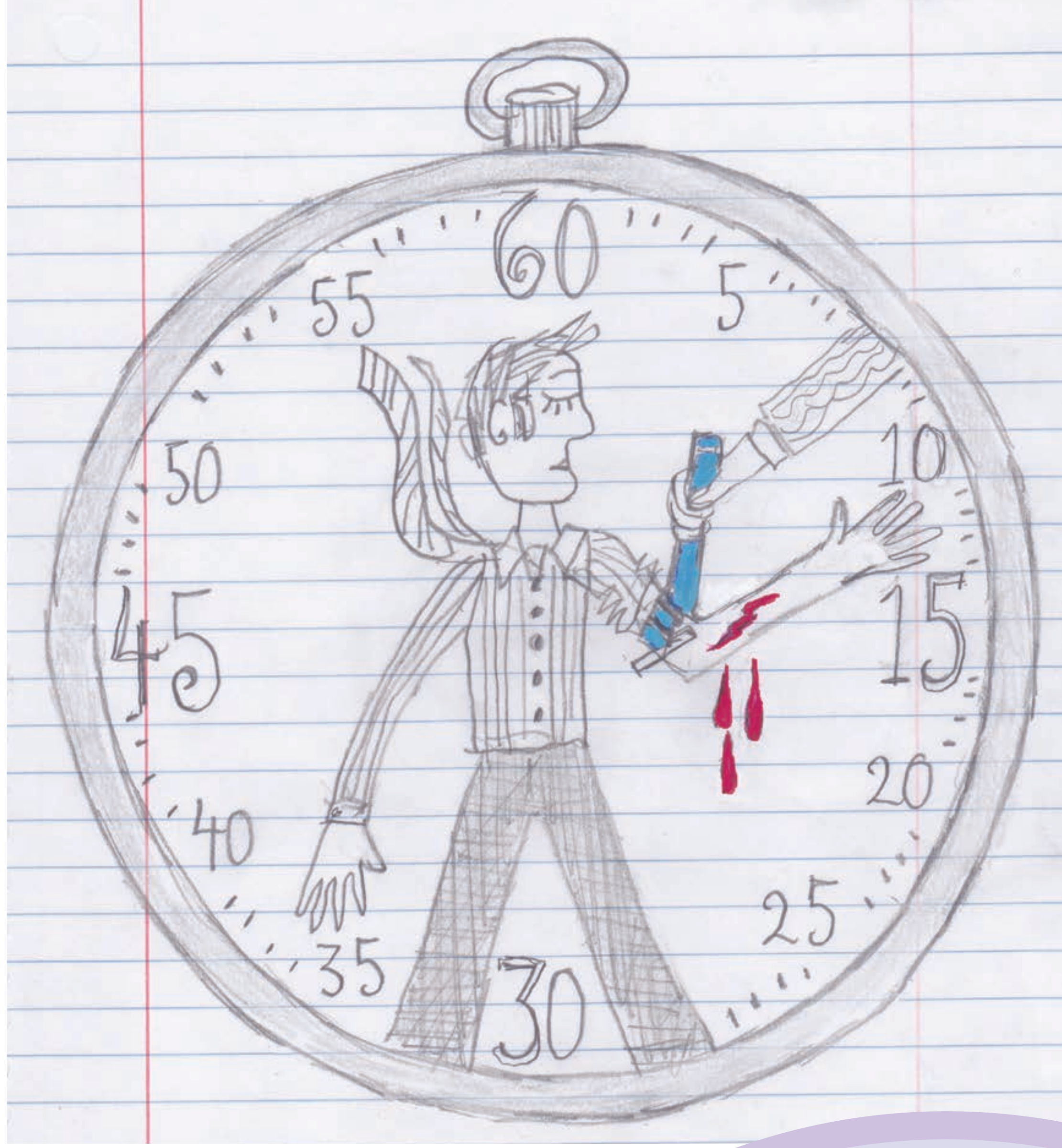
Tourniquet Kit

Victims of gunshot wounds or motor vehicle accidents often die of severe blood loss before emergency services are able to get them to a hospital. Yet, with simple instruction, bystanders could save many of these people.

A White House initiative under President Obama called Stop the Bleed has rolled out a program in response to this public health issue, and Pitt's Andrew Peitzman (MD '76, Res '84) founded the consortium that's coordinating the regional campaign. (Peitzman is the Mark M. Ravitch Professor, Distinguished Professor of Surgery, and UPMC vice president for trauma and surgical services.)

Throughout the next three years, funding from UPMC will support bystander intervention training and basic first aid for trauma wounds in communities across Pennsylvania, Ohio, and West Virginia. The $1.3 million grant will also support the strategic placement of bleeding-control kits (similar to AEDs) in airports, gyms, and supermarkets. Packed with gauze, tourniquets, and topical clotting agents, the kits are designed for laypeople to apply pressure to stem the loss of blood until an ambulance arrives.

If trained properly, says Peitzman, anyone can save a life. ***—Micaela Fox Corn***



CATHERINE LAZURE

PROMISED program participants

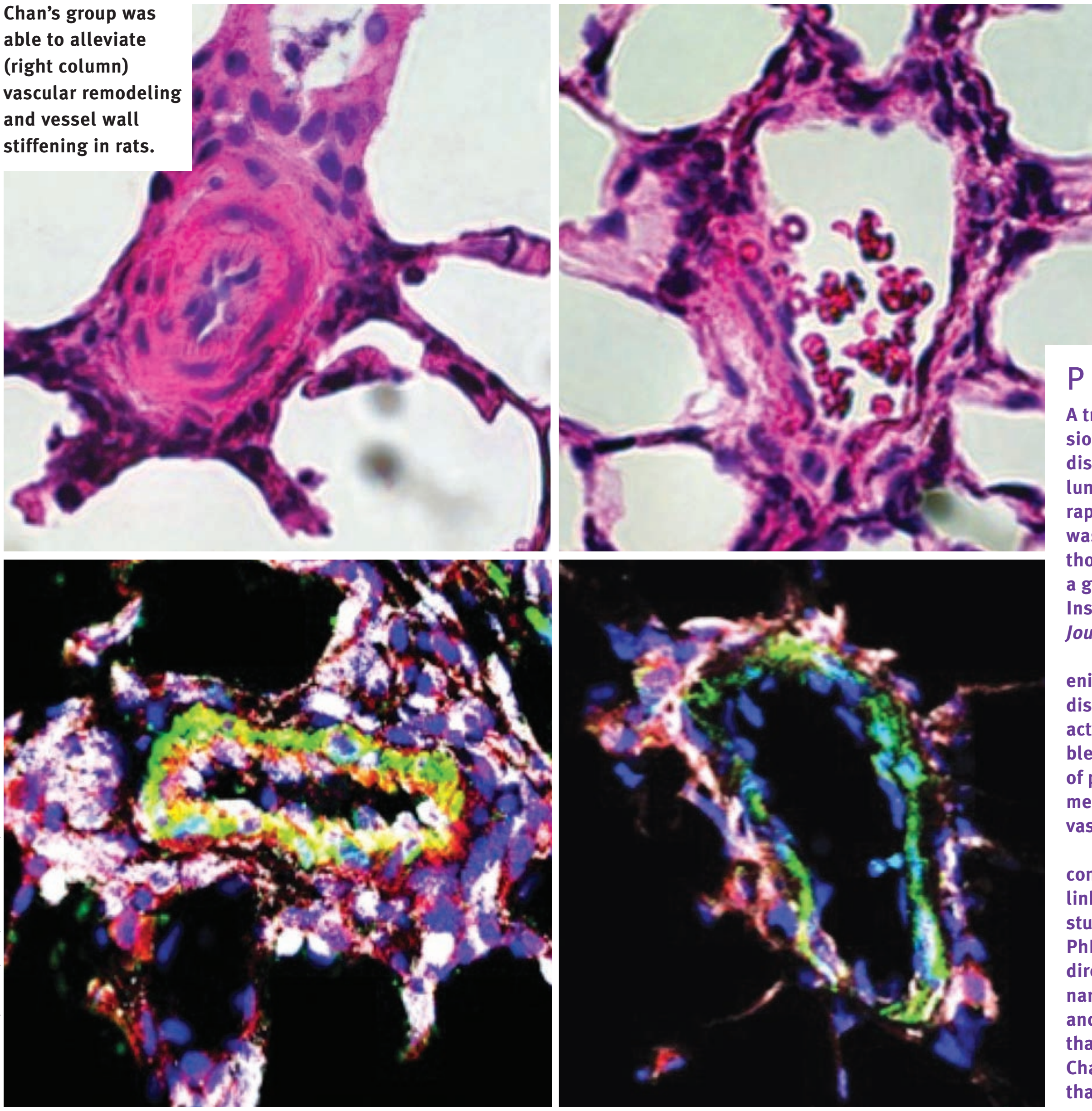
"HELP ME TO HELP YOU!"

"Too often as mentors, we are inclined to do for our mentee or tell our mentee which direction they should be going in," says Pitt's Doris Rubio. When in fact, "you need to help the mentee help him- or herself." For its inaugural career coaching event, the Professional Mentoring Skills Enhancing Diversity (PROMISED) program attracted nearly 50 participants to Pittsburgh in September. Hailing from 17 territories and states, the mentors learned how to support young scientists from underrepresented groups, with the goal of strengthening diversity in the biomedical research workforce. PROMISED is the brainchild of Rubio, codirector of Pitt's Institute for Clinical Research Education (ICRE), and is funded by the National Research Mentoring Network and sponsored by the National Institutes of Health. A second two-day career coaching training program is scheduled for May 2017.

—Christine Schauer

FOOTNOTE

One day, when current third-year Stanley Liu was a research associate at Stanford, a 412 number flashed on his phone screen. He assumed the number belonged to his alma mater, Carnegie Mellon, and that he was about to be solicited for a donation. Instead he heard an unusually last-minute offer from Pitt med admissions: *A seat has opened up in our fall class! Can you be here for the White Coat Ceremony on Sunday?* It was Wednesday. Liu e-mailed his boss—in Taiwan—who called back at 3 a.m. to say, *Go for it!* With a few dress shirts and khakis, Liu hopped the first flight to Pittsburgh on Saturday morning. "I haven't seen anybody beat my time yet," he says.



Chan's group was able to alleviate (right column) vascular remodeling and vessel wall stiffening in rats.

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PH BALANCING

A trademark of pulmonary hypertension (PH), a puzzling, progressive disease of the blood vessels in the lung, is vascular stiffness caused by rapidly proliferating cells. Not much was known about PH's early triggers, though—that is until August, when a group from Pitt's Vascular Medicine Institute published a study in the *Journal of Clinical Investigation*.

The group found that physical hardening of pulmonary arteries early in the disease sets off a cascade of molecular activation, making vascular cells scramble to meet the higher energy demands of proliferation. In other words, cellular metabolism is thrown off-balance by vascular stiffening.

"We really did not understand the component of the stiffness-metabolism link to disease progression until this study," says Stephen Chan, an MD/PhD, associate professor of medicine, director of the UPMC Center for Pulmonary Vascular Biology and Medicine, and senior author of the paper. Now that these molecular links are clear, Chan has begun customizing drugs that might inhibit or prevent PH. This approach might also work for other diseases characterized by vessel stiffening, including cancer. —*Kristin Bundy*

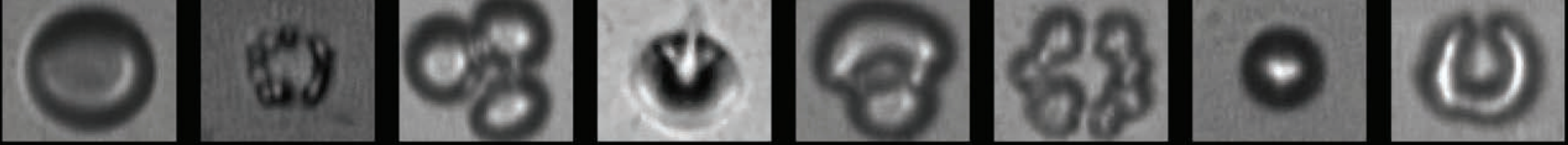
Name Dropping

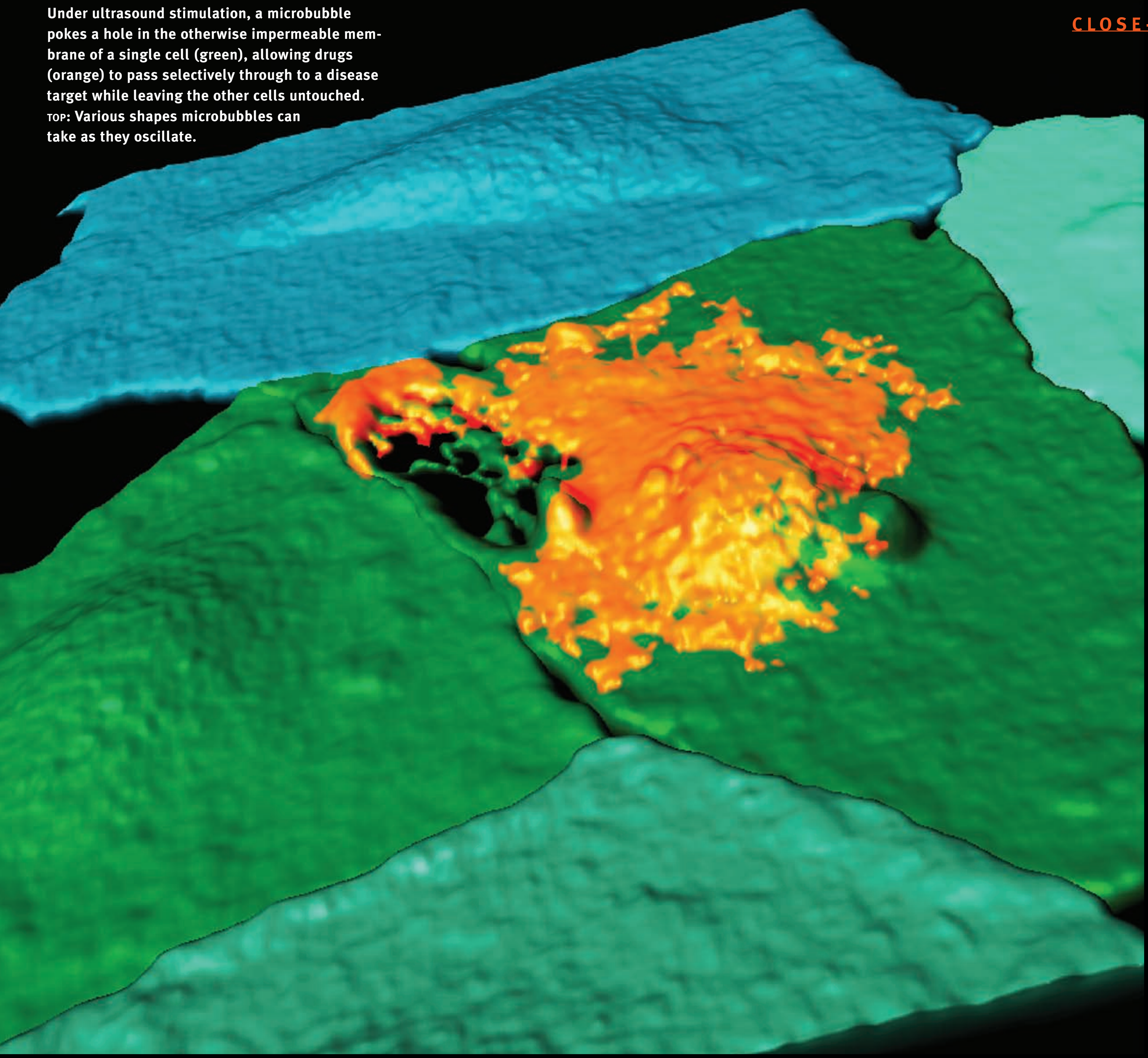
Pitt's science and technology symposium, Science 2016—Game Changers, captivated a crowd in October. The plenary speakers were the MVPs.

Dickson Prize in Medicine recipient **Jennifer Doudna**, a PhD, holds the Li Ka Shing Chancellor's Chair in Biomedical and Health Sciences at the University of California, Berkeley. Doudna and her colleague Emmanuelle Charpentier created a buzz in the world of science by repurposing a system that bacteria use to protect themselves from viruses. They showed that this RNA-protein system, known as CRISPR-Cas9, could quickly and easily modify genomes.

Mahlon DeLong, an MD, delivered the Klaus Hofmann Lecture. He is the William Patterson Timmie Professor of Neurology at Emory University and cofounder of ENTICe (Emory Neuromodulation and Technology Innovation Center). In 2014, DeLong received the Breakthrough Prize in Life Sciences and the Lasker-DeBakey Clinical Medical Research Award for his role in identifying neural circuitry abnormalities present in Parkinson's disease and building the foundation for effective deep brain stimulation treatments.

The Mellon Lecture was delivered by **Howard Y. Chang**, an MD/PhD. As a professor of dermatology at Stanford, he asked himself, *Why do skin cells act differently in different areas of the body?* He found that a molecule known as long noncoding RNA plays a role in programming chromatin—where genes reside—and directs the form and function of skin cells. Chang is pursuing further studies to see how these long noncoding RNAs may affect other genetic outcomes such as birth defects and cancer. In 2015, he won the Paul Marks Prize for Cancer Research from Memorial Sloan Kettering Cancer Center. —*Ali Greenholt*





Under ultrasound stimulation, a microbubble pokes a hole in the otherwise impermeable membrane of a single cell (green), allowing drugs (orange) to pass selectively through to a disease target while leaving the other cells untouched. TOP: Various shapes microbubbles can take as they oscillate.

IT'S A BUBBLE

When you hear "gas-filled bubbles," lifesaving medicine probably isn't the first thing that comes to mind. But that's the idea behind a recent *Proceedings of the National Academy of Sciences* paper from the lab of Flordeliza Villanueva, MD vice chair for preclinical research for the University of Pittsburgh Department of Medicine, director of the Center for Ultrasound Molecular Imaging and Therapeutics, and professor of medicine. Pitt postdoc Brandon Helfield was the paper's first author.

Villanueva's research on microbubbles has made headlines in the past. These gas-filled, smaller-than-red-blood-cell-size spheres are stimulated with ultrasound technology. To minimize side effects, the bubbles can be designed to transport therapies to specific biological sites as they move through the bloodstream. This noninvasive sonoporation, as it's called, has been used experimentally to break up blood clots and deliver drugs to the brain. It might also be used to stem tumor growth or identify early signs of cardiovascular disease.

Now, "we're able to get more of a granular look at what's going on that underlies these observations people have made on a whole-organ level," Villanueva explains.

—By Micaela Fox Corn

—Image courtesy Brandon Helfield, Xucai Chen, Simon Watkins, and Flordeliza Villanueva

Explorations and revelations taking place in the medical school

"how we turn the light that falls onto our eyes into something meaningful"

TO THE LETTER

A DOUBLE TAKE ON READING

BY KRISTIN BUNDY

As you read this, your brain is moving from one word to the next at a rate of 100–250 milliseconds per word, using context clues to make sense of the clusters of letters that formulate sentences. In essence, you're reading these words at a gist level. But if I pint a word that doesn't fit the context (e.g., pint versus print—see that difference?), your brain catches up a word or two later and says, *Hold on, that wasn't right*. You'll backtrack to make sense of it—a process called true-word recognition, or individuation.

This concept of reading as a two-phase process, first published by Pitt researchers in *Proceedings of the National Academy of Sciences* in July, is a new way of thinking about this uniquely human brain process. And it may help put to rest a 150-year-old debate about how the brain reads.

In the 1800s, neurologists had two possible explanations for what happens as we read and say the words in our heads. Either the brain converts the visual information of letters into sound, recognizing whole written words based only on these phonological representations, or there is a dedicated visual word center in our noggins.

As neuroimaging became more refined, researchers homed in on a brain region called the left mid-fusiform gyrus. Controversy ensued. One camp said that the brain area translates all visual information (words and objects) into their auditory form, while another camp insisted there's a brain region solely dedicated to words.

The Pitt group (which included psychology, neurosurgery, and neuroscience faculty) had the rare opportunity to stimulate the left mid-fusiform gyrus itself and record the results.

"It's a unique and amazing experience to be able to record directly from the human brain," says Avniel Ghuman, PhD and assistant professor of neurological surgery, who was the senior investigator of the study. Four study volunteers—each of whom had drug-resistant epilepsy and had chosen to have brain electrodes implanted to aid in managing their symptoms—elected to participate in the study, Ghuman says, adding thanks for their kindness and generosity.

During the procedure, scientists applied pain-free electrical current to the left mid-fusiform gyrus as patients described letters, words, and objects on the screen in front of them. Each patient experienced word-specific disruptions—that is, they misnamed letters and words. Sometimes they mistook letters to be other letters entirely; sometimes they envisioned fragments of words floating around the only word on the screen. Interestingly, however, they could still name objects and faces fairly normally.

Stimulating the left mid-fusiform gyrus "disrupted word processing in a very orthographic, letter- and word-specific manner," says Ghuman.

"We clearly induced severely disordered reading, and certainly this word-form area has been shown to be abnormal in individuals with [certain] reading disorders." (How similar the disordered reading he saw in the study is to acquired or developmental reading disorders remains to be seen, he adds.)

In another part of the study, volunteers simply read while the Pitt team recorded electrophysiological activity from the left mid-fusiform gyrus. Using machine-learning algorithms to analyze the activity, the researchers were able to discern what word a patient was reading at a given moment and track the process with unprecedented precision. From their analysis, two distinct phases of reading emerged: gist level in the first 100–250 milliseconds, followed by true-word recognition around 300–500 milliseconds.

"The idea that there's dynamic shift—that a single area can be involved in multiple stages of processing—is a different way of thinking," Ghuman says.

"The fact that you can see one area of the brain involved in early gist-level processing and later individuation processing suggests something way more nuanced than the classic view of the brain acting in an assembly line, [where] one part of the brain does its job and passes it on."

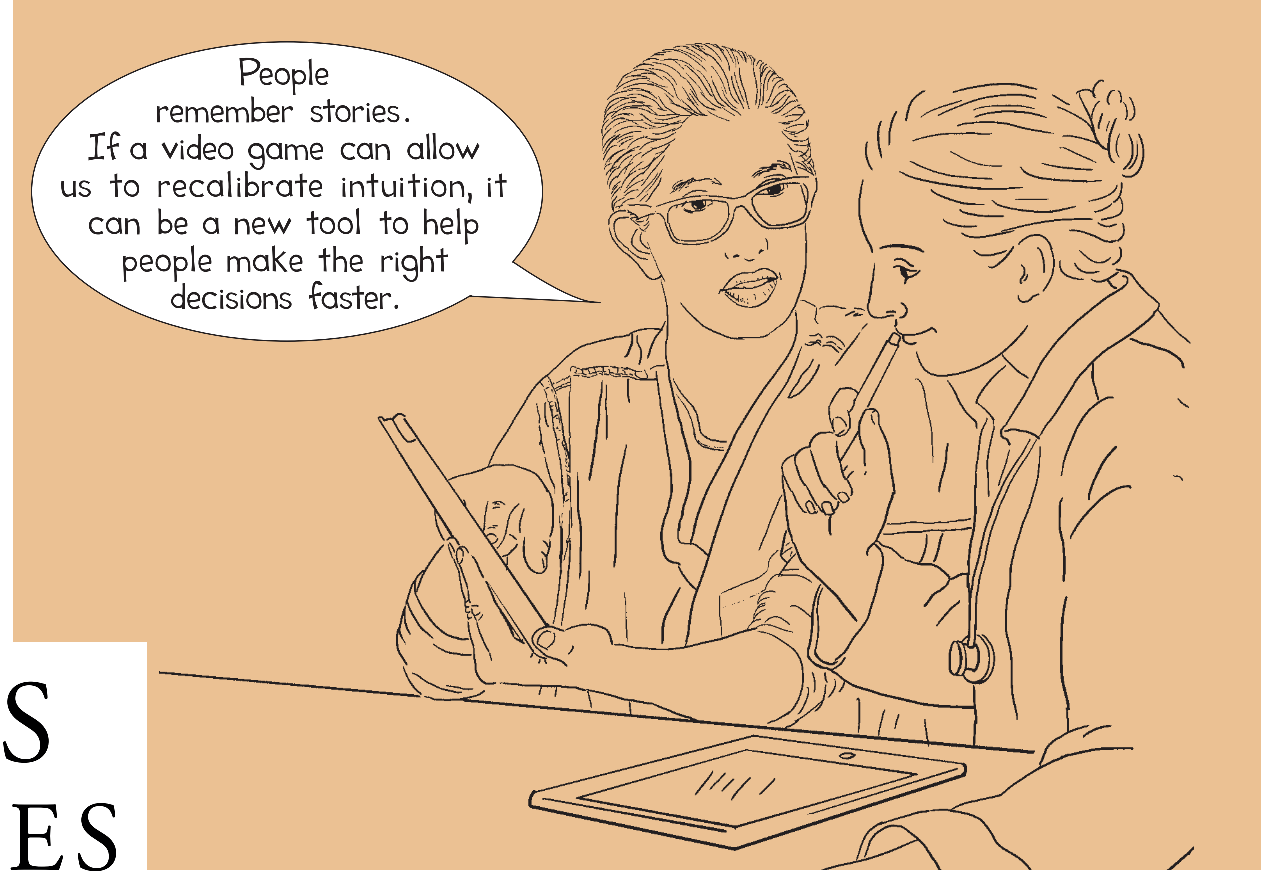
The investigators' evidence suggests that the left mid-fusiform gyrus is the visual information center for words and that its connectivity to other language areas of the brain is also important for reading. It's a cooperative exchange of information among different areas that makes reading possible. Or, as Ghuman puts it, "how we turn the light that falls onto our eyes into something meaningful." ■

TYPOGRAPHY: ELENA GIALAMAS CERRI

PLAY, DOCTOR

BY MICHELE D. BAUM

SERIOUS GAMES



PAUL BRITTENHAM

In critical care medicine, the difference between life and death often hinges on physicians' split-second decisions. For Deepika Mohan, an MD, MPH assistant professor of critical care medicine and surgery, the most important question isn't which decisions are made, but why.

"Most efforts to reduce physician error begin with the idea that decisions reflect knowledge, attitudes, and external constraints," she says. "I argue that intuition often forms the basis of physician decision-making—particularly in critical cases like trauma triage, sepsis, and stroke."

Mohan believes games may be able to sharpen physician judgment. Her study uses a video game, *Night Shift*, developed by Pittsburgh-based Schell Games, which simulates situations a physician may expect to encounter during a typical night in the emergency department—spiced up with a few curveballs and a narrative hook. *Night Shift*'s design is based on behavioral science principles about how people learn.

In October 2016, Mohan sat in a booth at the American College of Emergency Physicians (ACEP) scientific assembly in Las Vegas to recruit attendees to take part in a randomized, controlled trial on her new game. Participants were given iPads and asked to play either *Night Shift* or complete an educational module. Each then undertook a separate online task to determine the degree to which game-play or the educational module could influence decision-making.

"We were recruiting about 30 to 40 physicians an hour. Then someone sent out a tweet at 1:15, and by 1:30 we were swamped," says Mohan. "At 2:30, the conference organizer came up and said people thronging the booth and blocking traffic were creating a fire hazard. She said if we couldn't get it under control she was going to have to shut us down."

In all, 368 ACEP attendees took part, with 80 percent completing both parts of Mohan's study.

"The good news is that the game did, in fact, change practice," says Mohan, adding that the team saw "significant improvement" in performance on the virtual simulation compared to those who did an educational module. "The bad news is there are still some kinks to be worked out—bugs we discovered in the game and some other tweaking we need to do."

The team learned that games are potentially effective tools to change behavior, says Mohan. "That's something no one has really shown [in critical care], so that's pretty exciting. We're part of the way there but haven't hit the home run yet."

Mohan's study is funded by a five-year, $2.3 million National Institutes of Health Director's New Innovator Award, one of 41 conferred in 2015 to support "unusually creative new investigators with highly innovative research ideas" early in their careers. ■

Adapted from the School of Medicine's 2016 annual report.

ON THE NIGHT SHIFT

Those who play Deepika Mohan's serious game, *Night Shift*, enter the world of the imaginary Andy Jordan—an emergency medicine physician who has some problems.

Jordan's beloved grandfather, grief-stricken by his wife's death and incommunicado for several years, has mysteriously disappeared. Now Jordan—living at Grandad's and working as a new attending at the local hospital—needs answers—especially after finding that cryptic I'M NOT DEAD message in the attic.

This intrigue surrounds Jordan as he attempts to settle into his demanding new job. He has to learn the ropes quickly to efficiently interact with hospital staff, evaluate his patients, write clear orders, and make proper diagnoses and treatment decisions—if and when the cranky computer system cooperates. That old fellow in exam room 101 (Benjamin, nice, knows Grandad and may have information to help find him) isn't looking too good. Ben fell off his bike and is complaining of neck pain, with tingling and numbness in one hand.

Better order an X-ray and CT, and maybe a CBC and chemistry profile to be on the safe side. Hang on—someone just came in with a gunshot wound to the abdomen. Think fast, Dr. J.!

GETTY IMAGES

Pitt surgeons are adopting an approach to surgery that throws out some time-honored practices and gets patients moving again sooner.

OVERTURNING PROTOCOL

SURGEONS CHALLENGE THEIR OWN DOGMA

BY JENNY BLAIR

Picture a post-op surgical patient, and you might envision someone bleary, bedridden, fasting, on opioids, and tethered to tubes and catheters. But it doesn't have to be that way. As it turns out, some long-held surgical practices like restricted diets or IV pain medications actually have little basis in evidence—and often stress patients needlessly.

At Pitt, a set of research-tested protocols called enhanced recovery after surgery (ERAS, pronounced ee-rass) is overturning such practices, getting patients to eat, walk, feel better, and go home much sooner.

"I'd call it challenging dogma where there was no science," says surgery chair Timothy Billiar (Fel '90, Res '92).

Surgery and general anesthesia are physically demanding for patients. So ERAS holds that they should optimize their health beforehand. Through this protocol, they get help quitting smoking, losing weight, and building physical stamina before the operation.

"The stress of two hours of anesthesia is the same as the stress of running a 5K race at a high speed," says Pitt anesthesiology professor Stephen Esper (MD '07), a cardiothoracic anesthesiologist who codirects ERAS with assistant professor of surgery Jennifer Holder-Murray, a colorectal surgeon. The pair are spearheading the effort to institute ERAS across UPMC. "Why would you train for a race, but [not] train for your surgery?" asks Esper.

Patients' mental health, too, is something ERAS practitioners work to optimize, in part so they feel empowered to work toward recovery and in part because depression after major surgery can worsen outcomes. It's also important to provide patients with psychological support after frightening diagnoses, like cancer, and if they have substance-abuse problems.

Typically, the night before surgery, patients are told to fast in order to prevent vomiting during breathing-tube placement. But in ERAS, patients can take clear liquids like Gatorade and oral medications as late as two hours before surgery. This seems to do no harm during intubation, and the metabolic tank-up can reduce post-op insulin resistance and inflammation, as well as vomiting.

During surgery, fewer opioids are used, and IV fluids are carefully optimized to meet physiologic goals and avoid both dehydration and fluid backup into the lungs.

And after surgery, patients can drink liquids as soon as they wake up, then take oral medications and solid foods within 24 hours. Abdominal surgeons have long been taught to keep post-op patients from eating until the gut "wakes up." But studies have shown that's not only unnecessary, it's also hard on the metabolism. Rather than the traditional emphasis on pain control via bowel-slowing opioids, ERAS emphasizes using a variety of different pain medications, such as acetaminophen or ketamine.

Reducing IVs helps with another key ERAS goal: moving. Patients need to get out of bed soon after surgery. Lying around can delay bowel function and lead to metabolic problems or even blood clots.

These changes work. Studies of ERAS in colorectal and pancreatic procedures at UPMC found that patients go home at least two days sooner, and they suffer fewer complications—outcomes consistent with what other U.S. hospitals are experiencing. And, most important, those early discharges don't lead to more readmissions.

Danish surgeons developed ERAS in the 1990s; the approach has slowly made inroads in the United States. Since 2015, ERAS has been adopted in colorectal, pancreatic, gynecological, and gynecological oncology surgeries at six UPMC hospitals, and Billiar says its use will be expanded here. Keeping tabs on how ERAS is carried out is key, Billiar says: "It's really easy to slip back into old habits.

"You have to really get people to change their mind-set. When they do, they almost uniformly realize their patients are happier, [and] . . . the vast majority actually do pretty well. [Surgeons] almost always become rapid converts." ■

BLUE LIGHT SPECIAL

COBALT GOGGLES REDUCE INFLAMMATION FROM SURGERY

BY JASON BITTEL

ILLUSTRATION BY MICHELLE LEVEILLE

We tend to think of the immune system as the body's "good guys"—the infection-fighting force protecting us against harm from the outside world. That's a pretty accurate assessment. Yet the role these cells play is not one-dimensional. You see, sometimes it's the good guys, with the best of intentions, that do the most harm.

Just look at arthritis or inflammatory bowel disease. These are conditions where the body's good guys get all hot and bothered over a problem that isn't there. And when they can't find an outsider to blame, the body's own cells become the fall guys.

Or sometimes the immune system overreacts to an infection, which can result in sepsis—inflammation so pronounced that organs start failing.

The University of Pittsburgh's Matthew Rosengart, an MD, MPH, and associate professor of surgery and critical care medicine, has found a way to quiet the immune system (when it's useful for those physiological defenders to lay low). And he does so without using drugs and the side effects that can accompany them. Instead, he uses light.

In a paper published in April 2016 in the *Proceedings of the National Academy of Sciences*, Rosengart and colleagues showed that mice exposed to 24 hours of blue light prior to surgery (surgery is considered a "sterile injury") showed fewer signs of damaging inflammation and necrosis afterward. What's more, the benefits disappeared in mice with optic-nerve degeneration, showing that eyes are more than gateways to the soul—they're portals we can use to manipulate our own biology.

Exactly how or why this works isn't yet clear. Yet, "immune responses are energetically expensive, and so it pays to have them poised during times when threats are going to be maximal," says Rosengart.

The immune systems of humans and other diurnal creatures are more active while the sun is up. After all, we're much less likely to get injured or come into contact with pathogens while we're fast asleep. Blue light seems to have the opposite effect on mice, which are nocturnal.

Evolution appears to have selected for an immune system that takes its foot off the gas in response to certain light conditions. Rosengart is showing that the body cycles through states of vigilance and lax security as it perceives the likelihood of threats around it, and he's envisioning therapies based on those cycles. Light conditions that quiet the immune response in mice are likely to ramp up the immune system in people. And, if controlled properly, augmenting the immune response could be a powerful ally in the clinic, too.

Eyes are more than gateways to the soul—they're portals we can use to manipulate our own biology.

But why *blue* light? Rosengart says that of all the spectra of light that help synchronize circadian rhythms, blue and blue-green have the strongest effect. He did not get the same results with white or red light.

Clinical trials are already under way with pairs of cheap, disposable cobalt-colored plastic goggles that mimic the conditions that benefited the mice. (The mice didn't wear goggles.) Rosengart has some unpublished data that look promising for attenuating inflammation during certain procedures and conditions, but the results are still too preliminary to draw any conclusions.

In any event, don't be surprised if in a few years a doctor gives you a prescription for a pair of cerulean shades. A little light may go a long way.

Studies in mice show that blue light may be able to control the immune response.

A TINY PROTEIN BORROWED FROM ANCIENT CREATURES HAS THE POWER TO TRANSFORM MEDICINE—IF WE CAN JUST FIGURE OUT THE BEST WAYS TO WIELD IT | BY JASON BITTEL

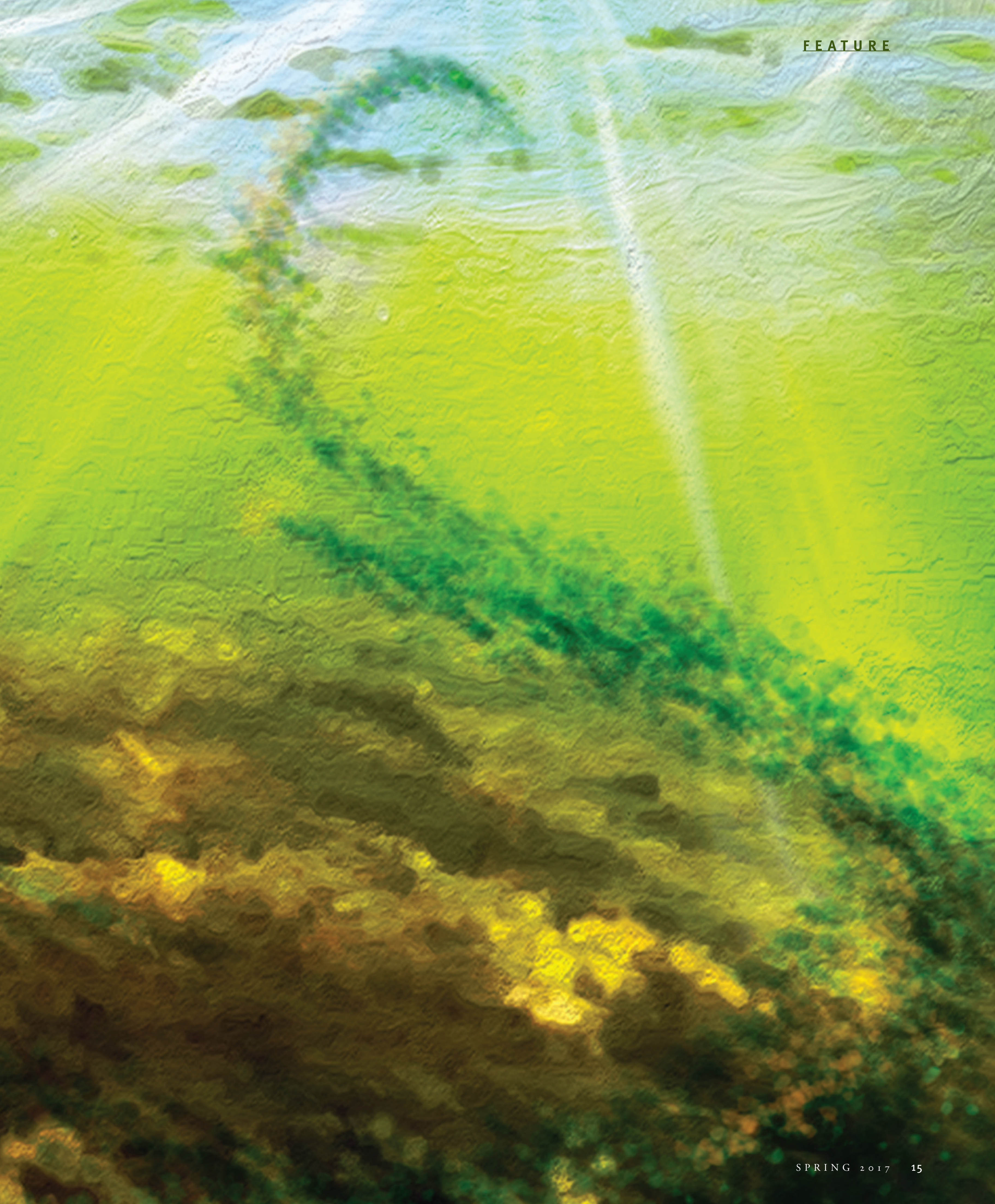
LET THERE BE LIGHT

It's daybreak in the swamp. As the sun peeks over the horizon, its rays crawl across the water and begin to penetrate the murky depths. Below, millions of single-celled organisms sense the light and start flapping their flagella in a desperate attempt to chase down the beams. These life forms eat sunlight by way of photosynthesis, and each day they must migrate out of the dark to harvest photons.

Why exactly are we talking about green algae and their daily sun salutations? Well, only because algae innards have yielded one of the greatest scientific tools of the modern era, and it seems fitting that we should give credit where it's due.

Most scientists believe single-celled aquatic plants like these emerged as many as 1.5 billion years ago. They are among the most primeval life forms. But in just the past decade—an infinitesimally small blink in the history of Earth—we humans have found a way to steal a piece of these creatures and inject it into mice, monkeys, and even humans. We call the tool optogenetics, and scientists at the University of Pittsburgh are using it to unlock some of biology's greatest secrets—from how the brain and central nervous system function to the circuits that govern mental health issues and chronic pain. Someday soon, optogenetics may even allow us to restore sight to the blind or turn whole organs on and off with little more than the press of a button on a remote control.

ILLUSTRATION | MICHELLE LEVEILLE



In 2007, a Stanford researcher named Karl Deisseroth and his then-PhD student, Feng Zhang, introduced these light-sensitive genes into the motor cortex of a mouse. Then, by surgically inserting a fiber-optic wire into the animal's skull, they found a way to bathe these cells in blue light. Turn the light on, and the animal would scamper around in circles. Turn the light off, and the mouse would immediately stop running laps and go back to whatever it was doing before—sniffing the walls or grooming itself.

As you might imagine, this was a pretty big deal. Not only did the researchers prove you could modify the behavior of an animal simply by flipping the equivalent of a light switch, they showed we could hack into and control *individual* neurons by genetically targeting them.

"I certainly had hope that it would be versatile and widely used," says Stanford's Deisseroth, who received the University of Pittsburgh's Dickson Prize in Medicine in 2015. "The potential was clear, but in science anything and everything can go wrong."

About that… The thing about optogenetics is that it's a simple technology, hewn from a simple organism. Flick a switch and see what happens. But porting that technology into humans is akin to taking the switch out of a toaster oven and using it to pilot a nuclear submarine.

You probably know that the brain is composed of neurons. But what you might not realize is that there are thousands of different kinds of these cells, and they differ in size, shape, and the way they interact with one another. Scientists have been sticking electrodes into the brain to stimulate this or that region since the 1700s, and while these experiments were revealing in their own ways, they lacked the finesse necessary to pick through the intricacies of the most advanced organ evolution ever spawned.

"There are just so many different components in the same area, and there's no way to reliably stimulate one electrically without stimulating everything else that's nearby," says Bryan "Mac" Hooks, an assistant professor of neurobiology at the University of Pittsburgh.

But now, the discovery of optogenetics has provided a workaround. All of a sudden, scientists can selectively activate specific kinds of neurons and see what happens. Conversely, through the addition of other light-sensitive opsins that act as inhibitors, like halorhodopsin and archaerhodopsin, they can silence neurons and record what happens (or doesn't) in their absence.

For Hooks, optogenetics means being able to study different kinds of neurons in the hopes of rooting out what circuits control plasticity. Some victims of stroke, for instance, are less able to recover than others. But if we could identify the neurons in the motor cortex that govern this process, then perhaps we could activate or dampen them as needed to make a patient's brain more willing to relearn how to walk, say.

"It's not too science fiction-y to imagine that different cell types have different gene expression patterns, and the products of some of these genes are a variety of ion channels, receptors, and intracellular signaling molecules," says Hooks. "If you find the drug that manipulates specific receptors or ion channels expressed by that cell type and can deliver it to the right place, then maybe you have an opportunity to help somebody who needs to reactivate plasticity in their brain following some kind of debilitating condition, like a traumatic brain injury."

Sarah Ross, who is also an assistant professor of neurobiology, is using a similar process to study the phenomenon of "wind-up." First described around 50 years ago, wind-up is what happens when pain receptors repeatedly fire messages at the brain to tell it something hurts, triggering bigger and bigger responses as time goes on. (If you're reading this with the fascination that can only come from never having experienced wind-up, then consider yourself lucky.)

Even though wind-up was discovered and studied half a century ago, the neural circuits responsible for the excruciating pain amplification have remained a mystery. But recently, Ross and her lab have been using opsins to investigate the condition.

"We showed, using optogenetics, that if you use inhibitory opsins to inhibit a particular subtype of spinal interneurons, you don't get the wind-up," she says.

Unfortunately, this doesn't mean doctors can flick a switch and turn off wind-up in post-surgery patients just yet. But they're not light-years away, either.

"Pain is a major low-hanging fruit," says Brian Davis, a professor of neurobiology and medicine.

If a particular organ is causing chronic pain, and we can identify the channels it uses to send those messages to the brain, then, Davis says, it should be relatively easy to express an inhibitory opsin in those sensory neurons and toggle them with optogenetics.

"You just have a little light, and when your pain gets bad, you turn on your light and the pain goes away," he says. "Think about that—think about the applications!"

In fact, Davis says we're closer than you might imagine. Hooks, Ross, and countless other researchers use mice that have been genetically engineered to produce opsins in particular cell types. But that's not going to work in humans, says Davis, because we're not transgenic mice. And that's where the viruses come in.

In the 1970s, scientists learned that they could use a virus's natural ability to penetrate cells as a way to smuggle other components inside. This is what's known as a viral vector, and they're already in use in humans. In fact, Davis is collaborating with a professor of microbiology and molecular genetics at Pitt named Joseph Glorioso, who has used these microscopic Russian nesting dolls to insert genes that coax a cancer patient's body to produce more of its own, natural opioids. So far, he has shown in a small clinical trial of 10 patients that the delivery system can reduce pain in people who no longer respond to strong pain relievers, like morphine.

While Glorioso's opioid work doesn't employ optogenetics, the virus he's working with, a defanged version of herpes simplex, is a natural neuron invader. This makes it an excellent candidate for becoming an opsin mule.

Davis, Glorioso, and their partners would also like to be able to control another important function—urination. "Spinal cord injury patients have a real problem with urination," says Davis, "and it's actually their number one complaint"—even over loss of sensation and paralysis itself.

For some patients, the worst part may be the constant need to empty the bladder mechanically or the annoyance of constant leakage. But for others who still retain some level of sensation, it's the extremely painful feeling of having to go but being helpless to do anything about it.

Yet manipulating an entire organ will be more difficult than overriding one pain channel. For starters, bladder release is regulated by two separate sphincters—one controlled by skeletal muscle and another by smooth muscle—as well as a muscular layer on the organ's exterior that aids with contraction. So the ideal application would seamlessly incorporate stimuli across this complex network, but do so in a way that is itself not more cumbersome than the symptoms the patients are already experiencing.

Here's a solution: How about a remotely controlled optogenetic bladder sock?

Don't scoff. Thanks to an aggressive outcomes program called SPARC (Stimulating Peripheral Activity to Relieve Conditions), which is supported by the National Institutes of Health Common Fund, Davis and others are already assembling the pieces. A collaboration involving Glorioso, Davis, Kathryn Albers (in the Department of Medicine), and William Goins (of Microbiology and Molecular Genetics) has already shown in a not-yet-published study that they could express channelrhodopsin in sensory neurons in the bladders of mice and cause a contraction with a blast of blue laser light. Another SPARC fellow, a colleague in St. Louis, has been developing a mesh embedded with micro-LEDs, complete with their own power source and ability to be controlled through telemetry. One of the biggest hurdles seems to be getting the optogenetic proteins to express in the right cells, at high enough levels, to actually trigger organ-wide responses.

Porting that technology into humans is akin to taking the switch out of a toaster oven and using it to pilot a nuclear submarine.

Consider the eyeball. José-Alain Sahel, who leads Pitt's Department of Ophthalmology, is using optogenetics to re-activate cells within the retina that have gone dormant. But it's not enough to simply turn the cells back on. Patients need to be able to translate natural light into the specific wavelengths that their cells have been newly programmed to be receptive to. This requires a special set of glasses equipped with cameras and a projection system.

There's still much about this approach that needs to be worked out, but in mice, the researchers showed that resensitized photoreceptor cells could exhibit a full visual cycle, activate cortical circuits, and contribute to behaviors that require some form of vision.

William Stauffer, assistant professor of neurobiology, has been trying to address some of these same issues posed by optogenetics—only the cells he studies are neurons that govern dopamine release. Among other things, dopamine neurons go crazy any time a creature experiences an unpredicted reward. This is why an unexpected bonus at work is more exciting than your monthly paycheck.

This may seem like a subjective difference—the bonus somehow just feels *better*—yet the brain's reaction is actually quantifiable. In the 1980s and '90s, a neurobiologist named Wolfram Schultz used single neuron recording in nonhuman primates to show that dopamine neurons responded to rewards that were better than predicted, but that these same cells were silent when the rewards were worse than predicted.

What's more, you can define these responses mathematically.

For Stauffer, who completed his postdoc under Schultz, optogenetics promised the ability to probe dopamine networks in new and exciting ways. However, he faced the problem of being able to target dopamine neurons and only dopamine neurons (specificity), as well as still being able to achieve high levels of light activation (sensitivity).

"Sensitivity and specificity are *not* independent," says Stauffer, "and it is often necessary to trade off one to get the other."

Fortunately, Stauffer's team was able to bypass this issue by using separate adeno-associated viruses as vehicles for two different opsins—one that was tasked with seeking out the right neurons and another that was designed to deliver high levels of light-sensitive proteins. The old one-two punch, as it were.

But what's even more important is what Stauffer did with his tag team of viruses: He injected them into a rhesus macaque monkey.

This was the first time cell type–specific optogenetics had been achieved in monkeys, notes Stauffer.

Mice have been the optogenetic gold standard for some time: they are small, quick to mature, and notoriously rapid breeders. And, you can order them genetically modified with the light-sensitive proteins already built in.

But mice aren't nearly a perfect model. For instance, the mouse brain is thought to contain about 70 million neurons. That sounds like a whole lot until you learn that the human brain contains 86 *billion*.

"Primate optogenetics will allow us to link structure to function like never before," Stauffer says.

Andrew Schwartz, a Distinguished Professor of Neurobiology, and colleagues figured out how monkeys, and then paralyzed people, could control a robotic arm with just their thoughts. He wants to improve upon that success with optogenetics.

Right now, we can activate peripheral nerves and the muscles they connect to with electric shock, says Schwartz. But this technique tends to recruit certain kinds of muscle fibers to action before others, a glitch that leads quickly to fatigue and lack of power. With optogenetics though, we could generate a small amount of force for a long period of time without getting fatigued. "That's what happens naturally," he says.

Furthermore, the development of opsins responsive to different wavelengths could open up all kinds of other possibilities.

"Suppose you have a bicep and a tricep," says Schwartz. "Say you put a red opsin in one and a yellow opsin in the other. Both muscle nerves join together and travel up the same nerve trunk, so you could put an array of LEDs at one spot on that nerve and selectively activate individual muscles."

As with other startling advances, optogenetics brings new ethical issues to the table. A researcher at Caltech was able to make a mouse attack a latex glove by flipping an optogenetic switch. This sort of demonstration opens the door to speculative scenarios about human behavior dictated by remote control.

Professional bioethicists, however, say practical ethical considerations are more immediately of concern; they cite the need to keep to a minimum the number of people participating in the very first clinical trials that gauge safety and efficacy.

Doctors would be forever altering the nervous system by implanting LEDs and other foreign material. And any time you talk about fiddling around in the brain, there's potential for incurring unforeseen complications. To quote a 2014 review in the *American Journal of Bioethics Neuroscience*, "Optogenetics interventions raise concerns not only for the person who is consenting, but also for the person he or she might become following the intervention, especially if the person experiences negative self-estrangement or significant disruptive personality changes."

The possible clinical applications of the technology are, of course, exciting. Who wouldn't want to be the first to restore sight, end the anguish of chronic pain, or help someone walk again?

But for Deisseroth, who originally coined the term "optogenetics," the appeal is as fundamental as the life forms that made all of this possible.

"I am most excited about the basic science applications," he says. "Some people are thinking about direct clinical applications, but by far the biggest excitement has always been the basic discoveries."

It's daybreak in the swamp, in other words. And we're just getting started. ■

Pitt people are showing how helpful it is to keep a big-picture perspective when approaching illnesses of all kinds—especially when the nervous system, including its master regulator, is part of that picture.

THE BIG PICTURE

MIND IS MATTER, PART II

BY ELAINE VITONE

A lot of docs bristle at terms like *holistic*, so evocative of crunchy, feel-good sales pitches that turn out to be thin on science. Yet evidence abounds of the link between the mind and the body. Notably, as we featured in our last cover story, Pitt investigators have mapped the neural network from a visceral organ all the way to the brain for the first time; that finding was published in *Proceedings of the National Academy of Sciences* (*PNAS*) in August.

Our organs don't live in vacuums, after all—they are part of the whole living, breathing *us*—and the systems of our bodies are in constant cross-talk. Hence it's no wonder that, for example, people with schizophrenia are more likely to have heart disease. Or likewise, that when you heal one ailing aspect of your being, the benefits can have a rippling effect.

Sometimes, potential cures are hiding in unexpected places.

In this second installment of our two-part brain-bodyography, we find out how valuable it can be to approach illness with a big-picture perspective.

ARTWORK | GREG DUNN

GUT FEELINGS

The placebo effect can be potent. In clinical trials for functional bowel disease, it's huge—to the tune of 40 to 50 percent. (In some areas, like cancer treatment, it's negligible.) Why are placebos so powerful in the GI realm? Because in many cases, the source of the problem isn't in the gut at all.

"The signals being sent to and fro, [from the brain] to the GI tract, are deranged, and you can't see that," says Pitt's David Levinthal (PhD '04, MD '06, Fel '12), assistant professor of medicine and director of UPMC's Neurogastroenterology and Motility Center. "It's just something that's essentially invisible to standard medicine. And that's the world of psychosomatic medicine, in a nutshell."


Davis


Gianaros


Levinthal

Levinthal coauthored the *PNAS* paper that was the focus of the first half of this double feature. That study mapped the neural anatomy connecting the brain to the adrenal gland—and paved the way for a more mechanistic understanding of psychosomatic illness.

Now, Levinthal is exploring the brain's links to the stomach and colon. So far, he's presented his preliminary findings at meetings for the Society for Neuroscience, the American Psychosomatic Society, and the American Neurogastroenterology and Motility Society.

In these and other organs Levinthal and his Pitt colleagues are studying, a common theme is emerging. Each organ appears to have neurological "siblings," if you will, elsewhere in the body. For example, the adrenal gland is controlled by a brain region that also controls core muscles. That insight has caused an *aha!* moment for the neurobiology community: If the adrenal gland—which is part of the stress response—and the core are both plugged into the same part of the brain, suddenly it makes sense why people swear by the stress-busting effects of exercises like yoga. Perhaps strengthening the one "sibling" can help fortify the other. And perhaps doing right by the "kids" can be good for the "parents," too. Because it's all part of the same network. One big, happy family.

In Levinthal's preliminary data, the colon appears to have a neuroanatomical sibling, as well—the leg musculature. And if you've ever been stuck in a hospital bed, or a cast, or anything else that has limited your walking-around time, that's a potential *aha!*, too.

"It's well known that immobility is on the short list of things that cause constipation," says Levinthal. And that amounts to much more than just discomfort—the wait for the bowels to come online and back to working order can lengthen post-op stay, Levinthal reminds. "It's important to establish that [function] before you let someone out of the hospital."

As for the stomach's neurological family tree, it's a bit more complicated. In Levinthal's rodent studies, the stomach appears to have two "parents" in the brain. One parent is a brain region that is also the parent of your adrenal gland's fight-or-flight response system. And the other parent? It's a brain region that governs the vagus nerve, which is a truly odd duck in neuroanatomy. Your vagus nerve is giant, extending from the brain stem itself all the way down and through you, influencing virtually everything about your physiology. "It's a visceral-sensory, visceral-motor, general-sensory, and skeletal-motor nerve all wrapped up in one," says Levinthal. (Talk about a Big Brother.)

So this "parent" brain region shared by the vagus nerve and the stomach—the insula, as it's called—is a seat of higher-order functions like emotion, cognition, empathy, and decision-making. "Which is really interesting," Levinthal says. Think fainting at the sight of your own blood or at the mere sight of a syringe: that's your vagus shutting you down.

Vagal responses, as these spells are called, can befall you with all sorts of triggers, from prolonged standing to low blood sugar to the prick of a needle, and the mechanisms of how all of this works are still unclear. Yet, says Levinthal, "Clearly, mind matters."

Similarly, the gut-churning nausea we feel in moments of emotional upheaval, like embarrassment, shock, or sudden loss, may well be the work of the vagus—the stomach's sibling.

The vagus-stomach network is "very clear" in Levinthal's rodent studies, and so far it's holding up in early studies of nonhuman primates, too. And now, with funding from the National Institute of Diabetes and Digestive and Kidney Diseases, Levinthal is undergoing training in a technique called transcranial magnetic stimulation (TMS), a noninvasive tool that will eventually allow him to safely map these neural networks in humans. Using a rapidly moving magnetic field that induces a current, TMS makes it possible to actually stimulate specific neurons on the surface of the brain from outside of the skull.

"You could use TMS as a probe, as a tool, to influence the system, and then measure some of those effects at the stomach level, or the colon, or other organs," he says. Eventually, he hopes what he learns will inform a new therapy possibility for people with the debilitating GI diseases he sees in his clinic every day. TMS is already FDA approved for patients with depression.

Additionally, this work is giving the team a new window into what brain areas may be involved in regulating the vagus, that supernerve so broad in its reach and so mysterious in its impact.

HEAD AND HEART HEALTH

In the '70s and '80s, we had a stereotype for a heart attack waiting to happen: a rage-filled, perpetually rushed, competitive, short-fused guy that we called a type A personality. This hypothesis launched an explosion of research, which, over time, revealed a more nuanced understanding of stress and cardiovascular disease. Really, hostility was the important part of this cardiovascular caricature—and you don't have to be a workaholic businessman to suffer its cardiovascular effects. Further, the research community found, factors like social support—or lack thereof—play important roles, as well.

For decades, the University of Pittsburgh has been among the top institutions studying stress and cardiovascular disease; Pitt has one of the oldest training grants in cardiovascular behavioral medicine in the country. Its director, Distinguished Professor of Psychiatry Karen Matthews, and her fellow Pitt giants in this field—J. Richard Jennings, Stephen Manuck, Thomas Kamarck, Anna Marsland, and Matthew Muldoon—have been at the forefront of disentangling such heart-health influences as psychosocial factors, genetics, environment, immune response, development, and age.

This rich head/heart-health history is part of what drew Peter Gianaros here 16 years ago as a postdoc—he then got a National Institutes of Health award and stayed. "I can't imagine being anyplace else in the world," he says. "We have leading neuroscientists and leading researchers in cardiovascular behavioral medicine in one place."

Gianaros, now a professor of psychology and psychiatry, studies the neurological basis for the sort of mental stress that sets blood pressure to the boiling point. Using fMRIs, he's working to establish the brain signature of people who develop stress-related cardiovascular disease, which he hopes might eventually be a way to flag people at risk. Gianaros has found that one brain region in particular lights up in those who have especially amped-up cardiovascular responses to stress: the anterior cingulate cortex. Recently, that very same region was also found to be hardwired to the interior of the adrenal gland—the body's stress-hormone factory—in nonhuman primates (as detailed by Levinthal with Pitt's Peter Strick, the Thomas Detre Professor, chair of neurobiology, and scientific director of the Brain Institute, and Richard Dum, a research associate professor of neurobiology).

Gianaros was excited to learn this particular finding holds up across species. "It just shows how [studies in animals and in humans] go hand in hand to converge on the ground truth," he says.

"The signals being sent to and fro, [from the brain] to the GI tract, are deranged, and you can't see that. It's just something that's essentially invisible to standard medicine."

Gianaros is also interested in how residing in socioeconomically disadvantaged neighborhoods can affect people's hearts and heads.

In recent years, investigators at Pitt and elsewhere have found that poverty truly is hazardous to your health, Gianaros notes. One study published in *PLOS ONE* in 2015 by Pitt's Mijung Park with Charles Reynolds and colleagues suggested it may even shorten our telomeres—molecular measuring sticks for our life expectancy. (See p. 30 for more on Reynolds's influential work on mental health.)

In a sobering paper forthcoming in *Cerebral Cortex*, Gianaros's team studied people who live in high-unemployment, low-income Pittsburgh neighborhoods. The team found that these Pittsburghers not only are more likely to have risk factors for heart disease, but they also have reduced levels of gray matter, especially in the brain's cortex—and these trends may not be happening independently of each other.

Granted, cause and effect is tricky to establish in observational studies like this. But, Gianaros says, one widely accepted maxim in medicine is that red flags for cardiovascular health—like elevated blood pressure, cholesterol, and glucose—are dangerous for the brain, too. In this study, the team noticed a troubling pattern in the production of the stress hormone cortisol among study participants. The researchers hypothesized that stress physiology "might be negatively affecting the brain, not just the heart or other organs of the body," says Gianaros. He's planning further studies to put these ideas to the test.

"The take-home message," he says, "is that what's bad for the heart is definitely bad for the brain, and disadvantaged areas create an environment that may be bad for both."

In the decades since the type A hypothesis, behavioral medicine and biological psychiatry have "exploded," says Gianaros, not only because now we have the technological tools to draw these connections, but also because the global health concerns of our time so often overlap.

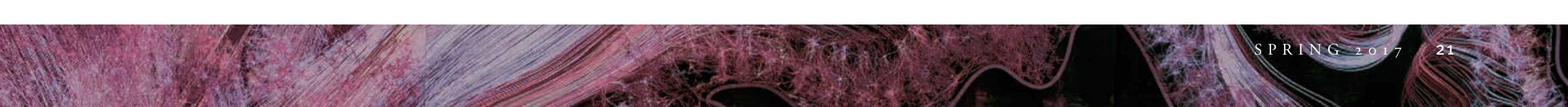
"I think that people are gaining appreciation that a lot of disorders of the brain don't exist in isolation from disorders of the body," he adds.

OH, THE (SENSORY) NERVE

About seven years ago, Brian Davis, a pain biologist, was studying a mouse model of pancreatic cancer when he noticed something odd. The tumor cells were releasing growth factors that bound to the sensory nerves within the pancreas, spawning massive neural growth and sensitization and making a bad situation even worse. What's more, the cancer then began to damage the nerves, causing them to send molecular distress signals to the immune system. Which then caused the kind of excessive inflammation that is *itself* cancer fueling.

"It wasn't a huge leap for us," says Davis, a PhD professor of neurobiology and medicine. "Sensory neurons drive inflammation; inflammation drives cancer. So what if we get rid of the sensory neurons?"

The team injected capsaicin—a natural, nerve-snuffing component of the chili pepper—into young mice with pancreatic cancer genes, wiping out much of their sensory nerves. "We didn't think it would stop the



The environment that sensory nerves create can determine whether cancer lives or dies.

cancer. We hoped that, at best, it would slow it," Davis says.

They were astonished to find that disease progression ground to a halt—especially in the mice who had almost all of their sensory nerves nulled. Though the animals did develop precancerous lesions, the tipping point never came. The study was published in *PNAS* in March 2016.

In December, Davis and his colleagues published a review paper in *Trends in Neurosciences* showing this was no fluke, making a damning case for nerves as cancer conspirators in humans. And in the realm of animal research (on prostate, stomach, and skin cancer), the team notes that such high-profile journals as *Science*, *Science Translational Medicine*, and *Cell* have published findings that—sometimes in metastasis, and sometimes even in forming a primary tumor in the first place—cancer fails to get a foothold when sensory nerves are out of the picture.

This unexpected new direction in Davis's research has underscored for him just how underappreciated our sensory fibers are. In fact, some pain biologists have given them a new name more befitting their status: metaboreceptors. Calling them pain fibers is "demeaning," he says—they're better than that.

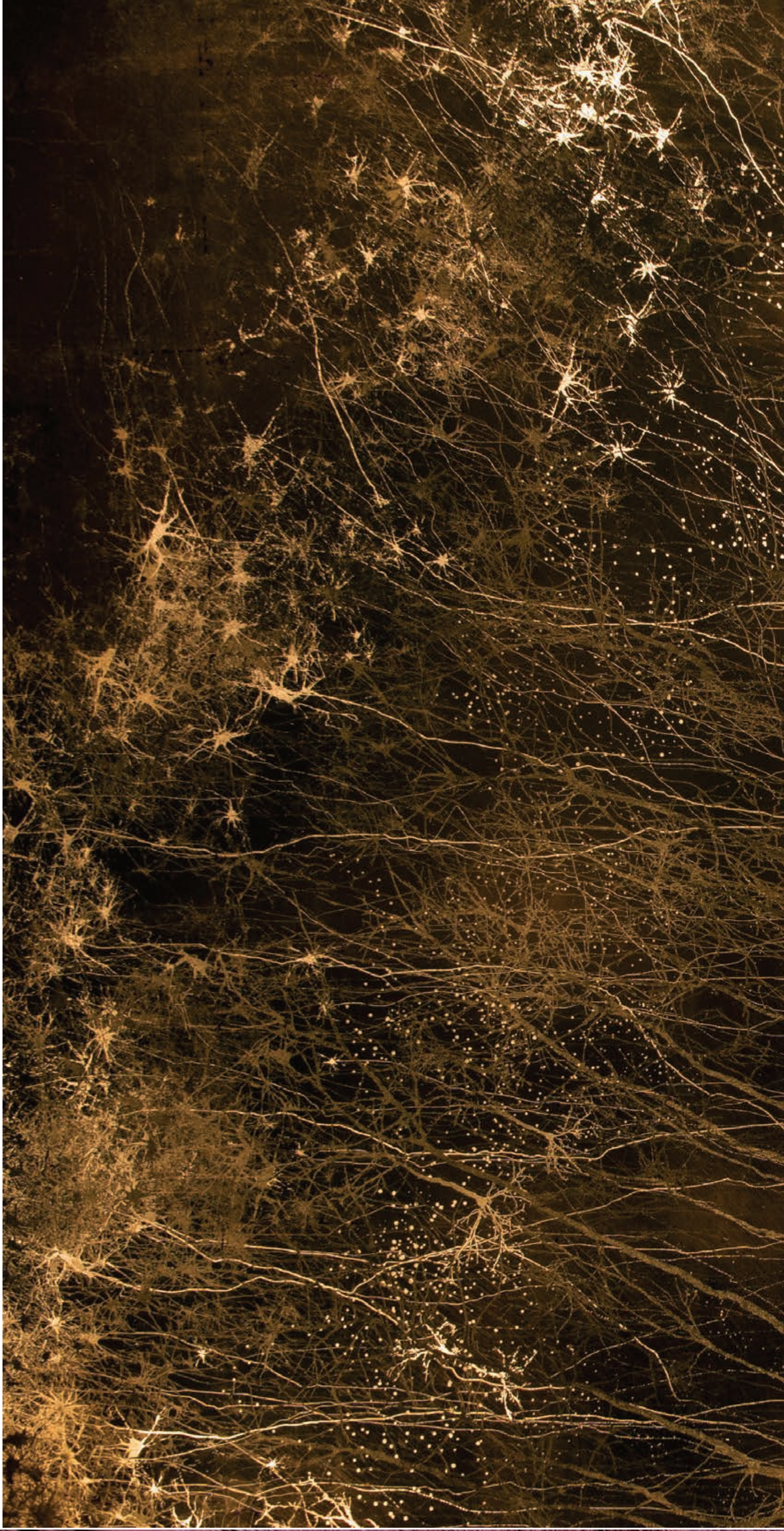
Perhaps, he says, "their normal day job is to help maintain peripheral tissues, to keep them healthy. They interact through the release of small molecules to coordinate the homeostatic mechanisms that every tissue needs. This is their real 9-to-5 job." And then, occasionally, they let you know you are sick or have an owie.

Neurons of all stripes communicate with one another about our sensory input, automatic functions, and motor movements, Davis explains. The brain integrates all of this information and sends descending input right back down through our bodies—including, if we're so unlucky, to tumors.

And this is where stress comes in.

"We *know* it's a bad prognosticator for cancer patients," says Davis. "We *know* that if you can control stress, if you use drugs that keep patients from being all freaked out, they do better."

The fuel to the fire that is cancer, he says, is "a very holistic kind of a thing." ■



MED SCHOOL AND THE MILITARY

BY MICAELA FOX CORN

STUDENTS OF VALOR

Early one morning in June 2002, **Sangki Oak** (Class of ’19) dressed for work and sat in the kitchen perusing the *San Jose Mercury News* over breakfast. Old ideas began to percolate as he read one story: Motivated by the attacks on 9/11, a safety for the NFL’s Arizona Cardinals had enlisted as a U.S. Army Ranger.

Oak had not known Pat Tillman’s name before that morning—he was no football fan—but he had been similarly moved to enlist after 9/11. Uncertainties about the lifestyle change had been keeping him at bay. He was comfortable—a 27-year-old hardware engineer helping to shape the dot-com boom in Silicon Valley. He’d worked hard to build his career ever since graduating from Duke University with a degree in computer science. His field was changing rapidly; it had dawned on him that he might struggle to be marketable again if he did a tour of military service.

Then again, the day job wasn’t always the most morally fulfilling, he thought. Tillman’s multimillion-dollar NFL contract surely must have been harder to walk away from.

Months later, Oak enlisted with the U.S. Navy as a medic because of an affinity for hands-on work, travel, and the ocean. It’s ironic, he says looking back, as he didn’t see the water during two tours in the mountains of Afghanistan.

COURTESY SANGKI OAK

LEFT: Sangki Oak at Pitt.
RIGHT: Oak sees patients at a clinic in Afghanistan.

PHOTOGRAPHY BY CAMI MESA, EXCEPT WHERE NOTED

He first deployed in 2009 to a base near Herat, where he was the sole medical provider to a unit of U.S. Marines. The first five months were fairly quiet. At a one-day pop-up clinic Oak set up and staffed in the village of Qal-I-Naw, more than 300 patients lined up outside. Most acute issues he was able to fix: a stitch here, a topical cream there—he had been trained to treat healthy marines. But for the more puzzling chronic conditions locals faced, he was at a loss.

One father, holding his limp, pallid child in his arms, smiled and nodded understandingly when Oak told him that there was nothing he could do for her. *I just don't know enough medicine*, the medic thought, ideas percolating again. "It was the straw that broke the camel's back," Oak recalls. "I needed to be a doctor."

As the deployment progressed, his unit shifted to the offensive.

"We stirred up the hornet's nest, and things got a lot more violent. There were a lot of casualties on my team. We actually were hit pretty hard." Oak and a couple of team members were sent to an American-Italian base and tasked with expanding capacity. Located near the village of Bala Murghab—a Taliban stronghold—the base was essentially a bubble.

"There was a line in the sand, basically, that if Western forces crossed, they would get lit up," he says.

The unit returned home, but it was soon asked to redeploy. Oak's contract was up, yet he didn't want his buddies to go without their "doc." He extended his contract and returned to Afghanistan.

Returning to the States in June 2011, he launched himself into premed courses at George Washington University, then a first round of medical school applications, followed by a second. Pitt had been a long shot (he claims), but the second-year student has since found his stride. He's spoken with Pitt med's student Military Medicine Interest Group about his experiences with casualties in the field and about caring for people in austere locations. Oak plans to work toward a Master of Public Health during the second half of med school.

In 2015, he traveled to Nepal with Team Rubicon. The 60 volunteers—military vets and civilians—offered aid following the 7.8 magnitude earthquake that tore through the Kathmandu area. Oak has also spent time in Syrian refugee camps near the Iraq border, assessing the conditions of the camps.

"The benefit of having done military service is you find a way to make [things] happen," says Oak, 41.

A coordinator of Pitt med's Global Health and Underserved Population Interest Group, he's intrigued by the potential of 3-D printing for addressing some of the challenges of providing care in resource-poor settings.

Last summer, he received notice from the Pat Tillman Foundation that he had been named a Tillman Scholar. Support from the foundation will allow him to hit the ground running soon after graduation as a health care provider in overseas communities that need him most. (He won't have to spend years paying off school loans.)

And, notes Oak, "Being a Tillman Scholar connects me to a larger community of veterans with the common goal of helping to make the world a better place."

LEFT: COURTESY SANGKI OAK. RIGHT: COURTESY KIMBERLY BELL.

ABOVE: Oak bonds with children in a village near Herat. **RIGHT:** Kimberly Bell and a fellow Army National Guard recruit in a medic exercise during active duty training.

Kimberly Bell

When **Kimberly Bell** (Class of '17) received her first bill in the mail from community college, she balked, then worried. Neither of her parents had graduated from college. (When she was born, her mom was 15 and her dad was a young U.S. Army medic.) There was no one to help answer questions like, *What do you mean "financial aid"? How do you fill out a FAFSA?*

Then a high school friend dropped her a line: *You know, the National Guard will pay for everything.* A month after graduating in 2005, Bell enlisted. *But I won't sign the contract unless I can be a medic,* she said. The Guard agreed.

Learning to be an effective first responder to natural disasters in Pennsylvania took rigorous drilling—one weekend every month and two weeks a year for six years. Bell did standard military active duty training, as well. (The Army National Guard can be called up as federal reserve troops.) She also completed EMT certification.

All the while, she was going to school. And raising a family.

In 2011, after transferring from community college, Bell graduated from Pitt with a bachelor's in biology. Her two daughters, 1 and 3 at the time, watched their mother cross the stage in cap and gown—and almost as quickly as the tassel turned, watched her sights set on Pitt med. During her final two inactive duty years with the Army National Guard (she was never called up), Bell applied to several med school programs and worked in the maternity ward at Magee-Womens Hospital of UPMC. By the time she became a first-year med student in 2013, she'd zeroed in on ob/gyn as a specialty.

It appears that the 30-year-old's approach to life is highly practical and strategic. (Think General MacArthur's island-hopping tactic.) In truth, Bell says, she has always been a dreamer—one laser-focused on adding "MD" to her name.

And now earning that MD is close enough to touch. The fourth-year says her time in the military has carried her here, by teaching her discipline, patience, and the value of a team.

"I formed such a great bond with the people I went through basic training and medic training with, because the situation was difficult, and we leaned on each other.

"Med school is just like that. We're all struggling in the same way, going through the same things, and we have each other. And I love it."


Kendra Parker-Pitts

OFFICER TRAINING

While **Kendra Parker-Pitts** (Class of ’17) was a Pitt undergrad, the biology and Russian major traversed the streets of Pittsburgh as an EMT. Those ambulance rides cemented Parker-Pitts’s love for emergency medicine.

Now, the high-speed fourth-year is participating in the U.S. military’s Health Professions Scholarship Program (HPSP). Through HPSP, prospective military physicians go through med school on the military’s dime and become officers in the army, navy, or air force.

Besides the six-week army officer training course Parker-Pitts took the summer after her first year, HPSP is not a big time commitment while you’re in school, she says. After graduation, she’ll serve on active duty in the army for four years in exchange for her four-year scholarship.

On bonding with some 300 recruits

“Military medicine in general isn’t a huge community, so it was nice to go and meet some of the people I’ll be working with in the future [at officer training]. And when I was interviewing for residencies, I ended up knowing pretty much everyone I was interviewing with [from basic training], which is something that doesn’t happen at all in the civilian world.”

On rotating at the VA

“The patients are wonderful. Not only is it amazing to be able to care for them after knowing how they served and protected us, but they are also lovely to work with. They are so thankful for the care they’re receiving. They know you’re all on the same team.” —*MFC*

TWO-WAY STREET

"'Tourniquet' used to be a dirty word" in civilian medicine, says Sangki Oak (Class of '19). Not anymore. A national campaign (with Pitt leadership) is teaching citizens to use bleeding-control satchels containing tourniquets and gauze to help victims of trauma wounds. (See p. 5 for more.) "I've packed hundreds of those kits" in the field, Oak says of his time in Afghanistan.

Military medicine practices have informed prehospital and emergency medicine for years. Triage, transfusion medicine, and telemedicine were all used in the military before they innovated the civilian world, notes Jo-Anne Suffoletto, of Pitt med and the VA. (By the way, Pitt's Ron Poropatich led early cross-continental efforts in army telemedicine when he was with the Department of Defense in the '80s.)

But the flow of ideas goes two ways. You can't innovate if you don't investigate, notes Poropatich. That's where academic medical centers come in.

The University's Center for Military Medicine Research is a frontline player looking into ways to improve trauma care (to the tune of up to $90 million from a recent DOD grant). The center also fosters major efforts in rehabilitation medicine, tissue engineering, vision restoration, bioinformatics, PTSD, and other areas. —*MFC*

JOINING FORCES

Alvin Thalappillil's (Class of '18) interest in veterans' health started close to home—with his brother, a veteran injured in the Iraq War, and his father, who served in India's military. So in spring 2016, he took a new minielective at Pitt med called Joining Forces: Caring for Veterans at the VA and in the Private Sector. The elective was inspired by the national Joining Forces effort, announced by former first lady Michelle Obama in 2011, to ensure the highest standard of care for American military families.

Thalappillil wanted to understand veteran patients within the context of their lives and what they were looking for from their doctors. "If you haven't seen war, it's a difficult thing to ask about. You have to be sensitive," he says.

But it's worth the effort, says Jo-Anne Suffoletto, assistant professor of medicine and associate chief of staff for education and innovative learning at the VA Pittsburgh Healthcare System.

"To miss asking patients about military service history is to miss a whole formative part of their life, and the impact it may have had on their overall trajectory."

Pennsylvania is home to the fourth-largest number of vets in the country (as of 2014, the most recent year for which data are available). And "there's a very significant veteran population in the Pittsburgh region," says Ron Poropatich, executive director of Pitt's Center for Military Medicine Research, professor of medicine, and retired army colonel.

Encouraged by student interest, codirectors Suffoletto and Poropatich are teaching the minicourse again this spring. —*MFC*

Reynolds (second from left) with colleagues and volunteers at Sangath in Goa, India.

THE SOUL OF PSYCHIATRY

REYNOLDS DEVOTES HIMSELF TO HELPING OLDER ADULTS LIVE WELL

BY SALLY ANN FLECKER

Charles F. Reynolds III is an affably serious man. He's a lover of Roman history and of Latin, who long ago studied philosophy. He presents himself as mild mannered, although you don't have to talk to him long before you understand exactly how sharp and penetrating his intellect is. But he's ever congenial; he easily could be cast as a benevolent pastor. His once ash-brown hair, now that he's 69, is mostly gray. He sports round wire-rim glasses and prefers a blue oxford-cloth shirt and dark-red tie when he knows he's having his picture taken. His friends call him Chip.

And there's a series of exercise videos that he "stars" in. This accolade is one he uses himself—with tongue firmly in cheek. In these videos, he stands behind a young trainer, following her example for an easy 10-minute workout. Dressed in a plain T-shirt and gym shorts, he marches in place, step-together-step-tap, and thrusts his arm as he does a leg kick. Some of the time, like many of us in an exercise class, he is in great form. Other times, again like many of us, he is a smidge out of step. He embellishes the march in place with enthusiastic arm movements. He stays unflustered.

SNAPSHOT BY ELLEN DETLEFSEN

Chip, as Reynolds is introduced simply in the video, is no generic volunteer. He is head of the Aging Institute of UPMC Senior Services and the University of Pittsburgh. The videos are produced by an Institute work group that is looking at lifestyle changes that may make a difference in cognitive fitness in the later years of life. The group would like to know, for instance, how much exercise it takes to stave off cognitive decline. Hence, the fitness videos with new routines sent out every week to participants in the study.

"They've been really popular with our clinical subjects," says Pitt's Judy Cameron, professor of psychiatry, who heads that work group and whose research looks at the neuroprotective effects of exercise on the brain. When the videos were played as part of a science outreach program at the tailgating party for Pitt's homecoming game, Cameron says that 450 people "exercised with Chip." She adds, "We teased him mercilessly."

Healthy aging has been a career fascination for Reynolds, who is also founder and director of the National Institute of Mental Health (NIMH) funded Center of Excellence in Late Life Depression Prevention and Treatment at Pitt. He has devoted decades to understanding, easing, and preventing depression suffered by adults in later life. A roll call of his many appointments offers a glimpse into the breadth and depth of this 44-year exploration. Reynolds is a Distinguished Professor of Psychiatry and the UPMC Professor of Geriatric Psychiatry. He's also editor in chief of the *American Journal of Geriatric Psychiatry*. His curriculum vitae is 78 pages long. He's at the top of his field.

Heartache steered him toward this work.

Reynolds was a senior medical resident at the Western Psychiatric Institute and Clinic when his grandfather died.

The first Charles F. Reynolds had enjoyed a good life. He was a successful cotton farmer, working the soil on a remote plantation in Mississippi, happily married to "Miz Naoma." Then in the late 1970s, he suffered a stroke. In the aftermath, the 90-year-old became so deeply depressed that he took his own life.

"The experience of losing a loved one to suicide made my academic and scientific interest in depression in older adults very much deeper and more personal," Reynolds recalls.

Reynolds had intended to spend the bulk of his days as a biological psychiatry researcher. But, he says, "I realized that the soul of psychiatry and its attraction for me was in treatment."

Although Reynolds did not abandon research, he focused his studies on immediate interventions that might provide improved treatment choices for the patients and families he and other clinicians cared for in their practices. His grandfather was always with him—as a reminder both of how merciless depression can be, and of the need for more effective treatments.

He's done a mountain of work to which geriatricians refer. (His publications have been cited more than 36,000 times.) Of particular note are three long-term trials on psychotherapeutic and pharmacologic interventions to keep depression at bay in older adults. Trial results were published in the *New England Journal of Medicine*, *JAMA*, and the *Archives of General Psychiatry*.

"Depression in older adults tends to be a chronic, relapsing illness," Reynolds says. "I like to say to my patients and their families, *We want to help you get well, but getting well is not enough. It's staying well that counts.*"

Because depression is also known to be a risk factor for dementia, one of these studies included a long-term, controlled clinical trial to combine a maintenance antidepressant with a cognitive enhancer, donepezil.

"Our work suggests the possibility that by appropriate treatment of depression, and with the addition of cognitive enhancers, we may be able to slow the progression from depression with mild cognitive impairment to depression with frank dementia," he says.

And, he adds: "If depression is a risk factor for dementia, then does preventing depression or treating depression delay, prevent, or attenuate the clinical expression of Alzheimer's dementia or vascular dementia? That's the big question. We think that it does [those things], but we don't yet have the data."

Through the years, Reynolds has directed other intriguing investigations. For instance, he developed evidence-based treatments for depression that can be carried out successfully in primary care settings that are rural or urban, inner city or suburban.

This is important because, as he puts it, "Most older adults don't want to see guys like me. They want to see primary care docs. My grandfather had not had access to mental health services. He was on a remote farm in Mississippi, a thousand miles away."

In an eight-year follow-up to the primary care study, Reynolds's team made the unexpected observation that patients in the intervention arm had a 24 percent better survival rate during the follow-up period than those who received usual care without the intervention. When Reynolds's team looked into the causes of death in the other group, they expected to see conditions like heart attack and stroke. Instead, the excess mortality was related to deaths from all kinds of cancer.

"We were puzzled by the finding. Could it be biologically plausible? Or is it just a chance finding?" he wonders aloud.

At first, they approached the question from a behavioral perspective, i.e., if your depression is getting treated, maybe you're more motivated to follow up with good medical care (which can translate to early detection of cancer or other conditions and adherence to prescribed medications). Maybe you'll be more likely to adopt a healthy lifestyle—start to exercise, cut back on smoking, eat better.

Discussing the finding with University of Pittsburgh Cancer Institute colleagues gave Reynolds more food for thought. It was plausible, they told him, that cellular and subcellular aging could explain the unexpected observation.

"We knew that chronic stress, as in depression, is associated with measures of accelerated cellular aging—for example, as exemplified by accelerated shortening of telomeres at the end of the chromosome," Reynolds explains.

"And so we've gotten very interested in delving into a number of areas related to the biology of aging—abnormal protein expression, abnormal metabolism expression, oxidative stress, decreased support for nerve cells, and blood vessel health."

His grandfather was always with him—as a reminder both of how merciless depression can be, and of the need for more effective treatments.

In October, the 2016 Pardes Humanitarian Prize in Mental Health was awarded to Reynolds "for pioneering work in geriatric psychiatry and the prevention and treatment of late-life depression." The award was shared by his colleague Vikram Patel at Sangath, an NGO in Goa, India, "for transformative work in advancing mental health care in resource-poor countries."

Reynolds has been collaborating with Patel on a trial studying the prevention of depression in late life. The trial, which explores the use of lay health counselors to provide early intervention in depression, is near and dear to Reynolds's heart both for its prevention of depression as well as its outreach to underserved adults.

The Pardes prize comes with a $300,000 cash award. Reynolds plans to donate his share entirely to Sangath. He wants the NGO to be able to further research on mental illness across the life cycle, which Patel and others there are pursuing.

Several times in our discussion, Reynolds emphasizes that his most gratifying work comes from collaborations. (The gushing comes from the other side of those collaborations, too.)

"It's been a wonderful journey," says Reynolds, "with great colleagues. Not only the medical school, but the other schools of the health sciences are really collaborative. People around here love to work with each other. We live much less in silos than do my colleagues and friends in other institutions."

Reynolds has tried to pay forward the mentoring and support he received from David Kupfer, Distinguished Professor Emeritus of Psychiatry, and Thomas Detre, the late senior vice chancellor for health sciences, who lured him here from Yale decades ago.

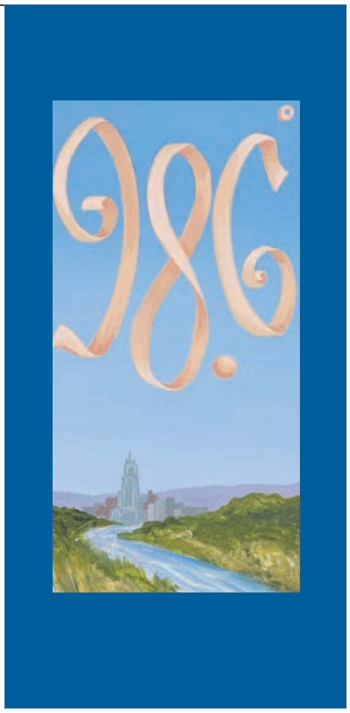
"I've devoted a lot of my own career now to mentoring younger scientists. In my NIMH center, since 1995, we have mentored and sponsored more than 25 NIH research career development awardees. We've been very successful in growing the next generations, plural, of investigators, PhDs and physician investigators in geriatric mental health research (from basic and translational science to applied and health services research). That's a part of my own legacy that I'm particularly proud of."

But another part of his legacy these days resides in Maine. Reynolds and his wife, Ellen Detlefsen (associate professor emeritus of library and information science), have pulled up their Pittsburgh roots to be nearer to one of their sons and his family.

Reynolds isn't ready to use the word "retirement" yet. In fact, he's planning to continue with his academic appointment through 2017 and with his role as coinvestigator on a number of projects around the country and in India. This is more of a recalibration, he says, of the balance between his professional life, family, and personal interests. Speaking of which, Reynolds is looking forward to spending lots of time with his grandchildren—Maggie, 4, and Kip, 7, who's "already skiing!" says Reynolds. He's all set for Kip to teach him the sport. "I've stayed in good shape. I'm pretty flexible for a guy in his 70th year."

This much is clear: You're not going to catch Reynolds standing still. ■

People and programs that keep the school healthy and vibrant



TYPE "O"

A UNIVERSAL DONOR

BY MAUREEN PASSMORE

In football, offensive linemen are the strength of the offense. They protect the quarterback and other teammates running or catching the ball. Usually the biggest men on the field, these players are known for strength, grit, and heart. University of Pittsburgh grad James Covert played on the "O line" for three of his four years on the Panthers team that went 31–5 in the early '80s. (The quarterback he was protecting then was his roommate, Dan Marino.)

Covert was a first-round draft pick of the Chicago Bears and a member of the 1985 Super Bowl XX championship team coached by Pitt and National Football League legend Mike Ditka. Covert's cocaptain on the Bears' offense, Walter Payton, called him the "best offensive tackle in the NFL."

So, what does a lineman do when he retires from the game? He continues looking out for others—just in a different way.

In 2007, after several years in health care sales, marketing, and acquisition initiatives with different companies, Covert joined the Institute for Transfusion Medicine (ITxM) as president and chief executive officer. ITxM specializes in transfusion medicine and related services. With its two blood centers, Central Blood Bank in Pittsburgh and LifeSource in Chicago, it provides many hundreds of thousands of units of blood products annually.

One of Covert's first goals for ITxM was to create a strategic plan, and a large part of that plan was research. He asked, *Why not forge a relationship with a biomedical powerhouse right here in Pittsburgh?*

With Covert's guidance, a relationship between ITxM and Pitt was solidified; that effort focuses on research on blood disorders and blood-related diseases and on serving people with those conditions. A joint gift from ITxM's Blood Science Foundation and ITxM's subsidiary, the Hemophilia Center of Western Pennsylvania, allowed for the creation of the School of Medicine's Vascular Medicine Institute (VMI). The VMI is directed by Mark Gladwin, the Jack D. Myers Professor of Internal Medicine, Distinguished Professor, and chair of medicine. Covert calls the partnership a "win."

"We committed the seed dollars, and once Mark got started, *boom!*, he really took off. He's a dynamo," Covert says. "That passion and energy is what has made VMI so successful."

Covert also credits another group of contributors. "People who give us the gift of their blood in order for us to treat patients are doing an altruistic act. The dollars we earn that go into the Blood Science Foundation really come from the community, and I feel strongly that the money needs to go back into the community."

When he was asked to join the Board of Trustees at Pitt in 2014, Covert saw it as another chance to help. "Pitt has given me so much in my life. I came from a small steel mill town near Pittsburgh and grew up and met my wife at Pitt," he says. "As my career since football has gone through changes, Pitt has prepared me for that.

"You can't say that about a lot of places."

Reprinted from the School of Medicine's 2016 annual report, Adaptation.

ANNIE O'NEILL

Covert helped start Pitt's Vascular Medicine Institute.

BOOSTER SHOT

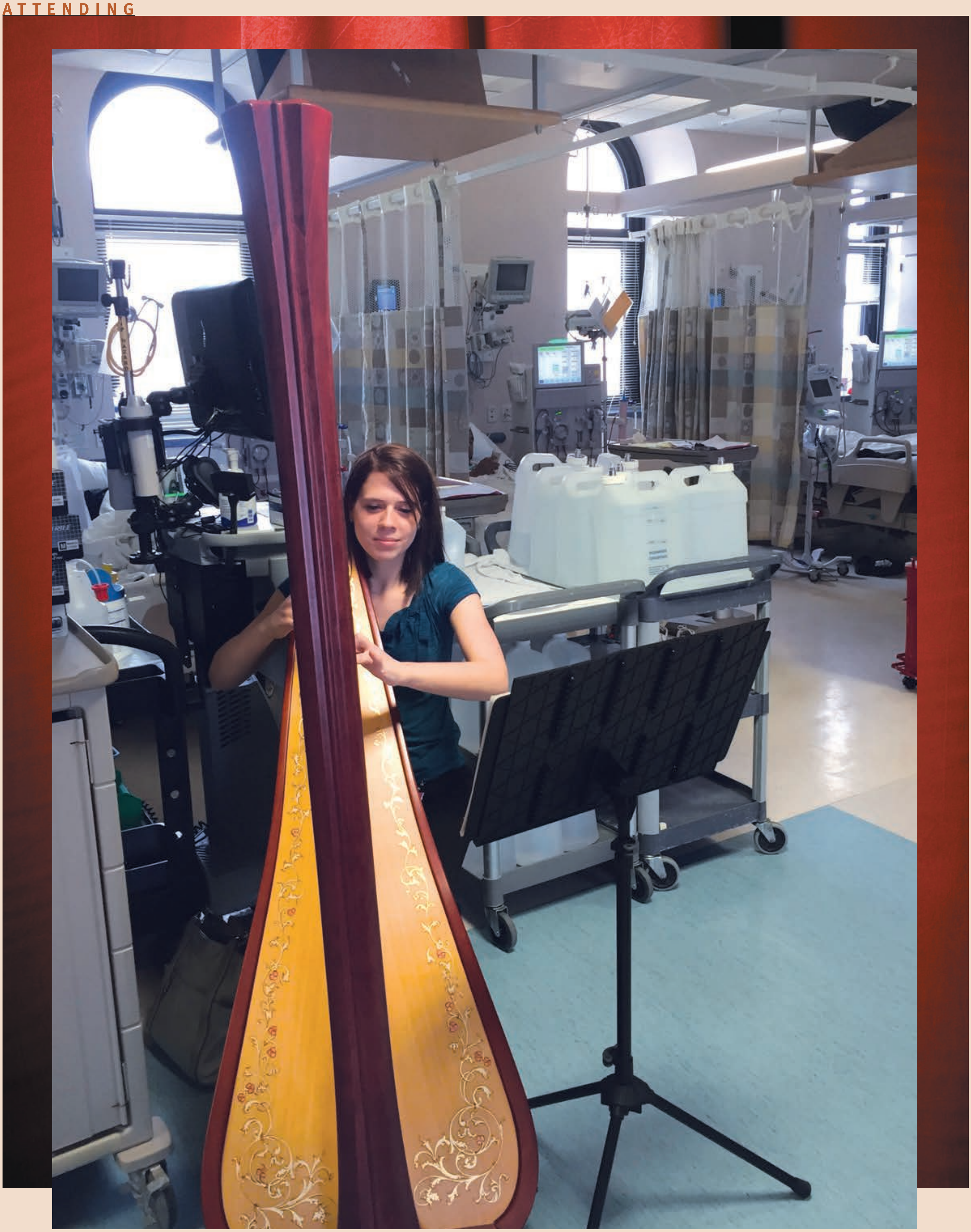
The first March of Dimes, in 1938, was fundraising genius in its simplicity: Get as many people as possible to donate one dime for polio research and care, and you could generate a tidal wave of support for medicine.

The national effort's success helped speed development of the killed-virus polio vaccine at Pitt, which was released in 1955. (It also landed president Franklin D. Roosevelt—who founded what later became the March of Dimes Foundation—a place on the 10 cent coin.)

But medical advancements depend on more than generous donations of cold, hard cash. Without large-scale field trials, the polio vaccine never would have reached the market.

That's why there's the **Pitt+Me** program of Pitt's Clinical and Translational Science Institute. Pitt+Me is a network of people who are committed to improving care in the community and worldwide. At this writing, 103,000 volunteers with 291 different conditions, as well as healthy volunteers, are taking part in 215 active studies—from trials focusing on child health to geriatric medicine and everything in between. If you're in Pittsburgh, maybe you've seen the bus ads. If you've flown the coop since graduation, look around; powerhouse academic medical centers across the country have similar programs.

At **pittplusme.org** you can check your—or your patients'—eligibility. (Follow @PittPlusMe to learn more.) The benefits abound, and you don't have to spend a dime. —*Micaela Fox Corn*



Harpist Audrey Kindsfather performs in the dialysis unit at UPMC Presbyterian.

LEFT: Pouya Joolharzadeh (violin) with Sae Jang (cello), founder of MusiCare, play for a palliative care patient. **RIGHT:** Amol Mehta (saxophone) and Justin Arnett (guitar) play in the dialysis unit.

MUSICAL MEDICINE

"IT'S NOT ABOUT ME ANYMORE"

STORY AND PHOTOS BY JENNIE DORRIS

Pitt med students Sae Jang (Class of '17) and Pouya Joolharzadeh (Class of '19) carefully put on tissue paper–thin yellow hospital gowns and bright blue gloves. They are outside the room of palliative care patient James Dorsey (not his real name). Dorsey has been at UPMC Presbyterian for almost a month.

But the med students aren't here for rounds. Jang picks up her cello, and Joolharzadeh gets his violin. They walk into the room, and Jang asks Dorsey if he'd like to hear some music. "Something from the '50s or '60s," he replies.

Jang sits in the corner of the room and starts playing "Yesterday" by the Beatles. Joolharzadeh follows with Bach while Jang stands close to Dorsey. Nurses gather outside the door. An infusion pump beeps nearby.

About three years ago, Jang started MusiCare, a program that gives medical students opportunities to perform for patients. Michael Chiang (Medical Scientist Training Program, Class of '21) and Shawn Tahata (Class of '18) helped formalize MusiCare in the Clinical Experiences curriculum and expand the program, which now brings students to play at UPMC Presbyterian and Children's Hospital of Pittsburgh of UPMC.

"I think that feeling of doing something positive for patients is really empowering as a medical student, especially in the first two years, when you are [mostly] studying from books and memorizing. It reminds us why we came to medical school," Jang says.

Across the hospital, Audrey Kindsfather (Class of '20) is playing harp in the dialysis unit. Behind her, patients take videos of the performance on their phones. A man getting dialysis tears up. "I think it's beautiful," he says. "I just wish I was in a different situation."

Kindsfather, who joined MusiCare last year, co-coordinates the program with Joolharzadeh and Elena Nikonova (Class of '19). Kindsfather's harp wouldn't fit in the palliative care rooms, so she and Jang expanded the program to the dialysis unit and to Children's with help from Jane Schell, an assistant professor of medicine at Pitt.

Kindsfather, who started playing piano at age 6 and took up harp at 12, sees the time she spends organizing the group and performing as self-care.

"It takes care of our mental health," she says.

Schell, who is the faculty advisor for MusiCare and hosts informal musical get-togethers at her home, says this group of students is ahead of the curve.

"When we go into medical school, it's so easy to get focused on the physiology. It's very easy to become dehumanized in the medical setting. Our patients have a lot of suffering. . . . Music helps our patients and our staff feel like humans. That, in and of itself, is therapeutic."

That is the impressive thing, to see medical students really pick up on that piece," Schell says.

Now in her fourth year of medical school, Jang engages with patients directly as part of the curriculum. While she was doing her rotation in thoracic surgery, a patient caught her eye. She had seen the patient daily for weeks during rounds and decided she could deepen the connection by playing music for her.

But when Jang brought her cello into the room, she realized the patient didn't recognize her. Because Jang had been focused on getting through the medical checklist when she saw her, they hadn't established a relationship.

"I remember this incredible feeling of guilt. Since then I've really changed the way I talk to my patients. In my initial interviews, I've started to ask them, 'What's one thing that's really important to you as a person?'" Jang says.

Joolharzadeh has found that performing music in the hospital has not just changed how he sees patients, but also how he sees music itself. While getting a bachelor's degree in music, he struggled with performance anxiety—his hands would shake to the point that he couldn't play.

"So far, playing for these patients has made that anxiety diminish, because it's not about me anymore," he says.

MusiCare is now among the variety of clinical settings where med students can volunteer for course credit. Nikonova, a pianist, would like MusiCare to grow to include residents and other physicians.

"Music itself bypasses everything and goes for the straight emotional appeal. For medical students it's cool because we can speak with residents and doctors and patients of all ages. Everyone will gather around a source of music when it's performed," Nikonova says. "There's nothing [else] that gives you that kind of room to breathe in the hospital." ■

CLASS NOTES

Woolley

’50s Had Scope and Scalpel existed when **Jane Woolley** (MD ’54) was a student, she might have been a playwright for the annual theater production. In the 1980s, Woolley penned comedies for staff parties while serving as founder and chief of staff of the anesthesiology group at USC Verdugo Hills Hospital in Glendale, Calif. The plays enlivened the work environment and got the medical and administrative staffs working together better, she says. Now retired, Woolley is cofounder of the Big Hearts for Little Hearts Desert Guild, a fundraising engine for Loma Linda University Children’s Hospital whose charity events have funded life-support equipment and a pediatric pharmacy. This year, the hospital is building a much needed clinic in southwestern California’s remote Coachella Valley. “The Desert Guild was the catalyst to make this epic event happen,” Woolley says.

’80s For **Stacey Berg** (MD ’85, Pediatrics Resident ’88), science fiction and research both seek answers to the question, “What if?” *Dissension*, her debut science fiction novel published in March 2016 by Harper Voyager Impulse, answers what might happen if humanity were fighting a regime of cloned soldiers (a sequel is forthcoming this spring). As associate dean for research assurances at Baylor College of Medicine and director of the developmental therapeutics program at Texas Children’s Cancer Center (among other titles), Berg is proud to be on the committee of Pediatric MATCH, a nationwide Children’s Oncology Group study that will identify children with genetically abnormal tumors that can be matched with targeted drugs. Berg, a lifelong Steelers and Penguins fan, is still deeply in tune with Pittsburgh; she even has Mineo’s pizza shipped in every year when she runs the Houston half-marathon (pizza isn’t as good in Texas, she says).

Berg

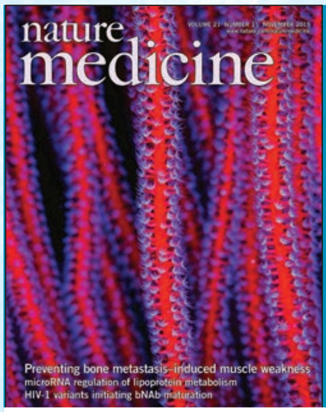
When transplant surgeon and immunologist **John Fung** (Transplantation Research Fellow ’86, Transplantation Clinical Fellow ’89) trained at Pitt med, the legendary Thomas E. Starzl served as his mentor. After completing his fellowship, Fung worked alongside Starzl for nearly two decades investigating, says Fung, “drug development, new procedures, and the elucidation of new pathways in liver immunity,” research that’s shaped the field of transplantation surgery. Fung was honored with Pitt’s inaugural Thomas E. Starzl Professor in Surgery, and he received the Thomas E. Starzl Prize in Surgery and Immunology in 2015. He is chief of the University of Chicago Section of Transplantation Surgery and founding director of its new Transplantation Institute.

Fung

’90s **John Mahoney** (MD ’90) won Pitt’s 2016 Sheth Distinguished Faculty Award for International Achievement. Though Mahoney “caught the bug” for international work before entering medical school, his role as associate dean for medical education at Pitt has really sent him globe-trotting. In one of his projects, Passport to Care, native speakers teach students medical language skills as well as “the cultural differences that come out in language.” Mahoney notes that despite differences, “we all want the same things for our children and for our countries.” He brings that idea to Pitt’s collaboration with Nazarbayev University in Kazakhstan, where Pitt has helped establish a medical school. What started as training faculty and building a curriculum will end in something much bigger, he says. “We’re going to change health outcomes in the entire country. That’s pretty exciting.”

Mahoney (left) and Pitt’s Loren Roth

Surgeon **S. Tonya Stefko** (MD ’97) directs the Orbital, Oculoplastics, and Aesthetic Surgery Service at UPMC; at Pitt, she was recently promoted to associate professor of ophthalmology with secondary appointments in otolaryn-



For someone who hated swimming as a child, **Theresa Guise** (MD ’85, Internal Medicine Resident ’88) has come a long way. After being persuaded to try scuba diving in adulthood, she became fascinated by underwater flora and fauna. Guise is now an award-winning underwater photographer in addition to a notable endocrinologist. Her photo of red whip coral, which resembles the skeletal muscle fibers she studies, was selected for the November 2015 cover of *Nature Medicine* (left). In that same issue, her lab at Indiana University published a paper identifying the unique mechanism by which bone, when destroyed by cancer, causes muscle weakness. “That was my biggest career milestone, . . . the marriage between my hobby and my work,” Guise says. Her latest project continues to go below the surface; she’s developing a clinical trial to test drugs on cancer-associated muscle weakness. (In the photo to the left, Guise is photographing a tiger shark in the waters of Fiji as part of an effort to promote shark conservation. “An ocean without the apex predator shark is an unhealthy ocean,” Guise says.)

—Christine Schauer

JOURNAL COVER: NATURE MEDICINE, VOL. 21, NO. 11, NOV. 2015, MACMILLAN PUBLISHERS LIMITED. PHOTO WITH SHARK: PETER DE MAAGT. PORTRAIT: STEVE BROKAW.

gology and neurological surgery. A particularly fun ("in a geeky way," she says) area of service for Stefko includes her work with the North American Skull Base Society, for which she serves on the Scientific Program Committee. She emphasizes the importance of ongoing collaboration and teamwork in her field, noting that "nobody does skull base medicine by himself or herself."

'00s

When **Trevor Snyder** (Bioengineering and Surgery Fellow '07) wants to figure out how user-friendly his ventricular assist devices (VADs) are, he doesn't go to other engineers: He relies on accountants at his Oklahoma City start-up, VADovations. Watching them interact with the VADs gives him an insider's view of how patients might use the devices. Snyder, vice president of research and development for VADovations, says his Pitt education taught him that making a VAD patient-friendly is just as important as designing the pump itself. "I never would have known that if I hadn't worked in [Pitt's] clinical program with the artificial heart team." Lately, he's been developing a VAD for the smallest of users. Snyder and Pitt McGowan Institute's **Peter Wearden** (Thoracic Surgery Resident '01) received a Small Business Innovation Research grant from the National Institutes of Health to develop the first available blood pump for infants and toddlers.


Musahl


Owonikoko

Pittsburgh was not part of **Volker Musahl**'s (Orthopaedic Resident '08) long-term plan. After interning in orthopaedics in Berlin, Musahl decided to come to Pittsburgh for one year to train with his mentor's colleague, Pitt orthopaedic surgery chair Freddie Fu; one year became 16. Musahl is now director of the sports medicine fellowship program, cohead physician of the Pittsburgh Panthers football team, medical director of the UPMC Rooney Sports Complex, and associate professor of orthopaedic surgery. During that first year in Pittsburgh, Musahl researched joint biomechanics, specifically soft tissue in the knee and shoulder. Today, Musahl codirects the Orthopaedic Robotics Laboratory in the Swanson School of Engineering. What does Musahl love most about teaching residents and fellows? "Closing the circle so that former students become colleagues. But you remain their mentor for a lifetime."

After studying in Nigeria, Germany, Baltimore, and Philadelphia, **Taofeek Owonikoko** (Clinical Hematology/Oncology Fellow '08) says, "Everything sort of came together for me when I was in Pittsburgh." Drawing on inspiration from Pitt mentors like the late Merrill Egorin and Chandra Belani, Owonikoko conducts translational research on small-cell lung cancer as an associate professor of hematology/medical oncology at Emory University. Owonikoko, who is also medical director of the phase I research program and codirector of thoracic oncology, has developed a growing tumor bank to address the lack of sufficient models for taking leads from the lab to the clinical level. In a study published in the *Journal of Translational Medicine* in 2016, he found that human tumor grafts grown in rodent models were a much better testing ground compared to traditional human cell lines. Findings from ex vivo study of these grafts matched findings of a phase II trial. He hopes to have a direct effect on patients with small-cell lung cancer, who currently have limited treatment options.

—Ali Greenholt, Cara Masset, Rachel Mennies, Christine Schauer, and Susan Wiedel

EDWARD DUBOVI

WHEN OLD MACDONALD HAS A VIRUS


ROBERT BARKER/CORNELL MARKETING GROUP

Dubovi with his 14-year-old cockapoo, Chelsea.

On any given day, Edward Dubovi (PhD '75) may peer into his microscope to discover the cells of an alligator, an elephant, or a goat.

"Maybe we're confronted with an outbreak of [miscarriages] in sheep," says the Cornell professor of virology. "Or maybe it's an upper respiratory issue in a cat."

Whatever the species, it's Dubovi and Cornell University's Animal Health Diagnostic Center's job to track down the virus responsible for the outbreak. Most of the facility's work focuses on agricultural animals like horses and cows; dogs come in third.

When a mysterious respiratory illness started making its way through the dogs of Chicago in 2015, Dubovi's laboratory was called in to find the culprit. He'd isolated a canine influenza virus back in 2004 and first thought it might be the same strain. But after two weeks of genetic analysis, Dubovi says, they were able to pinpoint the source of the outbreak as a different virus that had been seen in dogs in China and Korea several years earlier.

But finding a match still left one question: How does a virus jump across an ocean?

The flu isn't caused by a pathogen that can lie dormant, like malaria or HIV, explains Dubovi. That means for the virus to make its journey, it would have to have traveled in a sick pup. And this is how Dubovi suspects the virus made landfall—incoming companion animals aren't scrutinized nearly as thoroughly as imported livestock.

"Were this a virus of pigs or cows, everybody would have gone nuts," he says.

Although the dog virus isn't something most pet owners need to worry about—unless you live in Chicago, of course—it's an interesting example of what Dubovi's lab offers. That is, a bridge between the research labs developing theories about emerging viruses and everyday people who need solutions.

"Right now, everyone's jumping up and down about Zika virus," he says. "The diagnostic world is coming up with testing and technology to come to grips with that."

And it's people like Dubovi who are looking through the eyepiece of the microscope. *—Jason Bittel*

WILLIAM J. “DOC” DOYLE

JAN. 26, 1952–OCT. 21, 2016

Colleagues call William J. “Doc” Doyle, a Pitt professor of otolaryngology, a giant in his field. “I realized immediately he was a genius,” says Charles Bluestone, Distinguished Professor Emeritus of Otolaryngology, recalling their first meeting in 1974, when Doyle was a PhD candidate in anthropology at Pitt. Doyle’s training allowed him to follow his early passion for research on the middle ear, especially the Eustachian tube, where damage or disease appeared to be causing more deafness in Native American groups than others. Doyle’s PhD thesis provided evidence that their skull shape made them more susceptible to middle-ear problems.

Doyle

Doyle directed the ear, nose, and throat research lab at Children’s Hospital of Pittsburgh of UPMC from 1986 until his death. “He wrote paper after paper,” securing funding from the National Institutes of Health from 1978 to his current $7 million NIH grant, Bluestone says. “He is the world’s authority on middle-ear physiology and pathophysiology. No one is his peer.” Doyle’s magnum opus on gas exchange in the middle ear was published online in January in *Annals of Otology, Rhinology & Laryngology.*

Eugene Myers, Distinguished Professor Emeritus of Otolaryngology and chair emeritus of the department, says Doyle was “at it right up until the end,” working in the department’s walk-in hyperbaric pressure chamber in the Oakland Medical Building. “He certainly was a leader in his field and a very valuable member of our department for decades.” —*Marty Levine*

W. Doyle obituary ©2016 University Times. *Reprinted with permission and adaptations.*

JANICE MENDELSON

OCT. 22, 1922–JUNE 25, 2016

The Vietnam War had been under way only a few weeks when Janice Mendelson (MD ’47) joined the Army Medical Corps in December 1955. She credited her enlistment to an epiphany sparked by the sleep deprivation of surgical training. In the vision, she saw herself clad in brown, a clipboard in hand, scanning for an approaching plane. The scene’s portent was obvious to Mendelson, who had spent most of her youth in Tiajin, China, where her father was stationed as a U.S. Army physician in the 1930s. “She felt like if there were something she could do to help someone, she would,” says biographer Carmen “Penny” Marshall Adams, who compiled Mendelson’s entry in *Women Vietnam Veterans: Our Untold Stories.*

In 1959, when Mendelson achieved the rank of major, there were just eight female doctors in the army. As surgical advisor to the Office of the Command Surgeon for the Military Assistance Command in Saigon from 1970–71, the lieutenant colonel was the sole female army surgeon in the embattled country. “Vietnam was the greatest challenge of my life,” Mendelson said. “My mission was to help the Vietnamese military to provide the best possible surgical care and rehabilitation to the patients.”

Mendelson voluntarily extended her deployment from 12 to 18 months to oversee a model burn unit’s launch at Cong Hoa Hospital. Fluent in Mandarin and French, she worked with Vietnamese colleagues to refine skin-grafting and infection-prevention protocols in limited-resource settings, topics on which she would later publish.

Mendelson

A lifelong lover of international folk culture, Mendelson founded a dance group that met regularly on the roof of the USO outpost near Saigon. In San Antonio, where she resided after her 1980 retirement from the Academy of Health Sciences at Fort Sam Houston, Mendelson endowed the International Folk Culture Center at Our Lady of the Lake University. “You can’t hate a country whose dances you love,” she told the *San Antonio Express-News.* “This is my mission for world friendship.” —*Sharon Tregaskis*

EUGENE ORRINGER

NOV. 10, 1943–NOV. 10, 2016

“A ‘no’ from the NIH just means: Call them.” That was one of the many pieces of advice that Eugene Orringer (MD ’69) offered mentees throughout the years. The professor of medicine and director of the MD/PhD program for more than two decades at the University of North Carolina at Chapel Hill was a dedicated hematology researcher and physician. What Orringer enjoyed most in his career, as he told *Pitt Med* in 2005, was “helping young people.”

Orringer

Orringer directed the Education, Training, and Career Development Core at UNC’s Clinical and Translational Science Award program and led mentoring efforts for junior faculty members. Among them was Julia Brittain, now an associate professor of cell biology and anatomy at Augusta University, who says Orringer helped her earn her first K award from the NIH. She still applies his lessons, including picking up the phone to talk to grant officers. “I had to walk through the door, but he definitely showed me how to get to it,” she says.

Orringer was funded by the NIH from 1982 until the time of his death. He studied sickle cell disease, and he helped to establish the Duke-UNC Comprehensive Sickle Cell Center, one of only 10 NIH-funded comprehensive sickle cell centers in the country.

In 2006, Orringer received the Philip S. Hench Distinguished Alumnus Award, Pitt med’s highest alumni honor. —*Cara Masset*

IN MEMORIAM

’40s

GEORGE H. GRAY JR.
MD ’46
DEC. 30, 2016

KIRKLAND W. TODD JR.
MD ’46
SEPT. 27, 2016

JOHN J. GUEHL JR.
MD ’49
NOV. 13, 2016

RAYMOND A. YOURD
MD ’49
DEC. 11, 2016

’50s

LOWELL G. LUBIC
MD ’50
OCT. 9, 2016

CHARLES E. PIPER JR.
MD ’52
OCT. 4, 2016

JAMES S. BATES
MD ’53
JAN. 27, 2016

ROBERT C. SMITH
MD ’53
DEC. 15, 2016

BERNARD B. VINOSKI SR.
MD ’53
NOV. 29, 2016

SANFORD M. KLEIN
MD ’56
MAY 12, 2016

RICHARD A. WILSON
MD ’57
JAN. 2, 2017

’60s

BURTON S. HUTMAN
MD ’60
DEC. 24, 2016

JAMES G. PITCAVAGE SR.
MD ’60
DEC. 26, 2016

EUGENE LIPSON
MD ’61
AUG. 28, 2016

JOHN F. DELANEY JR.
MD ’64
NOV. 27, 2016

JOSEPH D. PHILLIPS
MD ’64
DEC. 10, 2016

DAVID L. STEINBERG
MD ’66
OCT. 18, 2016

STANLEY L. MALKIN
MD ’68
NOV. 24, 2016

JOHN K. WHITEFORD
MD ’68
FEB. 24, 2016

’70s

ROBERT H. EHRHART
MD ’74
NOV. 16, 2016

JAMES A. HIMMELBERGER
MD ’77
OCT. 3, 2016

CHRISTOPHER M. WEISS
MD ’78
NOV. 11, 2016

FACULTY

M. MICHAEL BARMADA
PHD ’99
DEC. 2, 2016

JOSEPH NWADIUKO

RECONNECTING DOCTORS IN DIASPORA

BY KRISTINA MARUSIC

HOWARD KORN

Nwadiuko wants to help medical professionals from developing nations make lasting change to health care systems in their home countries.

On a highway in Nigeria, as a bus barrels along at full speed, an oncoming car swerves into its path. The bus driver scowls but stubbornly holds course until the last second, when he jerks the wheel and careens out of the way, narrowly missing collisions with several other vehicles. Passenger Joseph Nwadiuko (MD '15), a 21-year-old American who plans to begin medical school at Pitt upon his return to the States, exhales.

This isn't his first bus ride, and by now Nwadiuko, whose parents immigrated to the United States from Nigeria, should know that traffic regulations in his ancestral land function more like polite suggestions than laws. The bus is full of physicians and volunteers like himself setting out on a public health service trip.

Harrowing ride aside, meeting his fellow passengers had an impact on him, Nwadiuko reports six years later. "When I asked physicians in Nigeria about their future career plans, I learned that many of them planned to go get advanced public health degrees here in the U.S. or in the U.K. … and then stay there."

Those discussions made Nwadiuko wonder how often Nigerian physicians in diaspora return home to help out—not just for brief medical mission trips, but in ways that create lasting change.

Upon his return to the States, he discovered little in the literature on the question, which later prompted a research project at Pitt.

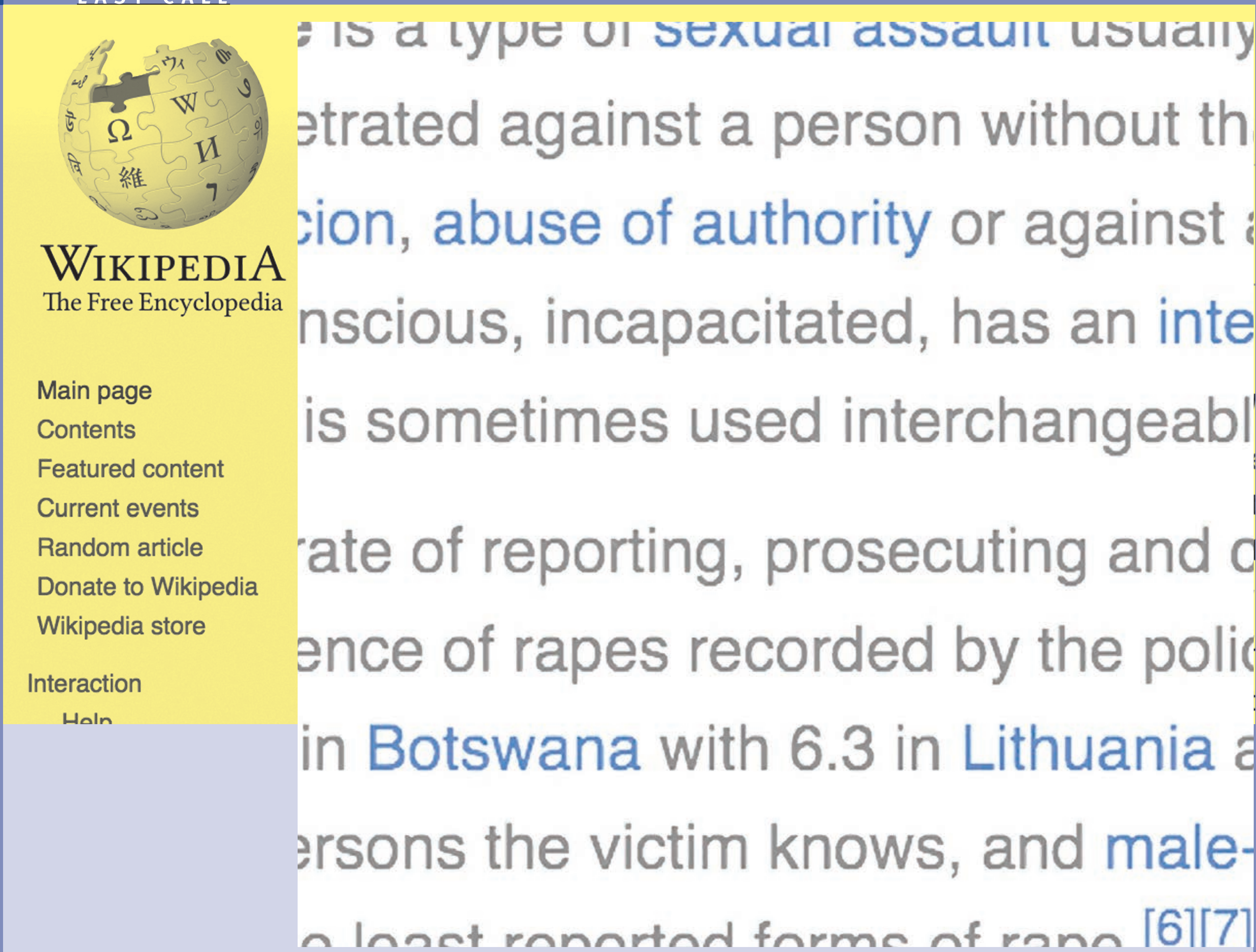
Nwadiuko learned that while many Nigerian-born physicians express a strong interest in improving health care in their home country, they often struggle to find a clear path to doing so because of a lack of information or reliable partners on the ground. (Take a look at his findings published in the June 14, 2016, issue of *Globalization and Health*.) When he expanded his research, he realized that the same thing held true in many parts of the world with struggling health systems.

Nwadiuko is now taking action on the problem as cofounder and executive director of the Diaspora Health Network, an organization that is equipping U.S.-based health care professionals originally from poorer nations like Nigeria, India, and Mexico to effectively give back to their home countries. (He's leading the organization while also training as an internal medicine resident at Johns Hopkins, his partner in founding the organization.)

The network's strategy consists of three steps: resources, training, and placement. Real-time reports on the needs of various health systems are provided through online "gateways" at diasporahealthnetwork.org. Training is offered by institutions teaming up with the Diaspora Health Network. For instance, UPMC's international division funded several attendees at a global health boot camp at the University of California, San Francisco. Once Diaspora Health Network participants are equipped to "do good, well," the next step is placement. The network is running pilot projects in India and Nepal, where participants are placed at universities to teach courses on health research in an effort to increase the number of trained health researchers.

"Our vision for the long term is to develop a diverse corps of physicians who have experience growing up within a low-income health system, but have also witnessed the potential of what an effective health care system can be," Nwadiuko says.

"If we can merge those two realities together, we can bring health care to everyone—regardless of how much money they may or may not have." ■



SCREEN CAPTURE: WIKIPEDIA

WIKI WOMAN

Barbara Page has her work cut out for her. She's a Wikipedia Visiting Scholar at Pitt's University Library System building content on women's health for the site. As of December 2016, there were only 1,232 women's health articles—a number of which were created by Page—with more than half (679) rated as "stubs" or "start-class." When she started this process, entries under these classifications included radical mastectomy, feminine hygiene, estrogen patch, endometriosis, cervical polyp, and breast self-examination.

Like most Wikipedia editors, Page—a part-time nursing student at Community College of Allegheny County who edits under her visiting scholar account "Barbara (WVS)"—is a volunteer. She's created 59 new articles and edited more than 250 others that have received 67 million page views in a little over a year. She would like to see more health students and professionals contributing to health topics on Wikipedia.

Page is most proud of the 375 edits she was able to make to the Wikipedia entry on rape, which receives an average of 4,000 page views every day. "I noticed [the page] lacked clinical content," she says. "There was nothing about injuries, medications, treatment, what to expect when you go to a hospital, or what type of counseling is available.

"Even if just one rape victim reads that article and understands what's going to happen to her at the hospital, it might make her feel as though she has some control over the process," Page says. —*Christine Schauer and Sharon Blake*

CALENDAR

FOR ALUMNI & FRIENDS

WINTER ACADEMY
FEBRUARY 15
The Breakers, Palm Beach, Fla.
FEBRUARY 17
Ritz-Carlton, Naples, Fla.
For information:
Jen Gabler at 412-647-3792
or jag188@pitt.edu

PITT DAY OF GIVING
FEBRUARY 28
For information:
Kelsey Thayer at 412-648-9090
or kelsey.thayer@pitt.edu

CLASS OF 2017 MATCH DAY
MARCH 17
Petersen Events Center
For information:
Ashley Knoch at 412-648-9059
or akk57@pitt.edu

PITT ALUMNI & FRIENDS PRESENTATION & RECEPTION BALTIMORE, MD
APRIL 20
6–8:30 p.m.
For information:
Rachel Edman at 412-647-4241
or rge6@pitt.edu

MAA EXECUTIVE BOARD MEETING
APRIL 26
Location TBA
Ashley Knoch at 412-648-9059
or akk57@pitt.edu
**Consider becoming an MAA board member. (Teleconferencing is available for four annual MAA meetings if you are not a local physician.)*

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

This doesn't smell/taste/feel/look right.

GETTY IMAGES

FOR REAL! TWEEN SCIENCE

For generations, kids forced to eat every last bite of a dinner they dislike have been savvy to the nose-holding trick: If you can't smell a food, you can't taste it very well, either. Without even trying, they've discovered that taste and smell are strongly connected to each other.

In fact, all of the senses—taste and smell, but also sight, hearing, and touch—are part of the sensory nervous system and are linked together. Our sensory nervous system helps us decode the world around us and figure out how to respond to it. We may get our first cues about the flavor of broccoli by smelling it, but our brain also decides whether it's delicious enough to swallow (or not!) by evaluating how it looks on our fork, feels in our mouth, and sounds as we chew it.

Some people have a condition called synesthesia, in which their senses actually overlap. Some synesthetes see each letter of the alphabet as having its own special color. Some feel an itch when they hear piano music. Some taste strawberries every time they see a chair. Do you think these different abilities would be annoying to live with? Or would they be more like superpowers?

—Lela Nargi

Auditory physiologist Thanos Tzounopoulos helped us see deep into our senses.

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THE OWL, 1964

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THE EXAMPLES BELOW ARE BASED ON A MINIMUM GIFT OF $10,000.

AGE	PAYMENT RATE	CHARITABLE DEDUCTION
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65	4.7%	$3,489.80
70	5.1%	$4,099.10
75	5.8%	$4,577.20
80	6.8%	$5,020.50
85	7.8%	$5,659.90
90	9.0%	$6,294.50

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