UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | FALL 2019

PITTMED

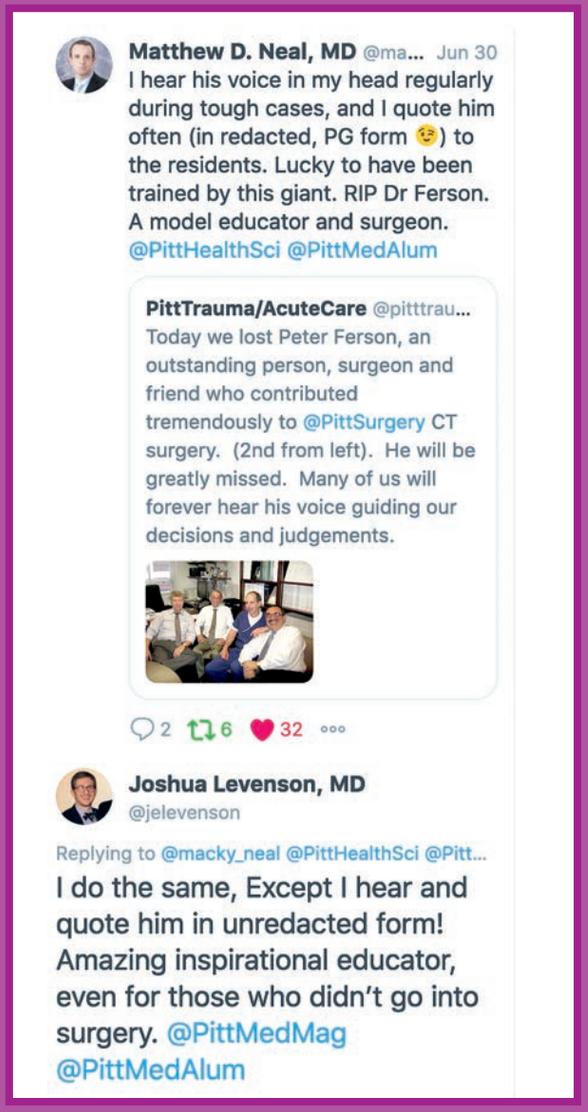
ONES THAT GOT AWAY

COVERS YOU DIDN'T SEE

OUR 20TH ANNIVERSARY ISSUE

CHIRP IN

Join the conversation on Twitter, @PittMedMag.



GET A HEALTHFUL!

The work of Pitt Med people often moves us. Here at the magazine, we tell those stories on these pages, through our monthly *Pitt Med Direct* e-mail blasts, and in our *Pitt Medcasts*.

If you're up for more inspiration, keep an eye out this fall for our sister publication, the brand-new ***Pittwire Health***, which will curate the most interesting and important news touching on health and wellness from throughout the University.

RESPECT

I always enjoy the magazine, but I wanted to say that the Spring issue article about the Tree of Life shooting ("Oct. 27, 2018" by Gavin Jenkins) was gripping, tautly written, respectful, and one of the best damn pieces of journalism I have read anywhere about it. Please pass along my thanks. I know many of the players involved. Gavin's piece was a fascinating window into a horrific morning; but in the end, it was inspiring how my amazing colleagues stepped up and moved toward the danger.

Andrew Nowalk
Biochemistry PhD '97, MD '99
Pittsburgh, Pa.

CORRECTIONS/ CLARIFICATIONS

In the Summer issue, we reported ("Trans Formation") that in the early 2000s, William Futrell, former professor and chair of plastic surgery at Pitt, was the only Pittsburgh surgeon performing gender-affirming surgeries. However, Richard Vagley (Plastic Surgery Res '89) tells us that in the early '80s he trained himself in these procedures and assembled a team around holistic evaluation, care, and follow-up for transgender patients. Vagley continued offering these services as part of his practice for about 30 years. We regret our error.

RECENT MAGAZINE HONORS

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

2019 Pittsburgh Black Media Federation Robert L. Vann Media Award Magazine/Feature (E. Dyer, "With Love, From Haiti")

2019 Press Club of Western Pennsylvania Golden Quill Award, Excellence in Audio Journalism—Medical/Health (S.A. Flecker, E. Vitone, and E. Lloyd, *Pitt Medcast*: "When Fred Met Margaret")

CORRESPONDENCE

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

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

For address corrections:

***Pitt Med* address corrections**
ATTN: Lauren Galloway
Forbes Tower, Suite 8084
3600 Forbes Ave at Meyran Ave
Pittsburgh, PA 15213
E-mail: LMG122@pitt.edu

CONTRIBUTORS

Editor in chief ERICA LLOYD says a magazine is like a house of many rooms, through which readers can pass as they please. Throughout the past 20 years, her commitment to making *Pitt Med* a welcoming home for readers has balanced poignancy and playfulness to access the humanity in science and medicine. "Storytelling has always been at the heart of what we do," says Lloyd, who combines narrative with other formats, like our Tough Questions section, to take on difficult topics. Lloyd has an MFA from the University of Pittsburgh and a BA from the University of Wisconsin. Before joining the parent club with her husband, Tim, she contributed to *National Geographic News*, *Popular Science*, *Wired*, and *Radiolab*. She is excited to see where *Pitt Med*'s story leads her next.

Art director ELENA GIALAMAS CERRI offers another magazine metaphor: To Cerri, the magazine's format leads readers on a journey of hills and valleys, "building up the pace and winding it down again." It takes a lot of effort to make design look effortless, but Cerri has done it again and again throughout the last 20 years. After the Pittsburgh native graduated from Carnegie Mellon University, Cerri's eye for design took her to Manhattan, as a designer at *ELLE* and the J. Crew catalog. The daughter of a physician and artist was destined to return to the Burgh and become *Pitt Med*'s art director. In October, she will celebrate another special 20th—her wedding anniversary with ophthalmologist husband, Hugo.

PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, FALL 2019 (SEPT/OCT/NOV)

VOL. 21, ISSUE 3

4

DEPARTMENTS

40 1/2

COVER

The photo of Gary Barr (MD '70) unicycling in Scaife Hall showed up in our inaugural issue, Fall 1999—30 years after it appeared in the 1970 *Hippocratean* yearbook. Dr. Barr is having fun, moving medicine forward, and, this time, rolling along with that first issue.
(Photo illustration by Elena Cerri. Photo: *Hippocratean*, 1970.)

24

FEATURES

PITTMED

PUBLISHER
Arthur S. Levine, MD

EDITOR IN CHIEF
Erica Lloyd

ART DIRECTOR
Elena Gialamas Cerri

SENIOR EDITOR
Elaine Vitone

ASSOCIATE EDITOR
Gavin Jenkins

PRODUCTION MANAGER
Chuck Dinsmore

INTERNS
Janine Faust, Alyce Palko,
Margaret Palko, Brian Salvato

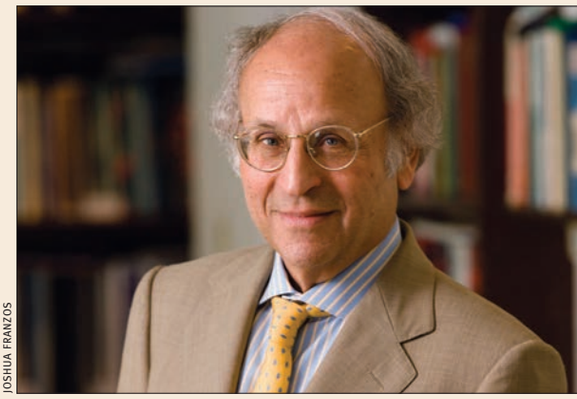
EDITORIAL ADVISORS
Lisa Barsom, PhD
Jeremy Berg, PhD
Michelle Broido, PhD
Paula Davis, MA
Robert Ferris, MD/PhD
Joan Harvey, MD
Joshua Levenson, MD '11
David Lewis, MD
Margaret C. McDonald, PhD, MFA
Loren Roth, MD
Steven Shapiro, MD
Peter Strick, PhD
Ann Thompson, MD
Bennett Van Houten, PhD
Simon Watkins,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

VICE CHANCELLOR, UNIVERSITY COMMUNICATIONS AND MARKETING
Ellen Moran

ASSISTANT VICE CHANCELLOR, MARKETING
Kate Ledger

University of Pittsburgh

Pitt Med is published by the Office of the Dean and Senior Vice Chancellor for the Health Sciences in cooperation with the Office of University Communications. It is produced quarterly for alumni, students, staff, faculty, and friends of the School of Medicine. PR 6749



JOSHUA FRANZOS

I learned from a book that crawdads don't really sing; I learned from my mother that if you go far enough into the wilderness you will hear them anyway. —Delia Owens

At Stone Harbor this August, I took time to consider, as Longfellow put it, how *waves, with their soft white hands, efface the footprints in the sands.* That ebb and flow has been a constant for eons. For now, I swim at low tide and jump the waves at high. (Maybe I'm influenced by the gravitational pull of the moon?) It's not surprising that creatures who live in coastal regions operate in 12-hour rhythms in sync with the tides. Pitt's Bokai Zhu has discovered that this clock, independent of our better characterized circadian clock, is still ingrained in us long after our slippery ancestors wriggled out of the sea foam. He began this work as a postdoc with the renowned cell biologist and Pitt Med alumnus Bert O'Malley. Using an algorithm that identified superimposed oscillations, Bokai found that the 12-hour rhythms of gene expression operating in the tissues of sea creatures are evolutionarily conserved in us. We have co-opted this ancient circatidal clock to benefit our terrestrial lives. For example, we've been able to increase the production of certain hormones related to metabolism during the "rush hours" of gene expression for these hormones. Those high-traffic times align with our dawn and dusk and our fasting and sleeping schedules—perhaps changing slightly throughout the month, though certainly not to the extent that tides do.

It's clear to me that serious study of evolutionary biology belongs in a medical school. We likely have much to learn about our own behavior and physiology from our sea ancestors. In fact, we've recently created a Center for Evolutionary Biology and Medicine to further catalyze such inquiries. Are there morbidities consequent to 12-hour clock deregulation, and if so, can we therapeutically reset the clock? Links between healthy limpets and sick humans may seem incongruous, but evolutionary biologists must live with the tension of contradictory observations. For example, the sickle cell mutation causes a very painful, sometimes lethal, disease. So why didn't we shed this mutation during evolution? Probably because sickle cells are not readily infected by the malarial parasite, malaria being a greater cause of mortality than sickle cell anemia. Nonhuman primates don't tend to get atherosclerosis, nor heart attacks; at some time in evolution, we lost the function of a gene (*cmah*) that protects our cousins. How did we benefit? We're better at long distance running! At least in mice, *cmah* loss increases running endurance and decreases muscle fatigue; if translatable to humans, this would have been an evolutionary advantage as we moved from the forest to the open savannah and had to hunt quickly over long distances.

Medicine is sprinkled with such apparent incongruities: We give stimulants for hyperactivity and nitroglycerin, an explosive, for angina. In fact, the ability to sit comfortably with competing ideas is our fount of creativity.

At the shore, between the swimming and the jumping, I relished the debut novel of Delia Owens, *Where the Crawdads Sing*. Owens is an acclaimed wildlife scientist, intrigued with how humans mirror and can learn from ancient animal behaviors. With extraordinary power and poetry, she writes now of Kya Clark, a very young fictional child who has been abandoned by her severely dysfunctional family and left alone in the only home she knows, a dense Carolina coastal marsh. She grows in isolation and learns from the gulls, the ferns, the insects, and the tides how to assess time, season, nature's rhythms, what to eat, and how to survive. She is shaped to an exceptional adulthood by the beautiful and violent secrets, often incongruities, that nature keeps and imposes on our own evolution.

We should go far enough into the wilderness to hear the crawdads sing, as Bokai Zhu has done!

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

OVERSCRIPTED WITH TELEMED?

Alexa, get me a prescription for antibiotics. Okay, it's not *that* easy to get antibiotics, but a study by Kristin Ray, assistant professor of pediatrics at Pitt Med, suggests that doctors seeing patients via video chat visits offered by commercial companies take a more liberal approach to handing out antibiotic prescriptions for children.

Her team's recent study found that these online doctors prescribed antibiotics 52 percent of the time for acute respiratory tract infections like the common cold, sore throat, or sinusitis. Such prescriptions are given 31 percent of the time during in-person physician visits.

Ray says it is important to critically examine the risks and benefits of delivering this type of care.

"I can understand there's a need for a trade-off sometimes—a desire for convenience—but we need to maintain adequate quality as we're opening up new ways to treat kids," she says. *—EBG*

Heartfelt Gap

When Utibe Essien was a resident at Massachusetts General Hospital, he struggled serving a non-native-English-speaking patient who had atrial fibrillation. He couldn't get the patient the newest, best medication because of issues with insurance. It got Essien thinking—what's the interplay between minority identity and access to the latest AFib treatments?

Essien, now an assistant professor of medicine at Pitt Med and an investigator at the VA Pittsburgh Healthcare System, recently answered that question with colleagues at Massachusetts General. Their research found that black patients with AFib were 27 percent less likely to receive the latest AFib drugs on the market when compared to white people with AFib.

The newest AFib drugs are easier on patients than the older anticoagulant (warfarin) for the condition. They have few dietary restrictions, and some can be taken less often.

"There've been fewer strokes and fewer deaths with the new blood thinners, and I think a lot of that is due to the ease of adherence," says Essien. "Due to the need for increased monitoring, [the older anticoagulant] can be quite disruptive to those who have a 9-to-5 or have to pick up kids."

Essien says the next step in his research is finding out the cause behind this inequality. *—Evan Bowen-Gaddy*

THE GEORGE A. ROMERO COLLECTION/ UNIVERSITY OF PITTSBURGH

FOOTNOTE

At medical schools, and in our larger society, we pay a lot of attention to health and, well, avoiding death. Sometimes we talk about what makes a good death. But what about that space in the middle? Yes, it's time to give a nod to the undead. Since George Romero's 1968 *Night of the Living Dead*, the horror genre has been a lot more fun. The Pittsburgh filmmaker and writer, whose work has been added to the National Film Registry, died in 2017; but his canon will forever be animated here at Pitt. Earlier this year, the Romero family donated his archives to the University Library System.

NOAH PURDY/FOOTHOLD STUDIOS

Overheard: Empowered for Sexual Health

Sharon Hillier, a PhD professor in Pitt's Department of Obstetrics, Gynecology, and Reproductive Sciences, as well as in the Department of Microbiology and Molecular Genetics, grew up north of Seattle in rural Skagit Valley. Hillier, who also is the Richard Sweet Professor of Reproductive Infectious Disease and vice chair for faculty affairs for ob/gyn, lived on a dairy farm and played with kids of strawberry, potato, and chicken farmers. One day, during her postdoc fellowship at the University of Washington, she was making rounds to HIV patients when she saw Marvin, a childhood friend who was suffering from the virus. Marvin died soon after that day. He inspired Hillier to dedicate her career to HIV research. She focuses on developing preventive HIV products for women and other receptive partners. Hillier's research has taken her all over the world, but she spends a lot of time in Africa, where her work empowers women to have a say in their sexual health.

How do antiretroviral drugs work against HIV?

[The disease] is all about replication, reproducing the nucleic acid. The retroviruses have transcriptase enzymes that replicate the RNA. The drugs that we use generally work in different places. There are some that actually stop replication at the integration point from when the virus comes into the cell. There are different drugs that have different mechanisms of action, but a simple way is they stop replication. You don't stop it outside the front door; you stop it before it gets into the rest of the house.

What products are you working on now?

There are two [experimental products] that I'm really excited about. There are vaginal rings: You twist a ring and insert it into the vagina, and it pops into shape. The little ring is made out of silicone, and it just sits in the vagina and releases antiretroviral for about a month at a time. We're also working on films. They're like a Listerine breath mint strip, but a little bit bigger. We're putting a bit of antiretroviral drug on the films. You put it over your finger, then put it in the vagina, and it unfolds. When it gets wet, it turns into a gel, but it just sits there. It would provide a week of protection at a time.

How do the African patients you see feel about these products?

A lot of women live in very difficult contexts. Maybe they're married, and their husband is having sex with other women. In Uganda, at least for many people, if you leave the marriage, you lose your children. The children stay with the husband. So, the woman has to decide if she wants to leave her husband and lose her children—or does she want to stay with her husband and maybe get HIV. For many of the young women in this study, they do find it incredibly empowering because it's something they can control. ***—Interview by Brian Salvato***

Faculty Snapshots

Richard Steinman received a Chancellor's Distinguished Teaching Award at the University's Honors Convocation this year. **As director of the MD/PhD Medical Scientist Training Program and Physician Scientist Training Program, Steinman is known for emphasizing scientific literacy. James O'Brien, a third-year PSTP student, says that Steinman requires students to perform "chalk talks," which are exercises that challenge students to articulate their project to scientists and people outside their field. "He taught me that scientists are storytellers, and to be successful, I need to learn how to articulate my work in a way that is simple and exciting," O'Brien says of his mentor.**

Steinman

Four other Pitt Med faculty members were honored with Chancellor's Distinguished Research Awards:

Since coming to Pitt more than 20 years ago, Derek Angus has become a leading voice in critical care research and practice, including the prevention and treatment of sepsis. He is a Distinguished Professor, the Mitchell P. Fink Professor, and chair of the Department of Critical Care Medicine.

Angus

Nathan Clark published in *Science* in 2018. The work of the associate professor of computational and systems biology focuses on understanding genes and genomes using evolutionary analyses. He will be joining the faculty of the University of Utah this fall.

Clark

JoAnne Flynn has transformed scientists' understanding of the immunology of tuberculosis by making groundbreaking changes to vaccine administration and introducing the nonhuman primate model. A professor of microbiology and molecular genetics, she is recognized internationally as an expert and thought leader in her field.

Flynn

Mary Phillips's contributions to our understanding of the neural basis of emotions led to the dissemination of a brain model that laboratories use worldwide. This work has shone a light on the neuropathophysiological basis of bipolar and other mood disorders. Phillips holds the Pittsburgh Foundation–Emmerling Endowed Chair in Psychotic Disorders in the Department of Psychiatry.

Phillips

Honorees each received $2,000 and a $3,000 grant to support their work. ***—Nichole Faina and @Pitt staff***

CATHERINE LAZURE

Touching fentanyl does not cause a toxic reaction.

PHYSICIAN TAKES AIM AT FENTANYL FEARS

Ryan Marino wants people, particularly first responders, to understand how fentanyl—a synthetic opioid 50 times more powerful than heroin—*doesn't* work.

"It's become an urban legend that fentanyl is contagious," says Marino (MD '14, Fel '19), a toxicologist and emergency medicine physician. In reality, fentanyl encountered by first responders cannot be accidentally absorbed through the skin or inhaled in sufficient quantities to cause a reaction.

"If that were possible, people would just touch drugs instead of injecting them," he says.

Even people who should know better can succumb to fentanyl fear, Marino adds, recalling an overdose that prompted hospital staff to seal the room (by stuffing towels under the door). One recent Texas broadcast noted that deputies self-administered naloxone nasal spray after feeling light-headed and overheated at a suspected drug scene.

"People are having real symptoms because of misinformation," says Marino, who started a Twitter hashtag #WTFentanyl, to counter fentanyl hysteria. Health care professionals around the country are using it to tag and debunk news reports. Information pinned to Marino's own Twitter account (@RyanMarino) also shares fentanyl facts.

"It's an obligation for me to spot these things and address them head-on," he says. —*Michele Baum*

MAFELIPE/GETTY IMAGES

FLASHBACK

Sometime in 1983, Jonathon Erlen was working at Falk Library's reference desk. It was a new job for Erlen, and things seemed to be humming along just fine. Then, in walks a man in full scuba gear; he picks out a medical journal, sits down in front of Erlen, and proceeds to read. The peculiar patron eventually left without a word. In the decades to follow, Erlen would dive into his roles with the Health Sciences Library System with gusto. Last winter, he retired as history of medicine librarian with teaching appointments in schools and centers throughout the University. The C.F. Reynolds Medical History Society, in which he remains active, has announced a lectureship in his honor.

JOAN HARVEY

FOOD FOR THOUGHT

"Let food be thy medicine, thy medicine shall be thy food." Hippocrates's quote is a wise one to live by. But what exactly constitutes a proper diet, and what should doctors tell patients about healthful eating? At the request of several students, Pitt Med presented its first Culinary Medicine course this spring to address these questions. Held at Phipps Conservatory and Botanical Gardens, the mini-elective spanned three evenings and was taught by volunteer chefs. The course focused on evidence-based Mediterranean, Dietary Approaches to Stop Hypertension (DASH), as well as plant-based diets. The 16 first-year students who took the course learned cutting techniques and food safety, and each class ended with a meal. "There's so much about dieting in the lay press, so it's important that we help students identify what topics are most helpful when talking to patients," says Joan Harvey, MD and associate dean of student affairs. (Above, from left: Jackson Mitzner, Emily Hacker, Vice Dean Ann Thompson, Harvey, Michelle Nanni, and Hermoon Worku.) *—Gavin Jenkins*

NAME DROPPING

Dina Katabi gets excited about the possibilities when combining computational power with radio waves. She is the Andrew and Erna Viterbi Professor of Electrical Engineering and Computer Science at MIT and a recipient of the MacArthur Fellowship. This October, at Pitt's Science 2019, she'll give the Klaus Hofmann Lecture.

Katabi

Katabi directs MIT's Center for Wireless Networks and Mobile Computing. One of her inventions uses machine learning to detect falls and monitor vital signs in the elderly (without the need for wearable sensors). Another allows the user to "see" through walls and blocked blood vessels. Several start-ups have sprung from her lab.

Here are some other talks not to miss at Science 2019. (All of these speakers belong to the National Academy of Sciences or the National Academy of Engineering, by the way.)

Medzhitov

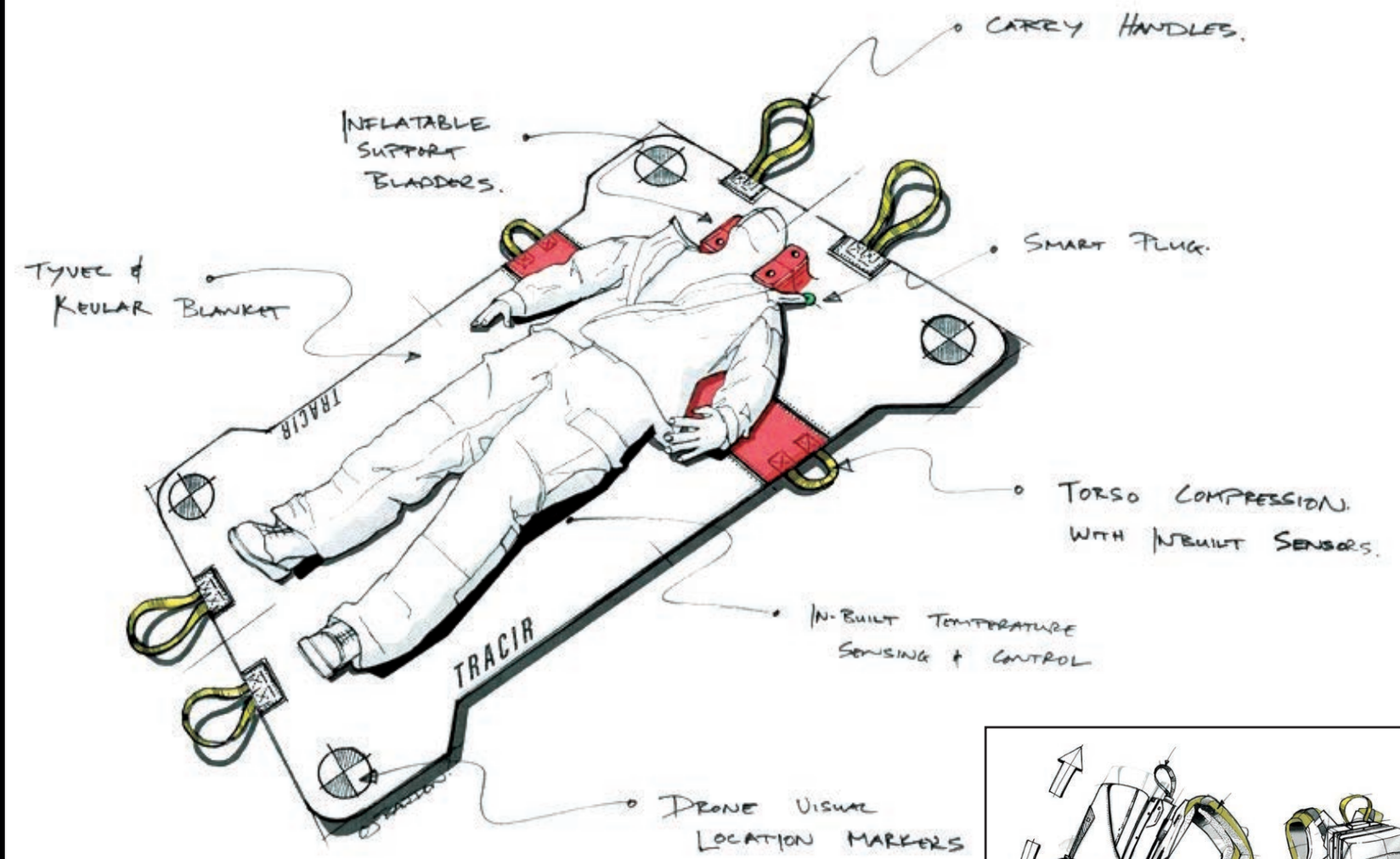
One of the world's leading immunology researchers will give the 2019 Dickson Prize in Medicine Lecture. That's **Ruslan Medzhitov**, Sterling Professor of Immunobiology at Yale University. Medzhitov has made fundamental discoveries regarding the protein he codiscovered known as Toll-like receptor 4 and the roles it plays in immunity and inflammation. He is a Howard Hughes Medical Institute investigator.

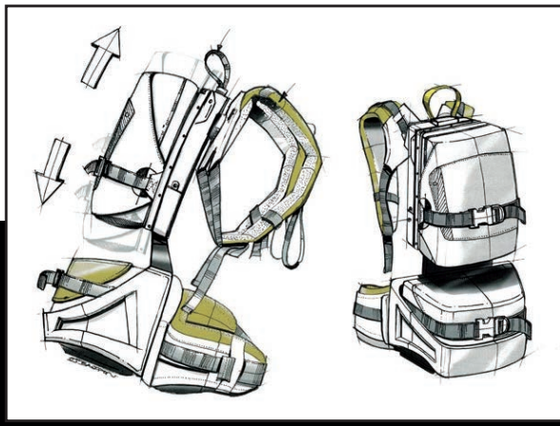
Sánchez Alvarado

Alejandro Sánchez Alvarado will give the Mellon Lecture. He's scientific director of the Stowers Institute for Medical Research and a Howard Hughes Medical Institute investigator. The Sánchez Alvarado Lab has developed molecular tools to explore the mysteries of regeneration in the planaria *Schmidtea*, hoping to also shed light on human health. (Our bodies replace probably 10 billion cells every day, his lab site tells us.)

Spector

Alfred Spector will give the Senior Vice Chancellor for Research Lecture. He was among the faculty at Carnegie Mellon University who developed the Andrew File System; Spector then went on to commercialize it at the company he founded, Transarc, which was eventually bought by IBM. He retired from Google in 2015 as vice president for research; he now serves as chief technology officer for the hedge fund Two Sigma. *—Erica Lloyd*





A GOLDEN BACKPACK

In 1993, during Ron Poropatich's 30-year stint in the United States Army, the pulmonary critical care medicine physician was caring for soldiers in Somalia. Using a $25,000 Kodak DCS camera capable of 1.54 megapixel images (iPhones today have 12 megapixel cameras), he would take a picture of a patient's "weird rash," fire up his satellite dish, and send the image to Walter Reed Army Medical Center, then in Washington, D.C., for a consult. Poropatich's work still focuses on helping patients who are miles away from a fully staffed hospital.

As director of Pitt's Center for Military Medicine Research, Poropatich is the principal investigator for the TRACIR project (TRAuma Care In a Rucksack). He's working with Michael Pinsky, MD professor of critical care medicine at Pitt, to develop a fully autonomous medical backpack for the United States Army. Pitt faculty from emergency medicine, surgery, and cardiology, as well as coinvestigators from Carnegie Mellon University, including robotics investigator Artur Dubrawski, make up the team.

Here's the idea: Fellow soldiers in the field remove the TRACIR backpack from an unmanned vehicle, apply a sensorized body-wrap to the wounded, and assess the injuries. TRACIR includes a full-body, autonomous stretcher. (Picture a smaller-scale Optimus Prime from the *Transformers* movies.) Biosensors on the body-wrap compare the soldier's baseline physiology to his wounded state. The stretcher releases robots to perform vascular access and administer fluid, blood, and vasoactive drugs.

The developers envision TRACIR also performing minor operations like needle thoracostomy for collapsed lungs.

TRACIR aims to extend the "golden hour," the time in which a critically wounded person has to receive urgent care with the best chance for survival.

"[After] a traumatic event, you really have to jump on that individual early, because there are inflammatory chemicals that get released from damaged organs," Poropatich says.

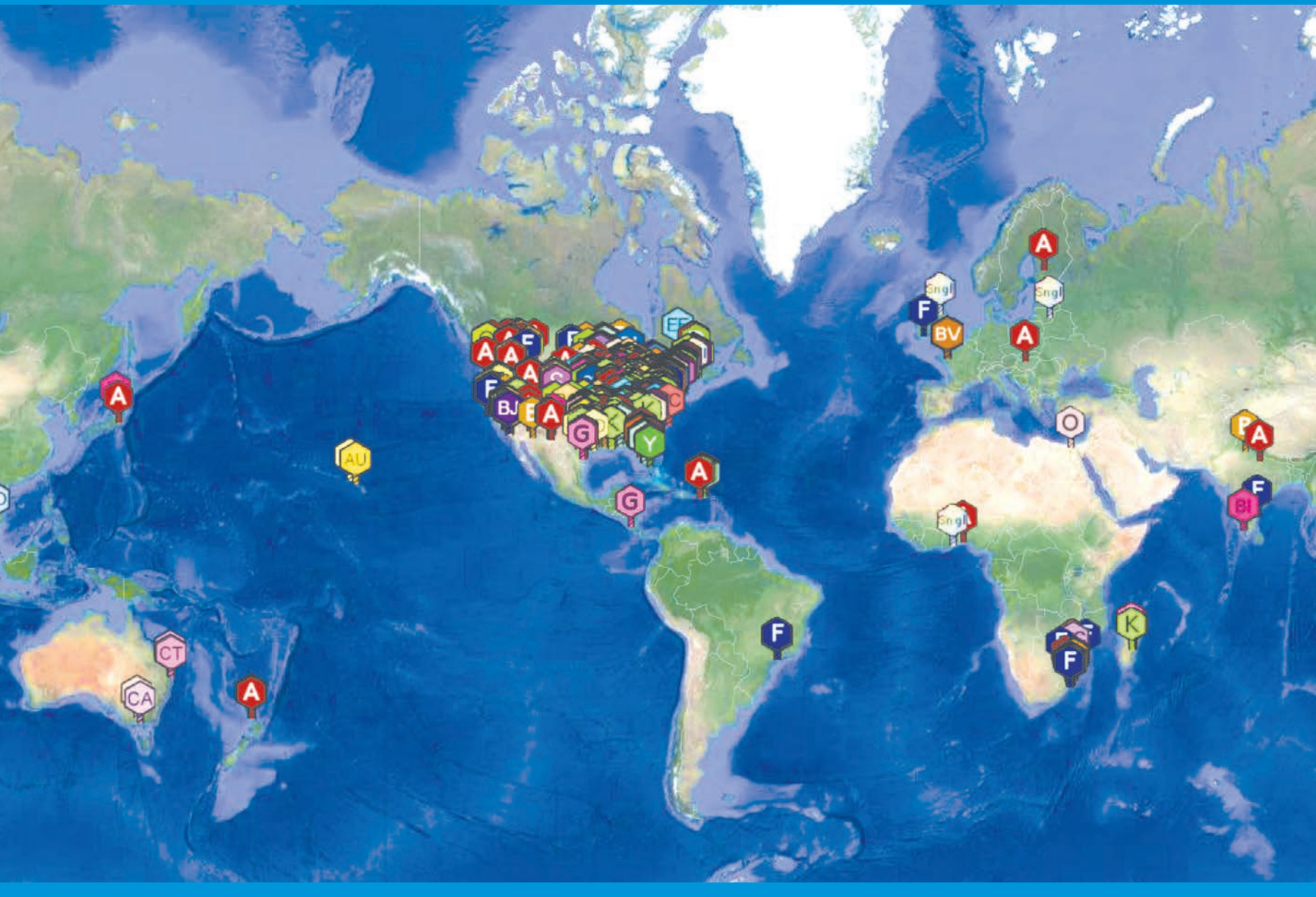
Using an algorithm designed from a UPMC prehospital clinical dataset of more than 5,000 trauma patients, TRACIR will learn more from every patient it treats. The challenge is condensing an array of computers and medical equipment.

"It's all got to fit into a backpack; so weight and power demand are really important. How long is that computer going to run? Build the algorithm, build some robot solution, then figure out how to make it small," Poropatich says.

The research team has nine years to turn science fiction into reality. The army wants to field test the rucksack in 2028. Seven years after Poropatich used one of the first digital cameras in Somalia, Sharp introduced the world to cell phones containing digital cameras. Maybe having a lifesaving rucksack by 2028 isn't so far-fetched? *—Brian Salvato*

—Images courtesy of the National Robotics Engineering Center

Explorations and revelations taking place in the medical school



An international network of students in Hatfull's SEA-PHAGES program has identified, analyzed, and categorized 15,000 bacteriophages. Three of those phages were used recently as part of a biomedical cocktail to save a British girl experiencing a life-threatening infection.

THE PHAGE HUNTERS

HATFULL'S LIFESAVING MENAGERIE

BY JASON BITTEL

Editor's Note: This story was adapted from a longer feature published in Pitt Magazine *this summer.*

In October of 2017, a British teenager named Isabelle lay on her deathbed. The girl had been diagnosed with cystic fibrosis at a young age, and even though she'd recently undergone a successful double lung transplant to alleviate some of her more life-threatening symptoms, a bacterial infection had since taken over her body. Antibiotics failed to kill or even contain the microbes. With no traditional options left, Isabelle's doctors reached out to Graham Hatfull.

You see, Hatfull is an expert on phages, viruses that hunt and destroy bacteria.

Most people haven't heard of phages, short for *bacteriophages*, but there are approximately 10 million trillion trillion of them on Earth, or about 10 million more than there are stars in the universe.

"Phage particles are the majority of all biological stuff on the planet," says Hatfull, who is the Eberly Family Professor of Biotechnology at the University of Pittsburgh.

Under an electron microscope, phages look like a lunar lander crossed with a robot spider. And like other viruses, they cannot reproduce on their own. Instead, a phage must hijack a bacterial cell's machinery to create copies of itself. It then multiplies inside the bacterium until there are so many that they burst out like candy from a smacked piñata. The bacterium dies as a result, while each new phage goes on the prowl for more hosts in which it can repeat the process.

Scientists have actually been using phages to combat bacterial infections since 1915, but the practice mostly fell out of favor with the rise of antibiotics. Isabelle's doctors hoped to harness phage therapy to combat Isabelle's infection.

Unfortunately, phages are what you might call picky eaters. Each one has evolved into a highly specialized predator of usually just one specific kind of prey. That's why even though phages are everywhere, they can't simply be grabbed from a puddle and injected into a sick person. Doctors need someone who can find precisely the right phage for the job.

That's where Hatfull comes in. He and his team at Pitt are among the world's leaders in collecting phages and learning what they do. They have also developed an international network of more than 150 schools that teach undergraduate students to process soil samples in the hopes of discovering new phages. Hatfull's freezer library currently includes more than 15,000 phages, roughly two-thirds of which are closely related.

With samples of Isabelle's bacteria in hand, Hatfull and his team were able to sift through their stores and isolate three candidates that might be able to go to war for the girl. One of these had been plucked out of a storm drain alongside the Heinz Memorial Chapel back in 2006 by a Pitt undergraduate named Tim Sampson. The other matches came from Rhode Island and South Africa. All three would go into the phage therapy cocktail as a way to prevent the bacteria from developing a resistance to any one phage.

Back in London, Isabelle's liver had begun to fail, but the team in Pittsburgh still had one obstacle to overcome. Two of the matches were temperate phages, meaning they infect bacteria but do not kill them outright. Luckily, Hatfull's lab had already experimented with a genetic modification to unleash a phage's inner bacteria-bursting beast.

After tweaking the cocktail, performing a litany of safety tests to make sure it didn't contain any toxins, and undergoing thorough regulatory approval, Hatfull's team shipped the serum off to London.

Isabelle was the first person in the world to receive genetically modified phage therapy.

"Almost overnight things started to clear up and heal," a grateful Jo Holdaway, Isabelle's mother, told CNN about the case that captured worldwide attention. "It was just amazing."

In six weeks, Isabelle's infection nearly disappeared. Hatfull and his team published Isabelle's groundbreaking case study in *Nature Medicine* in May 2019.

Today, more than a year since the June 2018 treatment, she still receives phage therapy on a regular basis, but her microbe levels are so low and her breathing so improved that she is no longer bedridden. Isabelle has returned to school and in many ways is living a normal, teenage life.

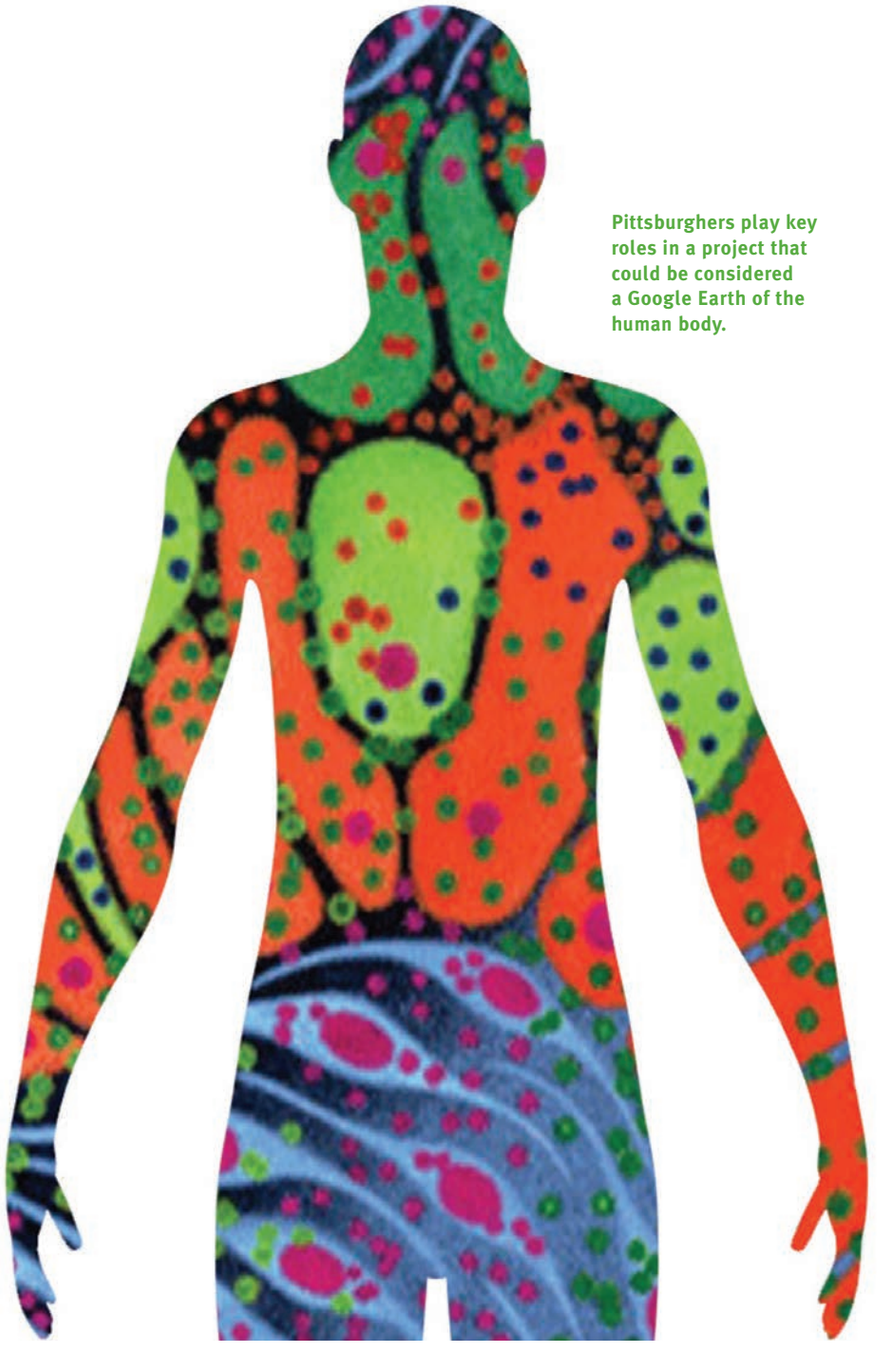
"This is a kid who we didn't expect to survive," says Hatfull. "That feels pretty amazing." ■

COURTESY GRAHAM HATFULL

ANOTHER DIMENSION

3-D ATLAS OF THE BODY, AT THE CELLULAR LEVEL

BY JACOB WILLIAMSON-REA



Pittsburghers play key roles in a project that could be considered a Google Earth of the human body.

NIH COMMON FUND

The Human Genome Project gave us identities and locations of genes. Yet to really understand wellness and disease, we'll need more than an address book. That's why scientists are creating the equivalent of a Google Earth of the human body.

In 2018, the National Institutes of Health launched the Human BioMolecular Atlas Program (HuBMAP), which was tasked with creating a comprehensive atlas of our cells and tissues.

Tomes of new maps are in the works, using data from individual cell types and images of each cell in representative tissue samples. The end goal: a high-resolution, 3-D atlas of us, down to our most basic building blocks, which shows not only where cells are, but their many functions, as well. The atlas will render the tens of trillions of cells within human tissue, clarifying how these cells organize, specialize, and cooperate.

Jonathan Silverstein, chief research informatics officer and professor of biomedical informatics at the University of Pittsburgh, and Nicholas Nystrom, chief scientist at the Pittsburgh Supercomputing Center, are coprincipal investigators on HuBMAP's infrastructure and engagement component. Silverstein also co-leads the steering committee of the HuBMAP Consortium with Michael Snyder at Stanford University.

HuBMAP collaborators elsewhere, at tissue mapping centers, will generate data about cell organization and variation within specific tissues and organs.

The Pittsburgh duo has developed the crucial framework to receive and manage data from the tissue mapping centers. High-quality, medically valuable data will come from advanced genomic sequencing, microscopy, and mass spectrometry for many different tissues, says Nystrom.

"When combined, these will provide a multimodal view of the tissues: physical appearance, genomic information, and protein expression, all at single-cell resolution. This is truly a medical first."

Ziv Bar-Joseph, the FORE Systems Professor of Machine Learning and Computational Biology at Carnegie Mellon University, leads a separate center focused on the development of computational analysis methods for HuBMAP.

"Upon completion, the 3-D map has the potential to be a major tool over the next few decades, just as the Human Genome has been since its completion," says Bar-Joseph. "This will be an amazing reference point in medicine and may lead to significant improvements in how we diagnose and treat disease." ■

TYPOGRAPHY: ELENA GIALAMAS CERRI

WORKLOAD CODE

BY HEATHER BOERNER

One hundred clicks. That's what it can take for a doctor using a typical hospital's electronic health record (EHR) just to order the right tests, check a history, and proceed with a patient's care.

A School of Medicine faculty member intends to change that. Among other things, Yalini Senathirajah's system would allow doctors to see the information they need at a glance, choosing which elements belong together on the screen.

MedWISE, an add-on to current EHRs, was designed by Senathirajah, a PhD associate professor of biomedical informatics. With the system now in beta phase, she's testing it to see if the approach helps physicians get the information they need without the cognitive load and potential for errors associated with most modern EHRs. And Senathirajah is looking for more recruits.

"I'm really keen to see: What will physicians do with it? I'm interested to see patterns and if they think of uses we didn't think of," she says.

"If the [EHR] system can be adapted by physicians to meet their needs, in public health emergencies it could be rapidly adapted to create new solutions without waiting three months for the IT department to provide a solution."

Senathirajah came up with the idea while working on her PhD in health care informatics at Columbia University. She was inspired by her own experience as a technical advisor for a large academic medical center. In that role, she got to see up close how EHRs don't quite go far enough to help physicians make timely and efficient medical decisions.

Here's how MedWISE works: Doctors can assemble information from a system's existing EHR into tiles, juxtaposing them on the same screen, and creating new elements. For example, physicians can create a calculator tile if the case requires, and even color-code the elements, or create specialty-specific items.

For example, as she's seen in beta users, "You [might] put all the important things in red and put them on the right," she says. "And then pull up brain scans and code them blue."

So far, the approach has been tried using data from the NewYork–Presbyterian Hospital. Senathirajah and colleagues have published indirect evidence of cognitive load reduction. Right now, the focus is testing the safety, efficiency, and other cognitive effects of the approach, and potentially using those results to develop a case for adoption by medical systems.

"MedWISE allows sharing configurations," she says. This could help physicians save time—if the next provider for that patient thinks the same way. And what if that clinician doesn't?

Will that user change the configuration? If not, could that cause medical errors? Senathirajah is now running a study of 66 physicians to find out.

Another study—of 32 clinicians, including physicians, nurse practitioners, and physician assistants—will compare MedWISE to usual EHR configurations to look at how long it takes users to complete specific tasks. Colleagues at Columbia University will participate. Senathirajah is looking forward to bringing her Pitt colleagues into the research.

"I'm lucky to have colleagues and students here that are so interested in solving this problem," she says.

"One reason I took this job is because my boss and others have been tremendously supportive and understood what I'm trying to do." ■

University of Pittsburgh School of Med.

PITTMED

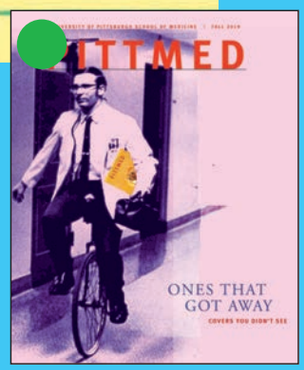
1 20th Anniversary Issue

our

~~MIXed~~

~~Methodology~~
~~Bonus Material~~
~~Behind the Zines~~
~~What We Left~~
~~On the Cutting Room Floor~~
→ The Covers That Got Away

This was almost the cover for this issue. (See legend.) How do we make these decisions? Keep reading.



LEGEND

- ACCEPTED
- REJECTED

Outtakes

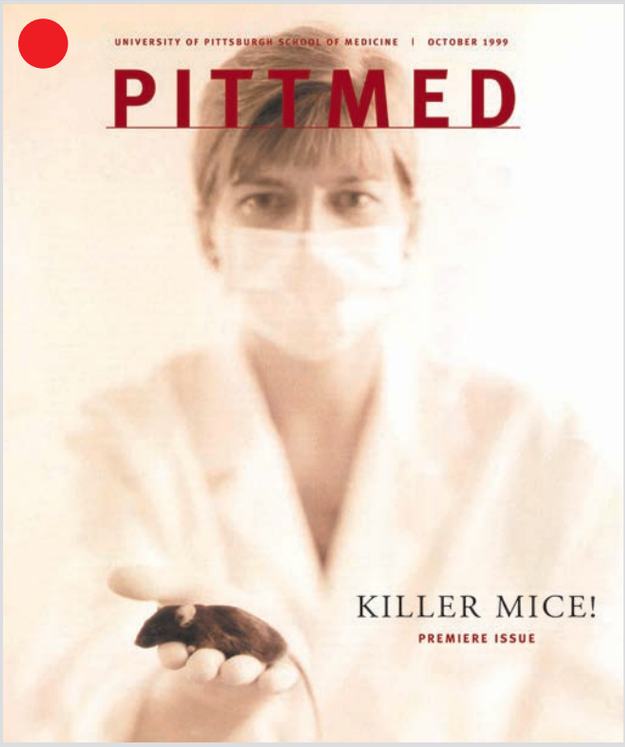
BY ERICA LLOYD

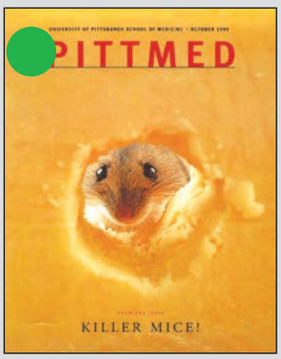
ART DIRECTION BY ELENA CERRI

Rarely are the images and words that land on our front cover the very first things we imagined. On the occasion of the magazine's 20th anniversary, we're sharing some of the thinking behind that process. Here, we offer a glimpse of would-be *Pitt Med* covers. Ones we didn't choose.

Sometimes, people ask us, "How do you do your graphics?" That's the realm of the discerning Elena Cerri, our art director. She fields and hones editorial suggestions and works directly with talented contributing artists to make these covers, and the rest of our graphics, happen.

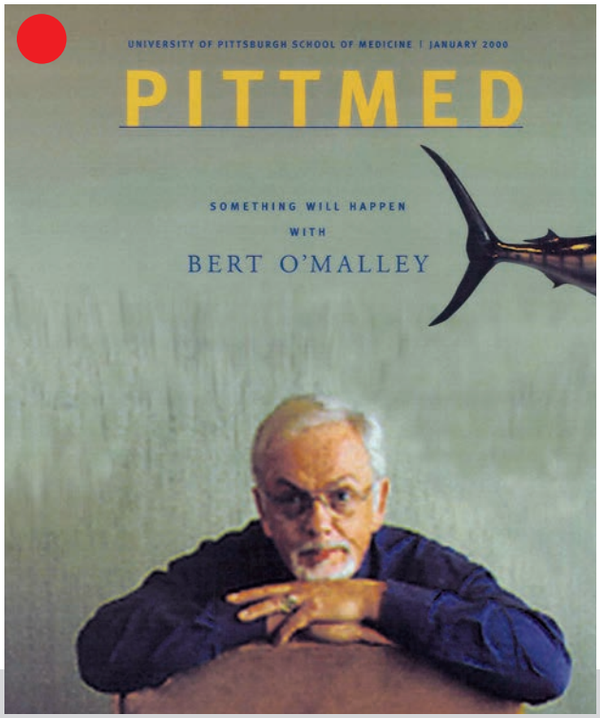
Note: Many of the rejected covers are shown as sketches because they did not get past the concept phase.

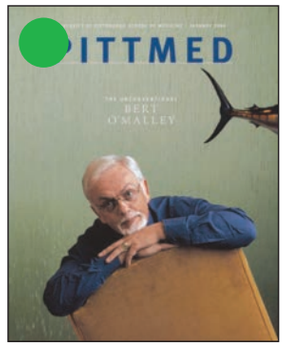




OCTOBER 1999

Our first cover story was "Killer Mice!" The Frank Walsh black-and-white photo (left) of Paula Monaghan-Nichols, who studied aggressive behavior, was too "film noir" for Art Levine, our publisher, who is also senior vice chancellor for the health sciences and dean of the med school. Pitt creative director, Gary Kohr-Cravener, found the cheesy mouse shot for a more straightforwardly playful approach.



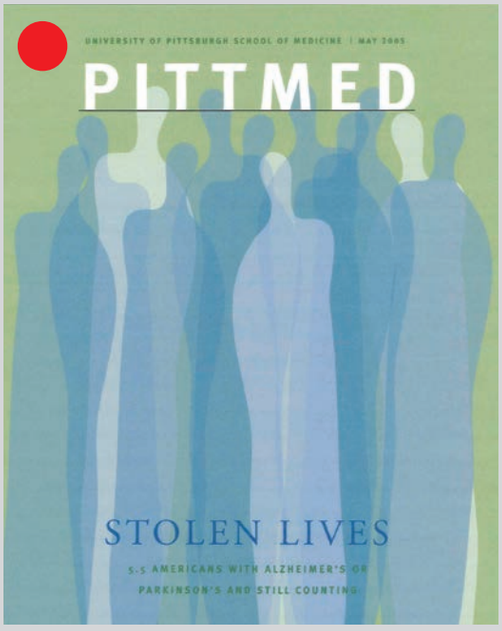


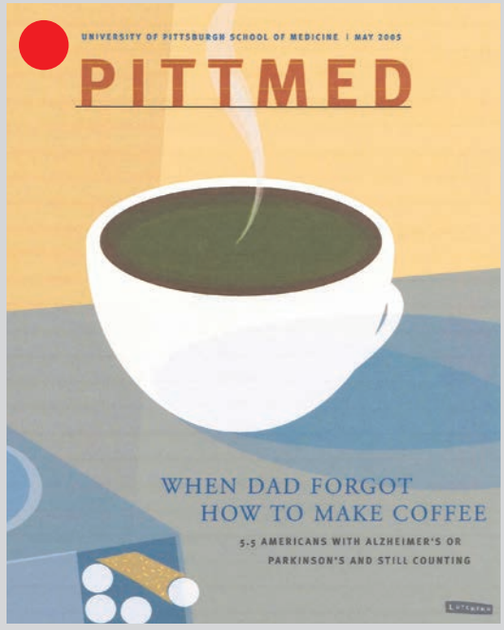
JANUARY 2000

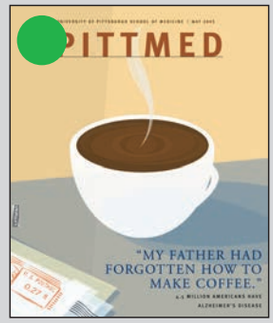
We wanted to do something unconventional with Bert O'Malley (MD '63), leading hormone researcher and known prankster. The dean encouraged us to tilt the distinguished physician-scientist. (Photo by Pam Francis.) Later that year, the dean made another suggestion: Stop using portraits on the cover. That lit a spark.

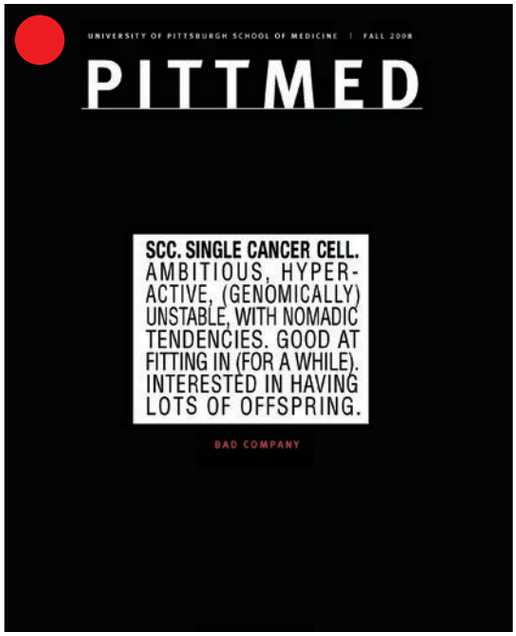
MAY 2005

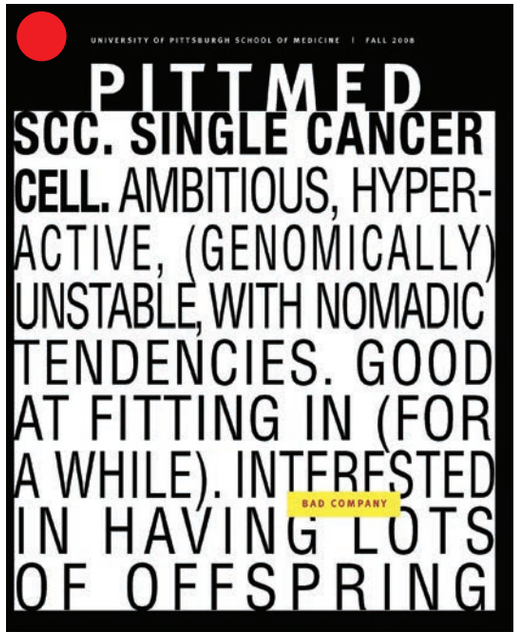
Illustrator Michael Lotenero proposed this crowd of shadowy figures for our first package feature, a 10-pager on neurodegeneration called "Stolen Lives." It worked well on the inside of the magazine, but felt vague for the cover. We landed on another Lotenero illustration for a companion story—Cindy Gill's essay on witnessing her father's decline into Alzheimer's. (Among other things, we substituted the cigarettes pictured with unpaid bills.) The coffee cup setting and line from the story signaled that an intimate narrative awaited the reader.

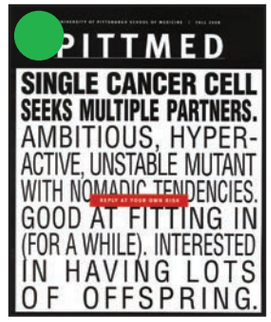










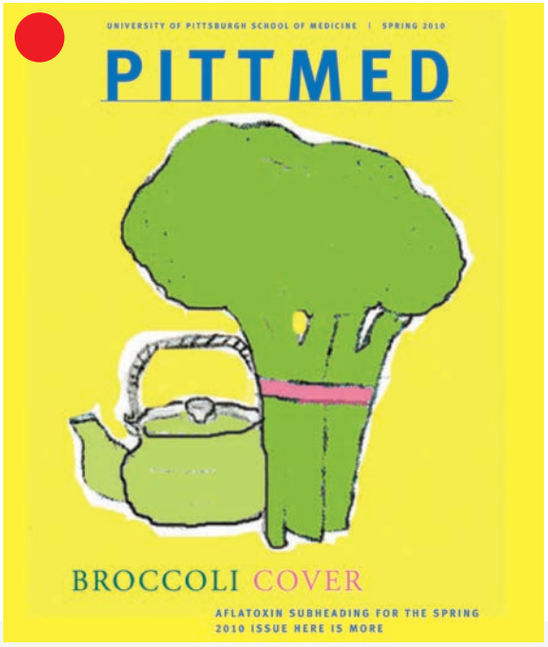


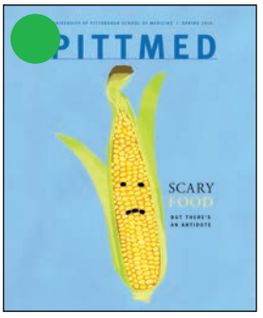
FALL 2008

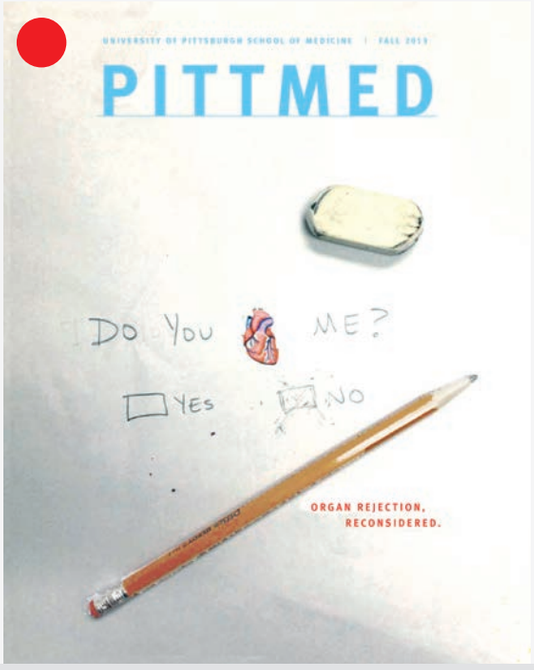
This feature was about shifting our thinking, and vocabulary, for cancer. Scientists no longer saw cancer cells as invaders; they were more like ne'er-do-wells among us, looking for opportunities to propagate.

SPRING 2010

Sometimes it's a toss-up. Illustrator Juliette Borda gave us two takes for a cover story on Pitt scientists helping populations likely to be exposed to a dangerous fungal toxin that grows on corn and peanuts in the tropics. The researchers were testing a broccoli-sprout tea antidote. We used the broccoli teapot inside the magazine. Not to be blithe, but who can resist scary corn?

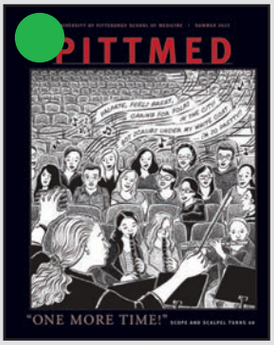






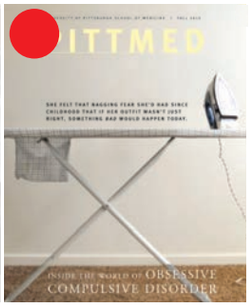
FALL 2013

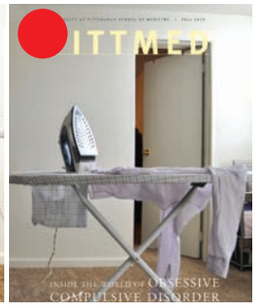
When scientists start rethinking organ rejection, there are lots of reasons to give a damn. (We were fond of senior editor Elaine Vitone's multiple-choice proposal, but did not, er, choose it.)

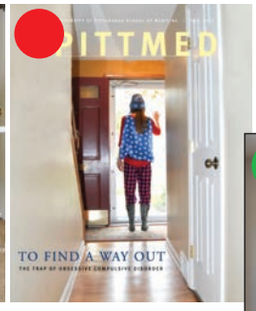


SUMMER 2015

Remember the 2015 Super Bowl halftime show where Katy Perry led a phalanx of improbably dressed dancers, including two in 7-foot-tall shark costumes? Remember how one of the sharks was out of step? No??? Well, we also missed the "Left Shark" incident, but learned of the resulting meme by covering that year's Scope and Scalpel production, which had its own version of the Left Shark. Em DeMarco, then a graphic journalist, created a comic for our cover story. While we loved her initial shark sketch, the reference was too obscure for a cover. We chose another DeMarco illustration showing the class coming together for the big production.

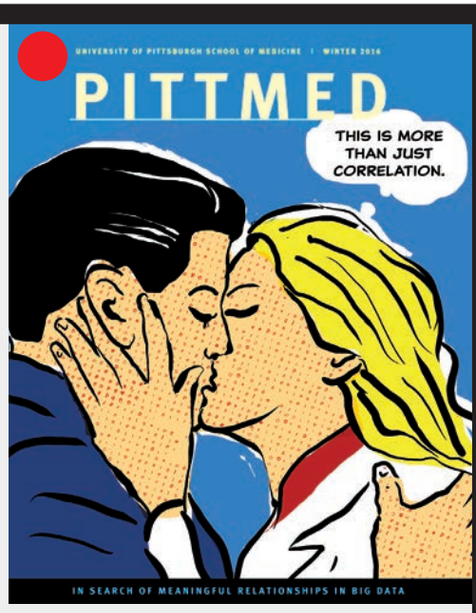






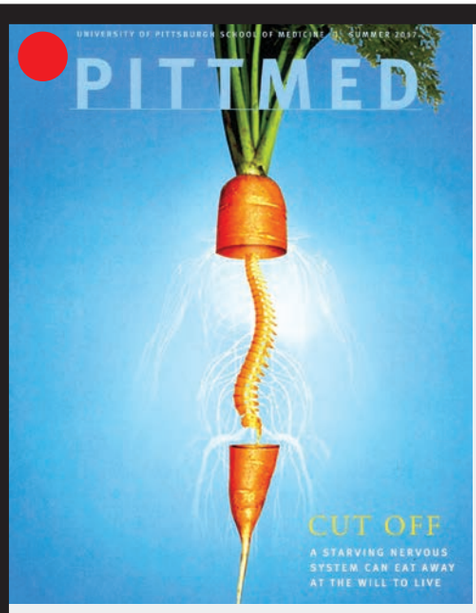
FALL 2015

Sometimes landing on the perfect cover is about iteration. Photographer Cami Mesa must have given us a dozen outtakes of ironing boards for our feature on obsessive compulsive disorder. Another Mesa shot we passed up: one of a young woman heading out in a silly unmatching superhero costume. That shot depicted a real exposure therapy, which our story's main character completed to overcome her difficulties leaving home because of OCD.



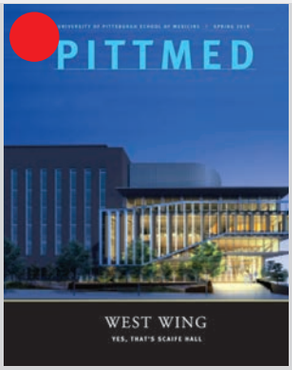
WINTER 2016

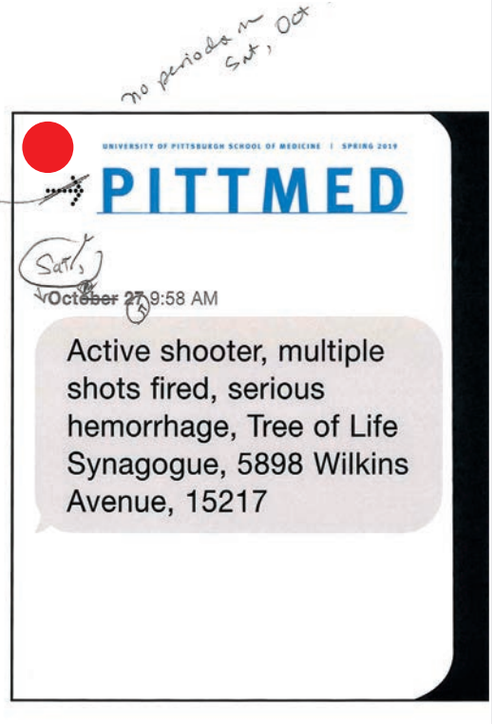
Illustrator Stacy Innerst created the Lichtenstein-esque cover concept (right) for the "correlation is not causation" idea. Though a fun spin on the search for "meaningful relationships in data," it was a no-go. Innerst's other offering: a Rube Goldberg machine interrupted by a cat. What could go wrong? (The cat was modeled after associate vice chancellor Maggie McDonald's late feline companion, Abbey. McDonald has been a key advisor to the magazine staff for 20 years.)



SUMMER 2017

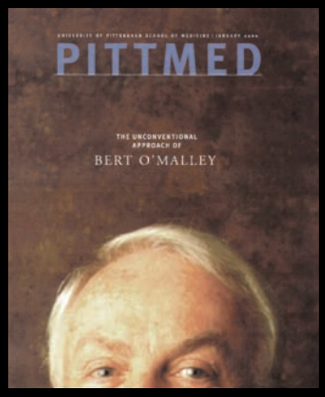
This astonishing story is about an experimental nutritive therapy Pitt docs administer via spinal fluid. It relieves certain forms of otherwise intractable depression. We asked Jesse Lenz to add nerves to his initial carrot spine concept, then asked him to take them away. In between was some editorial hand-wringing; yet less is more.

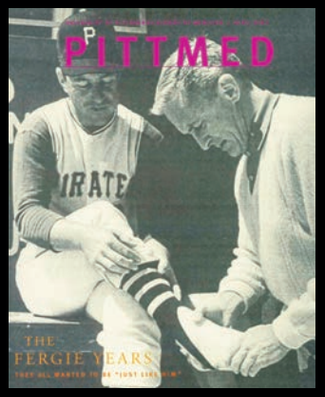


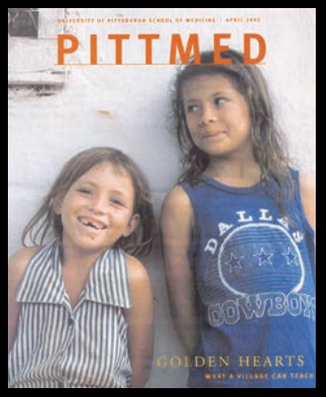


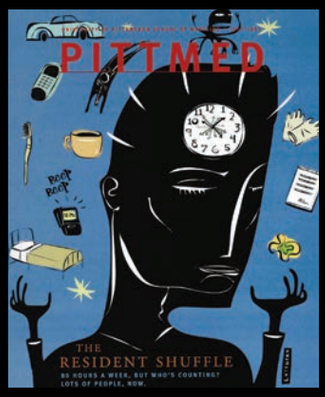
SPRING 2019

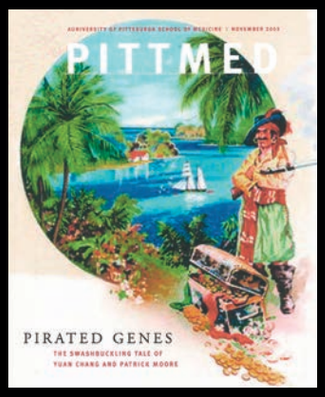
"West Wing," on the addition to Scaife Hall, was a potential cover. That's an important topic for the Pitt Med community, yet more profound was the Tree of Life shooting. How would we depict the medical response to the massacre? Bullet holes in glass seemed predictable. The cell phone alert would have felt appropriate if our timing had been more immediate; this issue came out six months after the horrific event. We went with a compelling line from Gavin Jenkins's story, set simply on army green.

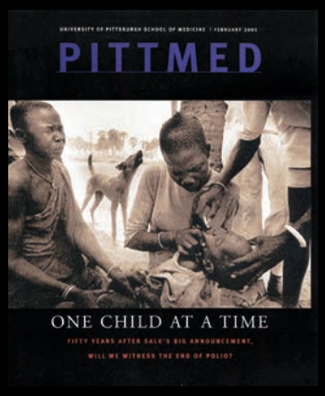


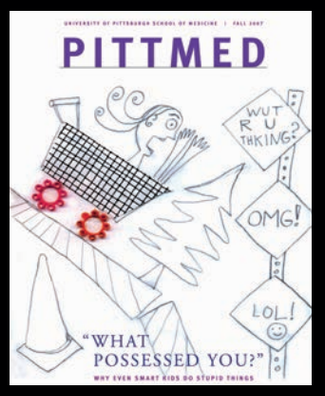


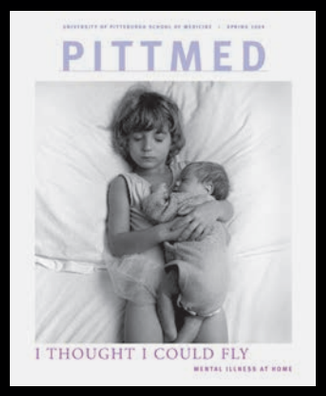


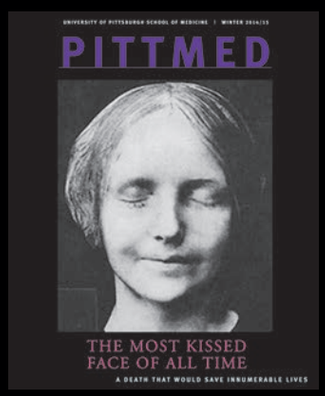


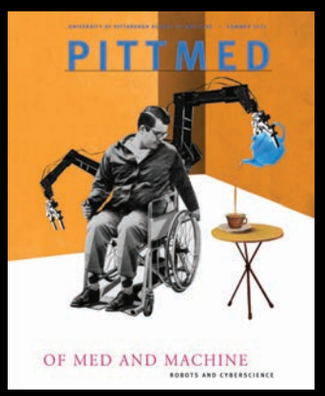


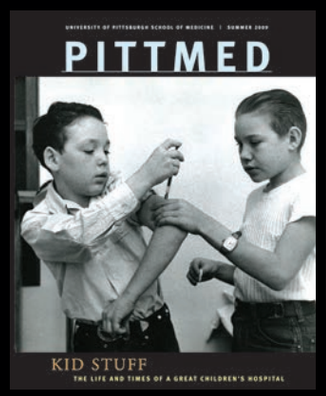


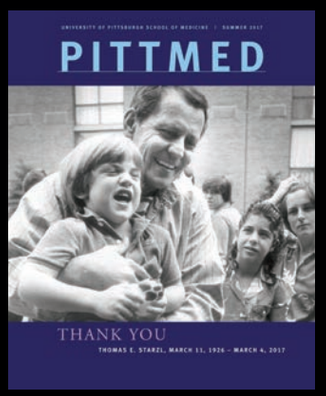


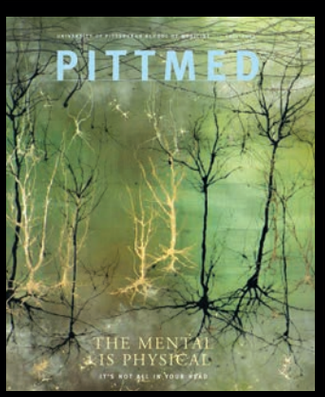


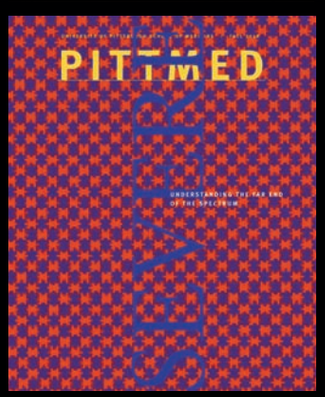


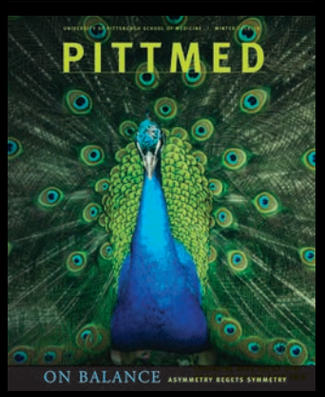


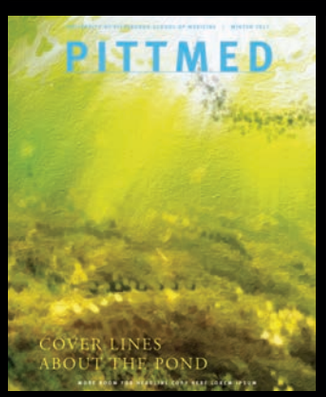


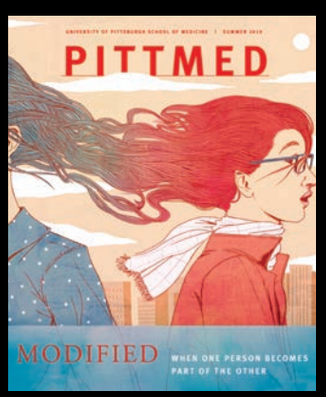












Other rejects, many of which we would have been happy to have on the cover.

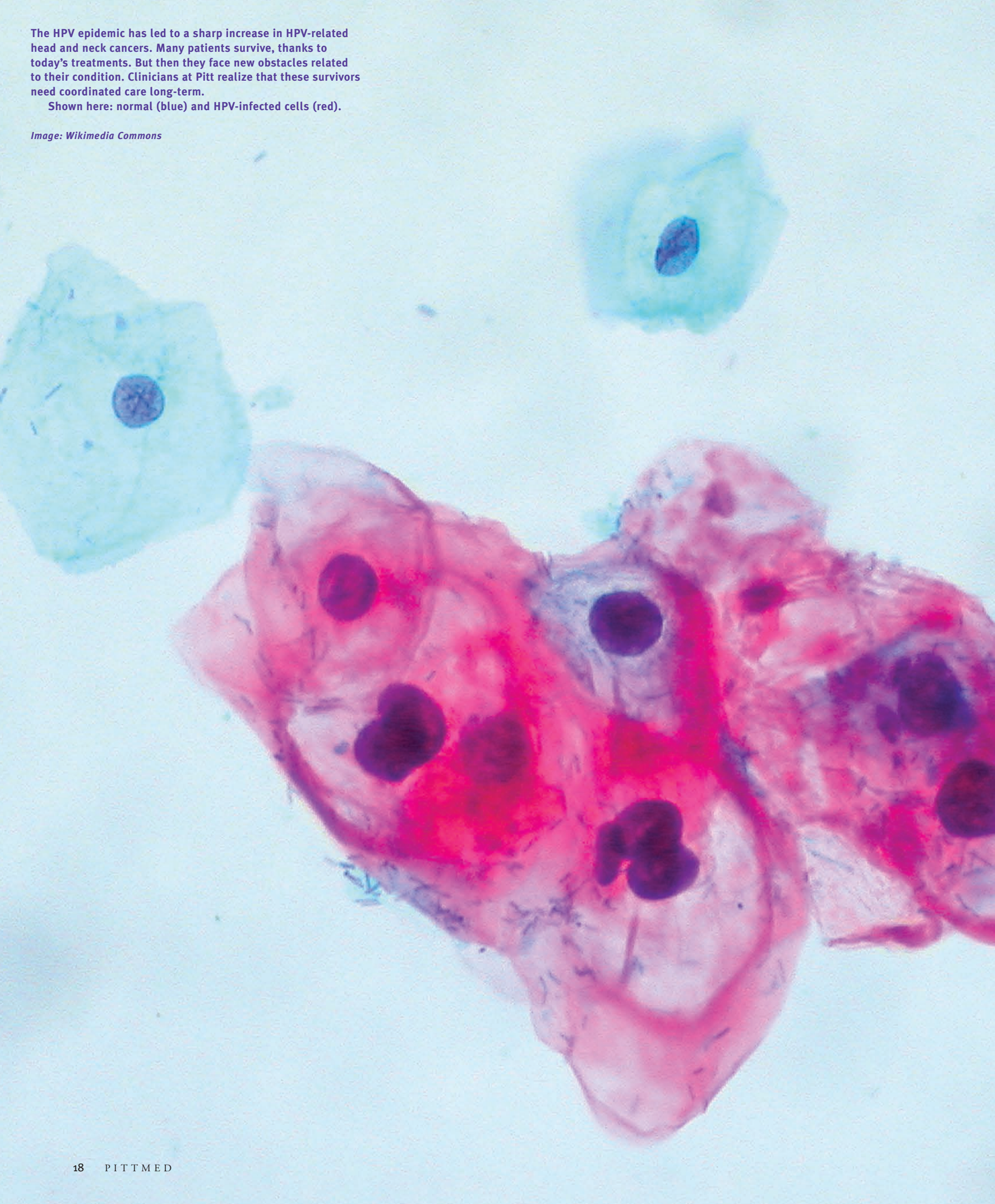
Cover contributors shown on these pages:

Juliette Borda
Charlee Brodsky
Esther Bubley
Elena Cerri
Em DeMarco
Greg Dunn
Pam Francis
Getty Images
Frank Harris
Michael Hirshon
Jim Judkis
Catherine Lazure
Jesse Lenz
Michelle Leveille
Michael Lotenero
Merck and Co.
Cami Mesa
Payette
Pictogram Studio
Pittsburgh Post-Gazette
Pitt Med students
David Pohl
Sebastião Salgado
Frank Walsh
Wikimedia Commons

The HPV epidemic has led to a sharp increase in HPV-related head and neck cancers. Many patients survive, thanks to today's treatments. But then they face new obstacles related to their condition. Clinicians at Pitt realize that these survivors need coordinated care long-term.

Shown here: normal (blue) and HPV-infected cells (red).

Image: Wikimedia Commons



LIFE AFTER HEAD AND NECK CANCER CAN BE A STRUGGLE

BY GAVIN JENKINS

SURVIVING SURVIVAL

Jonas Johnson presses his hand on Edward Christopher's neck. The examination room at the UPMC Head and Neck Cancer Survivorship Clinic is chilly on this June morning as Johnson, chair of the University of Pittsburgh Department of Otolaryngology, glides his fingers along the left side of Christopher's throat.

"Your skin is stiff," Johnson says. "Scar tissue doesn't go away."

Five years ago, Christopher was diagnosed with human papillomavirus (HPV) positive cancer on the base of his tongue, left tonsil, and the lymph nodes on the left side of his neck. After undergoing surgery to remove the tumors, he received radiation treatment and chemotherapy, followed by another procedure to remove his lymph nodes.

When he completed the treatment, he posted a picture on Facebook holding a sign that read CANCER FREE! That night, he and his family celebrated with dinner at an Italian restaurant.

Christopher felt lucky to be alive and grateful to Pitt doctors. He had no idea how difficult the years to come would be.

Half a decade later, he struggles to swallow bread, and when he eats cookies—a daily, midday treat—the 68-year-old has to dunk them in coffee first.

Johnson turns to Kathy, Christopher's wife, and explains that the rigidity in Christopher's skin is a side effect from radiation and chemotherapy treatments; this is what's been compromising his swallowing and speech. "He's gotta keep stretching [his neck] forever, or else he'll pay the price," Johnson says.

That price could be choking to death, which nearly happened to Christopher a few years ago. He had taken a big bite out of his dinner and couldn't swallow it like he would have before he had cancer. Kathy slapped his back until he coughed up the food.

Johnson spent decades fixated on removing cancerous tumors from patients through surgery. After an operation, when he saw a patient, his main concern was whether cancer had returned. If it hadn't, Johnson asked, "How are you doing?" The patient, who also was focused on cancer returning, usually replied, "Fine."

Later Johnson would learn how some simple tasks of daily living can be arduous for head and neck cancer survivors. Now he understands that when patients are asked specific questions about their lives, including the economic cost of being a head and neck cancer survivor, they indicate that they're far from fine.

"The results are shocking," Johnson says. "They are still shocking to me."

He credits Marci Lee Nilsen, a nurse who is a PhD assistant professor in Pitt's School of Nursing, with opening his eyes.

In 2016, Johnson and Nilsen created the Survivorship Clinic to help patients like Christopher improve their quality of life after beating head and neck cancer. Most patients grapple with dysphagia—difficulty swallowing—and trismus, commonly known as lockjaw. They might experience a loss of taste, tooth decay, dry mouth, and mouth sores. The side effects from radiation and chemotherapy can often cause patients to struggle to talk, hear, and sleep, as well. The combination of these treatments with surgery can also lead to mobility issues; many patients end up on disability. Insomnia and sleep apnea can exacerbate anxiety and depression (which also are common issues).

Getting care for these conditions can place a financial strain on patients who have already spent tens of thousands of dollars to overcome cancer.

Survivorship clinics for head and neck cancer are sprouting up across the country. Some of those clinics have more than a few specialists. UPMC's clinic patients see an otolaryngologist, audiologist, dentist, speech pathologist, and physical therapist in one day. And unlike any other survivorship clinic in the United States, they are charged just one co-pay.

When patients are asked specific questions about their lives, including the economic cost of being a head and neck cancer survivor, they indicate that they're far from fine.

The Survivorship Clinic also sets itself apart by how it monitors patients from the start. Nilsen and Johnson meet with patients *before* they receive radiation and chemotherapy, and then again a month after treatment is completed. After that, patients visit the clinic at least once a year, and depending on their needs, Johnson and Nilsen will coordinate with the appropriate primary care physician, dentist, or physical therapist.

Historically, the struggles of head and neck cancer survivors have been approached as an afterthought by many hospitals and primary care physicians. That's changing as providers recognize the fallout from treatments, which can be lifesaving but also life hobbling. Johnson and Nilsen have seen more than a thousand patients in their three years at UPMC's Survivorship Clinic. Their work has highlighted the importance of long-term care.

For Johnson, a renowned head and neck cancer surgeon who has been with Pitt since 1977, the Survivorship Clinic represents a new chapter in his career.

"I've reinvented myself," he says. "I say to my residents: *Don't think I've repudiated the last 40 years of my career. I still believe in surgery. But I've embraced the notion that we must recognize the trouble we cause [treating cancer], and we have to help people with it.*"

Johnson and Nilsen started out as mentor and mentee in 2014. Nilsen was a postdoc, researching how taxing it can be to communicate after head and neck cancer treatment. She needed to work with patients before and after surgery, and Johnson accommodated her with patients and space at UPMC's Eye and Ear Institute. She hadn't expected him to be so helpful.

"Sometimes people don't understand when you're coming from a nursing perspective," Nilsen says.

"A physician once told me it was 'fluffy stuff.' But, from the beginning, Johnson was really open and interested."

Later that year, Nilsen won an Oncology Nursing Foundation career development award to research long-term effects of head and neck cancer. The award supported the second phase of her project: clinical observation and a systematic review. While embedded on Johnson's team, Nilsen gave him research papers on dysphagia and trismus as part of her systematic review. She also sent him a decade-old research paper from the National Academy of Medicine about the need for a coordinated approach to survivorship care.

"It was more like a book, not a paper," Johnson says, with a smile.

"I drilled it into his head," Nilsen says.

Johnson and Nilsen, who are almost 40 years apart in age, began meeting weekly to discuss her clinical observations, as well as the literature they were reading. "Everyone was looking at problems like dysphagia and trismus separately," Nilsen says. "But if you can't open your mouth, how can you chew and swallow properly? The problems can all compound each other. And Johnson said, 'We need to do this better.'"

Pitt hired Nilsen in August 2016, after

A team led by Marci Lee Nilsen and Jonas Johnson helps cancer survivors get their lives back.

Photo: Tom M. Johnson

she completed her postdoc, and UPMC gave them the green light to open the Survivorship Clinic. When Johnson told Nilsen the news, she opened her mouth and tapped her front teeth, as she recalls:

"He says: *You're happy about this?* And I was like, *No. Teeth. Dentist. We need a dentist for this. Do you know how many times your patients ask about their teeth?*"

There's no shortage of these patients.

HPV is the most common sexually transmitted disease, with approximately 80 percent of sexually active people contracting it at some point. Passed through intimate skin-to-skin exposure, HPV is harmless in most cases, as the body clears the infection. However, the virus can remain latent for decades and be transmitted to another partner later. It also can develop into cervical cancer or head and neck cancer.

As the virus has risen to epidemic-level proportions, with an estimated 79 million people currently infected, the number of HPV-positive head and neck cancer cases has grown tremendously.

Unlike HPV-positive cervical cancer, which can be detected early through a Pap smear, HPV-positive head and neck cancer isn't usually identified early. Robert Ferris is director of the UPMC Hillman Cancer Center and Pitt associate vice chancellor for cancer research. His team is attempting to detect HPV-positive head and neck cancer through saliva, so doctors can treat it early on.

Because there isn't an early detection method, the increase in HPV-positive head and neck cancer cases snuck up on experts, climbing at a rate of 5 percent a year for three decades. In the 1980s, HPV-positive head and neck cancer made up 20 percent of all instances of cancer related to the sexually transmitted disease. Now it's close to half of all diagnosed HPV-related cancer cases and, says Ferris, it may even exceed HPV-positive cervical cancer cases.

"We didn't even know we were treating HPV-related cancer," Ferris says. "We were treating head and neck cancer; and then, little by little, we started seeing more cases of HPV-positive patients in every clinical trial that got reported over 20 years."

Unaware that they were treating patients with the virus-associated cancer, doctors gave HPV-positive head and neck cancer patients the same doses of radiation and chemotherapy as they did people with other forms of oropharyngeal cancer. Yet, it turns out that HPV-positive patients don't need such high doses; those doses seem to harm them. But doctors didn't know that until earlier this decade, after a series of de-intensification clinical trials, including one led by Ferris at Hillman.

Compared to people with other forms of oropharyngeal cancer, HPV-positive head and neck cancer patients are, on average, about 10 years younger (in their 50s instead of 60s), and their survival rate is much higher (close to 90 percent over five years compared to 40 percent).

Researchers don't know why these patients are so much more likely to survive, and Ferris says unlocking this mystery, as well as discovering why and when HPV causes cancer, could lead to better treatment.

"There's probably a Nobel Prize in it for whoever can figure that out," he says.

Mark Beck smiles as he waits in a Survivorship Clinic examination room. The eighth-grade history teacher feels grateful that he was able to finish another school year. "I would like to teach forever," he says. But Beck, a 47-year-old

long-distance runner, doesn't know if he'll be able to reach retirement without going on disability.

In 2010, he was diagnosed with HPV-positive cancer on his tonsils. Before he started going to the Survivorship Clinic, his swallowing had worsened every year following his treatment. Beck has had two near-death choking incidents, and sometimes saliva drips into his airway while he's teaching, making him cough. He doesn't go anywhere without a bottle of water because he also suffers from cottonmouth, which has made teaching all day challenging.

This year, he has struggled with his voice. It's normal early in the morning, but by dinner he can barely talk. He's been wondering why. Just minutes ago, Nilsen and Johnson told Beck he has residual radiation damage to his thyroid, a common side effect for patients nearing 10 years after treatment.

"I thought the cancer had come back, but they were like: *No, typical*," Beck says. "It wasn't a shock to them at all. They really know how to track stuff here."

Johnson and Nilsen do this through a patient reported outcome (PRO), a 60-question survey taken on an iPad as patients arrive at the Survivorship Clinic. The clinic team sees about 30 people every Thursday who are asked pointed questions about mental and physical health, sleep quality, neck discomfort, swallowing ability, and other oral issues.

The PRO responses also determine which specialists a patient sees. Patients examined by speech pathologist Tamara Wasserman-Wincko might need a fiberoptic endoscopic evaluation of swallowing (FEES). During this procedure, a thin, flexible endoscope is inserted through the patient's nasal cavity. The patient is given liquid or food (usually water or pudding) to swallow that has been dyed blue. While watching a patient swallow, Wasserman-Wincko and Johnson can check for aspiration. This evaluation also tells them if it's likely cancer has returned.

Christopher didn't need a FEES on this June morning, but because he described issues related to dysphagia on his PRO intake, Wasserman-Wincko wants to review swallowing techniques, or "effortful swallowing." They discuss his diet, talk about the importance of drinking water while eating. Each swallowing evaluation is tailored to the patient. Because Christopher's tumors were on the left side of his neck, Wasserman-Wincko advises him to turn his head left when swallowing.

"This helps patients to block off the weaker and impaired side of their throat when swallowing," she says. "If a patient had a tongue cancer, then food placement is key. A head tilt to the stronger side may help with transfer of food. We can't prevent stiffening from radiation therapy, but we try to slow it down by doing range-of-motion exercises."

Dental hygiene is another concern. Radiation can disintegrate teeth, and it changes the pH of the saliva. A survivorship patient has a pH level of 4 or 5, says Elizabeth Pawlowicz, an assistant professor in the School of Dental Medicine on staff at the Survivorship Clinic.

"It's like walking around with Coca-Cola in your mouth all the time," she says.

After an evaluation, Pawlowicz gives clinic patients mouthwash and fluoride, and she advises them to visit their dentist four times a year. She also advises patients to tell their dentist that they are prone to gum disease, tooth decay, fungal infections, and ulcers because of cancer treatment.

Sometimes, if a patient suffers from a combination of side effects, going on disability can come as a relief. David Lacivita, 59, conquered HPV-positive tongue cancer seven years ago. Doctors removed the lymph nodes from his neck, and now he has progressive fibrosis—he can't turn his head. Lacivita feels a shooting pain in his neck and shoulders whenever he reclines in a chair or lies in bed. A former bus driver, he sleeps only two to four hours a day because of the pain. He has been working as a landscaper, doing what labor he can, but is applying for disability.

"I go to work in pain, and I come home, and I'm in pain," he says.

At his June visit to the Survivorship Clinic, Lacivita is examined by Susan George, a physical therapist who is an adjunct instructor in the School of Health and Rehabilitation Sciences. She asks him to stretch out his arms and lace his fingers together. Lacivita does this without any pain, but he can't raise his arms above his head. A shock runs down his arms and his hands tingle when they get halfway to his head. He explains to George that he only recently started seeing a physical therapist.

"That's okay," George says. "But I need to coordinate with him."

Lacivita suffers from anxiety, in part, because of his inability to sleep. Physical therapy should help his mobility, but Johnson said that it's going to be difficult to undo the stiffness that has set in through the past seven years.

"We try never to say, *Get used to the new normal*. It's so evil to call this normal," Johnson says.

There are two ways to prevent more patients from needing a survivorship clinic: HPV vaccinations and changing the way HPV-positive head and neck cancer patients are treated, also called a de-intensification of therapy.

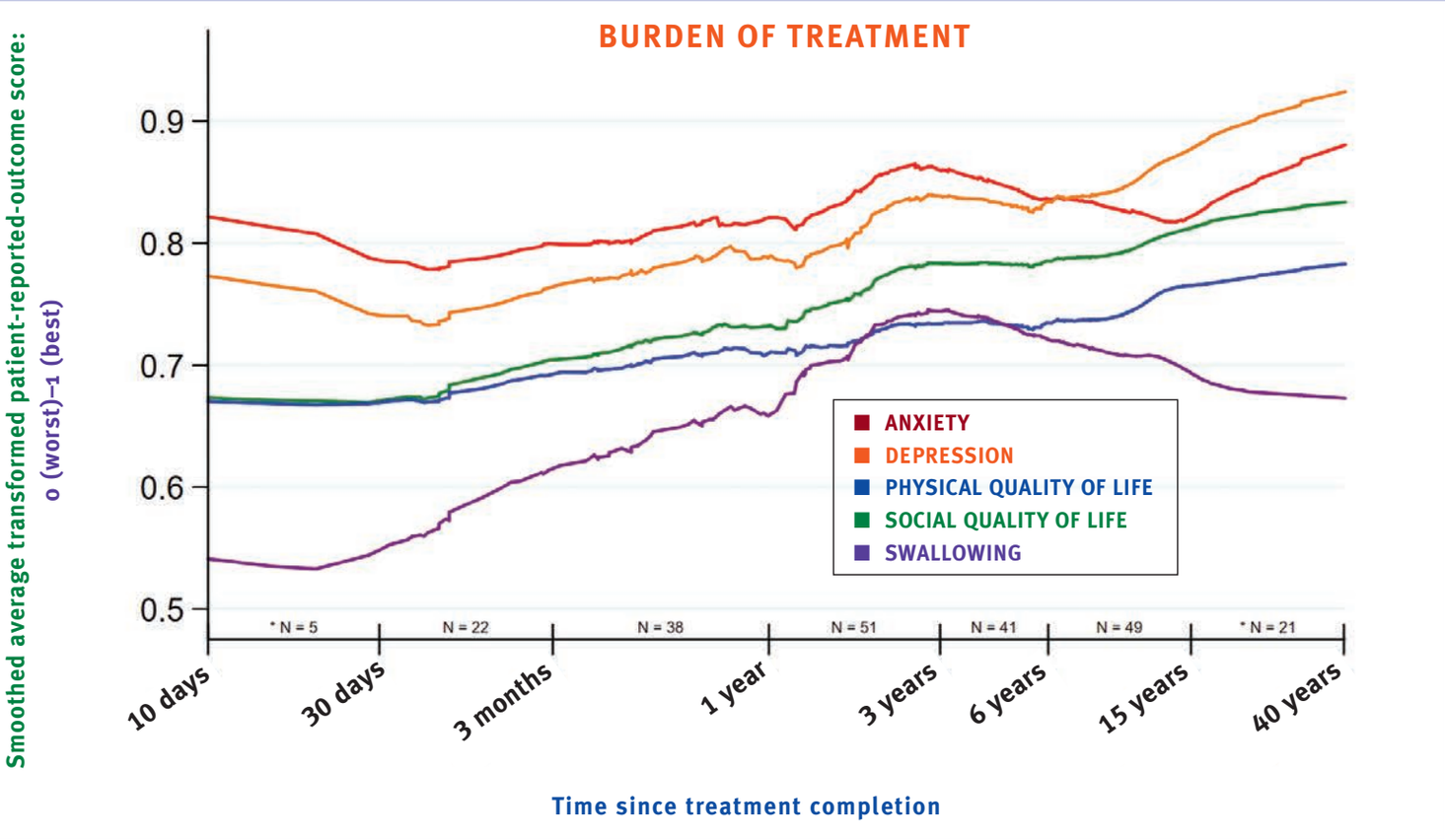
Normalizing HPV vaccinations in children is one possible solution. The Hillman Cancer Center has received funding for a grant from the National Cancer Institute to enhance awareness of the need for early inoculation. That effort is headed by Linda Robertson, assistant professor in Pitt's School of Nursing and associate director of health equity and community outreach and engagement; her team will work with pediatricians to increase HPV vaccination rates.

Hillman researchers are pursuing a number of ways to make treatment easier on patients. One team is developing a method that helps identify patients who will have trouble enduring radiation therapy.

Hillman is also the site of several clinical trials that aim to reduce dosages of radiation, eliminate chemotherapy, or attempt minimally invasive surgery. As part of a two-year trial that ended in July, surgeons used a transoral robotic device to perform surgery on 500 patients to reduce the dose of postoperative radiation. For example, if the dose would normally call for 70 gray (a radiation unit), the patients received a dose of 50 gray.

"We think if you can get 10 or 20 less gray of radiation that you'll have a better survivorship," Ferris says. "Fewer problems swallowing. Less scar tissue."

Ferris designed the trial, the first study of its kind using robotic surgery on HPV-positive head and neck cancer patients. Ferris won't know the trial's final results for months, but he says that 70 percent of participants were



GRAPH REPRINTED FROM NILSEN, MARCI LEE, ET AL. "BURDEN OF TREATMENT: REPORTED OUTCOMES IN A HEAD AND NECK CANCER SURVIVORSHIP CLINIC." *THE LARYNGOSCOPE*, JOHN WILEY AND SONS, 00:1–8, 2019.

In a study of 228 patients at the UPMC Survivorship Clinic, symptoms linked to anxiety (red line), depression (orange), physical quality of life (blue), and social quality of life (green) improved over time. However, patients stopped getting better at swallowing (purple) six years after cancer treatment ended and began to decline in ability, which doctors fear could lead to choking incidents.

able to skip chemotherapy and about half were able to receive a reduced dose of postoperative radiation therapy.

Ferris and his team are also exploring ways immunotherapy could be used in treating HPV-positive head and neck cancer. He argues that if the immune system has failed to control a chronic viral infection leading to cancer, then it makes sense to integrate an immune system booster. The booster would, ideally, turn back the clock and provide virus recognition that the immune system provides for most people.

"Especially since everybody on the planet is exposed to HPV essentially throughout their body just by normal human contact," Ferris says. "But we don't understand why some [patients' bodies] allow this virus to propagate, [or] how [the virus] hides out in the cell and turns it into cancer."

In 2012, Ferris created the Tumor Microenvironment Center at Hillman to examine how viruses are propagated and how the immune system fails. Later, Ferris took the high-risk patients from his de-intensification trial—the 30 percent who were not able to skip chemotherapy—and started a new trial. That trial focuses on replacing chemotherapy with immunotherapy and combining it with radiation. Ferris says the results he's seen give him hope in the potential of immunotherapy in treating head and neck cancer, yet he doesn't want to eliminate the possibility of using radiation or chemotherapy in lower doses. Radiation and chemotherapy, Ferris says, are beneficial because they can cause a type of cell death that elicits an immune response.

In the future, as immunotherapy is likely to become more common, radiation and chemotherapy could be used "in a kind of homeopathic way," says Ferris. He imagines lower doses that partner with immunotherapy—and minimize side effects.

Ferris would like to start clinical trials to test interventions that could reverse certain side effects.

"And the prerequisite to doing that was having the Survivorship Clinic open," he says.

The rapport between Johnson and Nilsen is one of the reasons why the Survivorship Clinic has been successful. Every week, they meet and go through two stacks of files: last week's patients and this Thursday's. Their prep work makes each Thursday run smoothly. From 8 a.m. until the last patient leaves, they move nonstop. Almost. There's typically a lull around midday, when Johnson asks Nilsen what she wants for lunch. She always asks for soup from the lobby. Nilsen jokes that she only works with Johnson for the free lunch.

One June day, when Johnson sets a bowl of chicken noodle soup in front of Nilsen, she says, "Why are you holding out on me?"

Smiling, Johnson digs into his white coat pocket and retrieves crackers. He sets them down next to the soup.

"That's more like it," Nilsen says.

Ferris calls Johnson and Nilsen innovators for recognizing the importance of survivorship care before most cancer experts. Their advocacy has helped make long-term quality of life for cancer survivors a priority throughout the Hillman Cancer Center.

"We've now partnered with the School of Nursing across Hillman and given specific titles, roles, and resources to expand the survivorship model, symptom recognition, and symptom management from the toxicities of cancer treatment," Ferris says. ■

The retina is key to both sensing and processing our visual world. Yet, as part of the central nervous system, it does not lend itself easily to transplant or regeneration.

OPHTHALMOLOGY REENVISIONED

BY ELAINE VITONE

COMING TO LIGHT

If you're ever unfortunate enough to land in a neurologist's exam room, one of the first things your doc will do is shine an ophthalmoscope in your eyes. Peering through each pupil, she'll spy a dome ablaze in sunset hues, four spindly veins branching out from the radiant "sun" that is the start of your optic nerve. This simple examination is one of the quickest ways to check in on your brain, because that dome—your retina—is a part of it, pushed out of your primitive central nervous system in-the-making a mere month into your becoming you.

Our eyes are central and essential to us. At just two and a half centimeters in diameter within our full-grown skulls, they hold nearly 70 percent of all our sensory receptors and helm almost half of our cerebral cortex.

And the retina is where the story starts.

It's the film in the camera. The place that first catches light along its spectacular conversion: from our encounters with our visual world to the sparks of our understanding. And somehow, in a process that still eludes scientists, the retina performs some local processing of the input it receives, as well, making it both hardware and software.

ILLUSTRATION | MICHELLE LEVEILLE

The nerves in your arms and legs are resilient; injure them and they can rebuild. But damage to the retina and optic nerve is permanent; because like your spine, they are part of your central nervous system. They don't easily lend themselves to transplant, either, unlike the cornea. Thus many diseases of the retina and optic nerve remain untreatable.

Changing that, experts say, will require an all-hands-on-deck approach: developmental biologists, stem cell biologists, physiologists, neuroscientists, mathematicians, engineers, pharmacologists, and surgeons all charging full force—and most importantly, doing it together. They'll need a common physical space, first of all, to get together on common scientific ground, as well as support and encouragement to test new ideas—even the bold, way-out-there ones that are a far cry from what most scientists in the grind of the grant life cycle would call "safe."

And all of this, says the University of Pittsburgh's Jeff Gross, is happening right here.

"We keep feeling like somebody should be saying 'No' at some point," he says. "They're really letting us do this."

By 2022, the whole department, which is now scattered across Biomedical Science Tower 3 and the Eye and Ear Institute, will set up shop along with rehabilitation medicine colleagues in UPMC's planned vision and rehabilitation hospital in Uptown. The nine-story, 410,000 square-foot facility was painstakingly designed to spec with both patients and scientists in mind, "room by room and bench by bench," Gross says.

There will be floors for both basic and clinical research, as well as surgical and medical care for ophthalmology patients. (More on the facility's patient-centered design and unique clinical offerings on page 30.) Spaces for teaching, spaces for incubating start-ups, and spaces for collaboration.

Gross, professor of ophthalmology and the E. Ronald Salvitti Professor in Ophthalmology Research, is scientific matchmaker in chief for a rapidly expanding cadre of Pitt scientists at the vanguard of vision-restoration research. In the past three years, the ophthalmology department has hired 18 new faculty members, with more to come. They're asking fundamental questions: How do photoreceptors within the retina stay alive? How do connections between the optic nerve and brain develop? How does the brain decipher the patterns of light in our sights? How do all of the structures of the eye develop in the first place?

And if and when any of the above fails—then what?

"Can you find ways to stimulate the regeneration?" says Gross. "Or can you supplement or bypass [damaged eye structures] through [electronic prosthetic] devices? Or gene therapy? Can you give [patients] something to repair dying photoreceptors? The department is focused on each of these issues—in different but overlapping ways."

The aggressive recruitment effort and bold new facility to match are the brain children of José-Alain Sahel, Pitt's chair of the Department of Ophthalmology, who came to Pitt three years ago from Paris.

Sahel speaks often of the tremendous support he's receiving to help him realize his vision. The new tower, which will be located next to UPMC Mercy, is part of UPMC's $2 billion investment in new specialty hospitals in the region. "The effort that UPMC is making in building this fully integrated facility is currently unique in the country," he says. And on the University of Pittsburgh side, Sahel is quick to add, Chancellor Patrick Gallagher has backed the ophthalmology department's expansion wholeheartedly as an area of strategic importance.

In 2008, Sahel founded Institut de la Vision in Paris. That colossal venture is in the same vein as what UPMC and Pitt are planning. In its first 10 years, the Paris institute launched several companies and created 1,000 jobs.

Sahel continues to advise his colleagues in Paris and has established a robust collaboration between the institute and its academic partner—the Sorbonne's scientific and medical school known as Université Pierre et Marie Curie—and Pitt/UPMC.

Before Pitt/UPMC even hitched their wagons to Paris, they had particular strengths in corneal biology, infectious disease research, immunology, drug delivery, neuroscience, information technology, engineering, and ocular biomechanics. Pitt is also home to the Louis J. Fox Center for Vision Restoration, perhaps the first multidisciplinary research program dedicated to optic nerve regeneration in the nation, which Gross directs.

In a nascent field known as cortical vision, scientists hope to learn to circumnavigate damaged eyes and optic nerves, placing electronic prostheses in their stead. This will require a deeper understanding of the seeing brain and how it works in tandem with our bodily hardware.

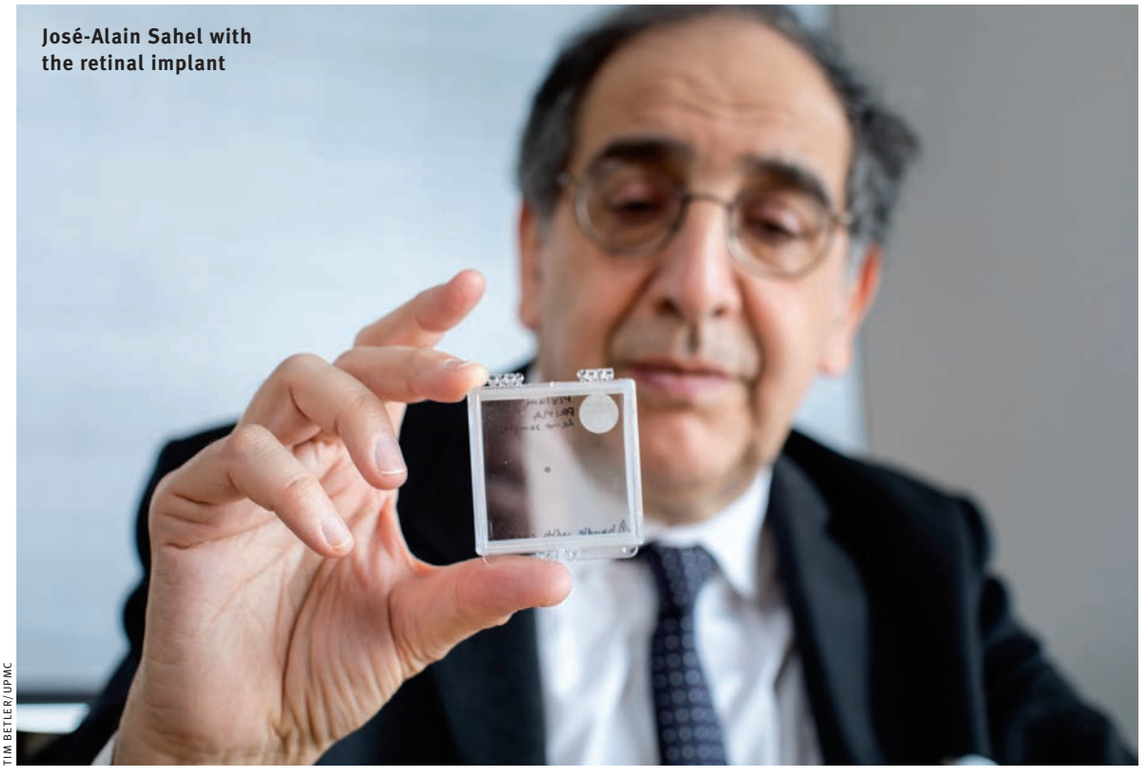
And now, the new intercontinental partnership is likely the largest biomedical research undertaking of ophthalmology in the world.

John Dowling, the Gordon and Llura Gund Research Professor of Neurosciences at Harvard University, mentor to Sahel, and luminary in the field of retinal biology, says this is exactly what he expected, because Sahel "has great taste in science. He knows the people who are likely to be very successful."

With Sahel at the helm, Dowling says, Pitt is on the path to number one in ophthalmology in the country, no question.

"He is a builder."

Gross says Dowling is just one of many advisory board members from around the world who've come to visit the exploding, reenvisioned department and left gushing at its promise, swept up in the feeling that this is the precipice of something huge.



José-Alain Sahel with the retinal implant

TIM BETLER/UPMC

MIND'S EYE

In a worst-case scenario, like a blast from a roadside bomb, the eyes and optic nerves might be destroyed altogether. But remember, the retina is an extension of the brain. Eyes and their wiring exist, essentially, to do our cerebral cortex's bidding.

"The brain," says Jeff Gross, "is what really sees."

In a nascent field known as cortical vision, scientists hope to learn to circumnavigate damaged eyes and optic nerves, placing electronic prostheses in their stead. This will require a deeper understanding of the seeing brain and how it works in tandem with our bodily hardware. "It's a long way off," says Gross. "But the pieces are all there."

In July, Pitt's ophthalmology department was awarded a $6 million grant from the Richard King Mellon Foundation. The massive gift will support Pitt in developing a Cortical Vision Program, through which it can recruit several neuroscientists researching vision and visual computation.

The latter, Gross explains, is the mathematical side of neuroscience—eavesdropping on, and computational modeling of, neurons within the networks. Visual computation demands a variety of approaches. "Some neuroscience, some math, some engineering," he says.

Gross adds that cortical vision will be the ophthalmology department's biggest area of expansion in the next couple of years. The first of these new hires, Patrick Mayo, was recently recruited from Duke University and will join the department in spring 2020.

FIXIN' CHIPS

If your brain is the computer, your retinas are chips. So, before José-Alain Sahel came to Pittsburgh, he and Stanford University's Daniel Palanker collaborated on a potential new therapy that could replace nature's chips with electronic ones. The latest and most promising iteration of that therapy is a retinal prosthetic device known as PRIMA, commercialized by Pixium Vision. Clinical trial organizers are now actively recruiting patients with end-stage atrophic dry age-related macular degeneration (AMD) for a three-year clinical feasibility study here in Pittsburgh. Study volunteers are already participating in France.

The new chip, a surgical implant, is pinhead sized, and, at 30 microns, no thicker than a human hair. The visual information goes from special glasses with a camera to a computer in the patient's pocket, then back to the glasses, where an infrared light beams the signal to the implanted chip. From there, patterns of light are sent to the brain. With training, patients could learn to use the chip to enhance their visual function—that's the hope.

This technology has a 25-year history. Previous attempts, though, either haven't worked or have fallen short of offering any meaningful improvement in vision. But PRIMA is expected to surpass its progenitors: It's the first wireless model. With 378 electrodes, hundreds more than on other chips, it's expected to drastically improve image quality. And it's the first chip to be surgically implanted under the area of macular degeneration, as opposed to on top of the retina or outside of the eye.

Joseph Martel, an assistant professor of ophthalmology at Pitt, is the principal investigator and will perform the delicate implantation procedure. He notes that while none of the study participants, who are legally blind, will suddenly be able to get behind the wheel, the technology has enormous potential to enhance quality of life.

"In these people who can't even see light, even if you can restore their ability to see shadows or a hand right in front of them, that's a very meaningful improvement."

ALGAE WIZ


Martel

Retinitis pigmentosa (RP), a leading cause of blindness worldwide, can result from any one of hundreds of molecular miscalculations. These missteps sabotage the production of a crucial protein, the absence of which robs photoreceptors of their function or causes them to die prematurely.

Experts are testing a wholly new workaround in a five-year safety and dose-escalation trial at three sites: UPMC here in Pittsburgh, Institut de la Vision in Paris, and Moorfields Eye Hospital in London. Using a technology called optogenetics, they'll target specific cells and reprogram them to become factories for a protein borrowed from nature—a light-sensitive substance usually only found in algae.

The reprogrammed cells, then, can detect light at specific wavelengths, which they can "see" using a specially designed set of glasses. The specs are equipped with a built-in camera, as well as a projection system. It's all linked to a pocket-size computer that generates images of the world around the person, in real time. (For more on the camera technology, see the next section.)

The therapy will be delivered via a viral vector, injected into "the jelly part of the eye," says Joseph Martel, the surgeon for the trial. He notes that other therapeutic approaches have been delivered under the retina—which is far trickier, not to mention riskier. The jelly, however, is a piece of cake. No one has to fly to Pittsburgh or Paris to learn the technique. And it takes minutes, not hours.

"These patients that we contact for these trials," Martel adds, "they're quite enthusiastic about participating. It's refreshing and definitely a nice change from previous visits where we were basically telling patients that . . . there's nothing we can do."

A NEW LENS

Consider the sea squirt.

As a little tyke, it's a freely moving being—a wee cyclops with a tail. And then, when it's ready to settle down with itself (it's hermaphroditic) and make some little squirts of its own, it finds a nice rock somewhere to retire, basically, as a sea sponge. In its new life chapter, its first order of business: eat its own eye. Then, in short order, its brain.

These fascinating creatures have an important lesson for us, says Ryad Benosman, professor of ophthalmology at Pitt, as well as an adjunct faculty member in the Robotics Institute of Carnegie Mellon. And that is: Anything that moves, sees. And Benosman, a world authority on computer vision, has come to realize, the thing most worth seeing is: movement.

Benosman, a mathematician by training, has undergone an unlikely metamorphosis of his own. He worked for years in robotics, designing omnidirectional systems. But as his frustrations mounted over the limitations of his prototypes (Exposure! Motion blur! File size! Power!), he grew curious about how this process comes so naturally to us and our kin in nature.

"Suddenly, around 2003, I understood that the problem was that if you want to really understand brains, you have to work with real brains," he says.

So, at his kitchen table, he began a self-guided exploration of the far-off field of physiology, focusing (ahem) on the eye. This organ, he found, has evolved the most across species, with efficiency robotics couldn't hold a candle to.


Benosman

After years of study, it dawned on him that brains simply don't care about what cameras churn through massive amounts of data and power to do, i.e., build hi-res renderings of every single point of light in the sky, blade of grass beneath our feet, and everything in between.

Instead, says Benosman, "You get information only when something happens." The stuff of real substance for the seeing brain is: change.

And if nothing changes, moves, or happens? Then the seeing brain idles. Nothing spent, nothing wasted.

Benosman conceived of a new type of sensor that captures and records only changes within a visual field between time points. He'd entered a discipline known as neuromorphic event-driven computation.

But it was all theoretical, he says, for years. Then José-Alain Sahel invited him to join Institut de la Vision in 2008. By 2015, Benosman had 45 people on his team, churning out implants, chipping away at optogenetic stimulation, building cameras and retinal prostheses (see previous sections for more on these technologies).

When Benosman presents on his work at conferences, there's a video he likes to play: a split screen showing the same drive through a tunnel in Paris, filmed by two different cameras side-by-side. On the left is a conventional camera. Though rendered in full color, it's kind of a mess. Scenes come at it too fast, causing blurry, pixelated blobs. And as the car emerges from the tunnel to the open air, the daylight completely blinds the camera.

On the right, using Benosman's invention, it's entirely different. There's no color—it's more of a flat plane of gray overlaid with what looks a little bit like a pen-and-ink outline of the edges of all that moves past the car. But there's no motion blur from computational catch-up. The important stuff is all there: individual tiles of the tunnel that locate the car in the space, and then, outside, streets and curbs and buildings of the intersection at what a Parisian would recognize as the Gare de Lyon. And there's no white-out of exposure, either. Light, dark, inside, outside, this camera doesn't care.

Benosman's innovation seeded a start-up called PROPHESEE, which produces cameras for driverless cars. The machine-vision technology mimics how our brains see.


da Silva

HATCHING PLANS

Hope and Terzo, the peregrine falcon couple who call the Cathedral of Learning their home, have vision far superior to our own. They can spot their next meal a mile away. And here's another fun fact: In each of their retinas, they have two structures that confer superfine-detailed vision. We humans only have one. For us, that structure is known as the fovea. The fowl equivalent is called the high-acuity area. (Fovea refers to the Latin "pit"; there are no actual pits in bird eyes.)

In the dome of the retina, this high-acuity area is a tiny spot within a little yellowish structure in the center called the macula. For us, the fovea contains about 200,000 cones—photoreceptor cells used during daylight conditions—compared to the whopping 6.4 million cones throughout the rest of the retina. And yet in humans, this tiny structure, which amounts to less than 1 percent of our entire retinal surface, has fully 50 percent of our visual cortex dedicated to processing what it takes in. In fact, losing a significant amount of nonfoveal cones is sometimes not even noticeable. But with foveal cones, it sure is.

For years, the National Eye Institute has supported scientists attempting to grow new retinas, to relieve patients facing macular degeneration, the leading cause of visual impairment and blindness in the developed world.

And it's working . . . almost. These seedlings of tissues, sprouted from stem cells, build layers of photoreceptors, ganglion cells, and interneurons. Unfortunately, however, no fovea-like structures.

But Susana da Silva, assistant professor of ophthalmology who joined Pitt this spring, thinks she knows why.

During her postdoc in the lab of Harvard University's Connie Cepko, da Silva studied retinal development in chickens. Because, as it turns out, uber vision is for the birds, broadly, and not just Hope, Terzo, and their high-flying friends. Chickens also have high-acuity areas like our foveae; but mice, zebra fish, and many other animal models frequently used in scientific studies do not.

By 2017, da Silva had identified the particular ingredients that can make or break chick high-acuity area development: retinoic acid (or rather, a complete absence thereof in a very specific spot) and FGF8. Then, she checked to see if the same was true in humans. And much to her delight, she found that it was.

"To our knowledge," says da Silva, "it's the first ever described molecular signature of the early human fovea."

Here at Pitt, she's setting up her lab, hatching plans, and preparing to follow through on her findings. She'll ask: What is downstream of retinoic acid and FGF8? Can these particular ingredients be tweaked to finally incubate new high-acuity areas in a dish? What signals do cells send to one another to decide on their fates?

"Development is all about the right time and the right place," says da Silva. Genetic manipulation is especially tough in these particularly tight time windows. Also, retinoic acid and FGF8 are all over the place during development, like in nascent limbs. Which is all to say: She has her work cut out for her. But nonetheless, da Silva is thrilled at the prospect of (sorry) pecking away at it.

SEE NEW PEOPLE, HEAR NEW PEOPLE


Gross

Of the many challenges in modern ophthalmology, regenerating the optic nerve is perhaps the most daunting. Pitt is growing a team of recruits with this bold goal in their sights. Among them, notably, is Takaaki Kuwajima, research assistant professor of ophthalmology who won a highly competitive, $125,000 career development award from Research to Prevent Blindness.

At the same time, says Jeff Gross, Pitt's Louis J. Fox Center for Vision Restoration director, no one is under the delusion that any one department or even one institution can go it alone toward a challenge this formidable.

Gross, a self-described cynic, apologizes. "I feel like I drank the Kool-Aid. But it's true. People really want to work together. I think that's the expectation," not just within the department, but the neuroscience community citywide.

Each year, the Fox Center has a conference—a 25-person think tank on optic nerve regeneration that invites experts from around the world. Stars from Institut de la Vision are now in regular attendance.

"We also bring in people who are studying regeneration in other parts of the central nervous system," says Gross. For example, Pitt's Thanos Tzounopoulos, an authority on the auditory nerve who is director of the Pittsburgh Hearing Research Center and Endowed Professor of Otolaryngology. It might sound (ahem) surprising given the specialized nature of these areas, however, says Gross, "Many of the parameters are the same."

There's plenty of cross talk between Pitt and its fellow Pittsburgh higher-ed institutions, as well—something unheard of in other cities. Each quarter, vision scientists from Pitt, Carnegie Mellon University, and Duquesne University get together, a couple of representatives from each institution giving a brief overview of their work.

"It's a bit like science speed-dating," says Marlene Behrmann, professor of psychology at Carnegie Mellon who is also an adjunct professor at Pitt. The scholars share tips, tricks, and technical and analytical approaches. The institutions put their heads together during candidate searches, as well, to fill in gaps.

Behrmann, who studies plasticity in the visual system following surgery for epilepsy, has a strong collaboration with Taylor Abel and Christina Patterson at Pitt and UPMC. She points out that the Pitt-CMU connection is longstanding, citing the Center for the Neural Basis of Cognition and other joint programs. And now, that cooperative relationship between the neighbors is "zoomed in many-fold," she says.

"In my view, a field grows exponentially when you have a critical mass of individuals," Behrmann says, each scholar carving out a particular niche, but with interests so intertwined. She adds that her own work has been enhanced enormously by Pittsburgh's neuroscience community.

"We've reached critical mass." ■

Views of the planned UPMC Vision and Rehabilitation Tower—in the Pittsburgh skyline and (top right) from Boulevard of the Allies.

Architecture renderings by HOK

SNEAK PEEK

At the moment, the UPMC Vision and Rehabilitation Tower is merely a gaping hole in the earth, clattering with construction in the shadow of UPMC Mercy. Come 2022, a nine-story, 410,000-square-foot facility will put Pitt ophthalmology researchers under the same roof with patients in an extraordinary space.

The team at HOK, the architects for the project, has carefully selected lighting, materials, textures, and audio throughout the planned building to help patients with visual impairments in navigating the spaces. For example, Chris Downey, a blind architect at HOK, introduced elements like sound as wayfinding.

Pitt's Department of Physical Medicine and Rehabilitation, chaired by Gwendolyn Sowa, was instrumental in the process, as well, and will have a presence on the fourth floor of the completed facility. Neurorehabilitation services will aid patients with low vision. A space for Pitt's Rehab Neural Engineering Labs will connect those investigators with ophthalmology researchers and clinicians.

The rehabilitation expertise is key; many diseases affecting vision also involve other senses, as well as balance, mobility, and cognition, explains José-Alain Sahel, Pitt's chair of ophthalmology.

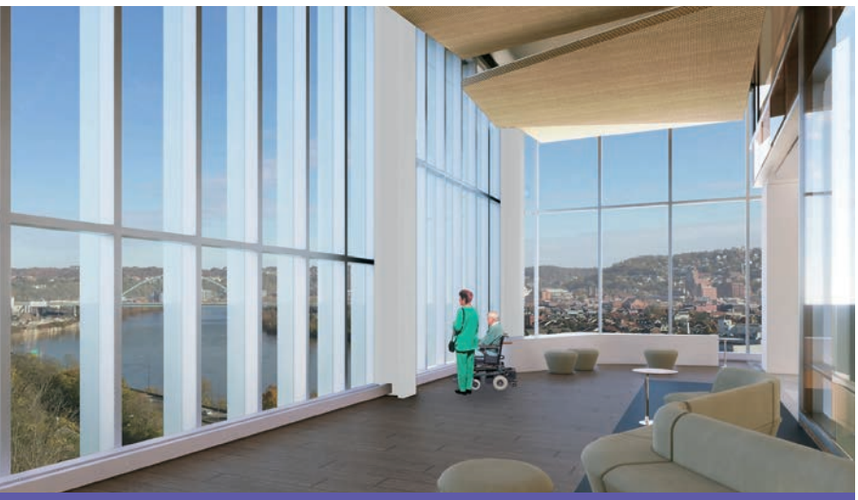
"It's a bold plan," says Sowa. "We believe that no other location in the world has paired vision and rehabilitation together in this way."

Sahel says patients will benefit from new imaging technologies, an area of great interest for his department. When he joined Pitt three years ago, Sahel's very first recruit was Ethan Rossi, a world leader in what's called adaptive optics. (Kunal Dansingani, Syed Mahmood Shah, and Jay Chhablani have also since joined the clinical imaging dream team.) Rossi is developing tools to visualize individual cells within a patient's retina, a capability that would enable Pitt ophthalmologists to quantify how well a given therapy is working. It could also help detect disease much earlier, which could improve outcomes.

Sahel is a firm believer that treatment is a beginning, not an end. Thus, the campus will feature a rooftop garden with test ramps and stairs, as well as an apartment and an indoor street scene, dubbed the street lab. In these spaces, patients will put new therapies and assistive technologies through the paces of everyday life, safely, with the support of the rehabilitation team.

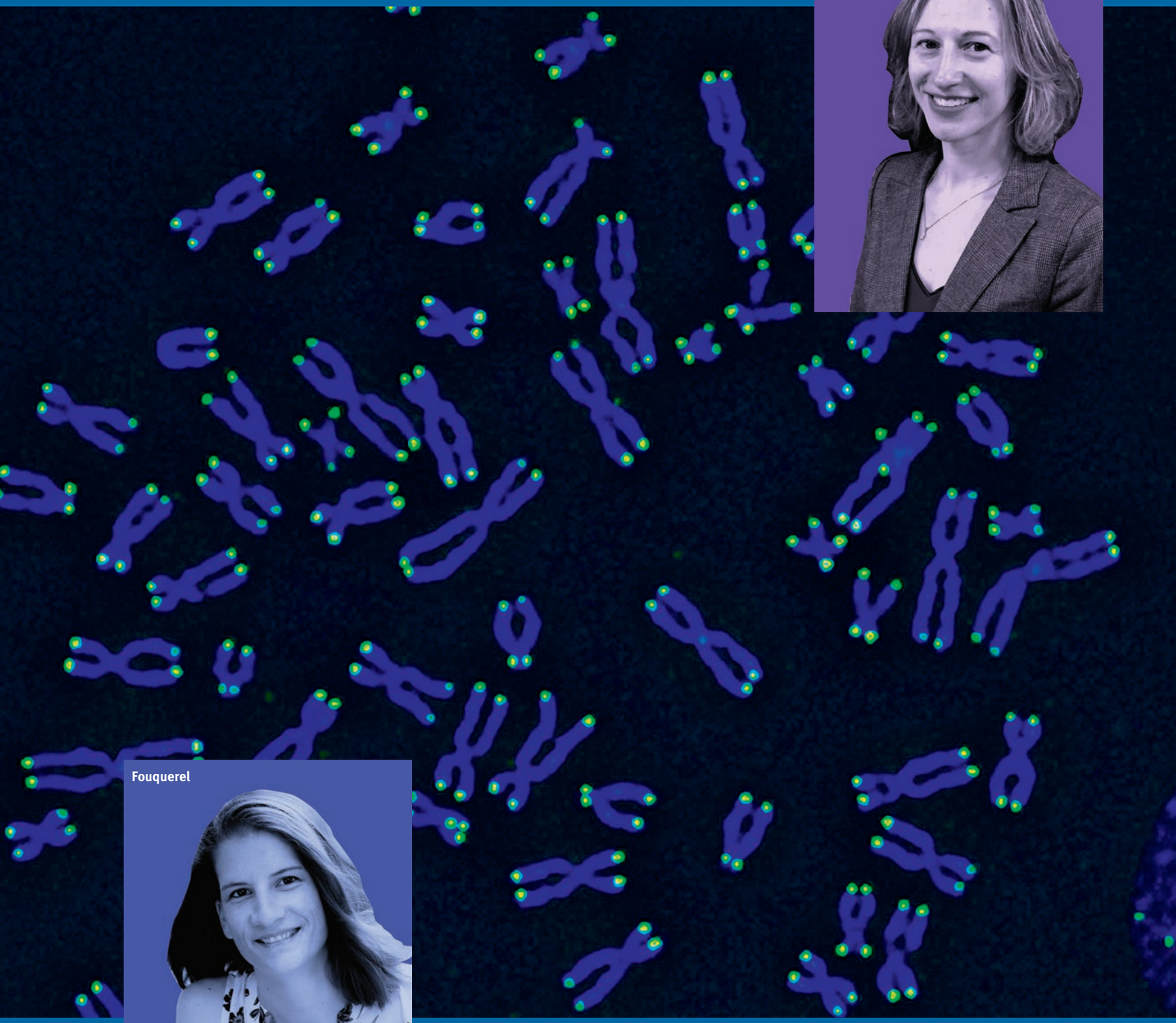
The street lab will feel a bit like a TV set—and in a sense it will be, cameras training on patient volunteers to measure their progress, step by tentative step, on the path toward a better drug or prototype, and a more independent life. —*Elaine Vitone*

UPMC Mercy is gaining the new Uptown facility as part of UPMC's $2 billion investment in new specialty hospitals in the region.



ABOVE: A view from the hospital, expected to open in 2022.

RIGHT: The building is designed to encourage collaboration, from the ground floor to the rooftop garden.



Opresko

Fouquerel

What do those caps on the ends of chromosomes mean for our health and longevity?

END GAME

MAIL-ORDER TELOMERE TESTING IS HERE. BUT WHAT CAN IT TELL YOU ABOUT AGING AND DISEASE RISK?

BY PATRICIA OPRESKO AND ELISE FOUQUEREL

Editor's Note: In our last Tough Questions*, we asked the University of Pittsburgh's Mylynda Massart and Jeremy Berg, What can genetics reports from consumer companies like 23andMe really tell you about your health?*

Some companies now offer tests to measure the tips of chromosomes, called telomeres, so that you learn more about how you're aging. What do these tests really mean? For answers, we tapped into the expertise of two telomere researchers—Pitt's ***Patricia Opresko****, professor of environmental and occupational health in the Graduate School of Public Health, and Thomas Jefferson University's* ***Elise Fouquerel*** *(Fel '18). Fouquerel, now an assistant professor, completed a postdoc in Opresko's lab.*

This article was adapted from The Conversation*, with permission.*

We are molecular biologists studying how chemicals, agents from the environment, and metabolism damage telomeres and affect their lengths and function. We're also interested in how damaged telomeres affect the health of our cells and genome. The idea of offering telomere length as part of a genetic test is intriguing since telomeres protect our genetic material. But equating telomere length with something as complex as aging struck us as tricky and overly simplistic.

We thought it would be helpful to probe: What exactly are telomeres? What are telomere tests? And what are companies claiming they can tell you? What's meant by age based on your birthday versus your "telomere age"?

Telomeres play a big role in keeping our chromosomes and bodies healthy even though they make up only a tiny fraction of our total DNA. The Greek origins of the word telomere describe where to find them. "Telo" means "end" while "mere" means "part." Telomeres cap both ends of all 46 chromosomes in each cell and protect chromosomes from losing genetic material. They are often compared to the plastic tips at the ends of shoelaces that prevent fraying.

What's the link between telomere length and human disease?

Telomeres are important for human health; and despite their protective function, they are not indestructible. Telomeres shorten every time a cell divides and shorten progressively as we age.

When telomeres become too short or lost, the chromosome tips are left unprotected and become sticky. This can cause chromosomes to fuse. To prevent further chromosome shortening and fusions, the cells enter senescence, a state in which they can no longer divide. Although they lose the ability to rejuvenate tissues, senescent cells can still promote inflammation and secrete factors that favor growth of nearby precancerous or cancerous cells.

Unfortunately, our lifestyle can actually accelerate the shortening. Environmental exposures such as sunlight, air pollution, cigarette smoke, and even inflammation or poor diet can damage cell components, including DNA. They do this by generating unstable oxygen molecules, or free radicals. Telomeres are particularly susceptible to damage by free radicals.

In collaboration with chemist Marcel Bruchez, at Carnegie Mellon University, we developed a new tool that damages only the telomeres. Using this tool, we discovered that oxidative damage to telomeres is sufficient to not only accelerate their shortening but also to cause telomere loss.

In previous laboratory experiments, scientists found that eliminating senescent cells from mice led to the delay or prevention of diseases and conditions associated with aging, including heart disease, diabetes, osteoporosis, and lung fibrosis. This work has led to the pursuit of new drugs called senolytics that could eliminate senescent cells in humans.

Is longer better?

Since short telomeres cause cells to senesce, this makes them interesting targets for healthy, disease-free aging. Also, since telomeres shorten

IMAGES: COURTESY OPRESKO LAB. PORTRAITS: COURTESY OPRESKO AND FOUQUEREL. PHOTO ILLUSTRATION: ELENA GIALAMAS CERRI

with age, regardless of exposure to toxins, this led to the notion that telomere length may provide information about a person's "true" biological age.

Commercial tests typically measure telomere lengths or amounts of telomeric DNA in a blood sample. Companies compare your telomeres to telomeres from people of similar age to try to determine the biological age of your blood cells.

However, just as individuals of the same age vary in height and weight, so do telomeres. If a child falls in the 40th percentile for height, this means compared to 100 girls her age, she is taller than 40. Charts similar to growth charts for children have been generated for telomeres.

People with telomere lengths below the first percentile are at risk for developing specific diseases including anemia, immunodeficiency, and pulmonary fibrosis, likely due to a gene mutation that impairs telomere maintenance.

At the other extreme, individuals with gene mutations that lead to very long telomeres, above the 99th percentile, are at greater risk for developing inherited forms of melanoma and brain cancers. Longer telomeres allow a cell to divide more times, and with every division there is a chance that an error during genome duplication produces a mutation that promotes cancer.

In a way, telomeres follow the Goldilocks principle. Too short or too long is not optimal.

Can telomere length predict health outcomes?

But what about telomere lengths in between the extremes? Studies involving hundreds to thousands of participants show general associations of shorter telomeres with increased risk for some diseases of aging, including heart disease, whereas longer telomeres are associated with increased risk for some types of cancers.

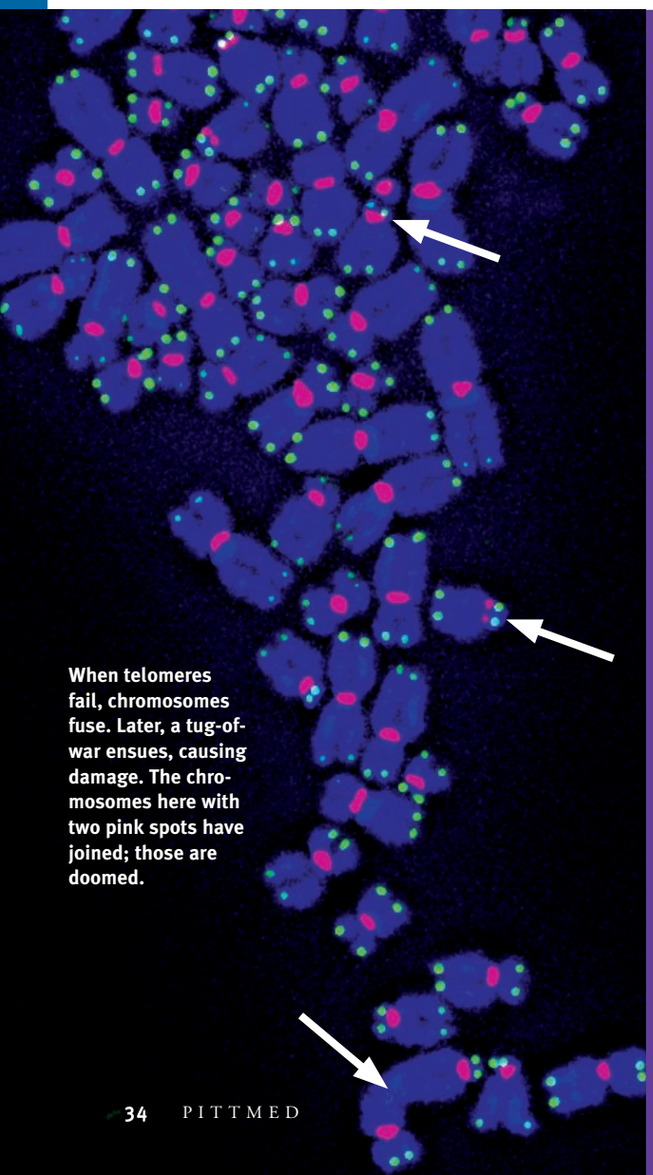
But translating these population studies to predictions about individual life spans and health is difficult. Some people with shorter telomeres do not develop heart disease in these population studies. More studies are needed to fully understand what an individual's telomere length means for that person's health and aging.

Large population studies show a healthy diet is associated with longer telomeres. Yet, claims about specific supplements for telomere health lack scientific backing.

If such a product could extend telomeres, would it be safe? Or would it increase your risk for developing cancer (because of longer telomeres)? Can protecting telomeres or slowing their shortening promote disease-free aging? We do not have the answers to these questions yet.

So, considering the uncertainties, should you have your telomeres measured?

Maybe, if the results would motivate healthy lifestyle changes. For now, a better investment for healthy aging would be to spend the money on exercise programs and nutritious foods instead. ■



When telomeres fail, chromosomes fuse. Later, a tug-of-war ensues, causing damage. The chromosomes here with two pink spots have joined; those are doomed.

THEY BLEW THE CAPS OFF

Scientists have long observed a correlation between telomere damage and cellular aging, but for the first time ever, researchers have demonstrated a cause-and-effect link between the two.

Research—led by Patty Opresko, professor of environmental and occupational health at the Graduate School of Public Health and coleader of the Genome Stability Program at the UPMC Hillman Cancer Center—shows how oxidative stress attacks telomeres, removing the lid on our chromosomes and allowing them to fuse to other, unwilling chromosomes.

"When the cell goes to divide, the chromosomes are now stuck together, so now you have a chromosome being pulled in a tug-of-war between two new daughter cells," says Opresko. "The forces of that tug-of-war cause the chromosome to break."

Scientists already knew that where you find oxidative stress—both smoking and air pollution can lead to this—you also find short telomeres. But according to Bennett Van Houten, the other leader of the Genome Stability Program and a professor of pharmacology and chemical biology, they didn't know precisely what caused telomere shortening. The literature suggests oxidative DNA damage at the telomere, but no one could precisely show cause and effect. One major source of oxidative stress in the cell generally is dysfunctional mitochondria.

The studies were possible thanks to Marcel Bruchez, director of the Molecular Biosensor and Imaging Center at Carnegie Mellon University. Using Bruchez's FAP (short for fluorogen-activating protein) tool, Opresko says they "attached a catcher's mitt," which was specially designed to receive light, to the telomeres. When they fired a laser at the mitt, it created oxygen molecules that harmed the telomeres and no other part of the chromosome.

They recorded this event, live on camera, with the help of Simon Watkins, Distinguished Professor of Cell Biology who directs Pitt Med's Center for Biologic Imaging. A high-definition video shows a laser beam ripping the lid off of the DNA packages and disturbing the cell. Elise Fouquerel, former Opresko postdoc who's now at Thomas Jefferson University, was the first author on a *Molecular Cell* paper describing this.

And when Van Houten's team targeted mitochondria with Bruchez's tool, they found that sick mitochondria caused increased amounts of oxidative stress, which directly caused telomere damage. That work is described in an August *Proceedings of the National Academy of Sciences*.

"Pittsburgh is the city of bridges, and none of this would have been possible without collaboration—the bridges built between these different labs," says Opresko. *—Evan Bowen-Gaddy*

GETTY IMAGES/PUNNARONG

VIGIL

When he tells us he is dying, he does it with blood.
He puts a color on his face that means
he has one foot already out the door,
dangling over nothing.

We gather. In a story someone is telling
he is seventeen. Deep sea fishing. And I see it—
sunburned, sticky with salt. Screaming into the horizon,
shivering at the way the sound hangs and fades
with no echo.

Now the space between each breath stretches, a stillness settles in.
He recedes from his body like the image on an old fashioned television
switched off. Slowly shrinking to black, leaving us staring
at our own reflections.

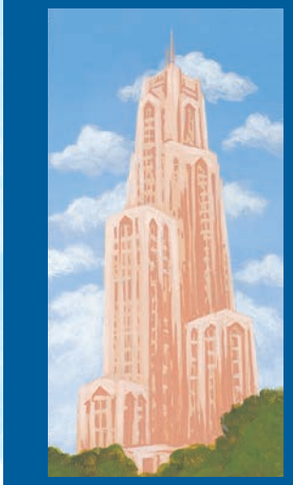
Looking at him, we know that absence can deepen.
A division by zero.

His eyelids, like heavy velvet curtains
drawn against an emptying stage.

—Amelie Meltzer

Pitt Med student Amelie Meltzer's (Class of 2022) "Vigil" was commended in the Hippocrates Prize, 2019 FPM-Hippocrates Health Professional Awards. It's included in the 2019 Hippocrates Prize Anthology*, which came out in May and can be ordered at hippocrates-poetry.org/order-2019-hippocrates.html.*

Reprinted with permission.



CLASS NOTES

'60s

After a rewarding tenure as a kidney transplant surgeon, **Nicholas Feduska** (MD '67) has been pursuing a career in residential real estate. As "the one who takes house calls but doesn't make house calls," Feduska treats his clients "as precisely," he says, "as I used to treat a patient." Feduska's alumni legacy lives on at Falk Library: In 1963, when Falk used to close at 7:30 p.m., Feduska—who "lived" in the library—circulated petitions to extend Falk's hours first to 10 p.m. and later to midnight, where they remain today, five nights a week. Why the change? "So many students were hungry for knowledge," he says.

'80s

Jennifer Campbell (MD '80) serves as councilmember for San Diego's District 2. She's the city's "Doctor on Call to Fix City Hall," shaping codes, laws, and national resolutions on behalf of her constituents. Campbell practiced and taught integrative medicine before joining public office—after "37 years in medicine, I felt this calling," she says. She decided to run in 2018 against an incumbent for her seat; she won with a 16 percent margin. "No physician had ever been on the city council," she says. "I bring a whole new way of looking at things as a differential diagnostician."

Campbell

Ismene Petrakis (MD '87) is a professor of psychiatry at Yale University, where she directs their addiction psychiatry residency; she is also the chief of Mental Health at Veterans Affairs Connecticut Healthcare System. Petrakis's research focuses on the opioid epidemic. As coprincipal investigator on a new VA Cooperative Study, she'll be researching the effectiveness of two formulations of buprenorphine in treating opioid addiction among veterans. The $40 million study—which "plans to recruit 900 subjects over 20 sites," says Petrakis—aims to increase treatment retention and prevent relapse in those struggling to recover from opioid disorder.

According to **Neal Kohatsu** (MD '82), "We need to think of health in the context of both one-on-one care and care of populations." He's a consultant in population health and preventive medicine and a volunteer clinical faculty member in the University of California, Davis Department of Family and Community Medicine. He recently directed a major smoking-cessation research program for Medi-Cal, California's Medicaid program, and helped to implement a quality strategy for the California Department of Health Care Services.

'90s

On July 1, **Aviva Abosch** (Neurobiology PhD '91, MD '93) became the University of Nebraska Medical Center's Nancy A. Keegan and Donald R. Voelte Jr. Chair in Neurosurgery. There have not been many women chairs of American neurosurgery departments. "I was fascinated as an undergrad," says Abosch, "by issues of consciousness—what distinguishes us from other parts of the animal kingdom? What's different about our brains?" Her current research on neuromodulation—a treatment she often uses for patients with epilepsy, movement disorders, and severe obsessive-compulsive disorder—contributes an ever-evolving response to this question.

'00s

Benedict Nwomeh (Pediatric Surgery Fellow '03) is a professor of surgery and pediatrics at Ohio State University (OSU) and vice chair of the pediatric surgery fellowship at Nationwide Children's Hospital. "The most important part of my work is figuring out what illness prevents a child from achieving their full potential and using my surgical skills to fix the problem," he says. Nwomeh directs OSU's pediatric surgery fellowship. He also helps train doctors to increase surgical capacity in sub-Saharan Africa: "As a native African," says Nwomeh, "a major passion of mine is giving back to the continent of my birth."

Nwomeh

Michael Gimbel (General Surgery Resident '03) is an assistant professor of plastic surgery at Pitt. His clinical practice focuses on reconstructive surgery, often for post-treatment cancer patients, "reconstructing many of the otherwise devastating defects that result from cancer removal," he says. This July, he transitioned his practice solely to UPMC Magee-Womens Hospital, where he serves as chief of plastic surgery and educates medical trainees.

"I find teaching surgery to be hard, much harder than surgery itself," says Gimbel. "But it is extremely gratifying." He was recognized with the Plastic Surgery Teacher of the Year Award in 2013.

'10s

Mari Mori (Biomedical Informatics MS '12) is an assistant professor of pediatrics at Ohio State University and a clinical and biochemical geneticist at Nationwide Children's Hospital—roles begun this year that mark "a big change in my career," she says. The MD treats both adults and children for inborn errors of metabolism, a grouping of rare genetic disorders in which a patient cannot convert food into energy. For her ongoing research on Pompe disease, the Pfizer/AGCM Foundation awarded Mori its Clinical Genetics Combined Residency for Translational Genomic Scholars Fellowship Award in 2015.

In July, **Jocelyn Fitzgerald** (MD '13) begins her final year of fellowship in urogynecology at Georgetown University in Washington, D.C. "I feel so strongly," she says, "about the ever-changing nature of women's bodies, and understanding their health care journey throughout the life span." The Physician Scientist Training Program alumna is also committed to outreach, serving as a member of the social media committees for the American Urogynecologic Society, *Female Pelvic Medicine and Reconstructive Surgery*, and the Society of Gynecologic Surgeons. Last year, she also traveled to Rwanda to treat women suffering from obstetric fistulas and to train local surgeons and physicians on obstetric care and treatment. *—Rachel Mennies*

WE KNEW YOU WHEN

DONALD MERCER

Mercer

Donald Mercer (PhD '68) wasn't expecting a press conference. But when his boss told him to put on his best lab coat, he did so, joining representatives from the University of Pittsburgh School of Medicine and Montefiore Hospital in front of the cameras.

The year was 1975, and the occasion was the announcement of Mercer's breakthrough cardiac research describing a quantitative blood test called CK-MB (cardiac isoenzyme of creatine kinase), which was capable of detecting heart attacks with nearly perfect accuracy.

Mercer's blood test saved patients from unnecessary treatment and eliminated false positives from ailments such as indigestion.

And it all came about because Mercer, then an assistant clinical professor in the Department of Pathology, had lunch with a colleague, chief cardiologist Murray Varat.

"We were talking about the Steelers or something. And the conversation turned to his frustration about these inaccurate tests. I thought if we could do something about these tests, we could not only save the hospital a considerable amount of money, but save many lives by placing the patients in the correct rooms to receive the appropriate treatment," says Mercer.

Nearly 45 years later, Mercer's test remains the benchmark for heart attack tests.

His paper on the test was featured as one of the top 40 of the 20th century in the 2006 volume of *Landmark Papers in Clinical Chemistry*.

After retiring from Pitt Med, Mercer in 1999 returned to his hometown of Wheeling, W. Va., where he was recently inducted into the city's Hall of Fame.

He dates his love of chemistry to working in the lab of a favorite professor at Wheeling Jesuit University, who steered him toward Pitt Med.

"Working in the chemistry lab my junior and senior years helped me focus on a career in chemistry," Mercer says. "I felt maybe I could take my chemistry skills and do something with them.

"And I did." *—Adam Reger*

MAX LEAKE

Second-year medical students learn how to intubate a mannequin "patient" under the guidance of William McIvor (Res '94), WISER's associate director for medical student programs.

OLDER WISER

The Peter M. Winter Institute for Simulation, Education, and Research (WISER) is 25 years old and in its prime. A leading simulation center, WISER has grown from a medical-student training hub into an educational powerhouse for providers at all levels of experience, specialty, and discipline. WISER's resources, says its director, Paul Phrampus (Res '00), "allow people to immerse in whatever they're learning." Students, he notes, "can practice over and over, applying their knowledge in a safe environment" before working with actual patients.

WISER's founding director, anesthesiologist John Schaefer, recognized the need for simulation-based education in 1994 and reached out to Pitt Med's legendary Peter Safar in the hopes of building the center. Their passion—coupled with a generous financial commitment from Peter Winter, chair of Pitt's Department of Anesthesiology at the time and the center's namesake—ultimately made WISER possible. Says Phrampus of Winter's commitment, "He put his neck on the line." *—RM*

PETER F. FERSON

AUG. 30, 1948–JUNE 30, 2019


Ferson

When the news broke that Peter Ferson (MD '73, Res '79) died this June, his former student Marcus Hoffman took to Twitter, calling for fellow alums to share #DrFersonMemories. "Everyone I knew had a Dr. Ferson story," Hoffman says. "He hammered home basics of surgery and operative approaches in a way that became enlightening."

Ferson, a cardiothoracic surgeon, professor emeritus of surgery, and the Charles Gray Watson Professor of Surgical Education, remained at Pitt for his entire career, educating more than four decades' worth of medical students and surgical trainees while primarily treating lung and esophageal cancer patients as a surgeon.

After Hoffman's initial invitation, #DrFersonMemories grew, filling Twitter with anecdotes both humorous and somber—a balance, according to many who contributed, that often characterized Ferson himself. "Things Dr. Ferson taught me:" wrote Temple Ratcliffe (MD '03)—"How to write admit orders. Simultaneous handshake/pulse check. … Most importantly: what loving your patients, learners, & profession looks like."

"[A]ll of us who were heavily influenced by him," says Hoffman, "can essentially hear him in our minds from time to time."

—Rachel Mennies

CHARLES FITZ

MAY 6, 1937—FEB. 22, 2019


Fitz

Charles Fitz, or "Chuck," was a father of pediatric neuroradiology, as well as "a terrific colleague," remembers Geoffrey Kurland, Pitt professor of pediatrics and the medical director for the pediatric lung transplantation program. "He carried a gruff exterior, beneath which beat a gentle heart."

Fitz was a professor of radiology at the University of Pittsburgh, as well as a practicing interventional radiologist and onetime UPMC Children's Hospital of Pittsburgh radiologist-in-chief. His colleagues recall him treating every trainee interaction as a "teachable moment."

Kurland fondly recalls how "[Fitz's] interaction was designed to teach residents to think more about each clinical situation, and to better formulate their questions in the first place," which often meant an easy answer to a student's question wasn't forthcoming. However, notes Kurland, "almost invariably, the resident would personally learn how great a teacher and colleague Chuck was."

Fitz's wife, Anna, also recalls his lifelong commitment to inquiry. "He wouldn't stop working until the day his colleagues would stop asking him questions," she says.

During his first faculty appointment at the Hospital for Sick Children in Toronto in 1976, he coauthored—alongside fellow faculty member Derek Harwood-Nash—the three-volume textbook *Neuroradiology in Infants and Children*. The textbook is one of the first for pediatric neuroradiology. Before his time in Toronto, he served as a physician in the air force.

"Many of us hope to leave behind a legacy: students we taught, papers we wrote, talks we gave, friends we made," says Kurland. "Chuck most certainly did all of that and then some."

—RM

Donations may be made to Children's Hospital of Pittsburgh Foundation, Radiology Research Fund. For information: Rachel McCune, rachel.mccune@chp.edu.

JAMES R. ZUBERBUHLER

AUG. 7, 1929–JUNE 24, 2019


Zuberbuhler

"Dr. Zube," as he was called, brought warmth and irreverent humor to the University of Pittsburgh for more than 40 years. Though he trained as an adult cardiologist, his passion for children drew him to pediatric cardiology "in an era," says his longtime colleague and friend Lee Beerman (MD '74), "when it was not even a specialty in its own right." Zuberbuhler "helped make pediatric cardiology and the care of children and adults with congenital heart disease what it is today," adds Beerman. He notes that Zuberbuhler had "boundless curiosity and passion for delivering the highest quality of care to his patients and families."

The former air force captain served as both a Pitt Med educator and, for nearly 30 years, director of pediatric cardiology at UPMC Children's Hospital of Pittsburgh. He "raised the use of the stethoscope, cardiac physical exam, and bedside approach to an art form," recalls Beerman. He authored more than 100 publications, including the 1981 *Clinical Diagnosis in Pediatric Cardiology*, still used today. When Zuberbuhler retired from his position as chief in 1994, Children's established the annual James R. Zuberbuhler Lecture.

In retirement, he built a collection of 900 photographs of wildflowers indigenous to Western Pennsylvania. For his online gallery, the ever-curious Zuberbuhler posted that he, of course, welcomed "comments and constructive criticism."

—RM

IN MEMORIAM

'50s

WILLIAM J. GARNER
MD '51
JULY 9, 2019

JOHN C. WAIN
MD '52
JULY 31, 2019

JOHN H. MOORE
MD '53
MAY 13, 2019

EUGENE W. DELSERONE
MD '56
JULY 8, 2019

JOHN ROBERT (BOB) DILLE
MD '56
MAY 5, 2019

CHARLES E. KOVAR
MD '56
JULY 22, 2019

'60s

GEORGE F. BUERGER JR.
RES '63, '68
JUNE 16, 2019

WILLIAM C. SCHMIDT
MD '63
SEPT. 6, 2018

JEROLD H. ALTMAN
RES '66
JULY 22, 2019

CHARLES S. STONE
RES '67
JULY 15, 2019

ROBERT KISILEVSKY
PHD '69
JUNE 5, 2019

'70s

TRUMAN E. MAST
RES '74, '76
MAY 17, 2019

NANCY K. ALBERTS
MD '79
MAY 11, 2019

FACULTY

JAMES A. GRAVES
RES '08
MARCH 14, 2019

DEFEAT INFECTION!

ROBERT J. O'CONNELL

BY CARA MASSET

PUWANAI SANGSRI/ARMED FORCES RESEARCH INSTITUTE OF MEDICAL SCIENCES. PHOTO ILLUSTRATION: ELENA GIALAMAS CERRI

Tracking infectious disease up close.

At a research clinic in Thailand, study participants became familiar faces during twice-weekly visits for blood draws. The volunteers had self-identified as being at high-risk for HIV infection, but they hadn't tested positive. During the course of the study, some participants became infected with the virus. The frequent blood tests indicated that they were in the throes of acute HIV infections, yet they otherwise appeared to be in good health. No symptoms to speak of.

The scientists, including Colonel Robert J. O'Connell (MD '97), were surprised. Previously, it was thought that people experiencing an acute HIV infection would present with clear symptoms. The team published its Thai clinic results, as well as results from clinics in East Africa, in the *New England Journal of Medicine* in 2016. "It was the very first time that [we] had the ability to so very carefully characterize what the virus was doing in the very beginning of human infection," O'Connell says of the study.

Inventing an HIV vaccine—and even a cure—was a primary assignment for Colonel O'Connell in his former role as director of the Armed Forces Research Institute of Medical Sciences (AFRIMS). The institute in Bangkok began when American and Thai armies worked together to stop a cholera epidemic in the 1950s. The partnership has grown into finding cures for infectious diseases that are of particular concern to soldiers. "When we do that and are successful, we generate products or knowledge that have broader public health benefits," he says.

As he served in this role, the military and civilian scientists in his circle studied not only HIV, but also malaria, dengue, and other tropical infections. He regularly travelled throughout Asia to oversee research projects in Nepal, Cambodia, and the Philippines and to speak at expert exchanges with military health services in such locations as China, Myanmar, Singapore, and Malaysia.

In July, O'Connell moved on to a new assignment: deputy commander of the parent organization of AFRIMS, the Walter Reed Army Institute of Research in Silver Spring, Md. "We conduct infectious disease and brain health research," he says. His new e-mail signature reflects the broader impact of his work: "Soldier Health. World Health."

O'Connell, born and raised a Minnesotan, earned his Pitt MD with assistance from the military's Health Professions Scholarship Program, then trained in infectious diseases and internal medicine with the U.S. Air Force Medical Corps in Texas. His research career began at Walter Reed. He became chief of the Department of Retrovirology at AFRIMS in 2013.

Today, AFRIMS has a partnership with Pitt, O'Connell notes with pride. The institute is working with John Mellors, who holds Pitt's Chair for Global Elimination of HIV and AIDS, to investigate an immunotherapy treatment for HIV that involves removing a patient's cells, priming them for a fight, and returning them to the patient's body.

When O'Connell reflects on his Pitt days, he says that on a practical level, he is most grateful for the medical training that guided him as a battalion surgeon during a one-year deployment to Iraq beginning in 2009. He's also thankful that he attended a university with legends who continue to inspire his work.

O'Connell remembers listening to talks by Jonas Salk as a visiting lecturer and Bernard Fisher on his first day of med school. "Jonas Salk pursued a product—[the polio vaccine]—that tangibly made an enormous impact on the world," he says. "On the other hand, Bernard Fisher made an enormous difference in the lives of countless women [by conducting clinical trials on breast cancer treatments]. He used evidence-based medicine to change the world."

O'Connell hopes to do both—develop products and gather evidence for the best ways to defeat infection. ■

WHAT'S UP, DOC?

Drop us a line at medmag@pitt.edu and tell us what you've been up to: career advancements, honors you've received, appointments, volunteer work, or publications. And if you have Pitt Med memories to share, we're all ears.

GET THEE TO A PUNNERY!

Twenty years of *Pitt Med* mag-ery. For these many moons, we've offered you our best headlines and other witticisms writ large. Thus, we feel entitled (oh, here we go) to a self-indulgent look back at some of our favorites. We present here a com-pun-dium, arranged by category, for those who can stomach it.

FILM AND TELEVISION

"Blood Brothers" (FALL 2014)

"Found in Translocation" (SPRING 2014)

"The King of Peptides" (FEBRUARY 2005)

"Sleeping's Beauty" (SUMMER 2012)

LITERATURE

"Gins of the Fathers" (FALL 2014)

"Good Night, Manic Mouse" (SPRING 2013)

"Oh, the Places You've Been" (SUMMER 2014)

MUSIC

"Baby Burn" (SPRING 2019)

"Get on Up" (SPRING 2015)

FUN AND GAMES

"Show and Telomeres" (WINTER 2014)

"Beta Up" (FALL 2012)

"Play, Doctor" (SPRING 2017)

IS THAT A TYPO?

"Damming Evidence" (SUMMER 2014)

"Antidote Anecdote" (SUMMER 2017)

"Viscous Cycle" (SPRING 2011)

"Yes we scan! Yes we scan!" (SPRING 2019)

COLLOQUIAL

"An Ounce of Regeneration" (SUMMER 2015)

"Sharpen Your Faculties" (SUMMER 2017)

"Between a Clot and a Hard Place" (SPRING 2018)

"Right Under Our Nodes" (MAY 2006)

"The Family that Assays Together" (FALL 2012)

OH, COME ON

"Chipped Liver" (WINTER 2015)

"Gluteal Morning" (SPRING 2007)

"Skulldiggery" (FALL 2006)

"Gains in Weight Research" (MAY 2006)

"Eye on Glaucoma" (FEBRUARY 2006)

"Ready or Clot" (SPRING 2015)

"HIV's HOV" (FALL 2014)

AND THE WINNER IS . . .

"Monkey Knee, Freddie Fu" (FALL 2007)

In 1991, Freddie Fu, chair of orthopaedic surgery, went to see what was ailing Johnny, a 12-year-old mandrill at the Pittsburgh Zoo who'd been grabbing and poking at his knee.

For links to these knee slappers, visit www.pittmed.health.pitt.edu.

CALENDAR

FOR ALUMNI & FRIENDS

For more information:
Jennifer Gabler at 412-802-8317 or
jag188@pitt.edu

MEDICAL ALUMNI WEEKEND
SEPTEMBER 20–21
Reunion Classes:
1959
1964, 1969
1974, 1979
1984, 1989
1994, 1999
2004, 2009
maa.pitt.edu/reunion

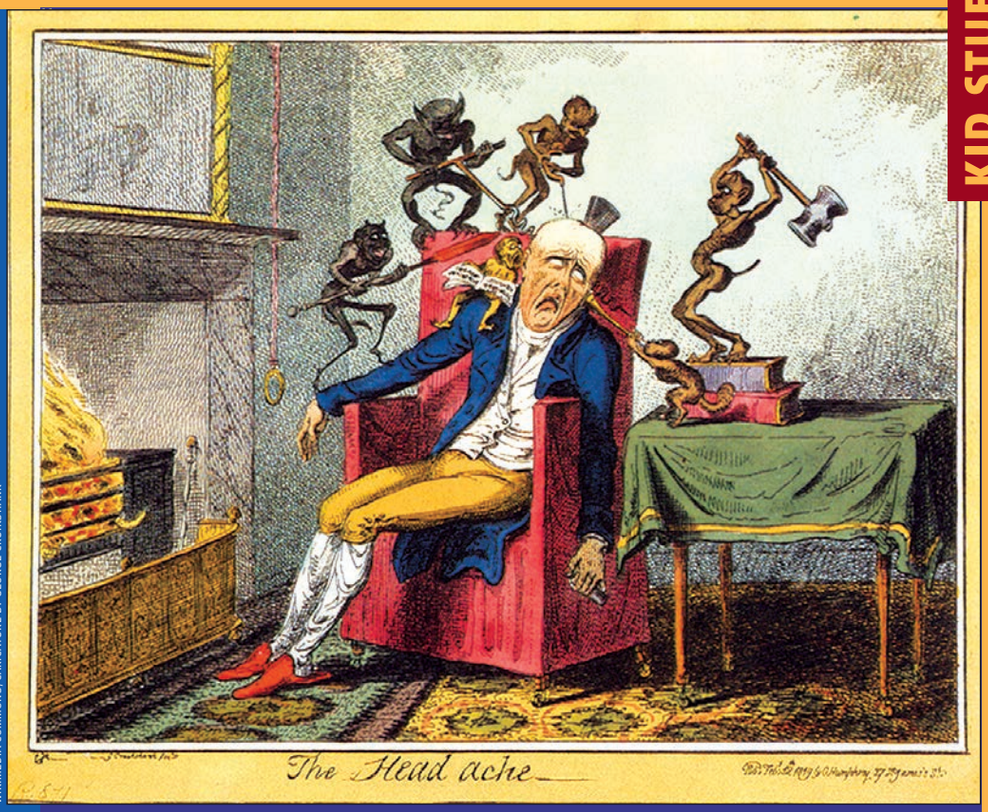
PITT HEALTH ACADEMY—SAN FRANCISCO, CA
SEPTEMBER 26
hsalumni.pitt.edu/event/SanFran2019
For more information:
Sarah McMullen at 412-623-4714
or msarah@pmhsf.org

SCIENCE 2019
OCTOBER 16–18
www.science.pitt.edu

PITT HOMECOMING
OCTOBER 23–27
homecoming.pitt.edu

2020 WINTER ACADEMY
FEBRUARY 14
The Ritz-Carlton, Naples, FL
winteracademy.pitt.edu

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



WIKIMEDIA COMMONS/CARICATURE BY GEORGE CRUIKSHANK

FOR REAL! TWEEN SCIENCE

Not all surgeries require general anesthesia. In fact, surgeons can, and often do, perform brain surgery on patients who are awake. While they cut into the brain, doctors will ask patients questions just to make sure they can move and speak properly. The brain itself has no pain receptors.

Why, then, do people get headaches? Most of us do at some point.

First, some good news: Only about 1 percent of headaches are caused by a serious condition like a brain infection or a blood bubble in a weakened brain artery.

Common headaches are a nuisance but easy to manage. They are often caused by tension and irritated muscles around the skull. The pain shows up in a membrane (the meninges) that lines the skull. Over-the-counter pain medications should do the trick to stop the pain.

When it comes to migraines, an especially distracting and debilitating type of headache, the pain comes from that same membrane, explains Robert Kaniecki, associate professor of neurology at Pitt. Patients travel from as far away as Hawaii to get migraine relief at the UPMC Headache Center, which Kaniecki directs. He knows a thing or two about cranium cargo, and he keeps model brains all over his office to help patients understand what's going on up there.

"The brain is cushioned by fluid and membranes, basically like a little water pillow," Kaniecki says. "The edges of that water pillow are where all those nerve endings and blood vessels are. The nerve endings in the membranes start to release chemicals, and those chemicals are very irritating."

Blood vessels around the membrane then swell and cause the brain to become inflamed. Some people get a heads-up right before a dreaded migraine sets in.

"About 20 to 30 percent will get a warning sign. Sometimes that is a change in vision, where they see lines, lights, or a patch of blurriness. That's called an aura," Kaniecki says.

If you suffer from migraines, Kaniecki suggests building a strict routine of sleep, healthy and timely eating, and exercise.

"Migraine brains don't like change," he says. *—Brian Salvato*

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

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

CHANGE SERVICE REQUESTED

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

LISTEN UP

Looking for something smart to download on your downtime? Check out *Pitt Medcast*, our award-winning audio series exploring matters of life, death, and well-being.

We've got an earful of stories and interviews on fascinating topics, like: autism, maternal mortality, and how useful 23andMe is to your health. And, coming soon, stories of Pittsburgh's "polio pioneers"—the schoolkids from Jonas Salk's clinical trials of the killed-virus polio vaccine. Subscribe today and never miss an episode!

bit.ly/pittmedcast

PITTMEDCAST

- iTunes
- RadioPublic
- SoundCloud
- Stitcher