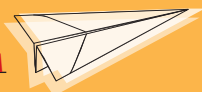


PITTMED



“IT WOULD BE LIKE SOMEBODY WAKING UP ONE DAY
AND BEING ABLE TO FLY.”



HAPPY AUGHTS

Sharon Tregaskis's interesting article on celiac disease ["Broken by Bread," Winter 2017/18 issue] prompted me to write a quick note of thanks for the great job *Pitt Med* editors and writers do on the magazine. Our family was recently affected by celiac, so it was very interesting to learn about Terence Dermody's work.

The article about Tom Smithgall's research was also most interesting ["Nef Busters: A team hunts down latent HIV," by Gavin Jenkins]. Tom was a wonderful mentor of PhD students during the time I helped recruit high-quality PhD candidates to the school, and I am not surprised at all that his superb research program is a wonderful training site, as well.

I have fond memories of helping the magazine staff find basic science faculty stories to write about when I was associate dean of graduate studies in the early 2000s. The magazine provides an important link to my time in the school, and I look forward to reading each new issue.

Keep up the great work.

Stephen Phillips, PhD
Albuquerque, N.M.

Dr. Phillips was associate dean and a faculty member at Pitt Med until 2006.

WHY NOT US?

At last count, @PittMedMag had 1,078 followers on Twitter. Are you one of them? If not, you're missing out on some good conversations. (Just saying—you seem like someone interested in healing and discovery.) Give your thumbs a workout by tapping in @PittMedMag. After that, check out #PittMedMondays on Instagram.

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Photographer **ROBIN JERSTAD** [cover, "Part of the Crowd"] loves "seeing the basics" in photography: "action, interaction, reaction." Jerstad, who was a staff photographer for the *Indianapolis Business Journal* for 22 years before going freelance, says that, sometimes, he learns from the people he photographs. At Morgan's Inspiration Island, the joy of the children was "really humbling," he says. "The way they approach themselves and the world around them, and their determination to go forward" inspired him.

EVAN BOWEN-GADDY ["Voyages Fantastic" and more], graduate of Pitt's Class of 2017, wrote his debut feature story for us this issue. He was drawn to writing about virtual reality because of a lifelong fascination with optics (and, yes, he wears glasses). "Voyages Fantastic" taught him the importance of background research—to ask the right questions during interviews so he could break down the complexities of the technology for readers. A Lower Merion, Pa., native, Bowen-Gaddy double-majored in astronomy and English. Bowen-Gaddy is now an intern at WHYY in Philadelphia. Previously, he interned with PublicSource in Pittsburgh, as well as here at *Pitt Med*.

SAVE THE DATE

MEDICAL ALUMNI WEEKEND
OCTOBER 5-6, 2018

Reunite with your fellow Pitt Med classmates from graduating years ending in 3 and 8.

For info: Ashley Knoch, akk57@pitt.edu, 412-648-9059.
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Water's no problem for the PneuChair. Learn more on pp. 29 and 34. (Photo courtesy HERL)

PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, SPRING 2018
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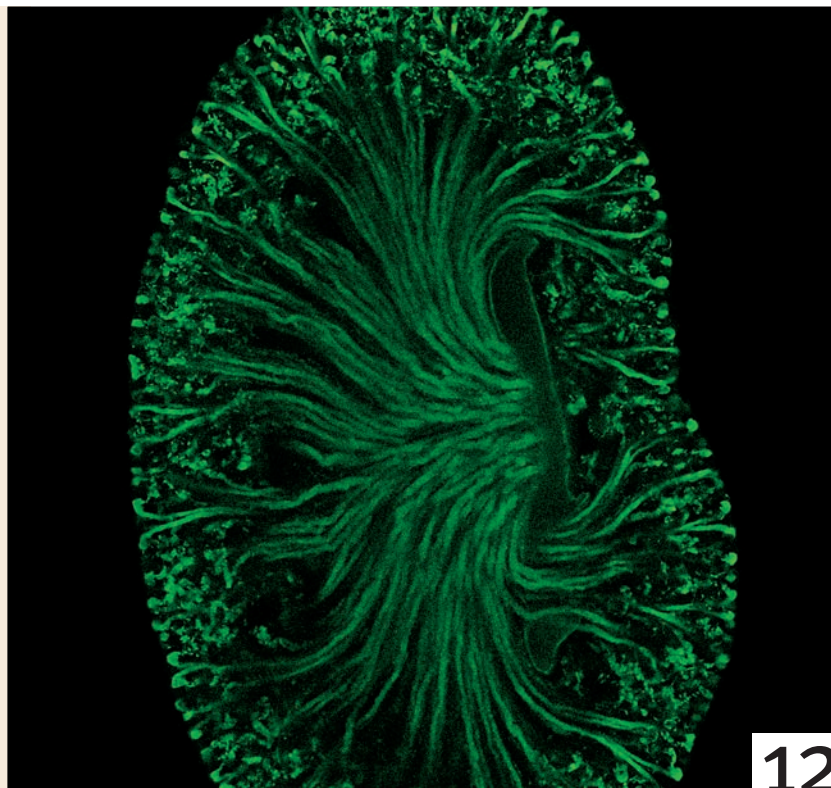
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The PneuChair, designed by Pitt engineers, allows everyone access to water activities.
(Cover: Robin Jerstad, © 2018)



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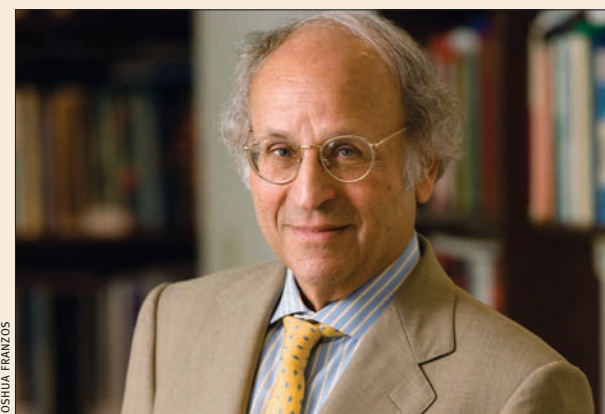
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How can a three-pound mass of jelly that you can hold in your palm imagine angels, contemplate the meaning of infinity, and even question its own place in the cosmos?

—V.S. Ramachandran



JOSHUA FRANZOS

Hovering just above the optic nerve are a pair of tiny structures in the brain, the suprachiasmatic nuclei (SCN). They sense daylight and work with genetic clocks in every cell to govern our circadian rhythms. If one's SCN are damaged, one's body slips its tempo, creating hormonal cacophony. Pitt's Colleen McClung studies how our internal rhythm section performs and its relation to mood disorders and addiction; she's especially interested in the adolescent brain. Her recent observations suggest that lasting neurodevelopmental deficits can result if this system becomes chronically out of sync.

The SCN fit on the head of a pin. It's astonishing to consider the power they have over us. Scores of brain structures are equally critical, but none operates in a vacuum. And neither do the best scientists.

Colleen is in fine company in our Department of Psychiatry. The University of Pittsburgh has been the leading recipient of awards from the National Institute of Mental Health for 19 of the past 20 years. The department's emeritus chair, David Kupfer, used to test the collaborative nature of potential recruits by taking them to dinner to see whether they'd share tastes of their meals. The department's synergy has been critical to Pitt's dominance in the field. Through our Brain Institute, we are building on that spirit, creating a Bell Labs for the mind.

The Institute, led by scientific director and National Academy of Sciences member Peter Strick, thrives from the interplay of Pittsburgh's all-star lineup of 150 neuroscience experts in dozens of departments throughout Pitt and also at Carnegie Mellon University. Neuroscientists and clinicians here partner also with experts in engineering, philosophy, artificial intelligence, data analytics, and imaging.

So many advances in neuroscience originated on our campus. To name just a few, in addition, of course, to the polio vaccine: Pittsburgh Compound B, which allows for early detection of Alzheimer's disease; the world's most advanced brain-computer interface technology that allows a user to control a robotic arm and hand with just thoughts; the first Gamma Knife in the United States for brain surgery; and the discovery that some cases of severe and otherwise unrelenting depression can be alleviated by balancing metabolites.

And now, we finally have powerful tools to explore previously uncharted and enigmatic gray matter. I'm so taken with the possibilities, that in my own lab, which has focused on DNA damage and repair, we are now also beginning to investigate the molecular underpinnings of Alzheimer's disease. Who knows—I may become our 151st neuroscientist!

Furthering my own understanding of this extraordinary organ has not lessened my reverence for it. I like the way Ramachandran, a neuroscientist at UC San Diego, put it:

Especially awe inspiring is the fact that any single brain . . . is made up of atoms that were forged in the hearts of countless, far-flung stars billions of years ago [and] now form a conglomerate . . . that can not only ponder the very stars that gave it birth but can also think about its own ability to think and wonder about its own ability to wonder.

That three-pound mass of jelly must be the greatest wonder of our world.

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*

Cancer Detective

The National Cancer Institute is funding further evaluation for PancreaSeq, a genetic test developed at Pitt and UPMC that employs next-generation sequencing. The technique is highly sensitive in detecting genomic alterations associated with various types of pancreatic cysts and, more importantly, pancreatic cancer.

A team led by Aatur Singhi, MD/PhD member of the Department of Pathology and a surgical pathologist, developed PancreaSeq in 2013 and spent four years testing it on nearly 600 patients. The results were impressive—with high accuracy, PancreaSeq identified mutations that signaled the presence of a common tumor type, as well as cysts that would later become cancerous. Fifteen percent of pancreatic cancer cases originate in cysts, so this test will help surgeons decide whether to remove the growths.

“It detects whether a cyst will ever turn cancerous, which could save money on further screening and reduce patient anxiety,” says Singhi. A second version of PancreaSeq, which will include testing for additional genes, will be released in 2018.

—Liberty Ferda



Elsie and Henry Hillman

FOOTNOTE

How many exclamation points should this thank-you get? In September, the Henry L. Hillman Foundation committed \$30 million over 10 years to the Hillman Fellows for Innovative Cancer Research Program at Pitt and UPMC

Hillman Cancer Center. The gift ensures the fellows will be able to continue to explore potential treatments such as stem cell therapy and immunotherapy. Without the foundation support, says Robert Ferris, who heads the Cancer Center, “this life-changing work would simply not be possible.”

A heart and transplant hospital will be one of three new specialty “digital” hospitals.



NEW HOSPITALS FOR A NEW PITTSBURGH

UPMC Mercy, Presbyterian, and Shadyside hospitals are about to get an upgrade. Last fall, Jeffrey Romoff, UPMC president and CEO, announced plans to collaborate with Microsoft on a \$2 billion project to build a new specialty “digital” hospital on each of these campuses. Mercy’s campus will house a new Vision and Rehabilitation Hospital, Presbyterian’s will add the Heart and Transplant Hospital, and Shadyside’s will include the Hillman Cancer Hospital.

The Microsoft partnership will redesign clinical experiences and advance research, notes Steven Shapiro, Distinguished Professor of Medicine and chief medical and scientific officer of UPMC. For example, it will allow immunologists at the medical school to tap into Microsoft’s “deep AI” expertise.

More information on Microsoft’s involvement will be released later this year, but for now, Romoff says, “We will apply technology in ways that will transform what today is often a disjointed and needlessly complex experience for patients and clinicians.”

The plans are part of UPMC’s continuous investment in health care growth for the region, note UPMC officials. The hospitals should be completed between 2020 and 2022. Romoff compared his goals for UPMC to those of Amazon in the retail world: “Amazon has jumped over the traditional retailing giants. . . . UPMC desires to be the Amazon of health care.” —Evan Bowen-Gaddy

Faculty Snapshots

In October, Mary Phillips was awarded the Colvin Prize for outstanding achievement in mood disorders research by the Brain and Behavior Research Foundation. Phillips, an MD/MD (Cantab), who holds the Pittsburgh Foundation-Emmerling Chair in Psychotic Disorders, uses neuroimaging techniques to measure the structure and function of different brain regions. In a video produced by the Brain and Behavior Research Foundation, Phillips says, "If we can talk about mental illnesses as being brain disorders, that's hugely helpful to many people suffering with the disorders."



Phillips

Donald Yealy (Res '88), chair and professor of emergency medicine who is also a professor of medicine and of clinical and translational science, was elected to the National Academy of Medicine. He is known for his research and national standard-setting efforts in treating sepsis, pneumonia, and respiratory failure. Yealy says the honor gives him access to leaders in medicine, science, and policy. "Pitt has led emergency medicine internationally for decades, and this offers recognition of that, along with future opportunities for more ways to improve the health of those with or at risk for acute illness or injury," Yealy says.



Yealy



Luketich

Pitt cardiothoracic surgeons are among the most highly regarded in the country by their peers. In December, James Luketich, Henry T. Bahnson Professor of Cardiothoracic Surgery and chair of cardiothoracic surgery, received a letter from the Thoracic Surgery Foundation announcing that his team was ranked number one in the "TSF Top 20" report, recognizing the faculties that have received the most TSF funding since 1993. Pitt has been awarded nearly \$1.1 million, surpassing the University of Pennsylvania and University of Washington, in Seattle, which were second and third, respectively.

—Nichole Faina

Overheard Stroke Detector



Several years ago, emergency medical technician **Matt Kesinger** found out that a patient he'd rushed to the hospital had had a stroke, and he hadn't caught it. This is a common scenario because there's been no quick and accurate way of detecting strokes outside of a hospital. Caused by an interruption of blood supply to the brain, stroke is the number one cause of disability in America. Only specialized hospitals have equipment for full diagnosis and treatment, and brain cells die every minute during a stroke; so going to the right hospital is crucial.

Kesinger became determined to do something to address prehospital care. His passion led him to enroll in Pitt Med and, eventually, to the development of AlphaStroke, a mobile screening device that detects stroke on the spot. Last spring, the AlphaStroke project won \$700,000 in the Rice Business Plan Competition; as a result, Kesinger was invited to ring the Nasdaq closing bell.

Why is a stroke-screening device needed in ambulances?

We know the classic signs—slurred speech, one-sided weakness—but only 40 to 50 percent of cases at most present that way. The rest depend on the part of the brain affected. With heart attacks, medics administer an EKG . . . to determine whether a heart attack has happened or is happening. There's nothing like that for stroke. So, many stroke victims go to the wrong hospital. There's an acronym for it, DIDO—door in, door out time: how long it takes to go from the wrong hospital to the right one. The longer it takes, the higher the probability of brain damage.

There are only 12 ambulances in the U.S. equipped with CT scanners—the [standard] technology for diagnosis and treatment for strokes—and each costs over a million dollars and must be operated by a neurologist.

How exactly does AlphaStroke work?

This handheld, portable device is connected to electrodes that measure brain waves. Using EEG and evoked potential, it can identify asymmetry in brain waves with 85 to 95 percent accuracy in less than 3 minutes. We created a scale of 0 to 10: the higher the number the more likely a stroke has happened, and a 10 indicates large vessel occlusion (which is a big stroke).

What was your process for creating AlphaStroke, and what stage is it in now?

I came to Pitt Med and researched the problem with some great emergency medicine faculty. Then in 2014, I got the idea to create the device. I recruited electrical engineer Dan Willis to build it. My mentors at Pitt encouraged me to take a leave of absence to get AlphaStroke into the world and then return to finish my final year before residency. In April 2015, we incorporated and filed a patent, and by August 2015, we had some designs.

In May 2017, we successfully completed a clinical trial with 38 subjects at UPMC and Ruby Memorial Hospital in Morgantown. We are gearing up for a large efficacy trial that will take place at hospitals across the country; we expect FDA clearance in approximately two years.

—Interview by Liberty Ferda

Lots in Life

People who feel lonely and are chronically socially isolated are more likely to suffer from neuroendocrine and cardiovascular problems.

College-educated black women in New York City are five times more likely to suffer severe complications from pregnancy and childbirth than white women who never graduated from high school.

These are just a couple of the ways that wellness is inextricably linked to environment, race, and circumstance.

Collin Schenk (MD '17) recalls that when he was a med student, he and his classmates scrambled to gain the community engagement skills needed to create real change for patients whose health was degraded by their lot in life. "Our aspirations were high, but our impact wasn't." So before they graduated, Schenk, Alyssa Bruehlman (MD '17), and others from the Class of 2017 established the Social Medicine Scholars Program. The program will assist the school in producing leaders who thrive at the intersections of health care, policy, and the social determinants of health.

"I'm quite inspired by these students," says program director Thuy Bui, an MD and associate professor of medicine. "They created ripples, and I'm hoping to keep those ripples going." Bui envisions that, as they graduate, each crop of scholars will hand off their projects-in-progress to new scholars, lending longevity to the efforts. The scholars will benefit from Pitt's new Community Engagement Centers, the first of which is in Homewood; the centers aim to deepen the University's partnerships in neighborhoods throughout Pittsburgh.

Pitt's inaugural Social Medicine Scholars are Lauren Auster, Arthi Narayanan, and Rafa Ifthikhar.

—Kate Benz



Cancer Risk Yardstick

According to a new study, scientists can predict a patient's risk of developing cancer by measuring the length of a telomere, the "cap" at the end of every chromosome. One of the study's principal researchers was Jian-Min Yuan, MD/PhD professor of epidemiology at Pitt Public Health who holds Pitt Med's Arnold Palmer Endowed Chair in Cancer Prevention. The team studied white blood cells from more than 28,000 patients enrolled in the Singapore Chinese Health Study since 1993. Researchers found that patients with longer telomeres had an increased risk of prostate, lung, breast, and colorectal cancers.

Yuan says, in the future, he wants to use this information in a clinical setting. He also plans to study how telomere length changes in patients undergoing chemotherapy. After studying this, "we can predict if people whose telomere length changes more dramatically have a better prognosis, or if the people whose telomeres are more stabilized have a better prognosis," says Yuan.

Yuan says that early screenings of telomere length could help patients take preventive measures: "We want to identify these patients, so they can receive early treatment, before it's too late." —EBG

Changing the Status Quo

In the past 40 years, doctors haven't changed much about the way they treat ovarian cancer. In fact, throughout those decades, "we haven't put a dent in ovarian cancer outcomes," says Ronald Buckanovich, MD/PhD professor of medicine and of obstetrics, gynecology, and reproductive sciences at the University of Pittsburgh. That's why he'll be joining a team of scientists at Magee-Womens Research Institute to form the Comprehensive Ovarian Biology Research Center. The team intends to learn more about ovarian biology and develop better clinical methods.

Buckanovich, who has studied cancer stem cells for two decades, will serve as the director of the Ovarian Cancer Center of Excellence and codirector of the Women's Cancer Research Center. Funding for the research center totals \$6 million, which includes \$3 million from the Eden Hall Foundation and a matching grant from UPMC.

Buckanovich says that, above all, he wants to move the center's research from the lab to the clinic, ending the stagnation in ovarian cancer treatment. Beyond cancer research, the center will also broadly study ovarian development, which could help unlock answers to questions about infertility, premature ovarian aging, and other conditions. "This critical plum-sized thing in the abdomen is incredibly powerful," says Buckanovich. —EBG



PITT VISUAL SERVICES/AIMEE OBIDZINSKI

BRAINY FELLOWS

The Science 2017 festival featured poster sessions from the first generation of Roth Fellows, Pitt Med students who each received \$500 in funding to pursue scholarly projects related to behavioral medicine, psychiatry, or the nervous system. Eight are shown here with Loren Roth, Distinguished Service Professor of Psychiatry, for whom the fellowship was named: (Group shot, back row, left to right) Roth, Justin Arnett, Peter Jones, Cecilia Huang, Brittany Atuahene, Spencer Keil, and Eric Strobl; (front row) Lauren Goldschen and Kimberly Lin. Katherine Kruckenberg is not shown.

Name Dropping



Sabatini

Pitt's 2017 Dickson Prize in Medicine went to **David Sabatini**, an MD/PhD professor of biology at MIT, a member of the Whitehead Institute for Biomedical Research, a Howard Hughes Medical Institute investigator, and a member of the Broad Institute.

During Science 2017, Sabatini spoke of how he came to be interested in rapamycin, an antifungal produced by a bacterium first isolated from Easter Island (though it is actually quite common). Wyeth-Ayerst decided in the '80s

that it would not pursue studies with rapamycin. Meanwhile, Wyeth scientist Suren Sehgal was so passionate about his work that he had saved samples of the molecule in his home freezer. Sehgal sent a sample of the molecule to Sabatini's mentor, neuroscientist Solomon Snyder at Johns Hopkins University. Sabatini later discovered that the compound's cellular target was a pathway he called mTOR (short for "mechanistic target of rapamycin"). For a decade, his lab has been tweaking mTOR to explore questions related to how organisms sense whether they have the nutrients and mass they need to grow.

Sabatini recalled fondly how Thomas Starzl made rapamycin a commonly prescribed immunosuppressive drug. It's now seen as a potential therapeutic for a number of diseases. Notably, it's a promising anticancer agent; it also slows aging in mice. Sabatini knows of scientists who "self-medicate" with rapamycin. There's even a rap song about it, he is pleased to report.

Other heavy hitters also came to Pittsburgh to be part of the science festival:

Lynne Maquat, a PhD, gave the Hofmann Lecture. She is the J. Lowell Orbison Professor of Biochemistry and Biophysics and of Oncology at the University of Rochester Medical Center and director of the Center for RNA Biology, which spans Rochester's medical center and College of Arts, Sciences, and Engineering. She spoke on messenger RNA decay and human disease.

James Allison gave the Mellon Lecture on immune checkpoints and cancer. Allison is a PhD professor and chair of immunology at the University of Texas MD Anderson Cancer Center.

Terrence Sejnowski, a PhD who is the Francis Crick Chair at the Salk Institute for Biological Studies and a Howard Hughes Medical Institute investigator, delivered the Provost Lecture. He spoke about neuroscience in the information age. —Erica Lloyd



LIFE-ALTERING

As Jenny Perez (Class of '21) watched a team of doctors treat her husband, 25-year-old Greg Morgan, for a rare form of cancer, she decided to finally take the MCAT and apply to medical school. For years, med school was just a hope, something she talked about. But seeing the way doctors tailored their treatment for Morgan to align with his specific end-of-life needs motivated her. It also changed her view on patient care; she realized how critical quality of life is for patients.

"I feel like I can give back in that way," says Perez, who is class president. She hopes to become a neurosurgeon:

"When someone needs surgery for a brain tumor, you may not always be able to save their life, but you have the opportunity to make the rest of their life as good as it can be."

The couple lived in Seattle. He was a research assistant at the University of Washington. Perez had just completed her PhD in anatomy and cell biol-

ogy at Wayne State University School of Medicine in Detroit and was working as a senior fellow at the University of Washington School of Medicine.

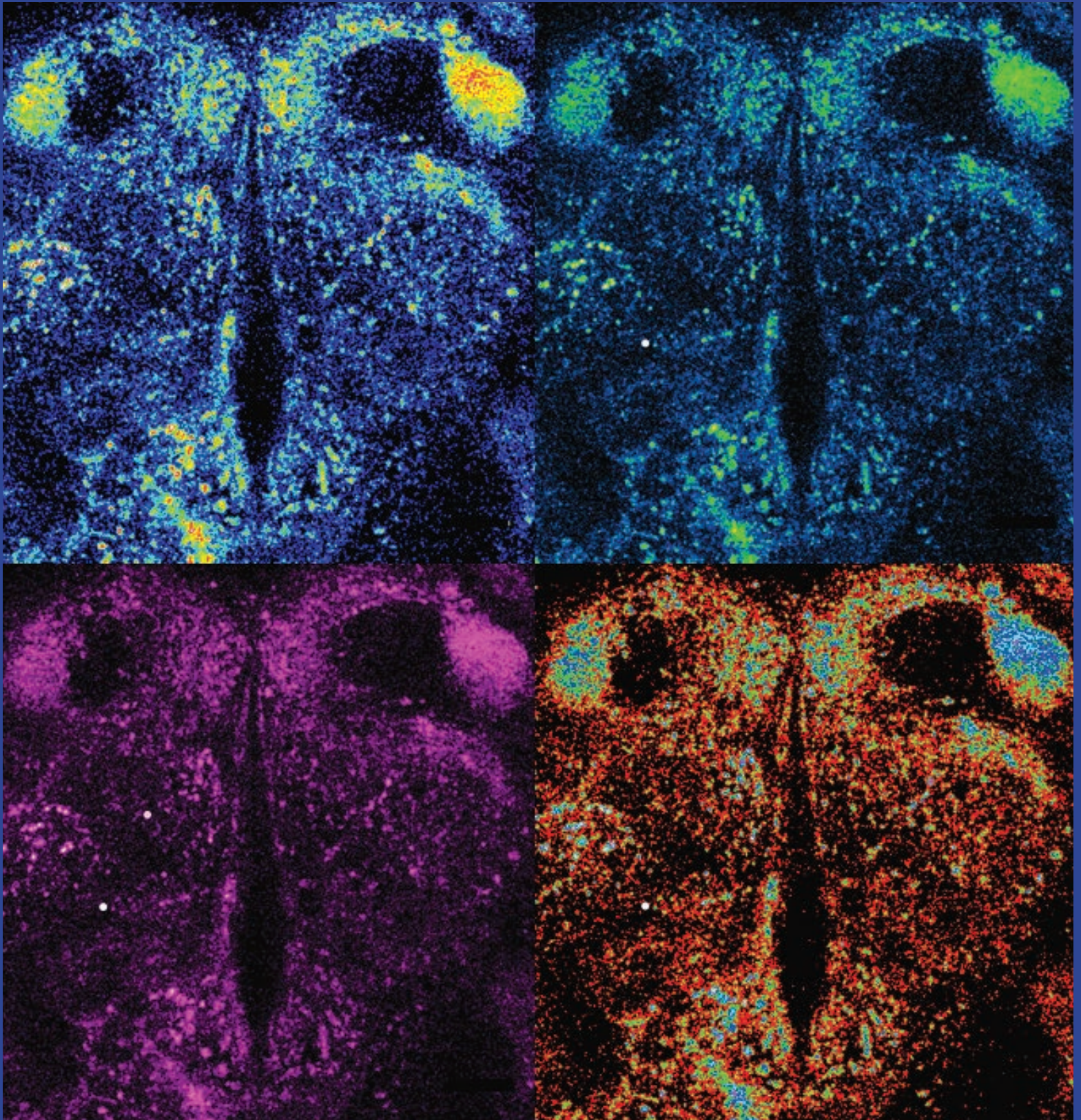
But then Morgan suffered a string of seemingly innocent symptoms—he experienced a swollen neck and headaches and lost his sense of smell. Morgan was diagnosed with sinonasal undifferentiated carcinoma, which accounts for only 3 percent of all head and neck malignancies. An aggressive round of chemotherapy and proton radiation therapy shrunk the original tumors, but the cancer had spread to his brain fluid. Through it all, Morgan's positive attitude never waned.

Perez says watching her husband die was a horrible, traumatic experience—the worst thing that ever happened to her. But, it also made her stronger and more patient.

"People get so worked up about things, and I'm just like, 'It's fine.' I'm able to remain calm so well now." —Kate Benz

INVESTIGATIONS

Explorations and revelations taking place in the medical school



Using fluorescent tools, Freyberg found that pH level may play an important role in how neurons talk to one another. Here, four different color filters illuminate dopamine in the adult fly brain.

DOPAMINE DISPATCHES

HOW NEURONS TALK AMONGST
THEMSELVES | BY WUDAN YAN

As a med student at the Albert Einstein College of Medicine, Zachary Freyberg met a woman with postpartum psychosis. She was catatonic when she arrived at the clinic. But after a few weeks of taking antipsychotics, she came out of her stupor.

In other patients taking similar drugs, Freyberg saw horrible side effects: Some developed diabetes or gained up to 40 pounds within the first month of treatment.

"I desperately wanted to understand the biological mechanisms underlying these diseases and how the medications interacted with them so we can create better treatments," says Freyberg, who's now an MD/PhD assistant professor of psychiatry at the University of Pittsburgh.

Although antipsychotics have been around for decades, no one really knows how they work. The one unifying clue in these processes: dopamine is involved. But precisely how the cells in our nervous system process it—or neurotransmitters in general, for that matter—has eluded scientists.

In August 2017, *Neuron* published a paper from Freyberg's team that may help crack open this mystery.

As an assistant professor at Columbia University in 2012, Freyberg started experimenting to see how neurons talked to one another. Using a new fluorescent tool called FFN206, he was able to visualize how dopamine moved around in the neurons of fruit flies: He watched as little sparks of turquoise

danced, then disappeared, on a screen when he forced neurons to fire—a signal that would unload dopamine.

Pleased to see that the system worked, Freyberg's next step was to figure out how the neuron loaded dopamine in the first place.

To move between neurons, neurotransmitters are packaged into microscopic sacs, or vesicles. Freyberg's collaborator, David Krantz at UCLA, had a few years earlier developed a probe—a pH-sensitive, fluorescent version of a protein called VMAT, which is known to help dopamine enter vesicles. When the vesicle gets acidic, the fluorescent signal dims; as the vesicle becomes more alkaline, the signal brightens. Freyberg knew that vesicles were acidic. He decided to try his hand at this new tool, curious to see what effect, if any, pH change would have on how much dopamine was loaded into the vesicle.

dopamine loading.

"At first, I thought it was a mistake, an artifact of the imaging. But it kept repeating," he says.

Freyberg then reasoned that if the vesicles were becoming more acidic, there must be a negative charge in counterbalance, controlling how dopamine was loaded. And on further study, he found that this was exactly the case. The source of the negative charge, as it turned out, was glutamate.

This seemed counterintuitive, because glutamate is also a neurotransmitter. Previously, researchers thought neurons would release only one neurotransmitter at a time to an adjacent cell. Freyberg's studies suggest that, actually, neurons can multitask and release two neurotransmitters at once. Further, the team found that neurons tailor the amount of neurotransmitter they release based on how

Although antipsychotics have been around for decades, no one really knows how they work.

After installing the pH-sensitive fluorescent VMAT probe into the brains of flies, Freyberg did a series of experiments and found that the mechanism didn't work as he'd expected. During periods of increased activity, the pH probe dimmed and the FFN206 signal rose, suggesting that the vesicles were becoming even more acidic than when they were at rest, which caused more

strong the incoming message is; the harder a neuron fires, the more acidic the vesicles get, which helps more dopamine get in.

Freyberg has validated the fruit-fly findings in mice. In the near term, he's looking to see if the concomitant release of dopamine and glutamate is relevant in neurological diseases. "That's the million dollar question right now," he says. ■

MED ED HEADS

A DAY TO CONNECT THOSE
WHO TEACH | BY ELAINE VITONE

Pitt Med has long had a rep for being the sort of place where scientists crosstalk easily outside of the departmental crowd they might normally roll with. All that confabbing has strengthened scholarship, community, and collaborations in enviable ways, says Dena Hofkosh.

Well, for researchers, that is. For educators, not so much.

“I realized that while there were many interesting and innovative educational programs, [medical educators] didn’t have a way of talking to each other across departments. So educational scholarship wasn’t so easy to see.”

In 2014, when Hofkosh, director of Pitt’s pediatric residency, added associate dean of faculty affairs at the School of Medicine to her title, she set to work creating a way to bring educators together from across the health sciences to showcase successes, share insights, and pool resources. The result: an annual event called Med Ed Day, sponsored by Pitt Med’s Academy of Master Educators, Office of Faculty Affairs, and Office of the Vice Dean, as well as the Office of Academic Career Development, Health Sciences. The Academy of Master Educators is now planning Med Ed Day’s third iteration for September 2018.

Last year’s event drew faculty, staff, stu-

dents, residents, and fellows from across the health sciences. Ohio State University’s Quinn Capers IV gave the keynote address on mitigating unconscious racial bias in the med school admissions process. (One gem of a takeaway: Training the Ohio State admissions team regarding bias didn’t increase the school’s acceptance rate of students from underrepresented groups, but it did increase the rate at which those students enrolled!)

The keynote was followed by a series of TED-style talks full of Pitt Med-ucators’ insights: teaching budding clinicians how to share the decision-making process with their patients; helping surgical residents think on their feet in the O.R.; using group video review of classroom encounters to help faculty members learn from one another; showing trainees how to spot the kinds of cognitive errors that can lead to misdiagnoses; and using students’ own genetic data to teach precision medicine.

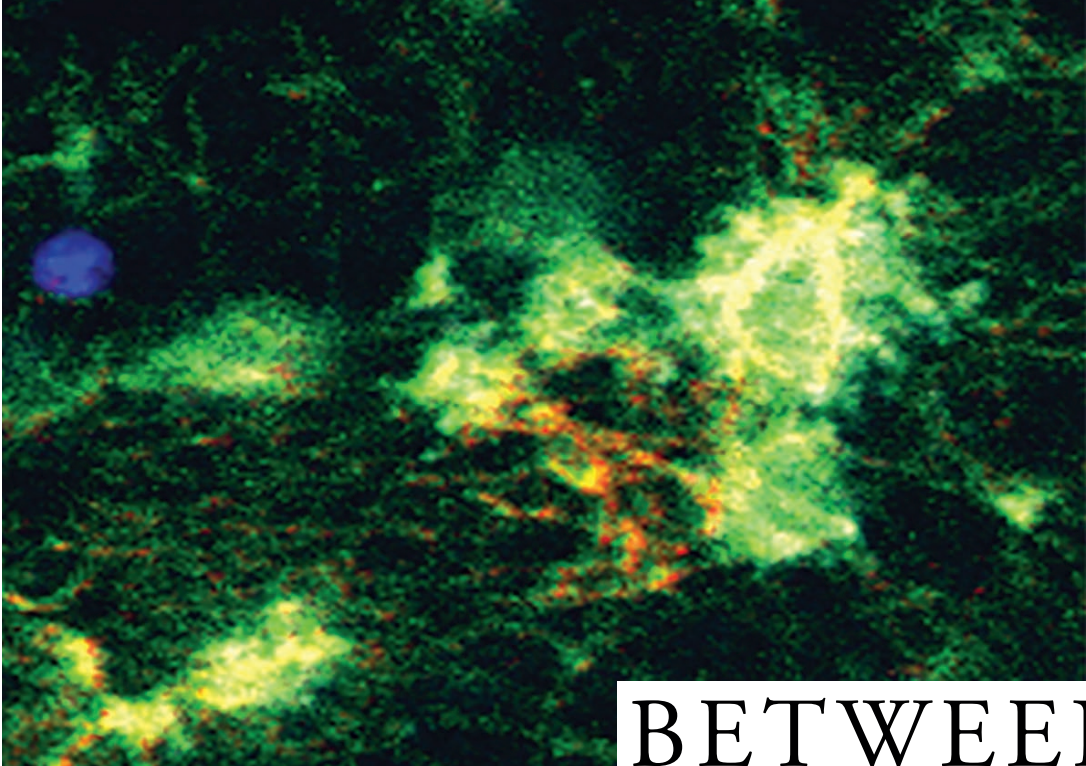
Some presentations described brand new curricular innovations coming down the pike; others were more established educational research findings, with supporting data on a curriculum’s impact on knowledge, skills, and

attitudes. The latter represented an exciting new shift in the field, says Ankur Doshi (MD ’00), associate professor of emergency medicine at Pitt who was on the Med Ed planning committee. Just as good medical practice is rooted in evidence, so is good teaching. “And we’re really moving toward that in medical education,” he says. Historically, grant support for medical education scholarship has been hard to come by—there are no National Institutes of Health grants devoted to it. But an increasing number of teachers are scaring

Just as good medical practice is rooted in evidence, so is good teaching.

up funding in creative ways; that’s a popular topic of discussion for Med Ed goers, he adds.

At the poster session last fall, crammed into the Biomedical Science Tower lobby, various Med Ed scholars networked around topics ranging from interprofessionalism to simulation-based instruction. In the thick of all that elbow-rubbing, a problem emerged, says Hofkosh: They needed a bigger room. ■



Platelets (green) produce an inflammation-boosting molecule called HMGB1 (orange).

WHEN PLATELETS GO BAD
BY ALLA KATSNELSON

BETWEEN A CLOT AND A HARD PLACE

Platelets—the body’s internal Band-Aids—are mighty shape-shifters. These cell fragments, which make up just 1–2 percent of your blood, roam your circulatory system in the form of tiny convex discs. When they sense damage to blood vessels, they home in on the injured site, attach to the vessel walls, and hit the proverbial Superman phone booth, metamorphosing into sticky, tentacled blobs. Through a slew of emitted and received molecular signals, these now-activated platelets entangle themselves with the threads of fibrin protein to stanch blood flow.

Sometimes, though, this crucial system malfunctions. Take trauma, for instance—the leading cause of death for people younger than 45. In about one in four trauma patients, the body’s ability to stop bleeding breaks down. Some 40 percent of trauma patients who die do so by hemorrhaging.

Ironically, those who survive acute injury must contend with an opposing concern: Activated platelets often stay sticky longer than they seemingly should, dramatically raising the risk of blood clots.

“One of the most incredibly frustrating things as a trauma surgeon is to resuscitate someone from the brink of death and get them through that vicious cycle of not being able to stop bleeding, and then have them die three days later from a blood clot,” says Matthew D. Neal (MD ’06, Res ’14, Fel ’15), assistant professor of surgery and critical care medicine

at the University of Pittsburgh.

Neal believes that the swing between these two extremes is caused by injury-induced signaling between platelets and the innate immune system, which regulates inflammation. This fall, his laboratory received a \$1.8 million grant from the National Institute of General Medical Sciences. He was selected for a Maximizing Investigators’ Research Award to elucidate such signaling and to tackle the major clinical problems it causes.

Neal and his colleagues aim to build on findings they reported in the *Journal of Clinical Investigation* in 2015; those showed that activated platelets express a molecule that opens the inflammatory floodgates. In turn, the same molecule keeps platelets in their sticky, activated form.

Researchers have long known that trauma kicks off inflammation, but that study provided some of the clearest evidence that platelets do more than just help stop bleeding.

“I think the involvement of platelets in the overall inflammatory cascade was really very surprising,” Neal says.

Modern trauma care and the evolution of the innate immune system are out of balance. Surgeons today may be able to save us from dire circumstances that evolution didn’t account for (multiple gunshots, car crashes...). But that medical magic is not always perfectly suited to the immune response: platelets can remain excessively activated, Neal explains,

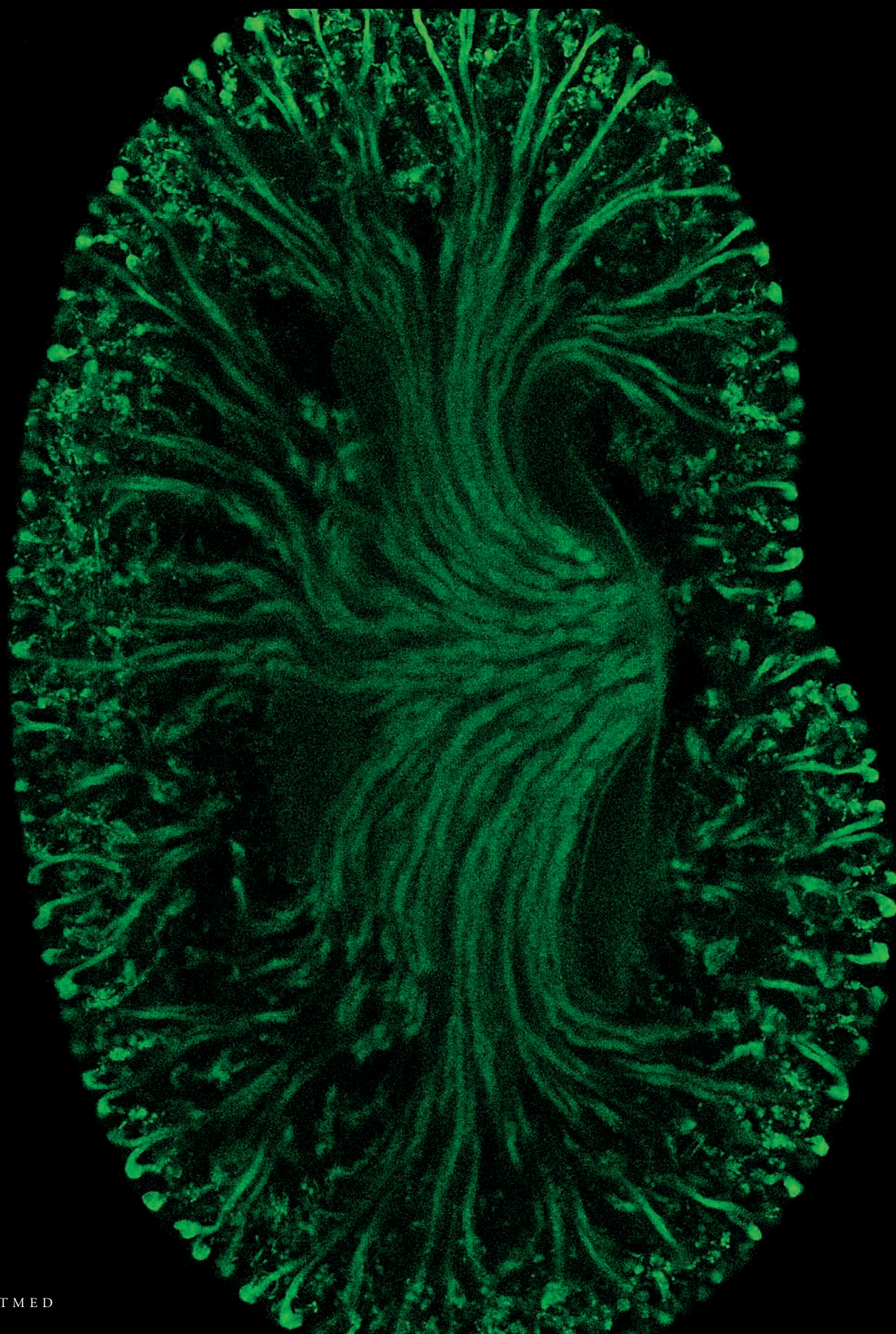
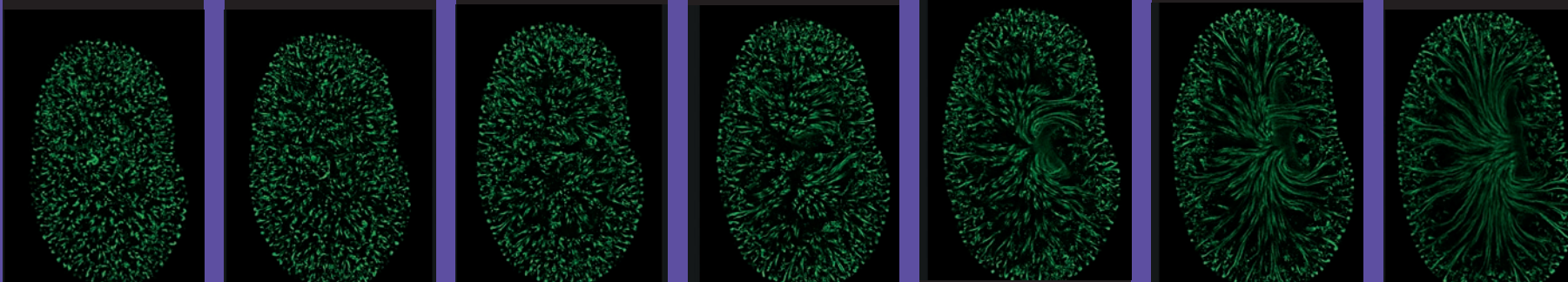
“doing their day job in places where they shouldn’t.”

Neal and his colleagues want to more clearly understand the innate immune signaling pathways that affect platelets and how this signaling causes blood clots to form. In a study forthcoming in *Scientific Reports*, the researchers will show that the interaction between platelets and immune cells called neutrophils revs up these pathways—and, along with them, clot formation.

The team is also studying how platelets change after trauma. They hope to identify characteristics that define the subset of platelets that are clot-forming troublemakers.

Such in-depth knowledge of platelets could yield many medical benefits, Neal says. In October, he received an additional grant from the Department of Defense in collaboration with bioengineer Anirban Sen Gupta at Case Western Reserve University to create synthetic platelets that could be used on the battlefield or in remote settings. The substance they developed appears to limit blood loss in mouse and pig models, according to two recently published studies.

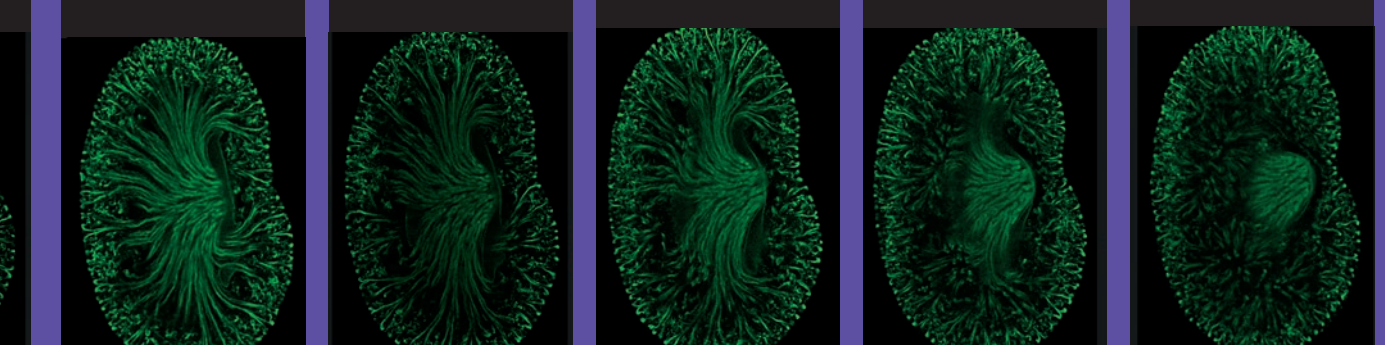
The grant also funds a nanotech project to create a molecular drone that can target activated platelets and deliver a drug that dials back their immune signaling and thus their clotting potential. That way, Neal says, “we can allow the platelet to do its day job, but attenuate the negative consequences.” ■



INTERSTITIAL TRAVELS: Pitt profs are aligning around immersive 3-D imaging technology to bring new understanding to their work.

For instance, Sunder Sims-Lucas and Jacqueline Ho, both assistant professors of pediatrics at Pitt, partnered with the Center for Biologic Imaging to generate these 3-D scans of a mouse kidney. The series shows a one-day-old transgenic kidney at different depths. The green channels highlight the duct system of the kidney, which collects urine from filtering nephrons.

No other university imaging center has the ability to create scans of entire organs revealing the cellular level at such high resolution.



VOYAGES FANTASTIC

20,000 VIEWS OF YOUR KIDNEY | BY EVAN BOWEN-GADDY

On any given day, Alan Watson is likely to be exploring an enclosure, moving through it with care, noting its contours. For a new perspective, he might reach up, pulling his body upward with one arm, then the other, like a rock climber scaling a wall. The spaces he surveys are not caves, nor are they man-made tunnels; they are blood vessels, the lining of an ovary or a lung, the white of an eye. The architecture of life-forms.

When Watson removes his virtual reality goggles, he might feel a little disoriented. But that's a small price to pay for an extraordinary view of an organ. Watson is a research assistant professor of cell biology at the University of Pittsburgh.

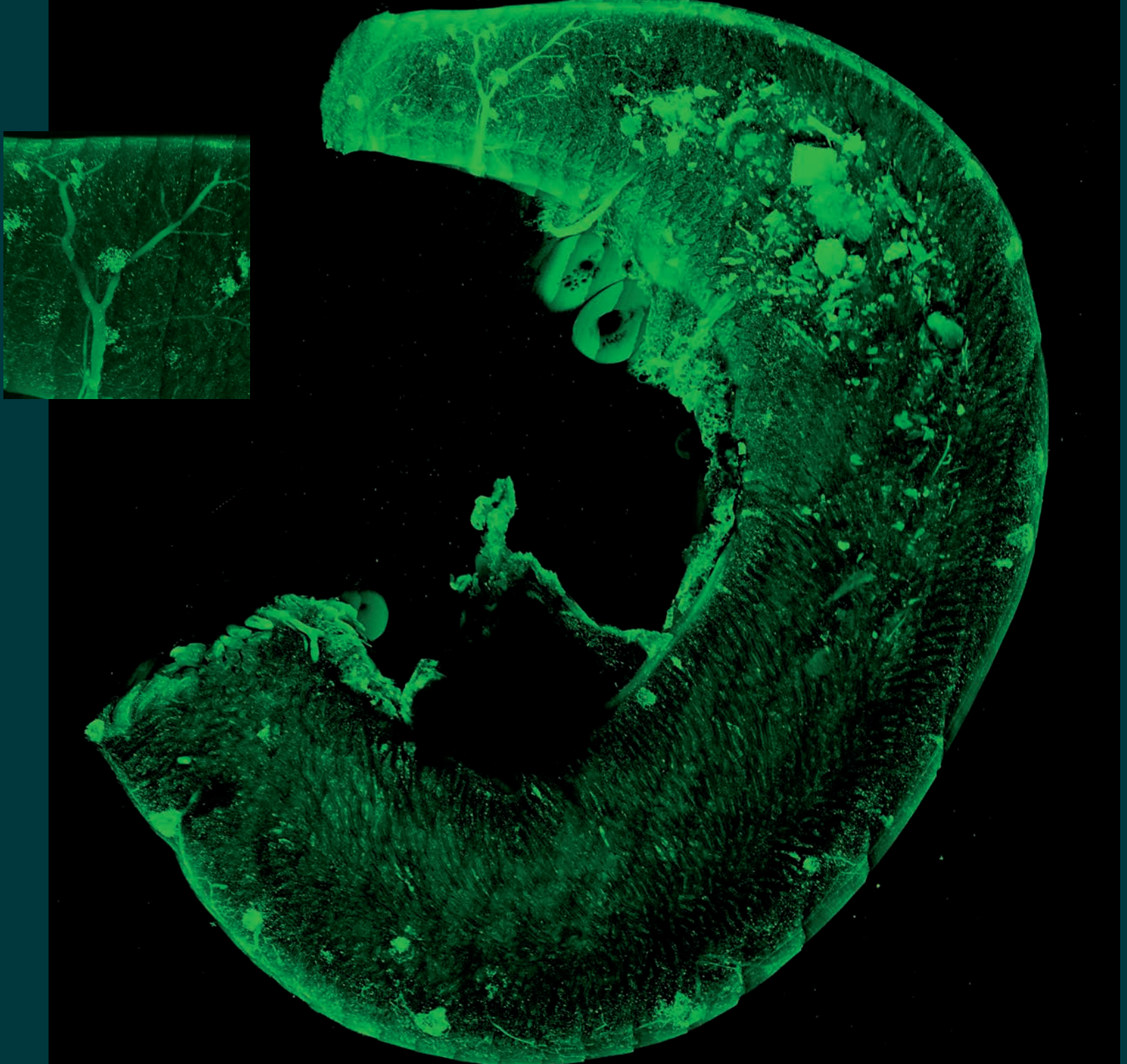
His fantastic voyages take place at Pitt's Center for Biologic Imaging (CBI), which is led by Simon Watkins, Distinguished Professor of Cell Biology.

In 2016, Watson was an immunology postdoc at Pitt's Center for Vaccine Research working with William Klimstra, associate professor of microbiology and molecular genetics and of immunology. They sought out the CBI with the intention of using one of the center's advanced microscopes to try to find a few virally infected cells within a mouse brain. This pursuit, Watson says, had him "staring at black."



Alan Watson demonstrates the VR system at Pitt's Science festival.

IMAGES COURTESY CENTER FOR BIOLOGIC IMAGING AND COLLABORATORS



Simon Watkins saw the trouble the young researcher was having, took the brain, and came back the next day with a high-resolution scan from deep into the brain, revealing hundreds of infected cells.

Watkins showed Watson what he'd used: a prototype of a unique "ribbon" scanner he'd been developing with Caliber ID, a company in Rochester, N.Y. The instrument is called a ribbon scanner because it's able to copy swaths of specimen at once. It'll do 16 scans of 1,000 by 1,000 pixels in a second; so it can put together massive 100,000 by 100,000 pixel swaths as much as 40 times faster "than anything else out there," notes Watson.

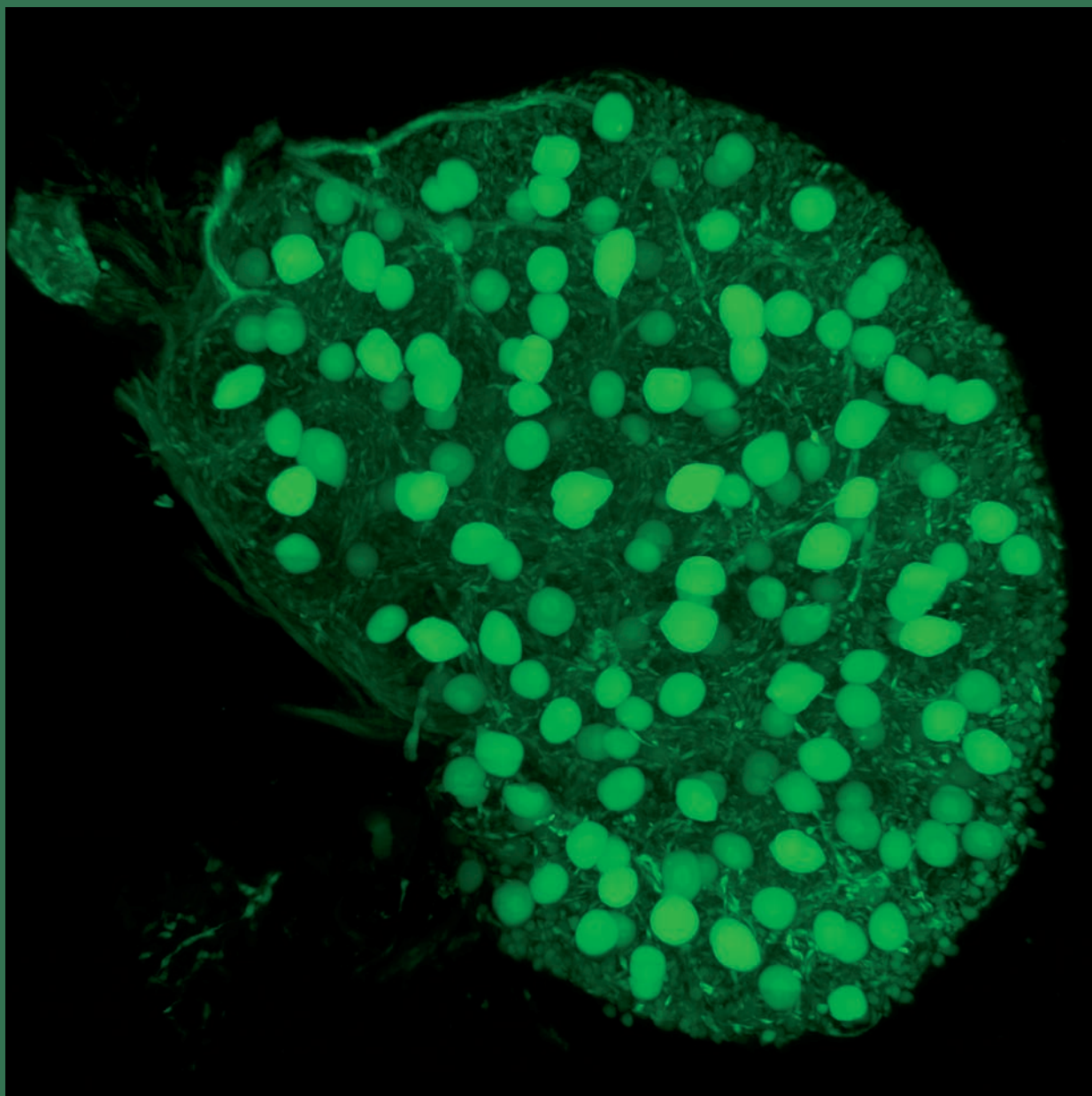
Watson was stunned by what he was able to see; and soon after, he started collaborating with Watkins. Watson is now on the CBI faculty.

The two scientists have since souped up the ribbon scanner. They added a powerhouse lens that Nikon gave Watkins to test. The lens is able to look deep, as well as deliver superb resolution. Usually you give up one capability for the other, says Watson.

"There are only three lenses like this in the world," Watkins says. CBI is the only imaging center with one.

Now the scientists are scanning *entire organs* in 3-D and at the cellular level.

No cellular biologist would try scanning whole organs with an ordinary microscope, says Watkins: "You just couldn't do it." (By "ordinary," Watkins is speaking of the type of high-end biologic research scopes of which Pitt's CBI has several.)



OPPOSITE PAGE: Joel Greenberger, Pitt's Claude Worthington Benedum Professor and chair of radiation oncology, is developing new drugs to counteract radiation from a nuclear disaster. By looking at the entire bowel of a mouse, Greenberger found that after radiation exposure, those circular green portions, called Peyer's patches, saw an influx of neutrophils, a type of immune cell. The neutrophils are the tiny green dots that make up the larger green circles in the image.

Greenberger is a big fan of using 3-D imaging in his studies: "Prior to Simon's techniques, all you had was the ability to sample organs. This also greatly reduces the need to repeat experiments."

THIS PAGE: To make organs transparent for 3-D scanning, Watson optically clears them using a chemical technique he developed. This 3-D scan of a cleared 12-day-old mouse ovary allowed Michael Buckenmeyer, a graduate student from the laboratory of Bryan Brown, assistant professor of bioengineering, to track individual follicles. Brown's lab focuses on regenerative medicine for unmet clinical needs in women's health.

By collaborating with colleagues at another scientific technology firm, Watkins and Watson have married these 3-D images to VR setups. They're making the system available to medical scientists throughout Pitt, who seem to be unanimously astonished by what they're learning from the immersive experiences. The researchers are suddenly able to see things no one else has seen.

In the less than two years that they've been applying the technology, Pitt people have already gained new understanding about vision loss, aneurysms, and other conditions.

Although its new capabilities capture every single pixel in 3-D, the CBI's approach is not about minutia.

"Imagine if you went to a football game, and you saw someone in a red hat," says Watkins. "If you were a bad scientist, you'd say, 'Every human being wears a red hat.' You have to see a thousand red hats to say, 'Well, 10 percent of these people wear red hats.'"

The ability to explore entire organs at a cellular level is unique to Pitt, Watkins believes. And it will be crucial to furthering our understanding of biology: "We need to look at whole systems," he says.

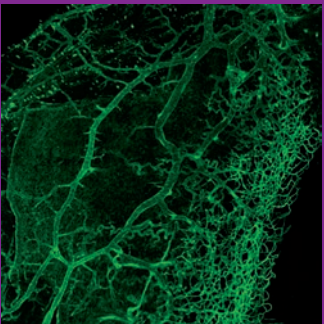
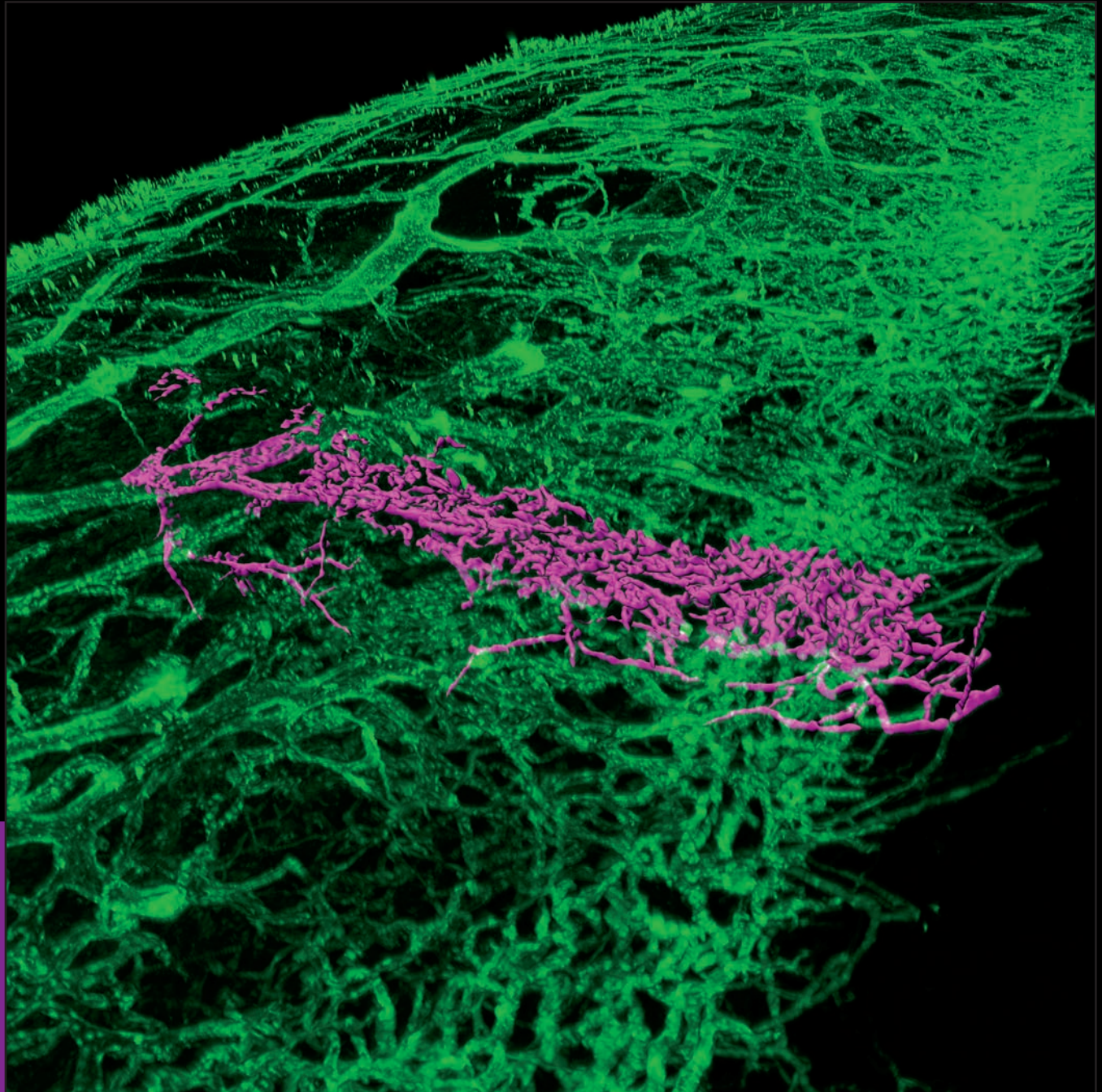
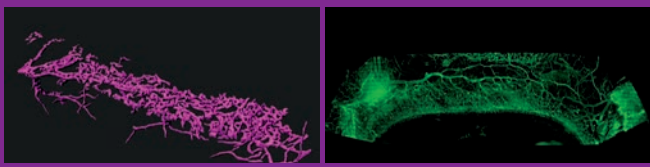
"When people look at subsamples, they miss things. When you see everything, you can make much more sophisticated observations."

It's a December morning at CBI, and George Spirou, codirector of the Rockefeller Neuroscience Institute at West Virginia University, sits with a VR headset, waiting to meet with Pitt researchers. He has a packed schedule ahead of him.

The ability to walk through Watson and Watkins's high-resolution scans comes with the help of syGlass, Spirou's West Virginia-based company that designs VR software to work with high-resolution microscopy. Spirou wants to find out more about how researchers are using the technology, as well as what else might be useful to them.

SyGlass, established in 2013, helps scientists interact with 3-D scans in 3-D, rather than on a typical 2-D monitor. "Why would you want to see a photograph of a room rather than walk into the room?" Spirou asks. "Because as you walk around and look around, you're going to learn a lot more."

He shows off his software. It's like Google Earth, he explains, in that



THIS PAGE: By using VR to explore the white of an eye, Nils Loewen saw outflow tracts that he couldn't before. It turns out that the collapse of these tracts (highlighted in purple) leads to glaucoma.

"you can see the Earth, but then as you zoom in, you load more detail."

Since Watson started using VR, he needs to remind his kids (who like to visit him in the lab) that the headset is not for games. "It's for serious work," he says.

Among the people Spirou will be meeting with today is Nils Loewen, associate professor of ophthalmology at Pitt. Loewen is determined to find solutions for people with glaucoma.

These patients have a plumbing problem, and it's happening somewhere deep in the eye, where even an ophthalmologist can't see.

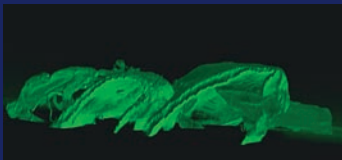
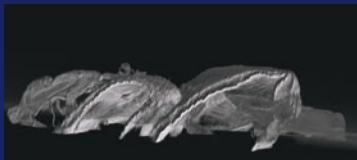
Glaucoma is the poor drainage of fluid through chan-

nels in the sclera, the white of the eye. Pitt's ophthalmology department has a whole host of strong microscopes, yet Loewen says they aren't powerful enough to see "the finer, more intricate parts of the outflow tract."

So Loewen turned to CBI. He now has a 1.2 terabyte scan of a pig eye that Alan Watson created from the ribbon scanner.

When he first saw the scan, Loewen wasn't sure what he was looking at. No one had ever seen outflow tracts in such detail.

By examining the scans with VR, Loewen's team learned that the tracts sometimes collapse. They're like the inflatable tube men you might see in front of gas stations



THIS PAGE: These are human cerebral vessels. Engineer Anne Robertson says she never would have been able to see the artery's fibers in this detail and over such a "vast" area without the CBI's novel techniques.



ROBERTSON LAB

or carpet stores, says Loewen. If there isn't enough pressure, the structures are not able to stay upright.

The utility of immersion has surprised Loewen. He was so taken with the experience, in fact, that he ended up buying a PlayStation and VR set for his home. (He's now a fan of the game *Bound*—"an uncanny amalgamation of modern dance, architecture, and psychoanalysis," he says.)

By the way, if you wanted to put Loewen's 1.2 terabyte scan data on CDs, you'd need 1,800 of them, or maybe a drawer full of thumb drives.

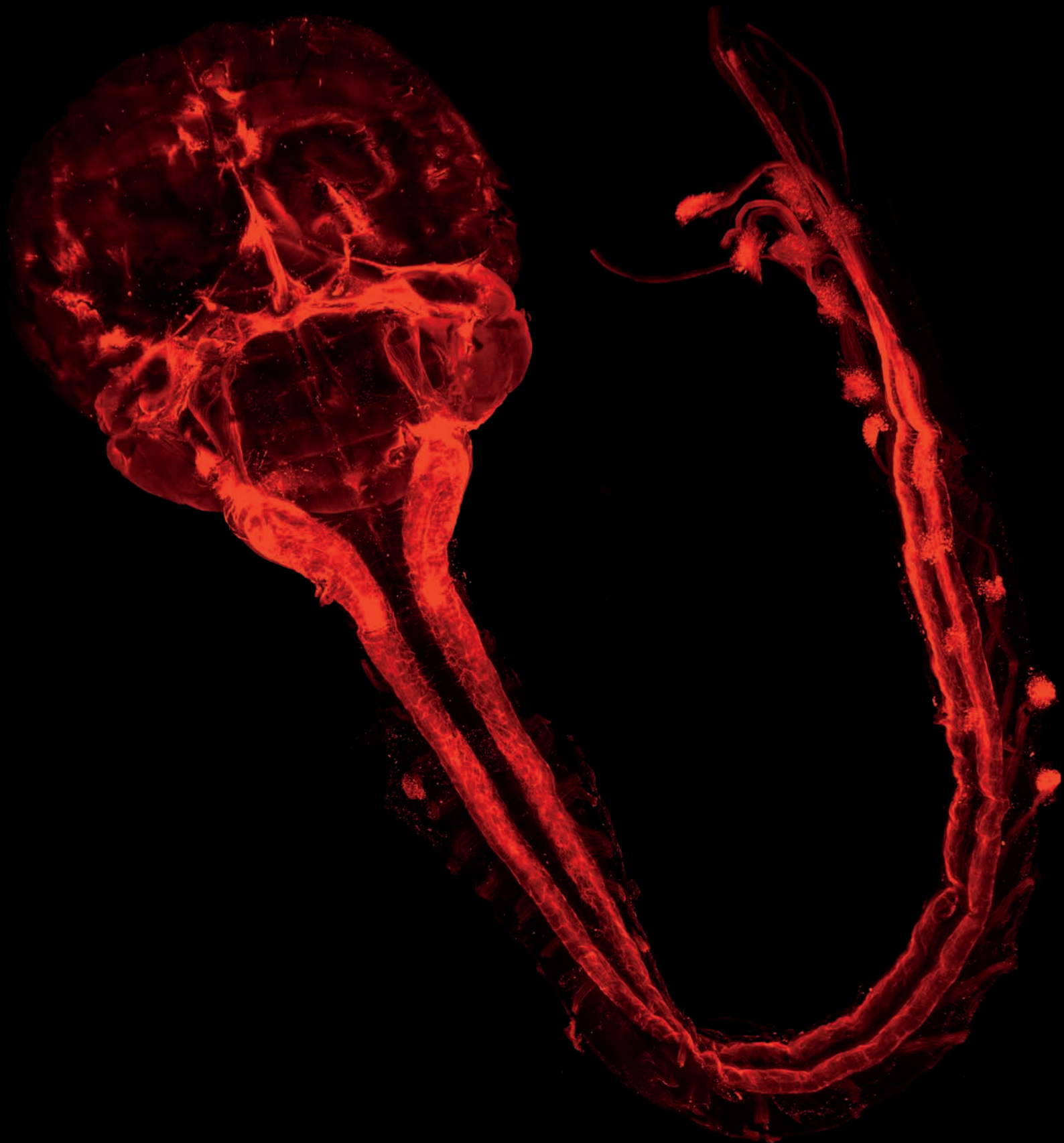
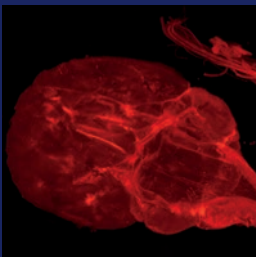
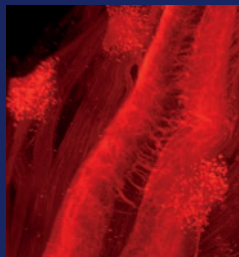
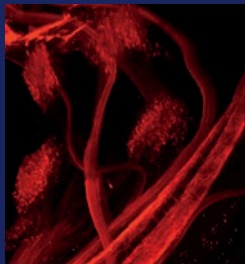
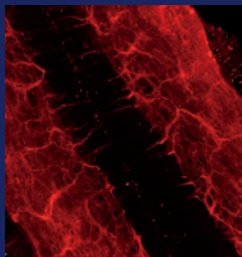
Imagine trying to upload and download terabytes of information on the Cloud as a routine. It's a nonstarter, Watkins will tell you.

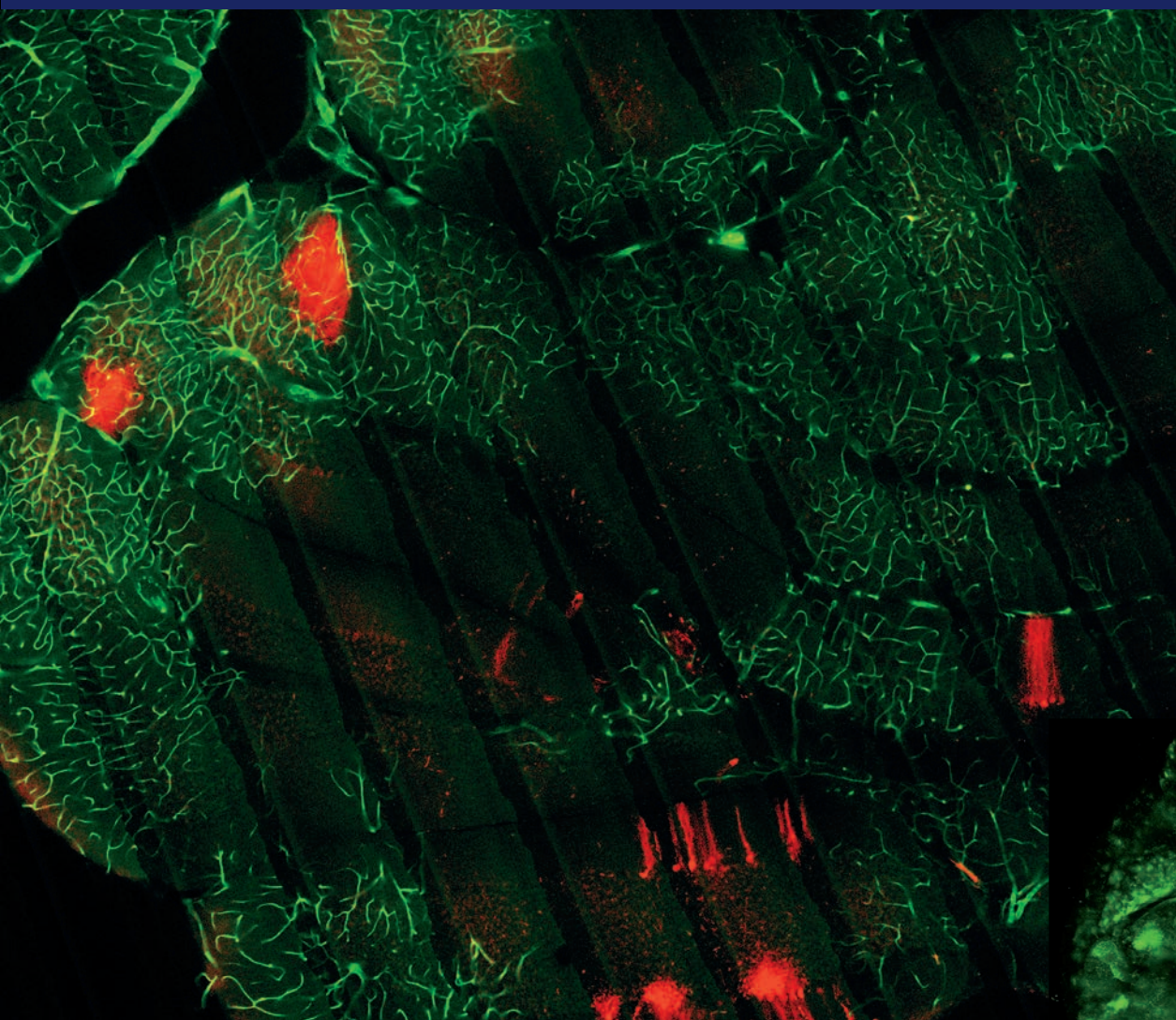
So CBI decided to build its own 3-D file storage system, aided by a supplement from the Defense Threat Reduction Agency awarded to Klimstra and Watkins.

"We call it our hive storage solution," says Watson.

After an expansion funded by the Department of Cell Biology, the hive can now hold a petabyte and a half (that equates to about 2.3 million CDs, or 1.5 quadrillion bytes). It clocks in at 10 gigabits per second.

Alan Watson, who started his career peering at brain





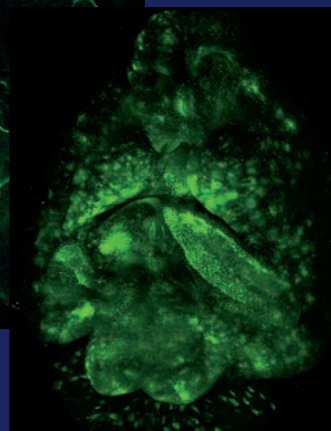
OPPOSITE PAGE: Kathryn Albers, a professor of neurobiology at Pitt, is interested in learning more about how the peripheral nervous system develops in relation to the central nervous system and, ultimately, to the brain. These 3-D scans gave her a view of the systems that she'd never had before.

Using CBI's 3-D technology, Albers's team plans to investigate how certain biomolecules (neurotrophic growth factors) expressed in peripheral tissues influence the development and growth of nerves.

The approach should let her explore how the entire nervous system is affected by these factors. "Connecting the periphery to the brain," says Albers, "has always been a very difficult thing to do because of the complexity and size" of the nervous system. "This is a technology that lets us put it all together."

THIS PAGE: Before Watson joined the CBI, he was a postdoc in William Klimstra's lab studying viral infection. This series shows a mouse brain infected with Venezuelan equine encephalitis virus

(red). When Watson first came to the CBI, he says he was "pecking and pecking here and there" to find a few infected cells. By scanning entire organs, Klimstra's team was able to identify infected regions throughout the brain. The investigators learned that collapsed microvasculature may contribute to the severity of the disease.



tissue, muses on what would be required to collect and scan data on an entire human brain at the cellular level.

Such an effort would probably take a year using the ribbon scanner (or a dozen with a more conventional scope); it would yield thousands of petabytes of information. That project is out of reach for the moment.

"We will do it eventually," Watson says. "Just not tomorrow." Until then, there is plenty to learn.

Anne Robertson is an engineer. She's interested in how blood vessels change after cerebral aneurysms strike.

Before she started working with Watson and Watkins, she'd section arteries to image them. That left her with a bunch of tiny donut-shaped samples that gave her hints about how structure relates to function but didn't tell her much about how fibers within the artery fit together.

The Pitt professor of mechanical engineering and materials science

and of bioengineering wondered, *How do you know whether one slice is representative?*

After she learned about the CBI's immersive techniques, she said to herself, *We can ask completely different questions!*

Looking specifically at the fibers of a longer section of artery (shown on p. 17) helped Robertson see how the fibers are intertwined, as well as their orientation. Examining calcification in the aneurysm wall revealed that the fibers wend around calcification rather than going through it or ending abruptly at its boundary. By surveying the structure before running computations, her team can develop a more accurate and sophisticated model for the artery.

Robertson was one of Spirou's many appointments that December day. During their meeting, she used the syGlass/CBI VR setup once again; this time she "entered" an aneurysm wall. Her assessment: "phenomenal!"

"When you're in 3-D, you all of a sudden see these things you've been trying to see in your head."



NATURE 2.0

Now with **MORE** Amino Acids!

BY SARAH C. BALDWIN

Think about it: life, in all its infinite and exquisite complexity, for the most part derives from a mere 20 amino acids that, strung together in myriad ways, make the proteins that make us go. Nature's pretty great, right?

For Alex Deiters, who's on the faculty at the University of Pittsburgh, great isn't quite good enough.

Because he's a chemist, he says, he finds "the functionality in those 20 amino acids very limited."

And because he's a chemist, he chooses to make new ones.

ILLUSTRATION | MICHELLE LEVEILLE

To understand Deiters's motivations, it's important to appreciate why anyone studies biological pathways and processes, from cell signaling to gene expression, in the first place: knowing at the molecular level how these processes work—and why they sometimes get tripped up—is essential to improving human health and understanding fundamental questions about life. (Like, *Why did we all end up with 20 amino acids anyway?*) One way to study these processes and the proteins involved is by manipulating them, then seeing what happens.

And scientists are getting pretty good at this. No doubt you've heard about that oddly named gene-editing technology, CRISPR-Cas9. The technology has been rocking the biomedical world for a few years—and it's likely to rock our worlds, as well, before long.

If your genome is your body's instruction manual and your DNA is the language it's written in, CRISPR-Cas9 makes pretty neat editing software for fixing typos, adding new sentences, and deleting entire paragraphs. By pairing a Cas9 protein with a guide RNA, the system can be used to locate, remove, and replace specific DNA sequences.

You might want to do this with a muta-

WON'T UV MINE?

Although Deiters finds Mother Nature lacking in imagination when it comes to amino acids, he admires her precision over where and when genes and proteins do their stuff. He'd like to offer scientists comparable sway by giving them the ability to place molecules under optical control.

Responsiveness to light is not intrinsic to proteins, so Deiters adds that function. To do this, he re-engineers the machinery of the cell to accept a light-responsive amino acid. This effectively expands the genetic code of a cell to 21 amino acids. The resulting extra and unnatural amino acid is modified with a light-removable chemical group that acts as a cage; the "cage" contains the amino acid so that it cannot perform its biological function. The caged amino acid is introduced to the protein at a selected site—in its catalytic center, say, or the area on the protein's surface where it interfaces with another protein. Once in place, the unnatural amino acid can then be exposed to UV light at a precise point in time. When that happens, the chemical photo-cage falls apart, and *voilà*: like a surprise guest popping out of a cake when the lights come on, the protein becomes active and starts doing what it is

The chemical photo-cage falls apart, and *voilà*: like a surprise guest popping out of a cake when the lights come on, the protein becomes active and starts doing what it is meant to do.

tion that causes Huntington's disease or sickle cell anemia, for example.

Compared to previous gene-editing technologies, CRISPR-Cas9 has been widely and enthusiastically hailed for its accuracy, speed, low cost, and scalability.

That said, the system is not immune to off-target effects.

Deiters, a professor of chemistry, knows just what to add to make CRISPR-Cas9 more precise: light.

meant to do.

Deiters has already used this tool to place numerous biological processes under light-control—he's changed how proteins move around (translocate), influenced how cells signal, and coordinated vital molecular assembly lines like nucleic acid polymerization and DNA recombination.

Which brings us back to CRISPR-Cas9. Three years ago, Deiters brought optical control to bear on the system, inserting a photo-

caged amino acid, thus effectively stopping Cas9 from snipping the targeted sequence.

And he recently published a paper with Bennett Van Houten, the Richard M. Cyert Professor of Molecular Oncology in the Department of Pharmacology and Chemical Biology, who studies DNA repair. By optically controlling a helicase, which unwinds DNA, they hope to provide insight into DNA repair pathways. That work could help answer questions related to cancer and aging.

Deiters considers CRISPR-Cas9 "a nice playground" for his photo-caging technology, but what really gets him excited is deploying his spatiotemporal superpower not in cell cultures, but in a living, breathing vertebrate, the zebra fish.

THINGS GET FISHY

A few years ago, as Pitt was recruiting Deiters from North Carolina State University, he met Michael Tsang, an associate professor of developmental biology who studies cell signaling. Tsang is especially interested in how fibroblast growth factors (FGF) activate the pathways required for an embryo to grow. In humans, abnormal FGF signaling has been associated with cancers and congenital skeletal defects.

To explore this signaling, Tsang looks at zebra fish embryos. Researchers are fond of using the small, horizontally banded swimmers to study development and disease not only because they're easier to house than mice, but also because they share 70 percent of our genes and have many of the same organs as we do. What's more, the fast-growing embryo develops outside of the mother, and it's transparent, providing a built-in window on the fish's development—and on the impact of genetic manipulations.

"Alex always had an interest in bridging biology and chemistry, and I'm always game to try things out," Tsang says, explaining how they came to join forces. The two began collaborating even before Deiters's final arrival at Pitt in 2013.

In the next two years, they published on light-triggered nucleic acid molecules to con-



trol gene splicing and gene expression in zebra fish embryos.

In 2014, they received the Kaufman Foundation Initiative Award for their efforts.

By 2017, Deiters and Tsang had introduced a caged light-responsive unnatural amino acid into a zebra fish enzyme that controls what's known as dorsoventral patterning.

"Dorsoventral patterning is a critical step in setting up the body plan of an embryo," Tsang explains. "It is one of the first phases of development, where the embryo has to decide the front and back of the body." If this patterning goes wrong, you may have, on one side, a central nervous system that's too small and, on the other, a malformed gut.

By exerting optical control over the signaling that regulates this process, Deiters and Tsang

were able to pinpoint the exact time window during which patterning is affected. The duo's proof of concept, Tsang says, can (so to speak) shed more light on "the pathways that are involved in, say, heart development. If we 'flip the switch' [at a given moment], we can see if we can change that development."

A converse approach is to create transgenic zebra fish lines with "mutations that replicate what happens in human disease, like cardiac defects," says Tsang. "The question then becomes, *If we flip the switch now, can we cure the disease?* And, hopefully, that will show us when to activate these pathways [with drugs] to rescue that phenotype in humans."

Introducing the brand-new amino acids into zebra fish has gone "remarkably well," says Deiters. The fish "now have a genetic

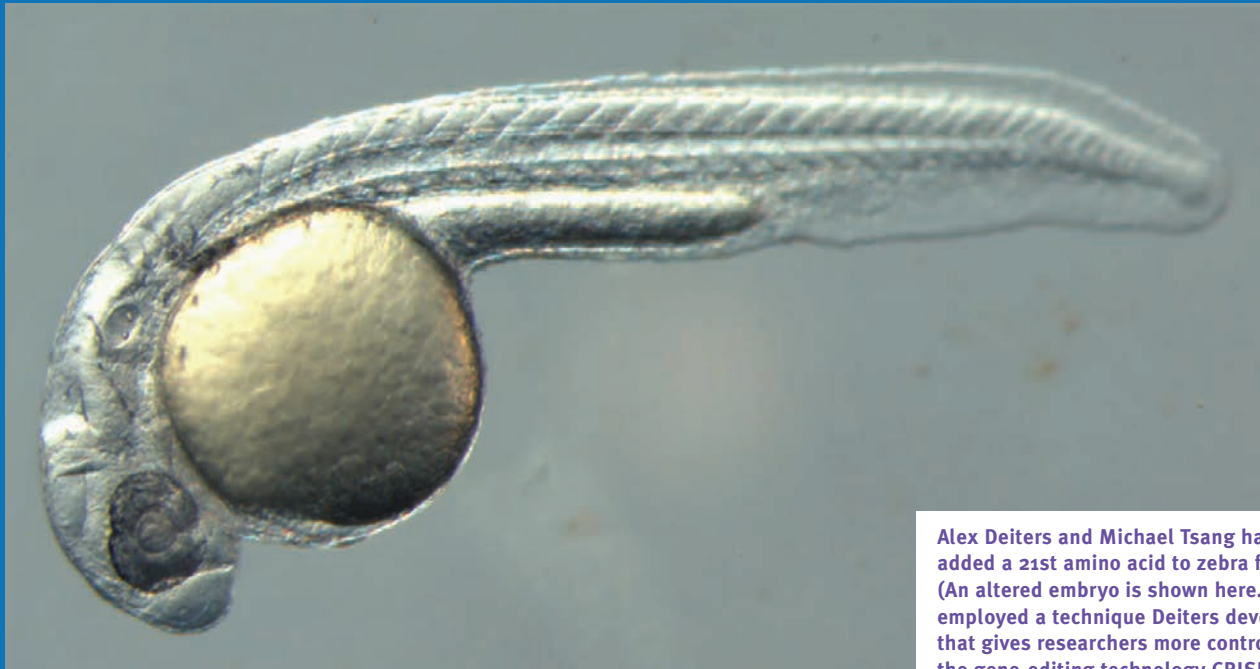
code that is expanded to 21 amino acids, where the 21st amino acid is synthesized by chemists and thus can be designed to have virtually any desired function—light activation being only one of them."

Deiters says, "We're improving the technology, making it more user friendly so others in the zebra fish community can adopt it."

He hopes to add more unnatural amino acids to the four he's published about so far; he wants to control additional zebra fish proteins. And he wants to make the process reversible.

"Right now, we can turn [a protein] on but not off. It would be cool to generate a light switch that goes in both directions, at a given time point in a given location, and do it in multicellular model organisms."

“Right now, we can turn [a protein] on but not off. It would be cool to generate a light switch that goes in both directions.”



COURTESY MICHAEL TSANG

Alex Deiters and Michael Tsang have added a 21st amino acid to zebra fish. (An altered embryo is shown here.) They employed a technique Deiters developed that gives researchers more control over the gene-editing technology CRISPR-Cas9. Such work might one day help patients with genetic disorders like sickle cell disease or cystic fibrosis.

NOT JUST A COOL TOOL

Both Deiters and Tsang are quick to point out that what they make are investigative tools, but they acknowledge the possible exciting therapeutic applications for humans. Imagine being able to treat cystic fibrosis by delivering CRISPR-Cas9 to a patient, but activating it selectively, using a fiber-optic probe to irradiate only the lungs, for example.

Deiters also makes a point of distinguishing between this kind of genetic editing—treating distinct cell populations, such as tumors, the lining of the respiratory tract, or blood cells—from altering the germ line, which refers to copies of the genome that may be passed down through generations. In a position statement for the National Institutes of Health, director Francis Collins calls the

latter “a line that should not be crossed,” stating that the “NIH will not fund any use of gene-editing technologies in human embryos.” Federal funds are not allowed to support such research.

In February 2017, however, a committee for the National Academy of Sciences and the National Academy of Medicine condoned modifying embryos to correct mutations that cause “a serious disease or condition” when no “reasonable alternatives” exist.

And last summer, privately funded researchers in Oregon reported using CRISPR-Cas9 to correct a common mutation in fertilized human embryos.

“The questions surrounding eventual use of CRISPR-Cas9 in human embryos are not new,” says Lisa Parker, director of the University’s Center for Bioethics and Health Law. “They center on safety of the interven-

tion and welfare of offspring, and on what is appropriate for parents to seek in (and for) their children and by what means.... We must also ask whether there will be equitable access to this technology, or if it will exacerbate health disparities.”

In any case, therapeutic applications are still “way into the future,” Tsang notes.

Zebra fish develop quickly. Scientists can inject an embryo, let it grow, and study the effects in just three days; yet the complexity of nature means that progress is slow.

“The operation (incorporating unnatural amino acids into an organism’s proteins) is surprisingly context sensitive,” says Deiters. The scientists can’t always get a protein to express, and they don’t always know why.

That unpredictability is a little frustrating, Deiters says, “but that’s why they call it ‘research.’” ■

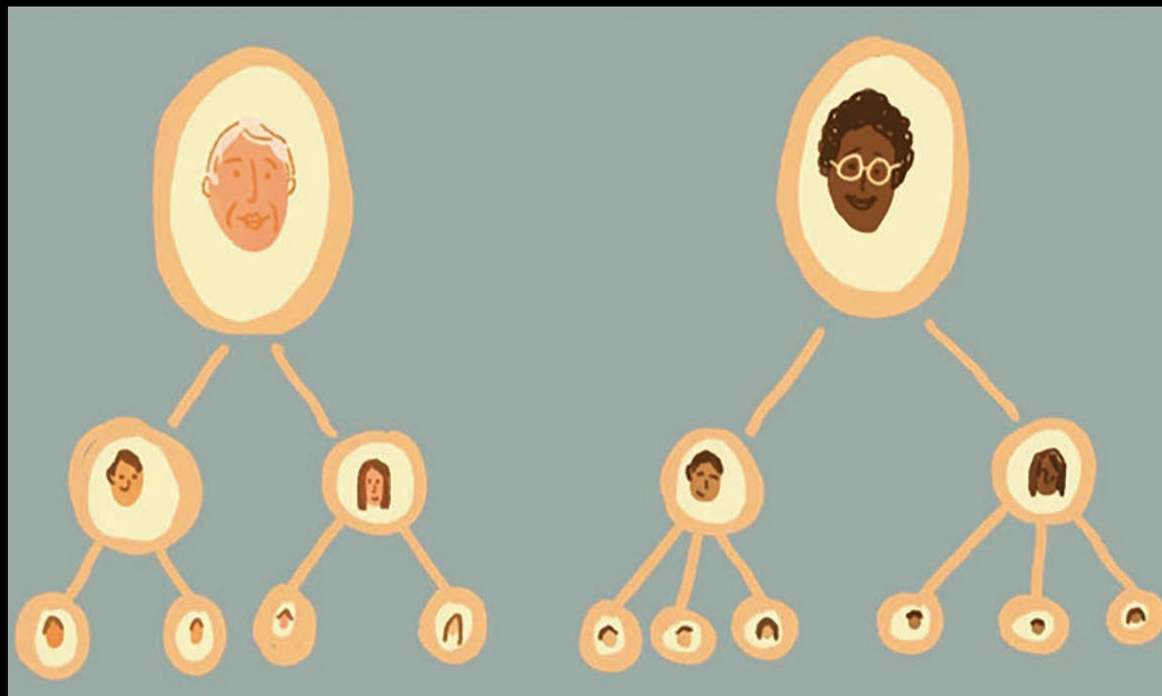


REPRESENT

TO MAKE PRECISION MEDICINE A REALITY,
RESEARCH ITSELF MUST CHANGE

BY ELAINE VITONE

ILLUSTRATIONS COURTESY THE NATIONAL INSTITUTES OF HEALTH



In August 1825, in a home near London’s Finsbury Square, a woman lay dying of postpartum hemorrhage, in spite of the usual remedies of the day—blankets and brandy, mostly. In a last-ditch effort, the team turned to an experimental and as yet controversial treatment; they drew several ounces of blood from her husband’s arm into a tumbler, then cautiously injected the still-warm fluid into the patient’s vein. Within hours, she “rallied considerably,” her doctor, Charles Waller, later wrote in defense of this “operation” and his now-famous colleague who developed it, James Blundell.

In the early days of human blood transfusion, not every patient was so lucky. Doctors didn’t know their type As from their Bs, Os, or ABs until 1902, and Rh-negative blood types weren’t discovered until World War II. In the meantime, people figured blood was blood. One patient’s cure could potentially become another’s fatal reaction.

The complexity and variety of the human form, as well as the diseases that ail it, continue to challenge scientists. We now know that a given cancer—or any other disease or injury, for that matter—will not look the same in one person as it does in another, nor will responses to a given treatment. And so the new drugs keep coming, because, about half the time, the medicine misses the mark. Either it doesn’t work as hoped, or there are side effects that might outweigh the benefits.

In many ways, the subtypes of diseases and disorders are blind spots. We still don’t know our As from our Bs.

Waller once said it was impossible to prove whether the full recovery of his historic patient was “produced by nature or by the remedy.” The past two centuries of clinical research history seem in answer to that, with tomes of papers full of comparisons between Treatment X and none at all. Blind, placebo-controlled trials are the reason why we’ve come such a long way from the days of blankets and brandy.

But now, we have a new problem: How do all these drugs compare against one another? For example, there are dozens of drugs approved for hypertension alone. Which one, if any, is right for *you*, given your genetics, environment, and exposures? To find these answers, clinical research itself must change.

In 2015, the National Institutes of Health (NIH) launched the Precision Medicine Initiative. Its centerpiece: a patient registry of 1 million volunteers from across the country, aptly named All of Us.

This historic recruitment effort began in May 2017 with volunteer number one, at site number one, the University of Pittsburgh and its clinical partner, UPMC. Why here? When the NIH reviewed proposals for the first sites to launch, the Pittsburgh team got the top score nationwide. Total funding is expected to exceed \$67 million.

On a recent chilly Tuesday afternoon, a small black screen on Steven Reis’s desk flashes a number in red. As of this moment, it tells him, 2,223 Pennsylvanians have signed up (and, as we go to print, 3,047). These volunteers amount to about 25 percent of all enrollees nationally, he says, adding that the enrollment effort is still in its beta phase—the national launch is expected to begin this spring.

Several new enrollment sites across the state are in the works, as well as a partnership with Giant Eagle to bring their pharmacists and technicians in on the game. Meanwhile, All of Us Pennsylvania is busily signing people up through community events, visits to public libraries (sponsored by a \$4.5 million grant from the National Network of Libraries of Medicine), e-mails to Pitt and UPMC staff, and letters to individual physicians. For practices in the Pittsburgh area, the program sends trained Pitt

students to pitch the program to patients in the waiting room. “We’ve been talking to providers throughout the region, and there’s a lot of enthusiasm,” says Reis.

When volunteers enroll, he explains, they come in for a brief visit for baseline measurements—weight, blood pressure, height, and the like—as well as blood and urine samples for genetic and other testing. Volunteers also complete a brief online questionnaire about their health, as well as a not-so-brief consent process. It takes so long, in part, because of what may be the most crucial part of the project: sharing their electronic health record information with the All of Us registry. All of the information is de-identified and secured using the latest and greatest cybersecurity technologies, notes Reis.

These data, along with periodic online surveys, and perhaps eventually metrics from wearable devices, will combine to create the largest and richest biomedical dataset ever assembled. Academic and industry researchers—and, to a lesser degree, citizen scientists, including high school students—will be able to request free access to these data. “You don’t know who’s going to come up with a discovery,” says Reis, who, as founding director of Pitt’s Clinical and Translational Science Institute (CTSI), has promoted a cross-disciplinary culture here, bringing design theorists, engineers, and others together with biomedical scientists to spark innovations. “People look at data differently depending on their background and skills.”

One of the main goals of this NIH initiative—and of the field of precision medicine itself—is to close gaps in care, says Mylynda Massart, an MD/PhD assistant professor of family medicine at Pitt who practices primary care at Matilda H. Theiss Health Center, a UPMC family medicine practice in Oak Hill that serves a diverse and underserved population. Take, for example, Massart’s own familial high cholesterol. The literature says statins can lower cholesterol and reduce mortality—but those conclusions are based on studies of middle-age Caucasian men. “So I don’t know what that data means for me. And I don’t know what that data means for an African American male sitting across from me in my office.”

Massart is a member of the national All of Us special populations committee, which is leading the charge in an ambitious goal: to enroll at least 51 percent of its 1 million participants from groups underrepresented in biomedical research. This includes racial and ethnic minorities, sexual and gender minorities,

and participants across the gamut of socioeconomic status and geography (rural, urban, and suburban areas). A range of ages will also be important; though the registry is currently open only to adults 18 and older, eventually, children and teens will be recruited, as well. A large-scale pediatric study is getting off the ground in Pittsburgh sooner—see “Tending to Children,” below.

Here in Pittsburgh, Massart cochairs All of Us PA’s stakeholder advisory board with Father Paul Abernathy, director of FOCUS Pittsburgh, a Hill District-based nonprofit that provides food, counseling, transportation, job training, and other services. Also on the board is Esther Bush, president and CEO of the Urban League of Greater Pittsburgh, a comprehensive social service/civil rights organization focused on serving African Americans and other groups. The Urban League has partnered with Pitt’s CTSI for more than a decade. Together, members of the advisory board will gather feedback from the community and incorporate it into the study.

Unfortunately, Massart says, there are reasons why underrepresented groups, especially African Americans, have historically been wary of medical research, the Tuskegee syphilis study being the most infamous example.

“We have to have open discussions about what happened historically,” she says, “and what things have been put into place to prevent that from ever happening again.” Sadly, she adds, those tragic episodes have contributed to health disparities within research. “We need to overcome that and reverse that process. That requires building trust and dialogue and

relationships, and so the community advisory board is helping us with that.”

Erricka Hager, a 29-year-old from Pittsburgh, first learned about All of Us when she came to work with the Urban League as a health advocate seven months ago. She decided to enroll, motivated by her grandmother, who, four years ago, was diagnosed with breast cancer—the first known case in their family tree.

“My son and my grandmother have a very strong bond,” says Hager. “It hit him hard.”

When she signed up, she did it for both generations. It was a way to honor her grandmother, Hager says, and to help ensure that there will be better detection and treatments available in case her two children are at risk for the disease.

At the Urban League, Hager works primarily with elderly African Americans, providing health education and advocacy, as well as recruiting for clinical studies. As she pitches All of Us and its merits, people might hesitate at first but warm to the idea when she explains her own reasons for joining. She reassures them: The registry is entirely voluntary and anonymous. Ask questions and learn as you go. If at any point you feel uncomfortable, you can opt out and elect to be removed from any studies going forward.

But if the volunteers stay—and All of Us hopes they will, for at least a decade—they will help seed a new era of scientific discovery.

“This is my way of taking hold of my health,” says Hager, “of being involved, and being at the forefront of the decisions that I want to be made for my future, as well as my children’s future.” ■

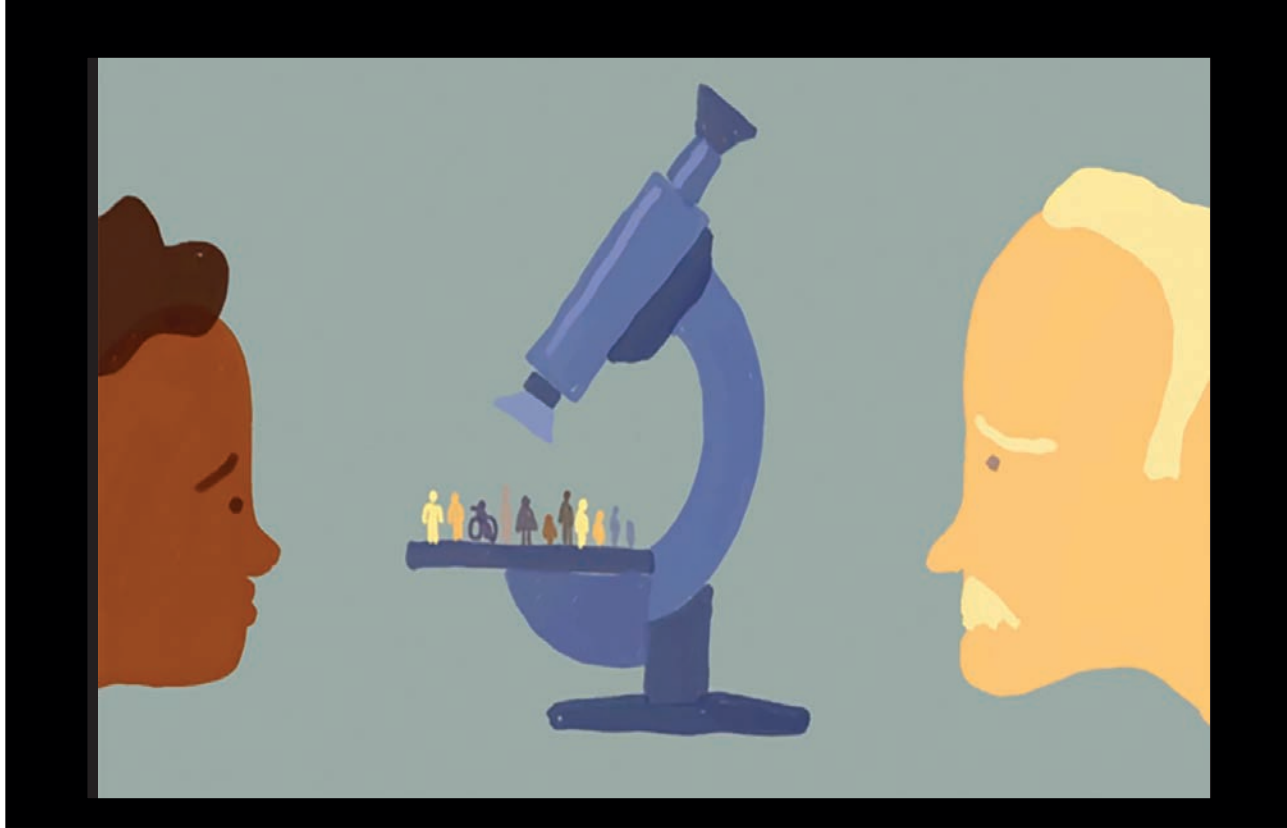
TENDING TO CHILDREN

What are the ingredients of a healthy childhood? What correlates with a young person graduating from high school, steady and ready to roll along the path to adulthood? These are essential questions, says the University of Pittsburgh’s Terence Dermody, who holds the Vira I. Heinz Chair of Pediatrics and is the physician-in-chief at Children’s Hospital of Pittsburgh of UPMC. He says Pitt and Children’s are uniquely poised to find the answers.

With startup funding from the Shear Family Foundation, the Pittsburgh Children’s Study recently began recruiting infants and children for a longitudinal epidemiological assessment that could make its official launch as early as January 2019. The sponsor team includes two Pitt ob/gyn profs—Janet Catov (who oversees the Magee Obstetric Medical and Infant Database) and Yoel Sadovsky (who directs the Magee-Womens Research Institute)—as well as George Gittes (professor of surgery and of pediatrics at Pitt and surgeon-in-chief at Children’s) and Steven Reis (Distinguished Service Professor of Medicine and director of the Clinical and Translational Science Institute, among other titles). The team hopes to enroll about 5,000 children in the study each year.

In addition to genetic and other biological data, the study will eventually encompass detailed interviews through periodic visits to schools and homes, conducted by personnel trained to answer questions and offer referrals as needed.

“That process itself may improve the health of kids in the community,” says Dermody, “and we’re excited about that.” —EV



PRECISION VISION THINKING OF YOU

The right treatment, at the right time, for the right person. Precision medicine—also known as personalized medicine—has been a focus at Pitt for a few years now. In the past year alone, big data and machine-learning projects here have begun to help doctors confirm when patients are suffering from acute kidney injury, they've helped identify which pancreatic cysts will progress to cancer (see “Cancer Detective,” p. 3), and they're predicting who is likely to benefit from a new therapy for treatment-resistant COPD. Also, a smartphone app for pregnant women considers each user's risk factors and barriers to care, helping them prevent preterm birth.

What else is on the horizon?

NICU NEWS: Premies often have a long road home from the hospital, not to mention a costly one. The average stay at the neonatal intensive care unit (NICU) is 17 days and costs about \$220,000. But recent computational modeling suggests many could be discharged sooner if their underlying conditions were identified through genome sequencing at birth and treated right out of the gate. To test this hypothesis, Jerry Vockley, an MD/PhD, chief of medical genetics at Children's Hospital of Pittsburgh of UPMC, and professor of pediatrics at Pitt, recently secured a five-year, multicenter grant of more than \$10 million from the National Center for Advancing Translational Sciences. The clinical trial is expected to launch this year.

BLOCK TALK: When a patient has a blockage in the heart, a cardiologist is likely to put in a stent, then head off any further trouble with antiplatelet agents—usually, a drug called clopidogrel (Plavix). But as the School of Pharmacy's Philip Empey, a PharmD/PhD, and colleagues reported in *JACC: Cardiovascular Interventions*, if you happen to carry a certain gene variant, you may metabolize the drug more slowly, and it may not work as expected. Such was the case for about a third of the patients Empey and his team studied, and those patients had worse outcomes: higher rates of death, stroke, or repeat heart attacks. Two years ago, UPMC Presbyterian implemented a protocol to iden-

tify patients who carry this allele as part of its standard of care.

GENE SCREEN: The field of pharmacogenomics—how your genetics influence your response to drugs—is growing rapidly. To date, nearly 200 drugs come with genetic-variant-related warnings, ranging from a heads-up about minor side effects to graver cautions. “The issue is, we've not had the genetic testing [results] to drive [prescribing] decisions,” says Empey. This spring, Pitt/UPMC researchers will begin providing that testing, inviting patients to volunteer for a study evaluating a panel of nearly 5,000 genes. The data will then be linked with the participant's UPMC health record. “So when [a doctor] goes to prescribe a certain medication, there might be a pop-up saying, based on this person's pharmacogenomics analysis, this drug may be less effective than another drug, for instance,” says Steven Reis, Distinguished Service Professor of Medicine, associate vice chancellor for clinical research, and director of Pitt's Clinical and Translational Science Institute. —*Elaine Vitone* ■





PART OF THE CROWD

THESE ENGINEERS DESIGN
FOR AN INCLUSIVE WORLD
BY GAVIN JENKINS

ABOVE: Children play at Morgan's Inspiration Island using PneuChairs, which were designed and built at Pitt's Human Engineering Research Laboratories.

Photo by Robin Jerstad

Brandon Daveler twisted the throttle on his Yamaha and hit a jump at full speed. It was the first American Motorcyclist Association race of the 2005 season, and Daveler, a 15-year-old thrill seeker who enjoyed working on engines, was confident he could win the District 5 title. But his life changed in midair.

Daveler flipped over the handlebars and landed on his head. Lying on the dirt track at the Greene County Fairgrounds in southwestern Pennsylvania, he heard the announcer yell, “Red flag! Red flag!” indicating that the race had stopped. The paramedics rushed to Daveler. He felt as though he were still sitting on the bike—like his arms were still holding the handlebars. But they were at his side on the dirt. After a life flight to a Morgantown, W.Va., hospital, he learned he’d suffered a fracture to his fourth and fifth cervical vertebrae and had quadriplegia. After months of rehabilitation, he regained movement in his arms but not in his wrists or hands.

An only child, Daveler relished his independence. He preferred racing to basketball because there weren’t teammates. The accident’s aftermath was shocking: The boy who repaired his bike alone at his home in Uniontown, Pa., had to ask people to scratch his head. When he returned to the ninth grade the following autumn, Laurel Highlands High School bought him a laptop and hired an aide to assist him. But the friends who came to his house to ride his dirt bike slowly stopped coming.

The physical and social exclusion was hard to accept then, and it remains a challenge today. “You’re always adjusting,” says Daveler, now a 28-year-old PhD student in the University of Pittsburgh’s rehabilitation science program. “I don’t think [adjusting to life in a wheelchair] ever ends.”

Pitt’s Rory Cooper believes the next generation of engineers will make life a lot easier for people with disabilities. His vision is to create a world where people with disabilities are included in all aspects of society, without physical or social barriers. And he is mentoring Daveler and others he expects will lead the way.

Pitt has been at the forefront of assistive technology since 1994, when Cooper

founded the Human Engineering Research Laboratories (HERL). In association with the U.S. Department of Veterans Affairs, HERL is a joint effort of the University of Pittsburgh School of Health and Rehabilitation Sciences and the School of Medicine, and it thrives as an interdisciplinary operation where computer, mechanical, and bio- engineers collaborate with physicians and occupational and physical therapists. Pitt associate professor of physical medicine and rehabilitation Brad Dicianno (MD ’01, Fel ’05) is its medical director.

Cooper, the FISA & Paralyzed Veterans of America Professor and Distinguished Professor of Rehabilitation Science and Technology, is also a professor of physical medicine and rehabilitation, of orthopaedic surgery, and of bioengineering. He credits his generation with raising the bar for wheelchair users from simply living healthy lives to participating more fully in society. “Now we’re in the crowd,” he says. “The next step is to be part of the crowd.” Cooper has played a significant role in this progress.

While earning his PhD at the University of California at Santa Barbara, he collaborated with a group of designers to create one of the first racing wheelchairs. He was the first engineer to use a solid frame to replace a traditional

folding frame, and he was one of the first to introduce a three-wheeled chair. He invented the SmartWheel, a feedback mechanism tracking the force and movements on push rims. The SmartWheel creates automated reports for doctors to optimize wheelchair setup and cater push styles to reduce repetitive stress and the risk of carpal tunnel and rotator cuff injuries.

Inspired by the data the SmartWheel obtained, Cooper moved the axle forward on his racing chair, which some have argued is the most revolutionary advance in manual wheelchair design history. He was the first to put fenders over the wheels on a racing chair to prevent the tires from bruising arms. Wheelchair racers often overcompensated for the crown on roads and crashed, but Cooper fixed that issue when he designed a crown-compensation mechanism to keep the chair rolling straight.

At HERL, Cooper oversees dozens of full-time employees in a 40,000-square-foot facility in Pittsburgh’s Bakery Square. Google is a neighbor. Cooper, a veteran who has a disability, hires many veterans, several of whom have a disability, as well.

Along one wall in Cooper’s office is a wood and wicker wheelchair from the early 1900s; in the corner, stands a foldable, steel Everest and Jennings wheelchair from the World War II era. The latter is similar to the wheelchair Cooper was given after his own cycling accident in 1980. When Cooper sees the chairs, he says he thinks about how far human engineering has progressed.

Cooper says the biggest change in wheelchair design over his career is that the focus is now on the person, not the chair. “The change happened when the consumers got involved [in engineering],” he says.

The engineer doesn’t know which of HERL’s 70 current projects excites him the most. “It’s like picking your favorite child,” he says. A couple of notable projects include a robotic bed that folds and then shifts like a conveyor belt to move people in and out of a wheelchair and a cueing kitchen that helps people with disabilities prepare meals safely with portable and sensing technology. HERL is also developing a few robotic arms: the Personal Mobility and



Manipulation Appliance (PerMMA) incorporates two robotic arms to help with everyday tasks, and StrongArm, which is mounted on a wheelchair, lifts users, transfers them, and then folds behind the backrest. And a team that includes Pitt Med physical medicine and rehabilitation assistant professors Robert Gaunt and Jennifer Collinger (both PhD engineers) and professor Michael Boninger, HERL's senior associate medical director, have been developing a brain-computer interface. The technology allows a user to move a robotic arm just by thinking about it. The user can even sense when the robotic arm is touching something. That project, based on science done by Distinguished Professor of Neurobiology Andrew Schwartz, has generated a lot of buzz.

Not surprisingly, considering Cooper's resumé, HERL is developing a couple of promising new wheelchairs:

With six wheels, MEBot (Mobility Enhancement Robotic Wheelchair) climbs curbs, and in 2017, it won the Blackwood

Design Award for best new concept.

The PneuChair is likewise making waves—it's a waterproof, motorized chair propelled by compressed air, and it won Pitt's Kuzneski Innovation Cup. In the spring of 2017, Morgan's Wonderland, a 25-acre theme park in San Antonio, opened a companion water park named Morgan's Inspiration Island. The fully accessible park uses PneuChairs from HERL. (See Follow-up on p. 34.)

A graduate student researcher at HERL, Daveler was the lead mechanical design engineer on PneuChair and MEBot. Daveler didn't travel to Texas with Cooper to see the PneuChair in action at the park, but he saw videos of children playing in the water in the chairs.

"It's rewarding to see the reactions of people when they see the devices in action," Daveler says. "But it really hit home" with the videos.

Daveler says the independent streak that led him into racing now fuels his desire to help other power chair users live self-sufficiently.

It's similar to what drives his boss: "It's really about making a difference in people's lives," Cooper says.

Along with others of his generation, Cooper made it easier for Daveler to return to school following his accident, to be "in the crowd."

On July 23, 1980, Cooper suffered a severe spinal cord injury while stationed in Germany. He was a U.S. Army sergeant pedaling a bicycle along Berliner Strasse in the town of Worms, heading to see his future wife, Rosemarie Emans. A bus forced him into oncoming traffic, and he was hit by a truck.

Months after the accident, Cooper returned to his home state and enrolled at California Polytechnic State University, San Luis Obispo. The Americans with Disabilities Act was a decade from becoming law. Public buildings weren't required to have ramps or elevators. Cooper often had to be carried up stairs to labs, where the tables were too high for him;

in classrooms, he turned desk chairs backward and hunched over them to take notes. Cooper and his friends who faced similar challenges were frustrated with technology dating from the Truman administration. They were inspired to research wheelchair designs, saying, *Nobody's going to change it unless we change it ourselves.*

So that's what they did. Twenty patents granted or pending later, Cooper's contributions have gained notice. His office shelves are decorated with an array of pictures, plaques, and awards. Among his many honors: the Secretary of Defense Meritorious Civilian Service Medal and the American Association for the Advancement of Science Mentor Award.

In 2016 alone, he was recognized nine times with national and international honors. Last year, Partnership for Public Service gave him the Samuel J. Heyman Service to America Medal, also known as a "Sammie." And Cooper was just named a fellow of the American Association for the Advancement of Science.

Cooper is an avid marathoner. In 1988, he won a bronze medal in the Paralympic Games in Seoul. Since 1983 he has won a gold every year in the National Veterans Wheelchair Games. The medalist's visage has been featured on a Cheerios box. In his daily life, Cooper uses an 18-pound titanium wheelchair that he helped design. It looks like a racing wheelchair.

Daveler says he was mesmerized the first time he entered Cooper's office. He looks up to Cooper and is inspired by his achievements. Jonathan Duvall feels the same way.

On Feb. 13, 2007, Jonathan Duvall, a 21-year-old Pitt undergrad from Salem, Ohio, was sledding. A blizzard had pummeled the city, and a walkway created a natural jump. Duvall flew off it on an inner tube and landed on his head.

Duvall's friends gathered around as they waited for paramedics to arrive. Looking up at them, Duvall was shocked and scared. He had heard his neck crack, and he couldn't move.

"Kick my legs," he said.

Duvall assured his friends that he wanted to know whether he could feel it. So, they kicked, and when he felt their boots land, he hoped

it was a good sign. But it wasn't. He'd broken his fourth cervical vertebra and developed quadriplegia.

And four months later, after he had dropped out of Pitt and moved in with his sister in Ohio, Duvall wasn't depressed or angry. He was bored.

He wasn't mapping out his life like his friends were. He was watching television, and that was about it. But then he broke his leg during physical therapy and returned to Pitt to see John Horton, an MD assistant professor of physical medicine and rehabilitation. Horton had been working alongside Rory Cooper since 1998, and he asked Duvall if he had returned to college yet.

"I was like, *I can go back to school?*" Duvall says.

Like Brandon Daveler, Duvall is now a graduate student researcher at HERL and is earning a PhD in rehabilitation science. The two have become good friends. They each volunteer as peer mentors to other wheelchair users. Duvall founded Pitt's Students for Disability Advocacy group and was its first president. Daveler is its current president. They have discussed starting a consulting firm together.

Cooper says, "What makes [Duvall and Daveler] really stand out in this field is their personal insight and their persistence to learn and incorporate new advances and concepts."

Jonathan Duvall was part of a team that developed a pathway measurement tool: a three-wheeled device that collects data on sidewalk length, width, roughness, and tripping hazards. After winning first place and \$20,000 at the 2014 Randall Family Big Idea Competition, hosted by Pitt's Innovation Institute, the engineers launched their own company, Pathway Accessibility Solutions, or pathVu.

Duvall's interest in urban landscapes began shortly after his accident. Several months after he had returned to Ohio, he visited Pittsburgh to see his friends. His fraternity was hosting a party at a house on Semple Street in South Oakland. It was a warm day, and Duvall was hanging out on the sidewalk when one of his pals invited him inside. The house sat on a hill, and to get inside, Duvall needed to scale

two flights of concrete stairs. With a sarcastic smirk, Duvall asked how he was supposed to get up there.

"Pledges!" the friend yelled.

The fraternity's pledges carried Duvall up the stairs and into the house. (They made a second trip for his wheelchair.) Later, they carried him back down. Reminiscing about that night, Duvall calls it neat. But the event also drove home issues of inaccessibility. He says this barrier can play with your mind.

"If I was trying to get into a place, I felt like everyone was thinking, *Why is he making us go through this hassle holding doors?*" he says.

Pittsburgh is a particularly difficult city for people with disabilities to call home. Many apartments are in houses that are around a hundred years old and inaccessible, and new rental units, like the ones in Bakery Living, across the street from HERL, tend to be expensive.

More than 2 million Americans use a wheelchair for daily tasks, according to the CDC. However, the U.S. Department of Housing and Urban Development determined in 2011 that while a third of housing may be modifiable for wheelchair users, only .15 percent of U.S. homes were accessible to them.

Future iterations of MEBot could help. The robotic chair, now on its second version, can climb an 8-inch-high curb in 30 to 40 seconds. MEBot's first version took a few minutes to do this.

One recent December morning, Jorge Candiotti, a postdoc and MEBot's lead software and electrical engineer, demonstrated MEBot scaling a curb in the lab. Candiotti pressed a lever, and MEBot rose. Daveler explained that the point of the height increase was to make turning on light switches and talking to people at eye level easier.

MEBot runs on six wheels—two large center driving wheels that reposition to the front, middle, and rear of the frame and four smaller caster wheels (two in the front and two in the back) that are controlled with compressed air and move up and down freely. This design served as Daveler's master's thesis, and it has brought HERL closer to creating an indoor-



Rory Cooper, sitting in a wheelchair that he helped design, outside HERL's 40,000 square-foot facility in Bakery Square. He says that the most significant changes happen when consumers get involved in engineering.

Photo by John Altdorfer

outdoor chair that can handle various terrains.

Using the power controls, Candiotti rolled the chair in front of a curb-like platform. He pressed a lever, and the chair rose using compressed air.

"He's elevating the chair to get the front wheels up onto the curb," Daveler said. "And now, what will happen is he'll move the entire frame forward onto the curb."

The frame slid forward, and the rear caster wheels lifted off the ground. MEBot was on the curb. Even with Daveler's narration, the demonstration took less than a minute. The increased speed was a major improvement over MEBot's first version.

But, in 2013, when Daveler and Candiotti showed the simulation to Cooper, he challenged them to go further, to design it to scale a staircase. Daveler says it was an example of "Dr. Cooper being Dr. Cooper."

The MEBot team spent the next four months changing designs and running simu-

lations. But they couldn't come up with a way for MEBot to climb stairs without making major redesigns. It needed to be much longer, but that would have made it less maneuverable indoors, and the project's goal was to create a power chair that overcame obstacles both inside and out. Daveler concluded it wasn't safe for the 440-pound power chair to climb stairs.

He calls the day he accepted this and admitted it to Cooper one of his hardest times on the project.

The MEBot team is now switching the chair's power system from pneumatics to hydraulics. But Daveler might not be at HERL when the next iteration is complete. He plans to start a company around pneumatic-powered mobility devices when he graduates next year. After Jonathan Duvall finishes his PhD this spring, he'd like to continue at HERL and join the faculty.

When Daveler leaves HERL, he will miss

working in a lab where projects are designed, built, and tested in the same building.

And, he notes, "There aren't many universities that allow its students to go from having an idea to commercializing it."

He'll also miss working for Cooper, a mentor who has become his friend.

"Everything that he's done, and his passion to help people with disabilities and veterans, it's really inspiring."

Cooper says HERL's success wouldn't be possible without help from Pitt, UPMC, and the VA. And he wants to follow in the footsteps of the former two by growing globally. HERL already collaborates with labs in Japan and Germany; later this year, Cooper will begin to mentor graduate student researchers with disabilities from the United Kingdom and Germany.

"What we've done with Jonathan and Brandon, we're going to do that worldwide," Cooper says. ■



ROBIN JERSTAD

“LIKE WAKING UP ONE DAY AND BEING ABLE TO FLY”

ACCESS TO FUN



COURTESY PRISCILLA HANEY

Sammi Haney

Gordon Hartman needed a wheelchair that could get wet. He was building Morgan's Inspiration Island, the world's first fully accessible water park, in San Antonio.

But, as Hartman told the *New York Times* for a December video, “That didn't exist.”

Hartman reached out to Rory Cooper, director of Pitt's Human Engineering Research Laboratories (HERL) and Distinguished Professor of Rehabilitation Science and Technology, who has multiple Pitt appointments, including professor of orthopaedic surgery. It just so happened that HERL was developing PneuChair, a motorized wheelchair that uses high-pressure air as an energy source. Unlike traditional power chairs, which depend on heavy batteries and electronics, PneuChair is waterproof—a perfect fit for Morgan's Inspiration Island.

HERL loaned one PneuChair to the San

Antonio park last year; the park purchased three more, and it expects to have six more by the time it opens this spring.

Brandon Daveler, a graduate student researcher at HERL, was the lead mechanical design engineer on the PneuChair project. (See p. 29 for more on Daveler, Cooper, and HERL.) Daveler is also a power-chair user. He told the *Times* that being able to play at a water park would change the lives of children with disabilities: “It would be like somebody waking up one day and being able to fly. You're free. You can do it, like any other person who can go to a water park.”

The *Times* story and video chronicles 8-year-old Sammi Haney as she visits Morgan's Inspiration Island for the first time. Haney has osteogenesis imperfecta, or brittle bone disease, and uses a power wheelchair. She was born with 19 fractures and breaks a bone multiple times a year.

As the Haney family arrives at the park in the video, Sammi says, “This is going to be awesome!” and zips ahead of everyone. Soon after, she's dousing herself and spraying her older brother with a water cannon.

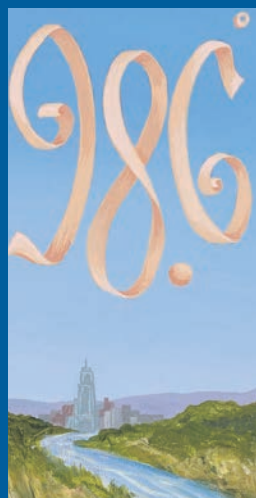
Cooper says he received 300 e-mails the day after the *Times* story came out. People were interested in using PneuChair in therapy pools, at beaches, and in rivers for fishing.

Cooper founded HERL in 1994 with the goal of helping to create a more inclusive world. And that includes access to fun. “It does affect your quality of life if you're excluded from these summertime activities,” Cooper says.

“Seeing the smiles on those kids' faces when they got to go to the water park for the first time and actually do things on their own was such a reward.”

As the *Times* video closes, a happy Sammi Haney sings, *I can swim in the water. I can swim in the air.* —Gavin Jenkins

*People and programs
that keep the school
healthy and vibrant*



GRATITUDE ON WHEELS

AVATARS FOR KIDS

BY EMMALEE C. TORISK

In May 2017, Cris Colaluca graduated from Mohawk Junior-Senior High School in Bessemer, Pa. He's among the first in the country to earn his diploma with the help of a robot. VGo is a 4-foot, roughly 20-pound, remotely controlled avatar with a video screen face and wheels; it allows immobile patients to participate in experiences they normally would miss.

For his senior project, Colaluca, 19, started a GoFundMe campaign in order to buy three VGo's for Children's Hospital of Pittsburgh of UPMC, where he has been a patient for years.

As a boy, Colaluca was diagnosed with electrical status epilepticus during slow-wave sleep (ESESS), a rare form of epilepsy syndrome that typically develops in childhood. In addition to experiencing seizures while asleep, ESESS patients struggle to understand speech and language (what's known as receptive dysphasia), as well as to express themselves in speech (expressive dysphasia).

Colaluca's complications prevented him from attending school beginning in the second grade. He felt isolated from his peers, and his education suffered. But that changed in seventh grade when Mohawk administrators ordered him a VGo. Now he is paying the favor forward by donating to Children's.

"I was thinking it would help the kids go outside their rooms and explore and do something

they can't really physically do," Colaluca says.

His GoFundMe campaign is sponsored by VecnaCares, the nonprofit branch of Massachusetts-based Vecna Technologies, which manufactures VGo. The Verizon Foundation and country music artist Jimmy Wayne helped promote the campaign.

In the end, Colaluca's senior project over-shot its goals, raising enough for five robots. The first three went to Children's: two donated by the Verizon Foundation and one by Pat McAfee, a Pittsburgh native and retired Indianapolis Colts player. The GoFundMe donations bought two VGo's for Colaluca's alma mater, Mohawk Area School District. (The campaign is still active.)

At Children's, the robots will be used to help patients connect with life outside the hospital room—keeping in touch with family and friends, continuing with school, and preparing for medical events through virtual tours of spaces like operating and waiting rooms. Users see through VGo's camera, and with a computer or iPad, they can direct the robot to look up, down, and from side to side. The user's face appears on the video screen as though he is talking on Skype. Microphones allow the robot to pick up sounds in its environment, and a speaker broadcasts the user's voice.

Andrew Urbach, professor of pediatrics at Pitt Med, has treated Colaluca through the years. He has seen how the avatar transformed his patient's life. "It's a part of him," Urbach says. "It gave him the freedom to develop as a person, and it changed him. I think that's where his passion comes from and why he wants other individuals who are struggling with similar issues . . . to have this available."

Vecna will donate a VGo for Cris Colaluca's use, as well. (The Colaluca family credits business author Eva Rosenberg for helping make this happen.) That new VGo will go off to college with Colaluca in the fall. ■

CHILDREN'S HOSPITAL OF PITTSBURGH OF UPMC



Colaluca with a VGo

BOOSTER SHOT

From 2008 to 2012, 434 infants died in Allegheny County—that's slightly worse than the national average. And situations are more dire for African Americans. The county's racial disparity in infant mortality is 27 percent higher than the nation's average.

In an effort to decrease infant mortality, the **Richard King Mellon Foundation** granted \$4 million to Magee-Womens Research Institute and Foundation (MWRIF) to support the Magee Obstetrical Maternal Infant Database (MOMI) and \$1 million to MWRIF to support basic research relating to infant mortality. Working with MWRIF, Pitt and the RAND Corporation received separate grants of \$750,000 and \$625,000, respectively, to create algorithms to predict or score mortality risk.

The Mellon Foundation also granted \$5 million to establish the Magee Prize to recognize innovative women's health research. This October, the first award will be presented at a new international summit to be held in Pittsburgh. It will convene scientific and thought leaders in reproductive sciences and women's health research.

A team led by Pitt's Fuchiang ("Rich") Tsui, associate professor of biomedical informatics, will use the Mellon grant to develop predictive models that estimate risk of infant mortality. Using these models, RAND will develop intervention approaches that more effectively reduce risk.

"We hope to be a leading advocate for technologies and alternatives to models that relied on traditional office visits to promote healthy pregnancies," says Robert Edwards, chair of Pitt's Department of Obstetrics, Gynecology, and Reproductive Sciences.

"Infant mortality is an issue that the foundation and our community partners have been trying to solve for a very long time," says Mike Annichine, CEO of MWRI. —Kate Benz



CLASS NOTES

'80s

Robot, scalpel please. **Laligam**

Sekhar (Neurosurgical Resident '82), the vice chair of neurosurgery at the University of Washington, in Seattle, counts among his many research projects the development of an artificially intelligent robotic assistant, one that would "learn from various experiences"



Sekhar

during surgery. Sekhar, who has secured seven patents for his research, is additionally developing AI techniques to reduce treatment costs for patients with aneurysms. An expert in skull-based tumors and cerebrovascular surgery, Sekhar also instructs medical students and residents in a cadaver-based training lab at UW. Sekhar first helped develop a similar lab at Pitt and later recreated one at UW. These labs allow surgeons to learn the operations first on cadavers, Sekhar says, "so that in the operating room, they're well prepared."

'90s

Karna Murthy (MD '98), associate professor of pediatrics at Northwestern University, spent a lot of time on the phone in 2006. He called hospitals around the country to help pitch the Children's Hospitals Neonatal Consortium, an online database for physicians to share information on complex and rare conditions that newborns face. Early on, Murthy called **Beverly Brozanski** (MD '82), professor of pediatrics

at Pitt Med and medical director of the NICU at Children's Hospital of Pittsburgh of UPMC, who signed Pitt up. She says the consortium, of which she's a board member and an executive group member, has since brought "a collaborative spirit and forum" to neonatal intensive care nationwide. Thirty-four hospitals now share their NICU data with the consortium, aggregating information on more than 20,000 babies every year. Murthy serves as vice chair of the consortium.

'00s

Brian Keith McNeil (MD '01)

made TV appearances with NFL Hall of Fame cornerback Michael Haynes in September, prostate awareness month, as part of a Urology Care Foundation campaign called Know Your Stats. McNeil, who is the urology vice chair and residency program director at SUNY Downstate Medical Center, discussed men's health with Haynes as part of his role as a 2017–18 fellow ambassador with the New York Academy of Medicine. (Fellow ambassadors provide expertise to the media to help improve urban health.) He says it feels good to be in a position to keep men healthy. When McNeil was a teenager in West Philadelphia, his father died from prostate cancer.

Michael Lynch (MD '04, Emergency Medicine Resident '07, Medical Toxicology Fellow '09) became the Pittsburgh Poison Center's medical director in 2013. Back then, for the most part, callers needed treatment for ingestion of household toxins. Then calls about opi-



Brozanski



McNeil

oid overdoses flooded in. Last year, Lynch's team rolled out a "warm handoff" program. It's the first poison center in the country to tackle the opioid epidemic in this way, he says. Instead of merely referring callers elsewhere, the team extends a "warm hand" by assessing callers for addiction, connecting them directly to treatment options, and making follow-up calls. "I can't think of anything more poisonous" than opioids, says Lynch, assistant professor of emergency medicine at Pitt. He has been asked to join the U.S. Department of Health and Human Services Pain Management Inter-Agency Task Force.

The core problem underlying mental illness is communication—not between people, but between areas of the brain—says **Alik Widge** (MD '08), assistant professor of psychiatry at Harvard. "Different parts of the brain have intrinsic rhythms," he explains. When those rhythms get out of sync, people develop conditions like

PTSD or OCD. Widge combined his Pitt MD with a robotics PhD from CMU and is now designing an electronic device that fits into the brain to bridge communication gaps. It listens to which areas of the brain are out of sync, then "works with" the brain's inherent plasticity. Widge says the device isn't a permanent crutch. After enough therapy, it could be removed. "Our goal is to give people back some control over their own mind."



Widge

'10s

Antonia Chen

(Orthopaedic Resident '13) was one of only three physicians to make 2016's "40 under 40" list for the *Philadelphia*

Business Journal. Chen specializes in hip and knee replacement—"I help grandma and grandpa walk again," she says. She has also been researching periprosthetic joint infection and working with medical students as an assistant professor at Thomas Jefferson University. She's now moving to Boston to join Brigham and Women's Hospital as their director of arthroplasty research and an attending orthopaedic surgeon with an appointment at Harvard Medical School.

When **Tom Miller** (MD '14) got lost on a hike in New Zealand back in 2004, his travel mishap turned out to be fortunate after all. "To entertain myself, I imagined several of the characters that ended up in the novel," he says of his book published in February 2018, *The Philosopher's Flight* (Simon & Schuster). It's a fantastical tale set in World War I-era America about a young man breaking into the woman-dominated field of



Chen



Miller

JENNIFER ARNOLD

SIMULATION AND REALITY

philosophy. The book's subtitle, *Half Science, Half Magic—Entirely Fantastic*, could be the motto for Miller's dual career as a physician-author. He's finishing up his emergency medicine residency at the University of Wisconsin and working on a sequel, *The Philosopher's War*.



Londono

Ricardo Londono (PhD '15, MD '17)

received the Society for Biomaterials' 2017 Student Award for Outstanding Research. Londono snagged the honor for work he conducted in surgery professor Stephen Badylak's lab, yielding 22 peer-reviewed manuscripts and five book chapters. His work demonstrated that improperly decellular-

ized biomaterials can lead to encapsulation and scar tissue formation; he also examined the use of biologic scaffolds in esophageal and cardiac tissue repair. Londono, who authored *Annals of Biomedical Engineering's* most highly cited publication in 2015, is now a postdoctoral associate in Pitt's Center for Cellular and Molecular Engineering. He hopes his research can support safety regulations for biomaterials, which don't go through complete regulatory steps when used in clinical applications, he says, "because we lack adequate criteria for quality compliance."

— Evan Bowen-Gaddy, Charlotte Couch, Rachel Mennies, and Adrianna Moyer

For parents of babies who go home with feeding tubes, ventilators, and other artifacts of a stay in the NICU, leaving the hospital can be a daunting prospect. At the Johns Hopkins All Children's Hospital Simulation Center in St. Petersburg, Fla., newly appointed medical director Jennifer Arnold (Res '03, Fel '07) leads a team that helps parents of medically complex infants practice for life at home.

The immersive scenarios Arnold oversees feature computerized mannequins and a mix of auditory, visual, and olfactory cues—known as "moulage" in the business—that get participants' hearts pounding over what to do when, say, the baby has an airway emergency. "We don't want them so stressed that they can't learn," says Arnold, "but we want them stressed enough that their attention is focused." During a debrief, participants reflect and identify what they'll do differently in real life. The simulation center provides classes not only for parents, but also for hospital staff (on neonatal intubation and other procedures).

Arnold first encountered simulation during her fellowship at Pitt. "This," she thought, "is the best way to educate people." To test that theory, she ran a randomized, controlled trial on neonatal intubation. In their first encounters with real babies in respiratory distress, residents she trained at Pitt's simulation center had far superior performance to those in the conventional curriculum.

As the star of her own long-running reality show, the 3-foot-2 blonde is no stranger to stagecraft. When *Pitt Med* last spoke with Arnold in 2011, she and her husband, Bill, were beginning their fifth season as stars of *The Little Couple*. Since then, the show has followed them as they've adopted children, Will and Zoey. Everyone in the family has spondyloepiphyseal dysplasia, a genetic mutation that can lead to dwarfism.

In this season of the show, the Arnolds consider whether to move the family from Houston (where Arnold headed the simulation center at Texas Children's Hospital for nine years) to St. Petersburg for the doc's current role. When Arnold goes to Glasgow to give a keynote talk at a pediatric simulation conference, the whole family tags along to take in castles and haggis!

—Sharon Tregaskis



ABOVE: Arnold tells a group of school children including her son, Will (front row, black shirt), about training parents and doctors to help newborns at the simulation center at Johns Hopkins in St. Petersburg, Fla.



JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

BERNARD KLIONSKY

OCT. 8, 1925–NOV. 12, 2017

During a summer course in 2005, Bernard Klionsky showed his class of med students a slide that looked like a red, yellow, and brown blot. Klionsky, then a semiretired 80-year-old former vice chair of pathology at Pitt, asked the class to identify what they saw.

When a student suggested correctly that the image was a thrombus, Klionsky pushed her to be more accurate. “Give me a description a blind man could understand,” he said.

Klionsky, who died in November at 92, wanted the student to identify the image as a heart attack. He was fond of saying, “To most students, ‘heart attack’ is just a word. And it’s not enough just to know the word.”

To become effective doctors, Klionsky believed, students need to be able not just to diagnose a medical condition, but also recognize where each particular patient falls along the spectrum of a disease’s possible outcomes. Ultimately, though, this lesson—like all of Klionsky’s—was really about how to approach problems. He showed students how to become, as he put it, “highly trained problem solvers.”

Klionsky, a World War II veteran from Binghamton, N.Y., encouraged his four children to be problem solvers, as well, his son Daniel Klionsky recalls. Although the pathologist disliked sports, he’d take Daniel to Pirates games, where they’d calculate how a hit would affect a player’s average.

Klionsky’s own career as a Pitt pathology professor included numerous hits. Early on, he invented the open-top cryostat for collecting samples in the O.R., forever changing surgical pathology. He identified the structure of Fabry disease. He figured out how to end an epidemic of yellow hyaline membrane disease and low bilirubin kernicterus, once a major cause of death among premature infants. Klionsky was a driving force behind the medical center’s central laboratories and the Central Blood Bank. He served as director of laboratories at Magee-Womens Hospital of UPMC for 27 years.

The pathologist endowed a summer research fund for medical and undergraduate students. George Michalopoulos, MD/PhD, Maud L. Menten Professor of Pathology and department chair, says Klionsky was a mentor who will be missed. “He was universally respected,” Michalopoulos says. “He was suc-

cessful at everything that he tried.”

—Gavin Jenkins, with reporting from a 2006 Pitt Med story by Hattie Fletcher

ROLF LOEBER

JUNE 5, 1942–NOV. 6, 2017

Rolf Loeber, who gained international renown for his research on delinquency in youth, died Nov. 6. He was a Pitt Distinguished Professor of Psychiatry who also held appointments in psychology and epidemiology.

Through the Life History Studies Program, cofounded and codirected with his research partner and wife of 50 years, Magda Stouthamer-Loeber, he created three longitudinal studies. Beginning in 1987, the Pittsburgh Youth Study followed 1,500 boys to chart antisocial behavior through early adulthood, determining its risk factors and its effect on their lives. The Developmental Trends Study, begun in 1989, looked at similar factors among boys requiring clinical treatment. The ongoing Pittsburgh Girls Study has been examining 2,400 girls’ experiences of delinquency, depression, and substance use since 1999.

“Rolf was clearly a pacesetter internationally in the origin of several extremely important

large longitudinal studies of development,” says psychiatry department chair David Lewis, who collaborated with Loeber on a study of cannabis use in adolescents. Lewis notes that Loeber’s findings will continue to inform public policy, while the many investigators he trained will move the field in new directions.

Born in the Netherlands, Loeber earned a PhD in clinical psychology at Queen’s University in Ontario and joined the Pitt faculty in 1984. He was also a professor of juvenile delinquency and social development at the Free University of Amsterdam, Netherlands. He and Magda were intensely interested in the history of Ireland and its arts; together, they produced *A Guide to Irish Fiction, 1650–1900*. Loeber also published a biographical dictionary of 17th-century Irish architects.

When the couple was interviewed by *Pitt Med* magazine in 2007, he reflected on their research. “Our mission,” he said, “is to try and figure out the causes of violence in a community and the parameters through which we could actually bring about change.” —Marty Levine

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Loeber



Klionsky

IN MEMORIAM

'40s

ROBERT ERB GREGORY
MD '43
DEC. 13, 2017

HOMER G. MCCLINTOCK
MD '43
OCT. 1, 2017

HARVEY A. LINCOFF
MD '48
NOV. 25, 2017

HARRY S. BINAKONSKY
MD '49
DEC. 20, 2017

'50s

PHILIP BROSTOFF
RES '50, '51
JAN. 6, 2018

RICHARD W. HEMPHILL
MD '53, RES '57
JAN. 10, 2018

HAROLD BROURMAN
MD '55
DEC. 28, 2017

WALTER E. ECK
MD '55
NOV. 25, 2017

JAMES A. STUART
MD '56
AUG. 16, 2017

JOSEPH F. HAKAS
MD '57

NOV. 16, 2017

'60s

THOMAS M. GLUSHIEN
MD '60
MAY 4, 2017

GERALD F. LOFTUS
RES '63
NOV. 9, 2017

FRANK IRWIN MARLOWE
MD '63
SEPT. 15, 2017

MICHAEL C. BELL
MD '64
OCT. 15, 2017

WILLIAM G. DOODY
MD '64
JAN. 18, 2018

EDWIN J. MORGAN
MD '64
OCT. 19, 2017

WALTER F. O'DONNELL
MD '67
JAN. 9, 2018

DOUGLAS M. GRODIN
MD '68
NOV. 26, 2017

ROBERT D. BRICKMAN
RES '69
NOV. 19, 2017

'70s

JEAN E. RINALDO
MD '75
JAN. 4, 2018

JAMES A. CROZIER
RES '77
OCT. 19, 2017

MARY CHARLOTTE GOESSLER
MD '77
DEC. 8, 2017

'80s

GEOFFREY L. CHENTOW
RES '83
JULY 9, 2016

WERNER M. BLOOS
MD '85
JAN. 16, 2018

PAUL J. SCIOSCIA
MD '87
DEC. 3, 2017

'90s

VIRGINIA L. KNIGHT
MD '93
NOV. 21, 2017

FACULTY

JUDITH S. GAVALER
JAN. 5, 2018

RON SHAPIRO RENAL RECONSIDERED

BY SARAH C. BALDWIN

Waiting for “the one” may not be the best strategy when it comes to kidneys.

Ron Shapiro (Fel ’88) coauthored a 2016 *New England Journal of Medicine* article that marks a significant step forward in improving immunosuppression.

The *NEJM* authors reported on the outcomes of transplants for patients who underwent desensitization, a process that removes antibodies that contribute to organ rejection. Those who were desensitized before receiving kidney transplants from live donors who were deemed incompatible were more likely to survive (by 13.6 percent) than patients who remained on the transplant waiting list or received a kidney from a deceased donor. They were also more likely to survive (by 32.6 percent) than those who stayed on the waiting list and did not receive a kidney from a deceased donor.

In the United States about 100,000 people are on the waiting list for a kidney, yet only about 17,000 compatible kidneys are transplanted each year (of which only about 5,500 are from living donors).

Two leading nephrologists from Grenoble called these findings “revolutionary.” Shapiro is a bit more circumspect. The results are

promising, sure, he notes, “compared to sitting on the waiting list, because [those patients] have a 5 to 6 percent mortality rate annually. More patients die waiting for a kidney than those who are waiting for a heart, lung, and liver combined.”

Yet at the end of the day, says Shapiro, “transplantation is a drop in the bucket.” Some 660,000 people in the United States have end-stage renal disease, and more than 400,000 of them are on dialysis. “Their mortality at five years on dialysis if they’re not referred is 70 percent, which is worse than most cancers,” says Shapiro.

He’s more optimistic about potential advances, such as growing organs in test tubes. Better yet, he says, would be preventing end-stage renal disease in the first place.

Shapiro has delivered more than 600 lectures and grand rounds. More than 400 articles, 70 book chapters, and four textbooks bear his name. Much of his focus has been on immunosuppression protocols. And he’s transplanted, by his estimation, between 1,600 and 1,700 kidneys. Shapiro’s assessment of his

career trajectory? “It all kind of worked out.”

Richard Simmons, chair emeritus of Pitt’s Department of Surgery and a kidney transplantation specialist himself, hired Shapiro almost 30 years ago. He’ll tell you, “Dr. Shapiro is the epitome of . . . calm, cool, competent, and kind.”

Shapiro notes that he trained with “the greats,” including the late Thomas E. Starzl and Robert Corry, a trailblazer in pancreas transplantation, whose endowed chair Shapiro occupied at Pitt from 2007 until 2014. Earlier, Shapiro did a stint as a research fellow with Richard Lower, who in the 1960s, ’70s, and ’80s paved the way for heart transplantation at the Medical College of Virginia.

In July 2014—the day he turned 60, in fact—Shapiro accepted an offer to become surgical director of Kidney and Pancreas Transplantation at Mount Sinai’s Recanati/Miller Transplantation Institute. Three decades in the Steel City notwithstanding, it was a homecoming of sorts: Shapiro did his surgical residency at Mount Sinai in the mid-’80s. In addition to overseeing more than 200 adult and pediatric kidney transplantations a year, he continues to transplant “a fair number” of kidneys himself, “as well as the odd pancreas.”

After Starzl’s death last March, Shapiro wrote an article in *Clinical Transplantation*, of which he is editor in chief, praising his mentor’s contributions to the field and adding that “everything that he did was focused on improving the welfare of his patients.”

The student of greats learned well. According to Richard Simmons, Shapiro is “a perfect product of the Starzl genius in training.” ■



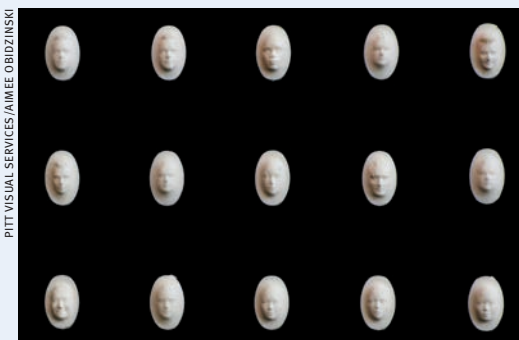
Shapiro

LISTEN TO YOUR MAA!

You’re overdue for a visit. Get yourself over to maa.pitt.edu to learn what your classmates are up to, register for Medical Alumni Weekend and other events, and then some. Don’t make me ask twice.

Remember who you are and where you came from. Connect with your **Medical Alumni Association**—@PittMedAlum on Facebook, Twitter, and Instagram.

And wipe that smile off your face.



PITT VISUAL SERVICES / AIMEE OBIDZINSKI

OVERCOME

A man, perhaps 6 feet tall and in his mid-50s, stands in the William Pitt Union. He wears a mustache, a collared shirt, and a coat that seems too light for this January day. He is sobbing softly. Opposite him is a black wall covered in 22,000 little white pills, each engraved with the face of someone who has died in the opioid epidemic.

The wall is part of the exhibition *Prescribed to Death: A Memorial to the Victims of the Opioid Crisis*. We've all seen the headlines: In the United States, 22,000 people died from a prescription opioid overdose in 2015, making drug overdoses, predominantly from opioids, the number one cause of all accidental deaths in adults—and that number is growing. Pennsylvania ranks fourth in the nation for opioid deaths. But according to the National Safety Council, one-third of people on these substances don't even realize they are taking an opioid. *Prescribed to Death* hopes to educate the public about the reality of the crisis. Its first stop was on Pitt's campus from January 30 to February 2. —Susan Wiedel

To learn more: stopeverydaykillers.nsc.org
and www.pittmed.health.pitt.edu/story/stepping-path-hell

CALENDAR

FOR ALUMNI & FRIENDS

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

MATCH DAY

MARCH 16, 12 P.M.

Petersen Events Center

**MEDICAL ALUMNI ASSOCIATION
EXECUTIVE COMMITTEE BOARD MEETING**
APRIL 11, 6 P.M.
University Club

HEALTH SCIENCES

ALUMNI & FRIENDS RECEPTION

APRIL 12, 6–8:30 P.M.

The English Oak Room
Cleveland, Ohio

**THIRD-YEAR MEDICAL STUDENT
PINNING CEREMONY**

MAY 4, 3 P.M.

Scaife Hall, Lecture Rooms 5 & 6

GRADUATING CLASS LUNCHEON

MAY 18, 11 A.M.

Alumni Hall, J.W. Connolly Ballroom

SCOPE AND SCALPEL

MAY 18, 7 P.M.

MAY 20, 2 P.M.

Central Catholic High School
McGonigle Theater

For information:

scopeandscalpelsociety@gmail.com

For tickets: scopeandscalpel.org/tickets

SCHOOL OF MEDICINE COMMENCEMENT

MAY 21, 4 P.M.

Soldiers & Sailors Memorial Hall & Museum

For information:

Rhonda Matthews at 412-648-9674

rmatthews@medschool.pitt.edu

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



FRANK HARRIS



FOR REAL! TWEEN SCIENCE

Maybe you've heard stories: A woman wakes up in her kitchen having cooked—and eaten—an enormous snack in the night. Maybe you've got stories of your own, like falling asleep in your bed, but finding yourself on the porch in the morning.

The common theme here: sleepwalking, also known as somnambulism. This disorder affects about 4 percent of adults and 17 percent of children in America. Stories about it may sound cool and funny. But sleepwalking can result in injuries, according to pediatrician Sangeeta Chakravorty. At Children's Hospital of Pittsburgh of UPMC's Pediatric Sleep Evaluation Center, she helps families deal with sleepwalking.

Sleepwalking can run in families or be caused by medicine, accidents, fevers, or stress. Scientists don't understand all the reasons why it happens. It seems that although it is supposed to be shut off as we sleep, the "walk" program in our brains somehow gets turned on while dreaming. When this happens, says Chakravorty, "skeletal muscles and nerves receive impulses and respond automatically, without the . . . knowledge of the sleeper. The body moves without the brain centers that control consciousness being fully engaged."

Sleepwalkers may do things other than walking. They might run, talk, pee, or eat snacks (maybe with the wrappers still on them). Children are more likely to sleepwalk because the electrical connections in their brains that link asleep and awake centers haven't grown strong yet. They tend to outgrow sleepwalking by the time they're teens. —Lela Nargi

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



LOCATION, LOCATION, DONATION

Ah, the joys and pains of fixer-upping: Painting your very own ceiling! The suspense of finally finding out what's hiding under that shag carpet!

If the appeal of renovation has seriously curbed, your house-flip is a flop, or you're just plain fed up and ready to downsize, **consider a real estate gift to Pitt.**

Whether it's a home, a lot, a rental property, or a vacation spot, your asset can provide you or your loved one with an income stream for life. It can also help make tax time less taxing. You can even designate a specific area that your gift will benefit—say, Scaife Hall's own renovation, now under way, or a researcher who's hammering out promising new cures.

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