

# PITTMED

“... that has changed how other medical schools have designed their curriculums.”

—Brad Dicianno, Pitt

“All of us know, in the next few years, unless you’re like Pitt, you won’t be able to survive, support innovative research, promote health for your patients. We look at Pitt and say, *He was ahead.*”

—Julie Freischlag, Wake Forest



“The quality of applicants continues to become more and more stellar.”

—Richard Steinman, Pitt

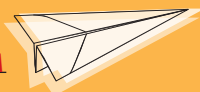
“Arthur Levine is a visionary and an inspiration to everybody in academic medicine.”

—Lloyd B. Minor, Stanford

“He wants to be number one. He wants to be number one in everything. One of the reasons I moved here was that the people in the administration were going to be supportive in aiming high.”

—Peter Strick, Pitt

THE MAN  
BEHIND THE  
MOMENTUM



**PERSON OF INTEREST**

I really enjoy your magazine. It makes me feel closer to home as an almost lifelong Pittsburgher.

I'm currently finishing my last year of internal medicine residency at Emory and applying to GI fellowships. Pitt Med changed my life; there, I built a group of lifelong friends, sometimes called the "Wu Crew," after our classmate Bryan Wu (MD '17).

In the Fall 2019 issue I especially enjoyed reading "The Phage Hunters" [by J. Bittel], "Food for Thought" [G. Jenkins' story about Pitt Med's new culinary elective], and the obituary for Peter F. Ferson (MD '73) [by R. Mennies].

I had the pleasure of working with Dr. Ferson in a small group. He once recalled for us a particularly bad Steelers game, during which he threw the remote. After that, he didn't watch football ever again. He preferred to place his passion elsewhere. I loved his no-nonsense, self-deprecating humor.

Keep up the great work!

Vladimir Lamm (MD '17)  
Atlanta, Ga.

**CORRECTIONS / CLARIFICATIONS**

In the Fall issue, we listed one of **Benedict Nwomeh's (Fel '03) titles incorrectly. Nwomeh directs the pediatric surgery fellowship at Nationwide Children's Hospital.**

**RECENT MAGAZINE HONORS**

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

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

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

**CORRESPONDENCE**

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

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

For address corrections:  
**Pitt Med address corrections**  
ATTN: Alexandra Rigby  
M-200K Scaife Hall  
3550 Terrace Street  
Pittsburgh, PA 15261  
E-mail: amr276@pitt.edu



Join the conversation on Twitter, @PittMedMag.



**Ryan Marino @RyanMarino · Oct 18**

I've received @PittMedMag for years & it's always inspired me to read about the visionaries from my home institution.

Never in a million years did I think I could be worthy enough to include. Getting this in the mail means more to me than I can say.

Thanks for believing in me.



**PHYSICIAN TAKES AIM AT FENTANYL FEARS**

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

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

"If that were possible, people would just touch drugs instead of injecting them," he says.  
Even people who should know better can succumb



Sometime in 1983, Jonathon Erlen was working at Falk Library's reference desk. It was a new job for Erlen, and things seemed to be humming along just fine. Then, in walks a man in full scuba gear; he picks out a medical journal, sits down in front

**CONTRIBUTORS**

For **FRANK HARRIS** ["The Man Behind the Momentum," "Blueprint," "Dean Machine," and "Polio Pioneers" podcast ad], creating more than 50 portraits for this issue was a personal record. He says it was "a pretty big job," but we think he accomplished the Herculean task with flying colors (or in black and white, as was the case here). Harris's work has been featured in *Vanity Fair*, *Harvard Magazine*, and *New Orleans Magazine*. He has two sons, and his partner, Teresa LaCaria, is a 2004 Pitt Med grad. Harris has been painting with his son, Maximus, who is on the autism spectrum; they aim to pitch a gallery exhibition of their work soon. Harris is also working on cover art for the Disability and Mental Health Summit, celebrating the 30th anniversary of the Americans with Disabilities Act.

A Chicago-based freelancer, **RACHEL MENNIES** [Class Notes] also has a connection to Pitt Med beyond her written work. Like Harris, she is partnered with a Pitt Med alum. Mennies says she enjoys keeping in touch with Pittsburgh through her writing. She is the author of *The Glad Hand of God Points Backwards*, finalist for a National Jewish Book Award and the 2013 winner of the Walt McDonald First-Book Prize in Poetry. Mennies is now writing a nonfiction book on insomnia and gender.

44

39

369



# PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, WINTER 2019/20 (DEC/JAN/FEB)

VOL. 21, ISSUE 4



4

## OF NOTE 3

New dean named.  
Health literacy boost.  
HIV in hiding.

## CLOSE-UP 7

Delivery persons heeded.

## INVESTIGATIONS 8

Man v. self.  
Nitty gritty details.  
Offbeat.

## 98.6 DEGREES 34

Buying time for a childhood disease.  
Sound approach to funding.

## ALUMNI NEWS 36

Modjoros on intimate medicine.  
RIP Crock, Dille, Fisher, Kisilevsky.  
Johnston teaches once, learns twice.

## LAST CALL 40

This med school is a dean machine.

## FOR REAL! 40 1/2

Blankies do heavy duty.



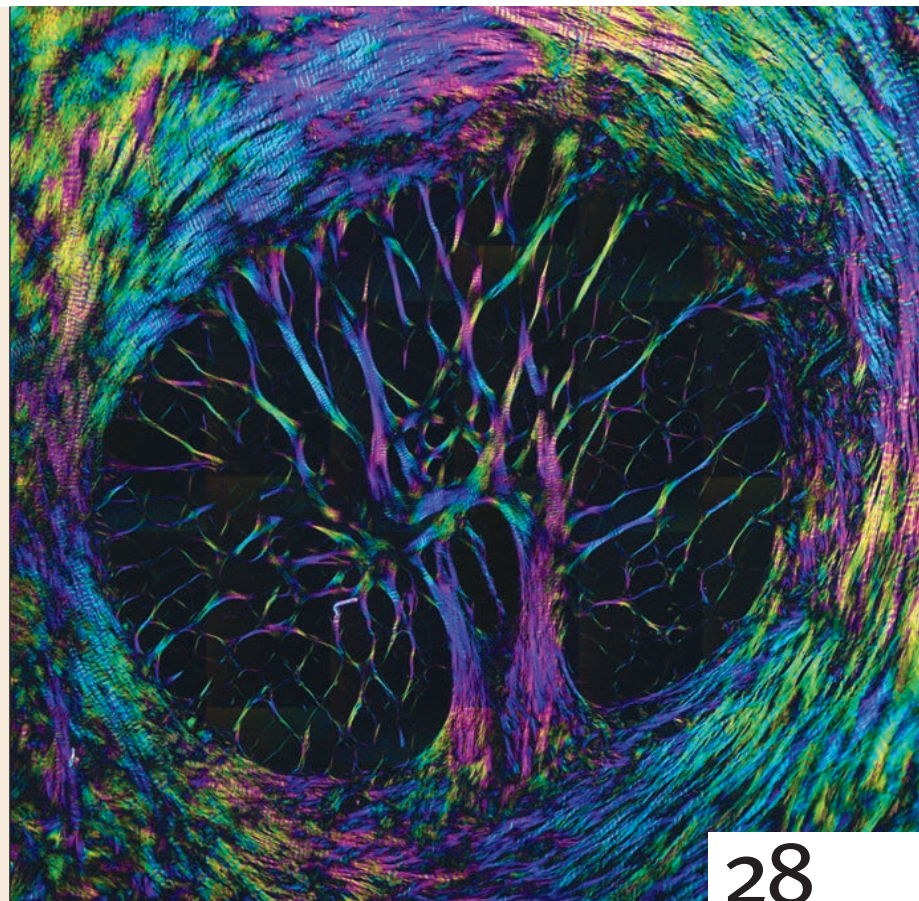
40 1/2



37

## COVER

Out of the mouths of colleagues: Art Levine's extraordinary legacy.  
(Cover: Illustration Frank Harris. Design Elena Cerri © 2019.)



28

## FEATURES

### The Man Behind the Momentum

12

A half-century ago, Art Levine set out to cultivate great science.

COVER STORY BY SHARON TREGASKIS

### Blueprint

18

The flourishing health sciences community here is very much by design.

INFOGRAPHICS BY ERICA LLOYD, ELENA CERRI,  
AND FRANK HARRIS

### Left of Bang

23

Doctors and public health experts trying to stop bloodshed.

BY GAVIN JENKINS

### The Forest, the Trees, and the Leaves

28

Ian Sigal surveys the ever-changing landscape of the eye.

IMAGE ESSAY BY ELAINE VITONE

# PITTMED

## PUBLISHER

Arthur S. Levine, MD

## EDITOR IN CHIEF

Erica Lloyd

## ART DIRECTOR

Elena Gialamas Cerri

## SENIOR EDITOR

Elaine Vitone

## ASSOCIATE EDITOR

Gavin Jenkins

## PRODUCTION MANAGER

Chuck Dinsmore

## INTERNS

Alyce Palko, Margaret Palko

## EDITORIAL ADVISORS

Jeremy Berg, PhD

Michelle Broido, PhD

Paula Davis, MA

Terence Dermody, MD

Robert Ferris, MD/PhD

Joan Harvey, MD

Joshua Levenson, MD '11

David Lewis, MD

Mylynda Massart, MD/PhD

Margaret C. McDonald, PhD, MFA

Kevin Rivera (Class of 2023)

Loren Roth, MD

Steven Shapiro, MD

Peter Strick, PhD

Ann Thompson, MD

Bennett Van Houten, PhD

Simon Watkins, PhD

Marshall Webster, MD, Res '70

## VICE CHANCELLOR, UNIVERSITY COMMUNICATIONS AND MARKETING

Ellen Moran

## ASSISTANT VICE CHANCELLOR, MARKETING

Kate Ledger



*Pitt Med* is published by the Office of the Dean and Senior Vice Chancellor for the Health Sciences in cooperation with the Office of University Communications. It is produced quarterly for alumni, students, staff, faculty, and friends of the School of Medicine. PR 6750

The University of Pittsburgh is an affirmative action, equal opportunity institution. © 2020, University of Pittsburgh

**T**he smallest sprout shows there is really no death;  
And if ever there was, it led forward life, and does not wait at the end to arrest it,  
And ceas'd the moment life appear'd.  
—Walt Whitman

The notion of regeneration can be considered in many ways. Here are three, starting with the fact that if you were a planarian flatworm, you could be cut into 16 pieces and, in a few days, there would be 16 of you. You'd grow 15 new heads along with all of your other important parts, and you'd be just fine. Every one of you, that is.

These fascinating animals caught the attention of Alejandro Sánchez Alvarado early in his career. No other researcher was paying attention to planaria when Dr. Alvarado decided to build a lab around them in 1995. First, he spent a year reading about thousands of species he might use for a career-building model. He decided on the freshwater planarian *Schmidtea mediterranea*, which is endowed with abundant pluripotent stem cells of a certain stripe that allow it to rebuild itself as needed.

Of course, you and I are not planaria, but there's a little flatworm in all of us. Human bodies churn out billions of new cells daily to keep things ticking, notably the skin and liver.

Dr. Alvarado visited Pittsburgh to give the Mellon Lecture at our annual Science Festival this fall. His lab at the Stowers Institute has developed molecular tools allowing him to uncover hundreds of genes related to regeneration and its intertwined mechanisms. Among other discoveries, he found a key molecular switch for regeneration that is not turned on in humans. Perhaps to the good, since evolution would likely not allow there to be 16 humans with identical affective and cognitive brains!

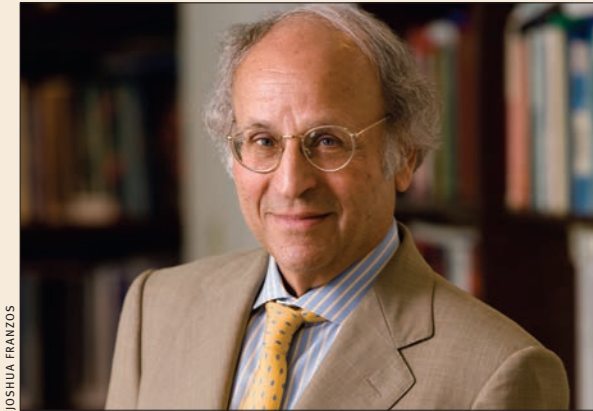
I keep thinking about Dr. Alvarado's talk, because it was brilliant, and because this is a time when resiliency and regeneration are needed more broadly.

In this regard, I was struck by a recent talk by Zanny Minton Beddoes, the editor in chief of the *Economist*. She speaks of the five shocks our society is now experiencing: the digital shock (artificial intelligence/big data); the economic shock (e.g., the manufacturing shift to high technology); the geopolitical shock (China's global ascendancy); the demographic shock (massive immigration waves); and climate. All five shocks are interdependent: We're undergoing a technological revolution that's creating a profound and widening skill and income inequality with great economic consequences. These consequences include demographic jolts as waves of migrants seek refuge from poverty and danger; in response, populism and nationalism are rising suddenly and globally. China seems poised to outpace the world. And our climate may well be out of control. As our climate system puts on epic and devastating spectacles, we can expect more shifts and shocks.

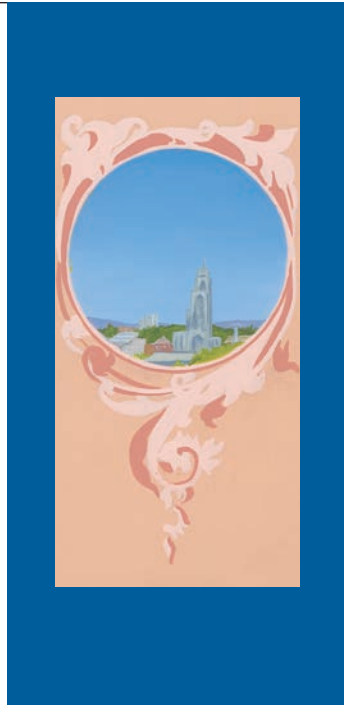
These can be frightening times, and it's easy to feel paralyzed. Yet, as Pittsburghers in particular have shown again and again, we have the ability to breathe new life into our world. After all, we got through the Industrial Revolution, which shocked our manufacturing and economic bases, led to massive but welcome immigration and global ascendancy, and turned the streetlights on in our smoky city at noon! This is our regenerative story. We reinvent ourselves and discover our own pluripotency.

Now for my own pluripotency, this little essay's third regeneration. Soon I will move to a new career as my decanal successor arrives: morphing into a physician-scientist intrigued with the challenges of research on the brain, applying what I know about cellular DNA damage and repair to neurons and glia, and hopefully keeping my own head—not 16!

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



JOSHUA FRANZOS



*Devoted to noteworthy happenings  
at the medical school*

## Shekhar Named Dean and Senior Vice Chancellor

Anantha Shekhar, an MD/PhD, nationally recognized educator, researcher, and entrepreneur who has made major contributions in medicine and life sciences, has been named senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of the School of Medicine at the University of Pittsburgh. His start date is set for June 2020.

Shekhar joins Pitt from Indiana University (IU), the nation's largest medical school, where he holds a number of leadership roles. These are: executive associate dean for research affairs, distinguished professor, associate vice president for university clinical affairs and research, executive vice president of academic affairs for clinical research at IU Health, and founding director of the Indiana Clinical and Translational Sciences Institute, the only statewide institute of its kind.

"This is a critical hire for the University of Pittsburgh," says Chancellor Patrick Gallagher. "Anantha's capacity to envision solutions, galvanize partnerships, and produce results is second to none, and his record of propelling both people and institutions to success is unparalleled. I could not be more excited to welcome Anantha into our community."

Shekhar has received continuous funding from the National Institutes of Health for basic, clinical, and translational research since 1989. He is known for sweeping and robust collaborations across the private, public, and philanthropic sectors.

### Among his many professional accomplishments:

- Growing the IU School of Medicine's research funding from the National Institutes of Health by 73 percent since 2015.
- Leading the Precision Health Initiative—a major strategic investment at IU with more than \$140 million in clusters such as genomic medicine and big data sciences. This initiative resulted in an estimated economic impact of nearly \$200 million in just four years, the hiring of more than 126 scientists, as well as the creation of four companies and recruitment of another to Indiana.
- Cofounding or leading five biotech companies, including Anagin, a



COURTESY/INDIANA UNIVERSITY

Shekhar

startup company that is developing treatments for post-traumatic stress disorder, traumatic brain injury, neuropathic pain, depression, Parkinson's disease, and Alzheimer's disease.

- Demonstrating a novel mechanism of action—the first in more than 70 years—that is being developed as a new approach to treating schizophrenia.
- Forming two commercial incubators within the Indiana Clinical and Translational Sciences Institute—one for therapeutics and another for medical devices—that currently host more than 15 companies in various stages of commercialization.
- Directing a laboratory that has developed highly regarded translational models for panic and related anxiety disorders that resulted in patents for novel therapies and the discovery of new treatments.

Pitt Provost and Senior Vice Chancellor Ann E. Cudd, PhD, who chaired the search committee, notes: "Anantha's exceptional and deep experience in basic research leading to novel, patentable therapeutics and in directing large, multi-institutional research initiatives, as well as being an award-winning teacher, will provide transformative contributions to our efforts going forward."

"I am honored and inspired to be joining one of the most respected medical and research communities in the world," Shekhar says.

"Building on the University of Pittsburgh's exceptional record of health sciences education, innovation, clinical excellence, and research preeminence is my top priority, and I look forward to advancing this goal in partnership with UPMC, for the greater good of society, in the months to come."

Shekhar will succeed Arthur S. Levine, an MD, who announced in January 2019 his intention to transition to a new research role within the University. (For more on his legacy here, see p. 12.)

—University Communications Announcement



AMIE OBIJINSKI/UNIVERSITY OF PITTSBURGH

## Overheard

### Jared Magnani: On Afib Literacy

Talking to a mechanic about transmissions can be frustrating if only one of you knows about cars. A lot of patients probably feel the same way when it comes to discussing chronic health conditions with their doctors.

The University of Pittsburgh's **Jared Magnani**, cardiologist and associate professor of medicine, wants patients with atrial fibrillation to become experts in their own care. Magnani, in collaboration with Tim Bickmore, a computer scientist at Northeastern University, is behind a pilot program that places smartphones with a mobile health app in the hands of Afib patients in rural Western Pennsylvania. The typical treatment for Afib, a heart rhythm disorder that can lead to blood clots, stroke, and heart failure, requires patients to adhere to a complex, long-term therapy to reset the rhythm and rate of blood flow. This includes tracking and reporting their symptoms, which can prove difficult for a first-year medical student, let alone a patient who is not health literate. The yet-unnamed app was designed as an intervention to coach patients on how to address the daily challenges of their disease. Study participants use the app to assess their symptoms, track their medicine intake, gauge their stress levels, and even record their own heart rhythm, thus returning some agency to the patient.

#### How did you end up pursuing this project?

As a cardiologist, I treat a lot of patients who experience chronic disease, and I find that there are tremendous obstacles toward their self care and their understanding of the disease. There are large barriers in terms of health literacy, as well as social limitations such as income, education, and transportation that impact how patients navigate health care. My aim is not to modify clinical care but to give something to the patient. The patient experience of atrial fibrillation is difficult because of its uncertain course. A patient could have a stroke at any time. Our goal for the patients enrolled in our program is to feel enfranchised so that they may deal better with *us*, so we can treat *them* better.

#### What can go wrong in the doctor-patient relationship when the patient isn't health literate?

At an appointment, a patient can hear a lot of gobbledygook—a lot of stuff said *at* them. We [doctors] do a poor job of listening, and we don't have a way of addressing the social determinants that will impact a patient's ability to adhere to health care. And, we don't have a way of addressing the anxiety, frustration, and depression that accompany chronic disease.

#### How does an empowered, health literate patient act?

That person is able to challenge their physician, ask questions, and clarify answers. I like that there is a platform included [in the app] that's about how to prepare for a doctor's visit. Users make a list by answering question prompts, and then review the list before the appointment. —*Nichole Faina*

## Class of 2023 Cheat Sheet

These incoming Pitt Med students have the kinds of backstories that reinforce one of our favorite topics: There is no one path to medical school.

**Marc Peretti was exposed to the rigors of medical school long before he arrived at Pitt Med this fall.** After graduating from Princeton University with degrees in mechanical and aerospace engineering, he followed his future wife—**Allison Serra**, assistant professor of obstetrics, gynecology, and reproductive sciences—to North Carolina, where she attended medical school. Peretti became a stay-at-home dad when the couple had their second child during Serra's residency at the University of California, Irvine. The Peretti-Serras moved to Pittsburgh when Serra landed a fellowship at UPMC Magee-Womens Hospital. Peretti gradually became interested in pursuing a career in medicine, and once their children entered school, he decided to apply to Pitt Med.

**After dropping out of high school, Solomon Johnson worked a series of odd jobs**—landscaper, dishwasher, stereo repairperson. Eventually, he landed a job as a busboy and bartender at a nightclub in New York. The nighttime hours gave Johnson time during the day to complete his GED and undergraduate degree at SUNY, Purchase. One day, Johnson read an article about a high school dropout who ended up attending the Geisel School of Medicine at Dartmouth, and he thought: *I could do that.* With support from a mentoring program, Johnson was able to gain valuable experience shadowing health care professionals before applying to Pitt Med.

**A few weeks before 9/11, David Wilson entered the United States Military Academy at West Point.** After commissioning as an officer, he completed two tours each in Iraq and Afghanistan. Later, he completed a program that included a master's in policy management at Georgetown University and service in the Pentagon. Though he found the work rewarding, he also craved change. He's now enrolled in the army's Health Professions Scholarship Program and will return to military service upon graduation from Pitt Med.

**Jasmine Hect was a first-generation college student at Wayne State University.** When a friend mentioned a lab researching brain development of babies, Hect's curiosity was sparked. She fell in love with the work and stayed after graduation to become the lab manager. Her mentors encouraged her to apply to MD/PhD programs, which would meld her interests in neuroscience research and the personal side of medicine. Now at Pitt, Hect says, "I feel like I'm exactly where I'm meant to be." —*Nichole Faina and Alyce Palko*

## FAR OUT

Screenwriter Geoffrey S. Fletcher once said, “I don’t have to go into outer space to write about an astronaut.” And Pitt docs don’t have to leave campus to assist with experiments in space. The McGowan Institute for Regenerative Medicine recently teamed up with the International Space Station U.S. National Laboratory. The collaboration will focus on microgravity life sciences research. What’s that? These folks will be doing out-there experiments like seeing if microgravity could allow 3-D printers to create complex tissue structures that are difficult to achieve under terrestrial conditions. Pitt people will develop Earth-based facilities to advance research and meet with partners; they’ll also coordinate with the ISS Lab on opportunities at the orbiting laboratory.

—Gavin Jenkins



## PAINFUL MYSTERIES

Endometriosis, a condition in which endometrial tissue forms outside of the uterus, creating lesions and scars, can take up to 10 years to diagnose. Approximately 6.5 million American women suffer from this painful disorder, and laparoscopic surgery is the only way to know if they have it. Women with undiagnosed endometriosis often seek emergency care for their pelvic pain, but the basic tests and imaging do not show abnormalities. This can result in years of pain without relief. In the meantime, “the impact on quality of life is massive,” says Nicole Donnellan, a Pitt associate professor of obstetrics, gynecology, and reproductive sciences who specializes in minimally invasive gynecological surgery.

As the director of the new Endometriosis and Chronic Pelvic Pain Center at UPMC Magee-Womens Hospital, Donnellan plans to transform how pelvic pain is diagnosed and treated. Using a tissue bank she collected from patients over eight years, she is developing a blood test to screen for endometriosis. In addition, she and other researchers will use the bank to learn more about the disease’s pathology and develop new treatment methods.

The center opened its doors in July. In addition to being a research hub, it provides comprehensive care to patients with pelvic pain, no matter the cause. Seventy percent of reproductive-age women experience pelvic pain; the cause might be gastric, urologic, neurological, or from something else. This means women in pain are often shuffled from doctor to doctor for years without relief. “My dream for the center is that we have a health navigator to fast-track people to the right specialist,” Donnellan says. “It’s my desire to empower my patients with options to make their day-to-day lives better.”

—Elizabeth Hoover

## HIV IN SPINAL FLUID

Doctors have managed HIV symptoms in patients for decades by driving infected cells into hiding. Though patients aren’t cured, they can maintain an undetectable viral load. But John Mellors, who holds the University of Pittsburgh Chair for Global Elimination of HIV and AIDS and is chief of infectious diseases, wanted to know where those cells might be lurking in the body.

With help from colleagues at Yale University and the University of North Carolina, Mellors and his team discovered that the brain acts as a sanctuary where HIV hides in spinal fluid.

The study, which was published in the *Journal of Clinical Investigation*, examined 69 patients who had been receiving HIV therapies for an average of nine years and for whom treatment had been working.

The study also revealed that these patients performed worse than noninfected controls on “a whole battery of spatial orientation, recall, calculation abilities, all kinds of performance tests,” notes Mellors. He says the study will both help how we treat HIV and how we think about viruses in general.

“We should be cognizant on a broader scale,” says Mellors. “The viruses we recover from may not be completely cleared from the brain.” —Evan Bowen-Gaddy



COURTESY MARISA ACOCELLA MARCHETTO

## IT'S GRAPHIC

Marisa Acoella Marchetto is a self-described “fashion-fanatic, about-to-get-married, big-city girl cartoonist with a fabulous life.” Then she found a lump in her breast. Her graphic novel, *Cancer Vixen*, was a creative response to her experience dealing with, and overcoming, cancer. A new genre known as graphic medicine uses comics to tell powerful stories about health and illness. Visitors to a 2019 Falk Library exhibition, *Graphic Medicine: Ill-Conceived and Well-Drawn!*, got a taste of Marchetto’s story (see frame to left). The work of five other graphic medicine artists was on display as well in the National Library of Medicine traveling exhibition. —Alyce Palko and Erica Lloyd

## Faculty Snapshots

**C**harles Darwin gave us the classic picture of gene evolution: parent genes passed on from one generation to the next, the most useful of them conserved. However, **Anne-Ruxandra Carvunis** studies a different kind of gene— orphan genes. The NIH gave Carvunis a New Innovator Award grant this fall to study a concept she pioneered, “proto-genes,” or genes that have no ancestors and seem to have emerged out of thin air. Carvunis is an assistant professor of computational and systems biology, a recipient of the L’Oreal-Unesco Award for Women in Science, and a Searle Scholar.



Carvunis

**Hydractinia**, a genus of ocean-dwellers that live on discarded shells, have the ability to tell whether other organisms are also hydractinian by touching them.

**Matthew Nicotra**, Pitt assistant professor of surgery and researcher in the Starzl Institute, received a National Science Foundation EDGE (Enabling Discovery through Genomic Tools) grant this year with colleagues at the University of Florida and National University of



Nicotra

Ireland to study the organism. Nicotra is interested in the fight-or-fuse genetics of these colony-forming salties. The “self” identifying mechanism used by *Hydractinia* can teach us about the innate immune system of humans, Nicotra believes. And this can help us understand how we recognize and reject transplanted organs.

**Dozens of Pitt and UPMC researchers have been awarded nine grants totaling more than \$32 million to curtail the opioid epidemic.** They’re investigating ways to improve prevention and treatment strategies for opioid misuse and addiction and to enhance pain management. The funding is part of the National Institutes of Health Helping to End Addiction Long-term, or the **NIH HEAL Initiative**. In fiscal year 2019, NIH HEAL awarded 375 grants across 41 states in an attempt to reverse the national opioid crisis.

“It’s clear that a multipronged scientific approach is needed to reduce the risks of opioids, accelerate development of effective nonopioid therapies for pain, and provide more flexible and effective options for treating addiction to opioids,” said NIH Director Francis S. Collins when he launched the initiative. —EBG and EL



Helping the Greater Pittsburgh Community Food Bank Produce to People program: from left to right, Jen Mihalo, Erica Hampton, Thuy Bui, and Ayo Ifidon.



## DELIVERY PERSONS HEED

The back of the car looks like the medical students just bought out a farmer's market. Several boxes rest there, filled with fresh produce—green cucumbers, yellow squash, red apples. Each carton is on its way to somebody's home on an October Saturday. They are almost too heavy to lift, but the students can manage one at a time. "It requires some muscle," says Thuy Bui, associate professor of medicine and director of the Social Medicine Fellows and home visit initiative at the University of Pittsburgh School of Medicine.

Partnering with the Greater Pittsburgh Community Food Bank Produce to People program, once a month, Bui and her med student team deliver the likes of broccoli, Brussels sprouts, and basic medical attention to patients in their homes. Their clients are referred through Alma Illery Medical Center in Homewood and UPMC Montefiore; people can also apply through the Community Engagement Center in Homewood (a Pitt partnership).

Casey Tompkins-Rhoades, a third-year medical student, says the program seeks out people "who sometimes get overlooked by the health-care system."

She and her classmates want to help break down barriers to good health that some Pittsburghers face—like limited mobility or financial issues.

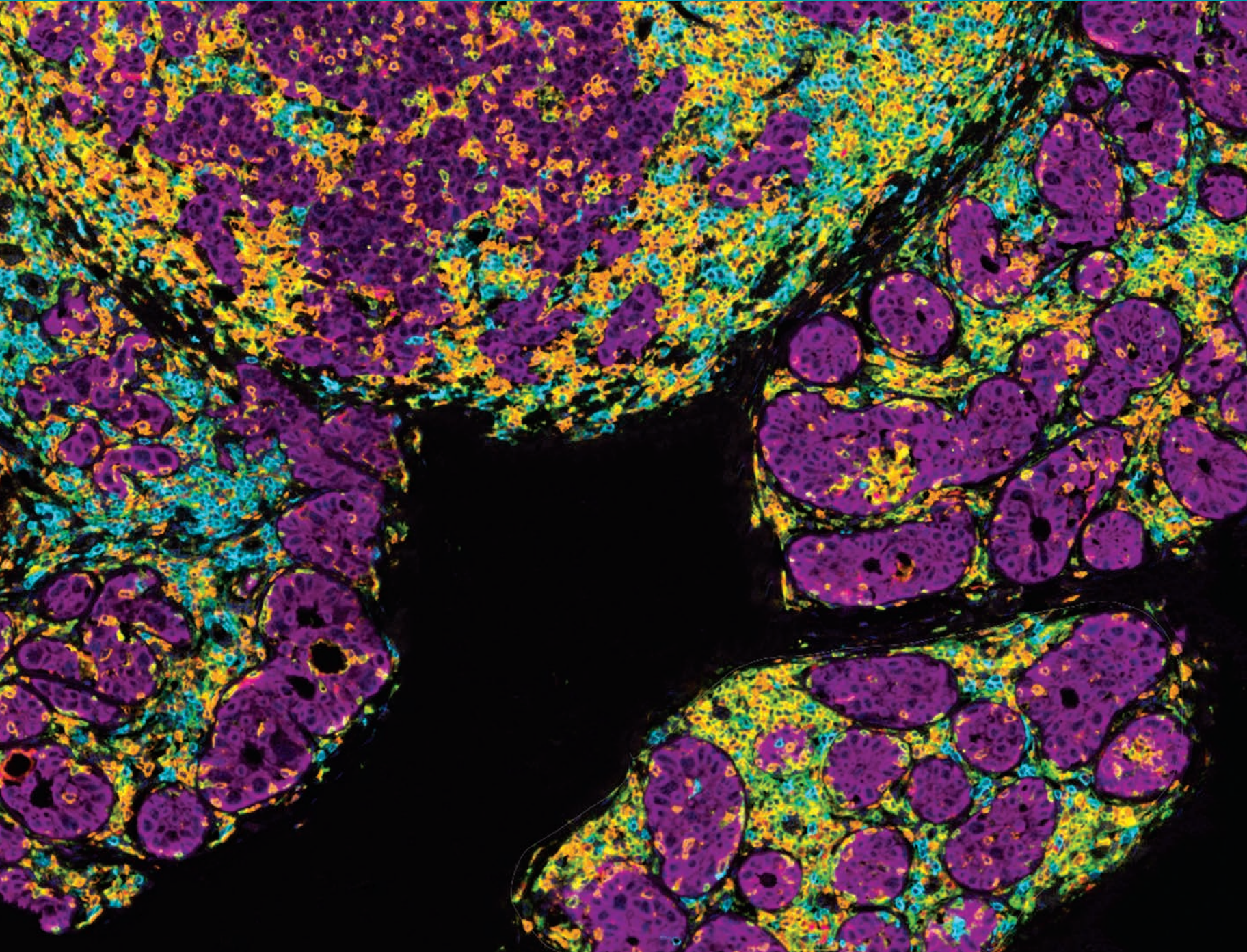
Lola Adebisi (Class of '21), lead student coordinator, describes how, after bringing the produce into a home, the team begins with a quick check of the patient's heart, lungs, and blood pressure. Then, the team addresses other topics appropriate to that patient.

If a patient has diabetes, for instance, the team might discuss sugar levels and help to set up the patient's next clinic visit with Bui, notes Adebisi. The team might also check on a patient's medications and take note of refills.

At the end of each appointment, the students make a point of asking patients about "whatever else is on their mind," says Adebisi, and this is where real connection happens. Adebisi says that she notices "how appreciative people are of seeing people of color in medicine. It's something I always take home with me and keep in my heart."

Something else she hears often: requests for return visits, with more fresh and colorful produce, of course. —Alyce Palko

—Photo by Aimee Obidzinski/University of Pittsburgh



Invasive ductal carcinoma (pink and purple) of the breast shows infiltration by various immune cells: CD8+ T cells (orange), B cells (cyan), and CD4+ T cells (green). Nuclei are blue.

# TO FIGHT CANCER, WE MUST FIGHT OURSELVES

THE IMMUNE SYSTEM OFTEN STOPS  
ITSELF FROM DESTROYING CANCER CELLS  
BY JASON BITTEL

People often think about cancer as though it's a foreign assault on the body. An alien growth. An invader that needs to be repelled.

But this is all wrong, says Dario Vignali, vice chair and professor of immunology at the University of Pittsburgh.

"The challenge is because it's not foreign. It's part of us," says Vignali, who is also coleader of the cancer immunology program and codirector of the Tumor Microenvironment Center at the UPMC Hillman Cancer Center. "It's transformed us, but it's, nonetheless, still us."

Interestingly, this is what can make cancer so damned difficult to combat. Tumors don't have a brain, says Vignali, but they do seem to know how our immune system works, and they use that knowledge to slip under the radar, short-circuit our defenses, and even co-opt the cells that should be fighting against them to do their bidding.

In 2019, Vignali and his team published two papers that explain some of the many ways tumors do what they do. But to understand them, you need to first understand a bit about how the immune system functions.

"We all know that one of the major cell types that can destroy cancer is called a cytotoxic T cell," says Vignali.

Also commonly referred to as CD8+ T cells, these battle-bots rove around in our blood looking for things they don't like.

When they find a target, such as a cell that's become infected with a virus, it's the CD8+s' job to annihilate it. Cancer cells can also draw the attention of CD8+s; however, the defender's search-and-destroy response doesn't always go as planned. Often, the CD8+s come screaming into the area, ready for a fight, only to power down like they've been hit with a tranquilizer dart.

Why? Well, it turns out that there's another type of T cell known as the regulatory T cell, or Tregs, whose job it is to make sure the CD8+s don't get carried away and start attacking things that don't need to be attacked. "Tregs are like the conductor of an immunological orchestra," says Vignali. "They are critical for ensuring that the immune system behaves itself. That it doesn't go too wild; that the parties aren't too festive." This helps limit unnecessary tissue damage that leads to autoimmunity or inflammation.

Scientists have long known that tumors tend to attract Tregs, which cause all the CD8+s that could be fighting the cancer to sort of go to sleep. But what's been missing is exactly how these cells communicate. That is, how does one kind of T cell make another kind of T cell turn off?

According to Vignali's April study, published in *Nature Immunology*, it all comes down to a couple of messenger molecules known as inhibitory cytokines—specifically,

cytokines known as IL-10 and IL-35. What's more, Vignali has shown that if you take away the Tregs' ability to produce those inhibitory cytokines, as he's done in experiments with mice, then the CD8+s can successfully eradicate the tumor.

In other words, we may be able to help our own bodies fight cancer by inhibiting the inhibitors.

Of course, there's more than one way to skin a Treg. And in another new study, this one published in *Immunity*, Vignali's team showed that a similar effect can be achieved by targeting a protein called neuropilin-1.

Neuropilin-1 "plays a key role in stabilizing regulatory T cells in this very hostile tumor environment," says Vignali. "So we discovered that if we target neuropilin-1, by genetically removing it from a Treg or blocking it with an antibody, now the Tregs collapse, and they don't work anymore."

And once the Tregs are down, the cytotoxic T cells can get back to work giving the cancer cells the boot.

All in all, if we're going to beat cancer, then we've got to get to know our own immune systems at least as well as cancer does.

"It's kind of like getting a car," says Vignali. "It looks great, but you don't really know how it works. So if it breaks down, you can't fix it.

"First we need to understand how it works. Then we can fix it." ■

There may be molecular switches that control life span and health span separately in the worm *C. elegans*.



IMAGE REPRINTED WITH TYPOGRAPHIC ALTERATIONS FROM NATURE COMMUNICATIONS; ARTICLE NUMBER: 3042; FRANCIS R. G. AMRIT ET AL. UNDER CREATIVE COMMONS CC BY LICENSE © 2019.

# NITTY

# GRITTY

THIS JUST IN RE LIFE SPAN AND HEALTH SPAN

BY ADAM REGER

**H**ow organisms manage to age well is not a question with straightforward answers.

In a surprising paper recently published in *Nature Communications*, Pitt researchers contribute to science's understanding of what promotes health span—the health and quality of life—which may be a better measure of aging than life span.

The team was led by Arjumand Ghazi, associate professor of pediatrics, developmental biology, and cell biology at Pitt. It all started when Ghazi was exploring the impact of the protein TCER-1 in the worm *Caenorhabditis elegans*. A long-standing dogma in the aging field has been that longevity and stress resistance go hand in hand, and genes that promote longevity often also support grit in the face of stress.

Ghazi's team expected the mutants lacking TCER-1 would be highly vulnerable. But when exposed to stressors—like extreme temperatures, harmful chemicals, or hostile pathogens—the worms without the protein were actually *more* resistant.

"It took us a long time to believe it," Ghazi says. In fact, they ran the experiments some 10 times over the next three years to

confirm these confounding findings. (In her lab, experiments are usually run at least three times.)

Interestingly, the researchers observed, the mutants lacking TCER-1 only showed enhanced protection against pathogens when the animal was fertile.

Why would this happen? Previously, Ghazi's lab had reported that TCER-1 promoted both longevity and fertility; perhaps the worms were diverting resources in fertility's favor at the expense of immunity, the team posited. They were allocating resources.

The team then tried boosting TCER-1 levels in a group of worms and found that fertility loss was less drastic in the presence of a pathogen. In contrast, in the control group—normal animals under the threat of infection—fertility took a big hit.

Ghazi speculates: "If everything is good, high levels of TCER-1 make an animal live longer and reproduce more." However, there's a price: When these worms get exposed to pathogens, they're not able to survive.

In addition to being more resilient, the worms without TCER-1 also showed improved mobility later in life. Named for its elegant movements, *C. elegans* is barely able to

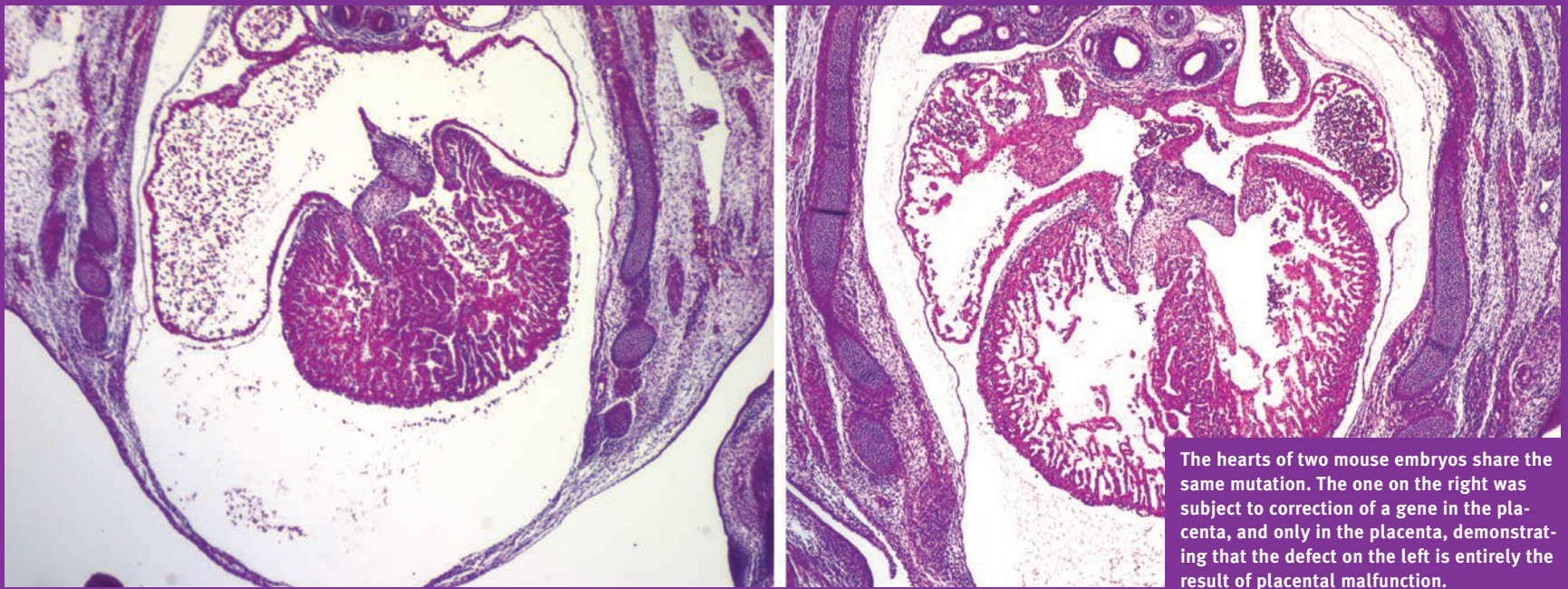
move by day 13 of its two-week life span. The mutant worms, however, were visibly spryer.

These findings bolster health span as a key part of understanding how organisms age. How long animals live is not, in itself, a good way to get a handle on the genes affecting the quality of their lives, Ghazi says.

Just as one 80-year-old human might be in a nursing home while another is out running marathons, she adds, the quality and health of life are of critical importance. Measuring health span is as challenging in worms as it is in humans, but in that challenge lie opportunities to understand the aging process more deeply.

Next, Ghazi hopes to test these findings in mice. Although she cautions against drawing parallels between worms and humans, the paper points toward exciting possibilities, like extending or preserving a woman's fertility or perhaps flipping a genetic "switch" to reallocate resources from fertility to immunity.

"This research makes a strong case for looking at whether higher organisms do the same thing," Ghazi says. "If that is the case, you can imagine manipulating it to affect the aging system, the reproductive system, the immune system." ■



The hearts of two mouse embryos share the same mutation. The one on the right was subject to correction of a gene in the placenta, and only in the placenta, demonstrating that the defect on the left is entirely the result of placental malfunction.

# OFFBEAT

PLACENTA HEALTH LINKED TO FETAL HEART DEFECTS

BY KRISTIN BUNDY

**I**n 1999, Yaacov Barak detailed findings in *Molecular Cell* suggesting a wholly new paradigm: a mechanistic connection between a placental defect and fetal abnormalities of the heart. “There was a lot of study into the causes of these heart defects,” says the associate professor of obstetrics, gynecology, and reproductive sciences at the University of Pittsburgh. “But they all focused on the heart.”

Barak stumbled upon this connection while studying the function of a gene known as PPAR $\gamma$  and its impact on fat cells. He performed a “knockout” experiment, in which the gene was disrupted in mouse embryos. The researchers hypothesized that without PPAR $\gamma$ —which encodes a protein considered the master regulator of fat cell differentiation—fat cells would fail to form.

Instead, they found that all of the embryos without PPAR $\gamma$  died early on because of placental defects. “And PPAR $\gamma$  is expressed nowhere else at the time of death except the placenta.” On top of that, they found heart defects in the embryos, but no evidence that PPAR $\gamma$  was expressed in the heart.

They decided it must be that whatever PPAR $\gamma$  does in the placenta must affect

the heart—and the data suggested as much. When they corrected PPAR $\gamma$  in the placenta, the fetal heart went back to normal.

Given that about one in 140 babies is born with congenital heart disease and must undergo surgery or endure frequent monitoring, you might anticipate that the news of this possible new therapeutic target was well received, especially by pediatric cardiologists.

But the biomedical community flat-out rejected the idea. It was an unambiguous experiment, says Barak, and still, “People said there must be an error they couldn’t put their finger on, or the results were just an anecdotal novelty.” Colleagues and grant reviewers called him delusional.

Barak, who came to Magee-Womens Research Institute in 2008, shelved the finding for years, focusing instead on placental development, fat cells, and PPAR $\gamma$  target genes.

Then, five years ago, he began to see his ideas crop up in the literature in epidemiologic studies. “Funny thing is, people didn’t remember where they heard the idea. We weren’t even cited,” he says. “Somehow what I did 20 years ago sank into the collective lore and remained because they knew something was there.”

In 2018, he applied for the Magee Prize,

a \$1 million grant for novel and out-of-left-field ideas to advance scientific discovery in women’s health. Competing against 26 other teams, Barak found his peers receptive this time, and won. The award was presented at the Magee-Womens Research Summit in October 2018.

With the award, he is currently collaborating with two researchers—Myriam Hemberger, an expert in placental development at the University of Calgary, and Henry Sucof, a heart expert of the Medical University of South Carolina. Their focus is to generate more precise mouse models, which, thereafter, they will use to interrogate the connection between the placenta and heart. “We’re doing this through different types of omics—mainly gene expression—as well as screens for potential hormones that might mediate the effect,” says Barak.

He also studies other unorthodox mechanisms. One that has caught his attention of late is how fat cells die. This is an offbeat approach, he says. “No one is studying it, and I think it’s one of the keys for understanding and treating type 2 diabetes.” He concedes such ideas might fall on deaf ears.

At least, at first. ■

# THE MAN BEHIND



A HALF-CENTURY AGO, ART LEVINE  
SET OUT TO CULTIVATE GREAT SCIENCE  
BY SHARON TREGASKIS

# THE MOMENTUM

**A**mong Arthur S. Levine's fondest memories of his Cleveland Heights childhood are the hours he spent with his cousin Don Glaser, a decade his senior. As local steelworkers leaned into the war effort, Don's parents, William and Lena Glaser, put in long hours at their mom-and-pop deli on the industrial side of town; extended family played a supporting role. "Every night, Don came to our house," Levine recalls. "We would play together, eat dinner."

Levine was 16 when Glaser, by then a junior member of the University of Michigan faculty, invented the bubble chamber, an apparatus that transformed the study of atomic particles and nuclear physics. Eight years later, when Glaser was awarded the 1960 Nobel Prize in Physics, Levine was in his first semester at Chicago Medical School.



In the next decade, Levine would earn his MD and board certification in pediatrics, complete a fellowship in hematology and oncology, and join the National Cancer Institute as a U.S. Public Health Service clinical associate. There he quickly ascended the ranks of physician-investigators, carrying out one of the first systematic investigations on the prevention and treatment of opportunistic infections in patients with cancer, as well as, with his colleagues, the first genetic and physical mapping of SV40, a mammalian tumor virus. Glaser, meanwhile, pivoted from physics to molecular biology, then launched Cetus Corp., the Bay Area biotech that would introduce polymerase chain reaction to amplify DNA and develop the cancer therapies interleukin and interferon. Says Levine: “We had a shared sense of how one contributes to the well-being of humanity.”

Around that time, Levine recalls having the transcendent, “F. Scott Fitzgerald moment” that would set the arc of his career. Lying awake at 3 a.m.—at about the same age Glaser had been when he met the king of Sweden—he took stock of his skills and aspirations. “Donald was a great scientist,” he says. “I thought I might not be a great scientist, but

He and colleagues discovered the first known protein that recognizes when DNA is damaged, for example by sunlight, and then, with other proteins, repairs the damage.

On his leadership potential, however, they heartily concur. Exhibit A: In 21 years as Pitt’s senior vice chancellor for the health sciences and dean of the School of Medicine, Levine has propelled Pitt Med from a good school with some well-known programs to a national treasure.

Exhibit B: In 2017, Levine got a call from “Building 1” at the NIH, asking if he would chair a blue ribbon strategic planning panel, “Advancing Biomedical Research in a Data-Driven Era” for the National Library of Medicine. The resulting report informed the current NIH strategic plan.

“Arthur Levine is a visionary and an inspiration to everybody in academic medicine,” says **Lloyd B. Minor**, a member of Pitt Med’s Board of Visitors and dean of Stanford Medicine. “He has helped usher in the future of medicine—most notably through his emphasis on facilitating and supporting basic science research.”

Since he was hired in 1998, Levine has overseen the creation of 10 academic departments and 10 new major centers and institutes. Of the medical school’s 31 current department chairs, he participated in recruiting and hiring 28—including **José-Alain Sahel**, perhaps the world’s top ophthalmologist physician-scientist. All five deans of the other health science schools have also been appointed during his watch. He’s simultaneously seen to a massive expansion of infrastructure—several million square feet of new construction and 10 core facilities—to support the research enterprise. Perhaps Levine’s greatest point of pride, however, has been the sustained rise in funds awarded to Pitt by the NIH, with the University consistently placing among the top five institutions in the nation, driven primarily by grants to the medical school, even as total NIH grant funding became more competitive.

Professor of critical care medicine and pediatrics **Ann Thompson** joined Pitt’s faculty in 1981; in 2014, Levine appointed her vice dean. “In the time he’s been here,” she



Early on in his deanship, Art Levine (shown here) proclaimed that every Pitt Med student would pursue a long-term research project. Ideas like this—initially met with skepticism—are now advancing biomedicine and have distinguished the school and its graduates.

Photo by Joshua Franzos

“In the time he’s been here, the institution has gone from kind of middle of the pack to one of the very best.”

I could be great at the kind of leadership that would further science and medicine, and, hopefully, do it in a way that is grand and elegant.”

Observers take issue with Levine’s stingy scientific self-assessment—he’s authored or coauthored 280 peer-reviewed papers, including early reports on naturally occurring viral recombinant DNAs and the molecular mechanisms that maintain the fidelity of the genome.

says, “the institution has gone from kind of middle of the pack to one of the very best.”

When Levine arrived in Pittsburgh, UPMC—the School of Medicine’s clinical counterpart and a vital financial partner—was under rapid expansion; as a consequence, clinical and academic faculty were joining Pitt at a brisk clip. Not everyone was happy in that growth environment; and while his predecessor, Thomas Detre, had focused on building Pitt’s clinical reputation, Levine was intent on cultivating similar excellence in the basic sciences. From the start, says **Jeffrey Romoff**, UPMC’s president and CEO, Levine has proven more than equal to the task. “Dr. Levine has navigated virtually every issue that emerged in the course of his





tenure—which was mine as well—with aplomb and intelligence,” he says. “He is fundamentally a gentleman and has a way of dealing with the subjects and the substance, rather than dealing with the noise.”

To wit: One of Levine’s first official acts was to mandate that all faculty provide his office with copies of their latest peer-reviewed papers. “I had assumed that was mostly for record-keeping and reference,” says Jeremy Berg, Pitt’s associate senior vice chancellor for science strategy and planning, whom Levine recruited from the NIH in 2011. “It turns out, he takes [them] home and at least reads the abstract.”

In 2018, those late-night reading sessions featured 1,800 papers—double the number pub-

lished by faculty in 1999. “I’ve always been amazed that whenever I mentioned a faculty member, he knew who they were, what they were working on, and how they were doing,” says Berg, formerly director of the National Institute of General Medical Sciences. “I couldn’t figure out how he managed to get so much information into his working memory.” The editor of this magazine recalls—every few months, for years—receiving reams of manuscripts the dean had identified as mutually interesting, with apologies that he might be missing some.

Such an egalitarian interest in the pursuits of all faculty, from the newest assistant professor to longtime department chairs, is rare, says

**Peter Strick**, founding scientific director of Pitt’s Brain Institute; Levine recruited Strick in 2000. “Art knows everyone on a first-name basis, follows their careers.”

And Levine isn’t finished when he’s read an abstract. Frequently, he picks up the phone to alert an author to another member of the faculty with complementary interests, a relevant animal model, or an apparatus that could further their work. “A lot of what I’ve devoted my effort to is encouraging people to socialize,” he says, “to take advantage of one another’s brains and their laboratories.”

That reach is not limited to national boundaries; the med school has significant clinical and research partners in Paris, Beijing,



and Palermo. (For 10 years, Levine served as scientific director of the Ri.MED Foundation, established by Pitt, UPMC, and Italian and regional Sicilian government entities to promote biomedical advances.)

While Levine relishes his self-appointed role as intellectual matchmaker, he's also formalized support for mentorship and collaboration throughout the School of Medicine. He's long advanced women in academic medicine. He appointed a number of "first" women department chairs, deans, and directors for Pitt's health sciences. And faculty development programs launched at his behest introduce junior hires to their counterparts across departments, coach them on the finer points of the tenure process and lab management, and connect them with senior colleagues who take a personal interest in their success. Levine, himself, hosts a monthly seminar for junior faculty from across the University. "He really wants to get people the exposure they need," says Berg. "He makes a commitment to both benefiting the careers of young people and also maximizing the investment the school makes when they're hired."

Levine's deep insights into the research enterprise have also been a boon for Pitt's recruitment of department chairs, institute directors, and the like. "His command of the range of important research issues within medicine is greater than that of anyone else I've ever known," says Ann Thompson. And when Levine brings senior scientists to Pittsburgh, they tend to stick around. "He can make sure that they're going to fit into this larger institution," she says.

**Angela Gronenborn** came to Pitt in 2004 as founding chair of the Department of Structural Biology (one of the country's few such departments in a med school). Since then, the UPMC Rosalind Franklin Professor of Structural Biology has stocked the basement of the University's Biomedical Science Tower 3 with a fleet of nuclear magnetic resonance spectrometers, cryogenically cooled electron microscopes, the array of gadgets used in X-ray crystallography, and a team of scientists who know how to use them. "Art has exquisite taste

"All of us know that, in the next few years, unless you're like Pitt, you won't be able to survive, support research, promote health for your patients."

"Art focused on his vision, that this would be the jewel in the crown of the medical school. He said, 'Just stick with it, and they will come because of it, and not in spite of it.'"

when it comes to science," says Gronenborn; those are almost the exact words used by dozens interviewed for this feature.

As a first-time department chair, Gronenborn asked Levine what professional development she should pursue to make the most of the opportunity, one still rarely afforded to women in the basic sciences. "He looked me straight in the eye, and he said, 'You know what you're doing—you go for what you think is best.'" His commitment has been unwavering, she says, whether she was requesting funds for new equipment, programmatic support, or feedback on a faculty search. "It always boils down to, *What is the best science you can do?*"

Back in 1977, Levine sat on the National Cancer Institute's Working Group on Education and Training. Two years later, as the committee concluded its study, the *New England Journal of Medicine* published "The Clinical Investigator as an Endangered Species," the first in what would become an increasingly strident series of reports on the shrinking ranks of physician-investigators—doctors best able to figure out how to bring breakthroughs in the lab to the benefit of patients.

By the time Levine arrived at Pitt, the school had a solid culture of medical student research participation. But it was optional. In 2004, Levine announced that, henceforward, every incoming student would complete an original project spanning the entirety of their enrollment. Despite an initial freedom to pursue anything from basic research to clinical

research, even creative pursuits like novels and film projects exploring the medical enterprise, the response was not universally positive.

Levine didn't balk at resistance from faculty and students, says **Steven Kanter**, who was vice dean at the time. And while the dean welcomed feedback to refine the policy, he didn't waver. "It was no different from the other kinds of things we did over the years," says Kanter, who now heads the Association of Academic Health Centers. "You have to be open and transparent and have a good, solid idea that's backed up with sound arguments. In a way, it's a privilege to be able to talk it through with very bright students and faculty—the idea gets better than it was originally."

Still, when **David Hackam** was summoned to Art Levine's office seven years later, the newly tenured professor of surgery and of cell biology and physiology felt an acute sense of dread.

"Getting a call from the dean is rarely a promotion," says Hackam. But that's what Levine had in mind. As an assistant professor, Hackam had launched START, a Department of Surgery program to engage students in clinical and research training. Levine had read the papers—both the young professor's and those authored by START participants—and he sought someone with the vision to propel the scholarly research project into its second decade. He invited Hackam to serve as associate dean for medical student research, then gave him *carte blanche* to invigorate the program. He counseled Hackam to hold steady as he imposed more rigor and introduced new coursework to help students make the most of the experience.

"Art focused on his vision, that this would be

the jewel in the crown of the medical school,” says Hackam. “He said, ‘Just stick with it, and they will come because of it, and not in spite of it.’” Today, requirements for medical students to pursue original research abound nationwide. “If duplication is the best form of flattery,” says Kanter, “Pittsburgh was flattered.”

These days, Hackam is the Garrett Professor at Johns Hopkins University, where he is also pediatric surgeon-in-chief and codirector of the Johns Hopkins Children’s Center.

“I learned a great deal from him about leadership,” says Hackam of Levine. “Art is a master of deploying subtlety and a master at using a sledgehammer when he needs it.” The sledgehammer was rarely wielded, in Hackam’s experience, in part because Levine has a knack for threading the needle himself. “He’s very wise and very smart, obviously, but also learned; incredibly so,” says Hackam. “Many leaders expect others to solve problems, but Art has a tremendous ability to come up with innovative solutions.”

Consider this: In 2006, the *Journal of the American Medical Association* published “Health Industry Practices that Create Conflicts of Interest,” coauthored by a mix of industry and academic medical center leaders. Soon after, Levine and **Marshall Webster**, then president of the University of Pittsburgh Physicians, chartered an industry relations committee to develop a policy governing everything from free lunches for medical students and the presence of sales reps in patient care areas to the distribution of drug samples, as well as industry-funded continuing education, ghostwriting, and faculty consulting.

That year, the biomedical industry spent more than \$25 billion marketing to doctors, including \$18 billion in free samples. The trick for the school would be preserving worthy upsides to the relationships—access to free samples for the neediest patients, plus clinical trials and other research partnerships—while curbing undue influence. Levine, whose first medical bag and stethoscope were graduation gifts from drug companies, demanded a proposal with teeth, complete with an actionable enforcement plan.

“It was my feeling, and that of my colleagues, that we needed to have a very precise, declarative policy,” he said at the time. A few months after the policy went into effect,

the American Medical Student Association awarded Pitt its Paul R. Wright Excellence in Medical Education Award, in recognition of the school’s commitment to professionalism, especially its initiatives to reduce pharmaceutical marketing influence.

Like the discussion around the scholarly research project, says Levine, the years of negotiation that led Pitt to institute one of the nation’s toughest industry policies reflects a mindset best articulated by 18th century English poet William Blake: “Without contraries is no progression.” (Levine has a deep appreciation for the humanities. He edited the *Columbia Review* as an undergraduate comparative literature major and aspiring poet.)

“Art has exquisite taste when it comes to science.”

Conflicting counsel comes from scientists, lawyers, ethicists, entrepreneurs, and academicians, he notes. In the end, this is to Pitt’s benefit, he says: “It’s hard for the brain to balance two competing ideas. Nonetheless, it’s those competing ideas and our effort to balance them that leads to creativity and productivity.”

Eight years ago, **Jeremy Berg** came to Pitt as part of the recruitment of his wife, **Wendie Berg**, to Radiology. Since then, Jeremy Berg has witnessed Levine consult widely and dig deeply before charting a course of action. “I always got the impression that if I said, *That’s a great idea! That’s brilliant!* he’d say, *You can do better than that.*

“No one would ever accuse him of being a hand-wringer,” adds Berg. “But he’s not afraid to ask people their thoughts and to listen. He doesn’t cut people off in the middle of their thoughts and say, *You’re wrong.* He just takes it all in.”

**Julie Freischlag**, CEO of Wake Forest Baptist Health, dean of Wake Forest School of Medicine, and a member of Pitt Med’s Board of Visitors, notes Levine figured out “way

ahead of the others” what sort of foundation and strong clinical partnership were needed to advance medicine: “All of us know that, in the next few years, unless you’re like Pitt with infrastructure and huge patient populations to study, you won’t be able to survive, support innovative research, promote health for your patients.”

“It is difficult to overstate Art Levine’s impact [here],” says Pitt Chancellor **Patrick Gallagher**. “[It has] been nothing short of transformative for the University, the city of Pittsburgh, the region, and, in many ways, the broader fields of medicine and health today.”

In January 2019, Levine announced that he will step down from his leadership roles when a to-be-named replacement can step in. But don’t look for him on the golf course. “There’s no biology to retirement,” says Levine. “You never heard of a lion retiring. They get up and go to work every day—hunting, foraging, and killing. And they do that until they crawl under a rock and die. They don’t retire; neither should we.”

Levine has already established a laboratory in the University’s Brain Institute. “Art is fearless both as a scientist and as an administrator,” says Strick. The Levine lab will probe cellular processes that may give rise to Alzheimer’s, the disease that in 2013 killed Don Glaser and affects 5.8 million Americans. Getting to the roots of the disease is imperative, says Levine.

“Every trial has failed to alter the course of Alzheimer’s by the time symptoms manifest,” he says, noting that as other biomedical researchers make progress against cancer and heart disease, the risk of living long enough to develop Alzheimer’s will only increase. “We have to try to understand what’s causing the disease and prevent it.”

Strick expects a significant uptick in participation in Brain Institute projects as Levine expands his lab’s research portfolio: “There are very few people who can read a CV and understand the talent in young people as Art can.

“He’s truly a remarkable judge of scientific character and scientific future.” ■

*Editor’s Note:* As we went to press, the Chancellor announced that Anantha Shekhar, an MD/PhD, will be Pitt’s new medical school dean and senior vice chancellor for the health sciences. See p. 3.



# BLUEPRINT

## THE BIG IDEAS

How do you take a good med school and position it in the very top tier of research institutions?

It seemed to happen naturally as Arthur Levine was pursuing some big ideas.

### Rear physician-scientists

So we have docs to translate new discoveries

**HOW?** ELEVATE MED STUDENT RESEARCH BY ESTABLISHING MANDATORY 4-YEAR SCHOLARLY PROJECT AND O'MALLEY RESEARCH AWARDS. ♦ PRESENT OTHER FORMAL OPPORTUNITIES LIKE CLINICAL AND PHYSICIAN SCIENTIST TRAINING PROGRAMS. ♦ PAIR EACH MED STUDENT WITH A PATIENT, SOMEONE THEY'LL GET TO KNOW OVER 4 YEARS WHO'S DEALING WITH A COMPLEX CHRONIC DISEASE. ♦ SUPPORT FACULTY EXCELLENCE BY TRAINING JUNIOR FACULTY ON RUNNING SUCCESSFUL LABS, OFFERING COMPETITIVE BRIDGE GRANTS IN RESPONSE TO DIFFICULT FEDERAL FUNDING LANDSCAPE, SALUTING AND LEARNING FROM MASTER EDUCATORS, AND PROMOTING DIVERSITY AND INCLUSION.

### Nurture basic sciences

**HOW?** CULTIVATE TOP TALENT AND BUILD ENVIABLE RESOURCES: ADD 10 DEPARTMENTS. ♦ BUILD ON INFRASTRUCTURE – 3 NEW BUILDINGS, 3 ADDITIONS, AND COUNTING. (THAT TRANSLATES TO SEVERAL MILLION SQUARE FEET OF NEW CONSTRUCTION AND RENOVATIONS.) ♦ EXPAND CORE FACILITIES. (LIKE IMAGING, GENOMICS AND OTHER OMICS, ... ) ♦ FURTHER STRENGTHEN DATA ANALYTICS CORPS AND LIBRARIES. ♦ ESTABLISH 10 MAJOR CENTERS AND INSTITUTES. ♦ START 7 NEW PHD PROGRAMS. ♦ LOOK OUT FOR THOSE JUST GETTING STARTED IN THEIR CAREERS, NOTABLY POSTDOCTORAL FELLOWS. ESTABLISH OFFICE TO SUPPORT THEM.

So we have discoveries to apply to the clinic

### Spark synergy

Connect the dots

**HOW?** SPONSOR SCIENCE FESTIVALS, SENIOR VICE CHANCELLOR LECTURE SERIES, AND OTHER HIGH-PROFILE SYMPOSIA. ♦ PUBLISH *PITT MED* MAGAZINE AND OTHER COMMUNICATIONS. ♦ HOST LUNCHES WITH MED STUDENTS. ♦ READ ALL FACULTY MANUSCRIPTS. ♦ CHAMPION UNIVERSITY-WIDE EFFORTS TO COMMERCIALIZE DISCOVERIES. ♦ POINT PEOPLE TOWARD POTENTIAL COLLABORATIONS AND RESOURCES.



# Increase health spans

The hope

Ask

WHAT'S THE RIGHT TREATMENT FOR EACH PATIENT?

WHAT ARE THE OBSTACLES TO GOOD HEALTH?

Prize

CREATIVITY  
DIFFERENT PERSPECTIVES  
TEAM SCIENCE AND CARE

- ◆ BY ERICA LLOYD
- ◆ ILLUSTRATIONS FRANK HARRIS
- ◆ DESIGN ELENA CERRI
- ◆ ALYCE PALKO CONTRIBUTED

## MAJOR PARTNERS

@

UPMC

OTHER PITT ENTITIES

CARNEGIE MELLON

GLOBAL AFFILIATES

PITTSBURGH

### THESE PARTNERSHIPS GO BEYOND THE EXPECTED, FOR INSTANCE:

**UPMC** is building a one-of-a-kind vision and rehab tower that's attracting some of the best scientists from around the world who want to end blindness.

Extensive relationships with all **Pitt** schools, notably the Dietrich School/Pitt Med Center for Protein Conformational Diseases partnership.

**Carnegie Mellon** and Pitt's joint graduate programs in neuroscience and computational bio have brought worldwide recognition to both institutions.

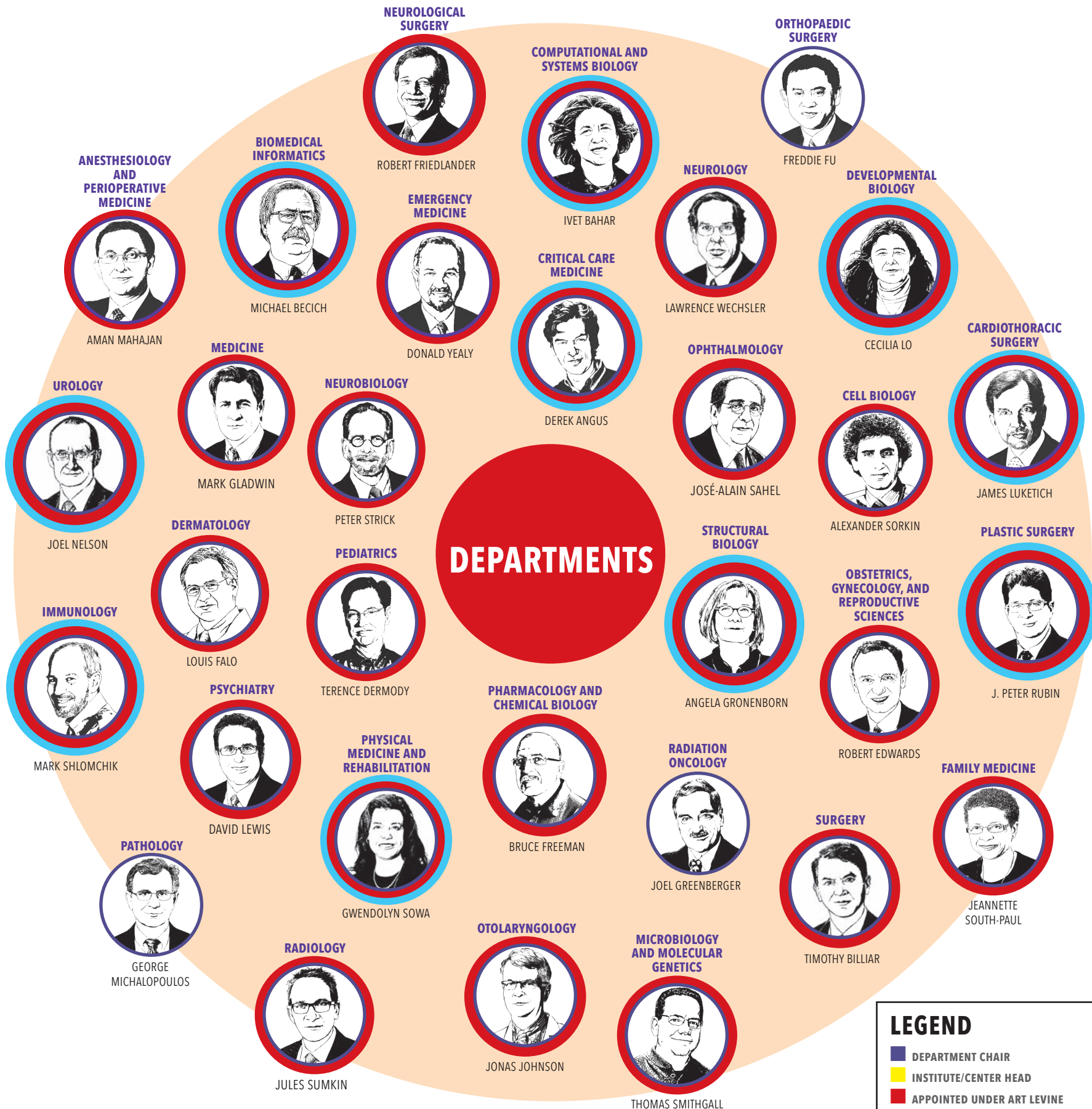
Pitt Med helped **Kazakhstan** establish a medical school and is training med students from **Tsinghua University**, "the MIT of China," in a two-year basic research program.

**Pittsburghers** will help find new cures. Our city is the first national site of All of Us, the NIH's historic precision medicine effort.

# BLUEPRINT

## THE MAKERS

Levine's winning formula: Lure in extraordinary people, support them, let them do their jobs.



### LEGEND

- DEPARTMENT CHAIR
- INSTITUTE/CENTER HEAD
- APPOINTED UNDER ART LEVINE
- LEVINE ESTABLISHED DEPARTMENT/INSTITUTE/CENTER

**INSTITUTE FOR  
PRECISION MEDICINE**



ADRIAN LEE

**VASCULAR MEDICINE  
INSTITUTE**



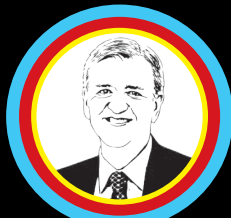
MARK GLADWIN

**AGING INSTITUTE**



TOREN FINKEL

**HEALTH POLICY  
INSTITUTE\***



A. EVERETTE JAMES

**CENTER FOR VACCINE  
RESEARCH**



W. PAUL DUPREX

**INSTITUTE FOR CLINICAL  
RESEARCH EDUCATION**



DORIS RUBIO

**BRAIN INSTITUTE**



PETER STRICK

Pitt becomes a place where cross-pollination is expected.

**MAJOR CENTERS**

**AND INSTITUTES**

Nearly **80 percent** of Pitt's 2018 NIH funding went to the School of Medicine. Since 1998, the University of Pittsburgh has ranked among the **top 10** recipients of NIH funding.

**NIH FUNDING  
AT THE UNIVERSITY  
OF PITTSBURGH**

**1998**

**\$169 MILLION**

**2018**

**\$578 MILLION**

**BTW, THAT TRANSLATES TO  
AN ESTIMATED 24,000  
ADDITIONAL JOBS.**

**THOMAS E. STARZL  
TRANSPLANTATION  
INSTITUTE**



FADI LAKKIS

**CLINICAL AND  
TRANSLATIONAL SCIENCE  
INSTITUTE**



STEVEN REIS

**UPMC HILLMAN  
CANCER CENTER**



ROBERT FERRIS

**MAGEE-WOMENS  
RESEARCH INSTITUTE**



YOEL SADOVSKY

**PITTSBURGH  
INSTITUTE FOR  
NEURODEGENERATIVE  
DISEASES**



J. TIMOTHY  
GREENAMYRE

**RESEARCH,  
UPMC WESTERN  
PSYCHIATRIC HOSPITAL**



DAVID LEWIS

**MCGOWAN INSTITUTE FOR  
REGENERATIVE MEDICINE**



WILLIAM WAGNER

**DRUG DISCOVERY  
INSTITUTE**



D. LANSING TAYLOR

\*HEALTH SCIENCES POLICY INSTITUTE EXPANDED AS A UNIVERSITY-WIDE INSTITUTE.

# BLUEPRINT

## FLOURISHING COMMUNITY

### PITT MED SCHOOL APPLICANTS

FALL 1998: 4,720

FALL 2019: 7,013

(FOR ABOUT 148 SLOTS)

### CLASS OF 2019 SCHOLARLY OUTPUT

346 Presentations

63 Awards

174 Submitted papers

46 Manuscripts in progress

108 Summer research projects

### PITT MED FACULTY DISTINCTIONS

2 AMERICAN ASSOCIATION OF ARTS AND SCIENCES MEMBERS

6 NATIONAL ACADEMY OF SCIENCES MEMBERS

7 PRESIDENTIAL EARLY CAREER AWARDS FOR SCIENTISTS AND ENGINEERS

25 NATIONAL ACADEMY OF MEDICINE MEMBERS

61 AMERICAN SOCIETY FOR CLINICAL INVESTIGATION MEMBERS

43 ASSOCIATION OF AMERICAN PHYSICIANS MEMBERS

204 ENDOWED CHAIRS

### ON THE SHOULDERS OF GIANTS\*

1 NOBEL LAUREATE\*\*

1 NATIONAL MEDAL OF SCIENCE WINNER

4 LASKER AWARDEES

\*DECEASED PITT MED FACULTY

\*\*NIELS JERNE AWARDED WHILE AT BASEL INSTITUTE FOR IMMUNOLOGY

### HEALTH SCIENCES THRIVE

#### SENIOR VICE CHANCELLOR



ARTHUR S. LEVINE  
MEDICINE

#### DEANS



BERNARD J. COSTELLO  
DENTAL MEDICINE



ANTHONY DELITTO  
HEALTH AND REHABILITATION SCIENCES



JACQUELINE DUNBAR-JACOB  
NURSING



A. EVERETTE JAMES  
(INTERIM)  
PUBLIC HEALTH



PATRICIA D. KROBOTH  
PHARMACY

### OUT OF THE LAB

The health sciences were fertile ground for innovation in FY 2019.

Invention disclosures: 308

U.S. patents: 83

Licenses, options, deals: 152


Start-ups: 15

### VERY HEALTHY

Pitt schools of the health sciences are among the finest in the nation. ♦ The School of Health and Rehabilitation Sciences is in the top 5 percent of schools in the United States at which to study health professions according to College Factual. *U.S. News and World Report* recently ranked its physical therapy program 1st and 4 other SHRS programs in its top 7. ♦ In 2016, *U.S. News* ranked the School of Pharmacy 9th

among 125 PharmD-granting institutions. ♦ Six School of Nursing programs were in the publication's top 10 in 2017. And Pitt Nursing ranked 6th in federal research funding in 2018. ♦ Pitt Dental Medicine ranked 4th in federal funding for dentistry programs for 2017. ♦ Pitt Public Health is among the top schools in the country in research dollars per faculty member.





Police guard the Route 91 Harvest Festival in Las Vegas following a mass shooting in 2017. Preventing massacres and other violent acts—a practice known as threat assessment—has become a focus for some in medicine, including Pitt Med's John “Jack” Rozel.

(Photo: Gian Sapienza/Getty Images)

# LEFT OF BANG:

PREVENTING A DISEASE CALLED VIOLENCE

BY GAVIN JENKINS

**W**hen Raquel Forsythe was a general surgery resident at University Hospital in Newark, N.J., in the late 1990s, she treated a 17-year-old boy who had been shot. He was mixed up in the kind of street violence that was endemic to his neighborhood.

Reading his chart, Forsythe noticed he also had diabetes. She began to talk to the teenager about controlling the disease, but he cut her off. “He looked up at me and said: *Do you really think my diabetes is what’s going to get me, Doc?*”

The young man had a point. Approximately 20 percent of homicide victims in this country are people who have already survived violent injuries like a gunshot wound. And African American children in America are about 10 times more likely to be victims of a gun-related homicide than white kids, whether they are directly involved or bystanders to conflicts.

Forsythe took his words to heart. Now medical director of trauma at UPMC Presbyterian and assistant professor of surgery and critical care medicine at the University of Pittsburgh, she believes doctors have an opportunity to intervene and try to break the cycle of violence. “As trauma directors, our role is to say: *Here’s a teachable moment. Now, what can we do to change whatever’s happening in your social situation that led to this injury? And how can we move forward to keep you safe?*”

If violence were examined like a disease, as recommended by Richard Garland, an assistant professor in Pitt’s Graduate School of Public Health and a former gang member, then “whatever’s happening,” as Forsythe puts it, translates to the symptoms. And Garland can recite those as if they are state capitals: poverty, a lack of education and job opportunities, addiction, mental health issues, and tendencies toward violence within one’s narrow network (friends or family within a community).

An activist and mediator in Pittsburgh communities for more than 25 years, Garland has seen how violence takes hold. “A boy grows up poor with his father in jail,” he says. “His mom is never home because she’s working multiple low-paying jobs. The boys on the corner are always there. So, he quits school,

and he gets caught up in drugs and gang life. Follows in his father’s footsteps.”

Garland, 66, wants to stop the disease from spreading further. He oversees Pitt’s Violence Prevention Initiative, which consists of two programs: Homicide Review and Gunshot Recurring Injury Prevention Services (GRIPS).

As gunshot victims recover at one of UPMC’s trauma centers, a social worker at the hospital asks if they’d like to meet with Garland and learn about GRIPS. If they say yes, Garland talks to them in the hospital. And after they’re released, he might help them find a job and move out of their neighborhood, thanks to donations from the Urban League, Allegheny Link, and the Urban Redevelopment Authority.

“Even if they say they don’t want help, I make sure they get my card,” Garland says. “A lot of times, they’ll call me later on, when they get out of the hospital.”

For patients with psychological needs that aren’t being met, Garland might help them connect with UPMC resolve Crisis Services (resolve is spelled with a lowercase “r”). The program’s 150-member staff (which includes mobile units) offers free crisis counseling and support to people of all ages.

John “Jack” Rozel is medical director at resolve and an associate professor of psychiatry and adjunct professor of law at Pitt. He also recommends cases to Garland and is beginning to build a partnership with UPMC’s trauma centers that will be similar to the one GRIPS has.

These partnerships won’t always be enough. Garland knows that some aggression can’t be

stopped. One afternoon, after visiting a gunshot victim in the hospital, he sought out the shooter through his connections and asked whether the situation could be settled peacefully.

“Dude looks at me and says: *Look, you gonna be the one who gives me 300 grand?*” Garland says. “And so he’s gonna go after him again, because it’s a pride thing. Dude says: *If I don’t do nothing to him, I can’t make it in this game. Everybody else is gonna be coming at me.*”

**R**ozel (Res ’04, Fel ’05) became resolve’s medical director in 2010. He and resolve’s clinicians focus on being “left of bang.” A term that comes from the U.S. Marines, left of bang refers to action prior to a deadly force incident. (Picture a timeline moving from left to right: “Bang,” or an attack, is in the middle of the line.)

Emergency medicine professionals like Forsythe typically deal with the right of bang, or the aftermath of violence. But that’s beginning to change. Violence prevention has become a focal point within the medical community here and elsewhere in the country, while experts in other disciplines examine how acts of brutality are born and how they spread.

Rozel’s work in this field falls under two categories: threat assessment, which is an evaluation of how much risk someone may pose, and threat management, an individualized plan to decrease the risk the person poses.

He says that “most acts of violence stem from a grudge.”

His resolve team members intervene in escalating disputes between neighbors, between bosses and employees, between tenants and landlords. And they step in to try to keep everyone safe in domestic disputes. (Our next issue will feature an expanded discussion dedicated to intimate partner violence.)

The resolve team also has helped prevent potential mass shooters from acting. One day, Rozel received a phone call from an outpatient psychiatrist—one of her patients was having homicidal fantasies. The patient, an adolescent boy, had admitted to thinking about shooting people at his school. Then Rozel heard from one of his contacts in law enforcement. The school resource officer had already flagged an



Mourners gather at a vigil on Franklin Ave. in Wilksburg, Pa., for mass shooting victims who were ambushed at a party in 2016. The death toll included five adults and an 8-month-old fetus. Richard Garland, of the Graduate School of Public Health, acts as a mediator to try to prevent conflicts from turning deadly. (Photo: John Heller/Pittsburgh Post-Gazette)

anonymous online profile of a person who'd been praising the 1999 Columbine High School shooting. After an investigation, they determined that the profile belonged to the boy.

"Everyone's really worried," Rozel says. "But no one is thinking, *This is a kid who needs handcuffs.*"

Through Rozel's coordination, the patient's parents sat down with their son's treatment team, school officials, and law enforcement. After what Rozel describes as a "frank and open conversation," the boy received the treatment he needed and successfully and safely returned to school.

A lot of people assume mass shooters suffer from a mental illness. Yet only about 25 percent of mass shooters have a psychiatric disorder. Rozel says that number is between four and 12 percent when all forms of violence are considered. In Allegheny County between 2001 and 2008, one in six homicide defendants were identified as having a psychiatric issue.

"Of the people with a psychiatric illness who act violently, some of them are absolutely

suffering from delusional beliefs. But there's not a clear connection for all of them," Rozel says. "It's more likely than not that they are engaging in violence despite the psychiatric ill-

ness, not because of it." They often struggle to interact socially or function physically.

While we are discussing misconceptions, Rozel would like to point out that our schools are safer than they seem—they're not where kids are typically killed. In 2019, the CDC reported that 98 percent of incidents involving children killed by firearms occurred outside of schools. Mass shootings in schools are terrifying and heartbreaking, yet still, when it comes to where children die from gun violence, "it's happening in the home and in the community," Rozel says.

He adds that many more high school and elementary school students are becoming trau-

matized from years of mass shooter drills. He'd like to see schools and communities focus as much on prevention, like recognizing people at risk of violence early on and fostering healthy

social environments, as they do on response to violence.

Rozel believes that threat assessment and threat management techniques work as well with a possible mass shooter or gang member as they do with someone who might harm a spouse. People who are close to engaging in a violent act tend to express their intentions, he notes.

"Most people don't just snap," Rozel says. "They usually threaten the person or people they intend to harm directly. Sometimes they tell a lot of people, and those comments often get thrown away. That person thinks: *People are always making threats. Or: He didn't really mean anything by it.*"

### "Most acts of violence stem from a grudge."

Listening is the key. Rozel learned that lesson as a freshman at Brown University, when he answered phones at a center with a suicide hotline. In high school, he had worked as an EMT and dreamed of a future in emergency medicine. But, at the hotline, he was astonished by how he could help callers simply by expressing empathy. After medical school at Brown, he moved to Pittsburgh and was mentored by Edward P. Mulvey, an expert on the links between mental illness and violence who directs Pitt's law and psychiatry program.

"Here I am now, over 25 years later, and listening is always the most important part of my job," Rozel says.

**P**olitical violence from extremists can start with a grudge, as well. Violent radical actors—white supremacists or Islamic extremists, for example—tend to be upset over what they see as injustice, and they want to respond to those perceived slights by creating what they believe to be a better society. When met with resistance, particularly any form of repression from a government, an extremist might escalate to violence.

"If they're already engaging in violence, they increase the level of that violence," says Michael Kenney, program director of international affairs at the Graduate School of Public and International Affairs (GSPIA), who examined al-Muhajiroun (which translates to the Emigrants) in *The Islamic State in Britain: Radicalization and Resilience in an Activist Network*.

"So, there's a classic action, repression, escalation, and violence dynamic," he says.

Kenney says that for most Muhajiroun he interviewed, Islamic extremism was a phase. The group spreads its ideology by attracting young men and women who want to rebel against their families and replace Western society with a caliphate. Many al-Muhajiroun work regular jobs while they are involved with the group. Eventually life—the desire to get ahead at work, start a family—tends to get in the way of starting a revolution. They leave the extremist group to lead normal lives.

White supremacist networks, like other radical groups, attract new followers online,

but they usually do it by claiming to have secret knowledge of a plot to harm white people, according to Kathleen Blee, the Bettye J. and Ralph E. Bailey Dean of the Kenneth P. Dietrich School of Arts and Sciences and the College of General Studies. Blee examined white supremacy in her 2017 book, *Understanding Racist Activism: Theory, Methods, and Research*.

Blee says that the plot often revolves around a fabricated threat that is imminent, and that urgency usually drives people to act violently.

White supremacist violence can spread through a contagion effect, according to Kenney. When a white supremacist commits a mass shooting, the shooter sometimes leaves a manifesto behind, and his words may inspire others. They may leave manifestos, as well, inspiring more acts.

"We have to be careful that we don't help glorify the perpetrators," Kenney says. "Because that contributes to the contagion effect. I do think the media has gotten smarter about not naming perpetrators or showing their image over time."

Extremist networks have expanded enormously through social media.

Blee notes that tech companies like YouTube have attempted to confront the spread of terrorism, specifically white supremacy, but they still have a long way to go.

"With YouTube, you're just redirected down an abyss of white supremacy very quickly," Blee says. "That means that people who aren't really searching for that topic get started on the process. They get pulled into these sites. Not just sites, communities."

**W**hat do we know about the biology of violence?

In 1949, Walter Hess won the Nobel Prize in Physiology or Medicine for using deep brain stimulation in animals to evoke behavior. Hess triggered aggression in cats by releasing weak electrical currents to different parts of the hypothalamus—a small region near the base of the brain that releases hormones and regulates body temperature.

"There's been evidence for a long time that the basic circuits for attack and rage, the

underlying elements of violence, are kind of built into the brain, hardwired," says Peter Strick, Distinguished Professor and chair of neurobiology at Pitt. "What we have above those basic circuits, are in a sense, the cognitive control circuits and emotional control circuits that modulate how we engage those very basic motor and behavioral programs."

To understand how the basic circuits become more easily triggered in some people, Strick points to Harry Harlow's classic study of monkeys. In the 1930s at the University of Wisconsin-Madison, Harlow separated infant monkeys from their mothers at birth and isolated them. When the monkeys became sexually mature, they attacked their cagemates and their human handlers. These were cagemates and handlers who had been friendly with the monkeys for years. The monkeys who had spent time with their mothers did not show the same unprovoked aggression.

This study may not translate directly to humans, in terms of maternal separation, but: "There's something about an early adverse life experience, when the brain is developing, that can lead to—particularly in these isolated monkeys—unprovoked aggression," Strick says.

Brain development can be stunted a number of ways—poor nutrition, living in poverty, and physical and emotional abuse are some of the most common culprits.

Strick says that when a child is harmed by factors like these, it can lead to depression, addiction, and violence as an adult.

"That's why the developing brain is a brain at risk," he says.

**T**he average bullet travels 2,500 feet per second, roughly 1,700 miles per hour. Bullet cases—the cylinder that holds the ammunition—are made of copper, steel, or brass. When these projectiles hit the human body, they don't cut a clean path through tissue like a knife would.

Forsythe knows this all too well.

"I am, unfortunately, an expert on gun violence," she says.

A bullet possesses energy, which causes injury outside the path it travels. It creates a

temporary cavity as it passes through tissue, and there is a ripple effect of damage. If a bullet from a 9-millimeter handgun pierces a human liver, it creates a hole that disrupts an area that is three-quarters of an inch wide. A bullet from a rifle damages everything within 3 to 4 inches around the cavity's path. If it strikes the liver, the organ is likely destroyed.

"A bullet can splinter bones and wreak havoc on the human body that lasts for years, if not for the rest of a person's life—if they survive," Forsythe says.

If someone managed to live after being shot in the lower intestines, they might have to wear a colostomy bag for life. If a bullet lodged

after the massacre, Lenworth Jacobs Jr., then a surgeon at Connecticut Children's Medical Center and regent with the American College of Surgeons, assembled experts from government and the medical and security communities to draw up the Hartford Consensus, a set of national guidelines to help people survive mass shooting events. From those guidelines, Stop the Bleed was born.

Stop the Bleed is a national campaign that focuses on teaching people how to perform emergency medicine tactics, such as how to pack a wound and apply a tourniquet.

In 2016, Forsythe joined a UPMC steering committee to implement a Stop the Bleed

While in prison, he earned his GED. After he was released, he moved to Pittsburgh and got a job at the Addison Terrace Learning Center talking with troubled teenagers about drug and alcohol issues. The experience inspired him to get his bachelor's degree ('92) and then a master's degree in social work ('96) from Pitt. Today, he's a member of Chancellor Patrick Gallagher's public safety advisory board; he works with nonprofit organizations and gives talks to law enforcement groups, as well as teenagers who are at risk of getting caught up in street violence.

"I'd like to think I wouldn't have joined a gang if GRIPS or resolve had been around

## Only about 25 percent of mass shooters have a psychiatric disorder. That number is between four and 12 percent when all forms of violence are considered.

in someone's spine, they might suffer from quadriplegia or paraplegia. When children are hit on a growth plate, they could end up with arms of different lengths.

On the morning of Dec. 14, 2012, Forsythe was seeing patients in UPMC Presbyterian's intensive care unit. While on rounds, a nurse informed her of the breaking news: A gunman had just murdered 27 people, including 20 children between the ages of 6 and 7 at Sandy Hook Elementary School in Newtown, Conn.

Forsythe felt an urge to take her oldest daughter, then in first grade, out of school. She wanted to drive her home and hug her tightly.

In the coming hours, as Forsythe continued to treat patients, she couldn't help but picture the crime scene inside Sandy Hook Elementary.

She also imagined the trauma surgeons at hospitals in Connecticut waiting for wounded children who never arrived. She became filled with frustration, and that led to a realization: Waiting at the hospital isn't enough; doctors have to do "whatever we can to get more people to the trauma center alive, so that we can try to do our jobs."

Forsythe wasn't the only doctor who came to this conclusion that day. A few months

program in Western Pennsylvania. In three years, more than 50,000 people in the Pittsburgh region have been trained on how to perform these life-saving tactics. On Oct. 27, 2018, police officers and EMS used their Stop the Bleed training to save the lives of SWAT team officers and worshippers at Tree of Life.

Forsythe wants kits of tourniquets and packing gauze to be as readily available as defibrillators. But she knows that's not enough to save everyone caught in the crossfire of a mass shooter. Or to save women attempting to escape violent partners. Or inner-city kids from becoming collateral damage.

She wants to do more than that's left of bang. So she and Rozel have testified at Pennsylvania House meetings and Senate Judiciary hearings to clarify the intersection of mental health and aggression and discuss gun violence as a public health issue. They are partnering with legislators and others—Rozel is working with gun shop owners—to address gun violence in less polarizing ways.

**A**s a teenager in Philadelphia, Garland joined a gang and spent a combined 23 and a half years in prison. His last stint (at 12 and a half years) was for conspiracy to commit murder.

[when I was younger]," Garland says. "But I don't know. I was all about gang life back then."

Garland admits he's one of the lucky ones.

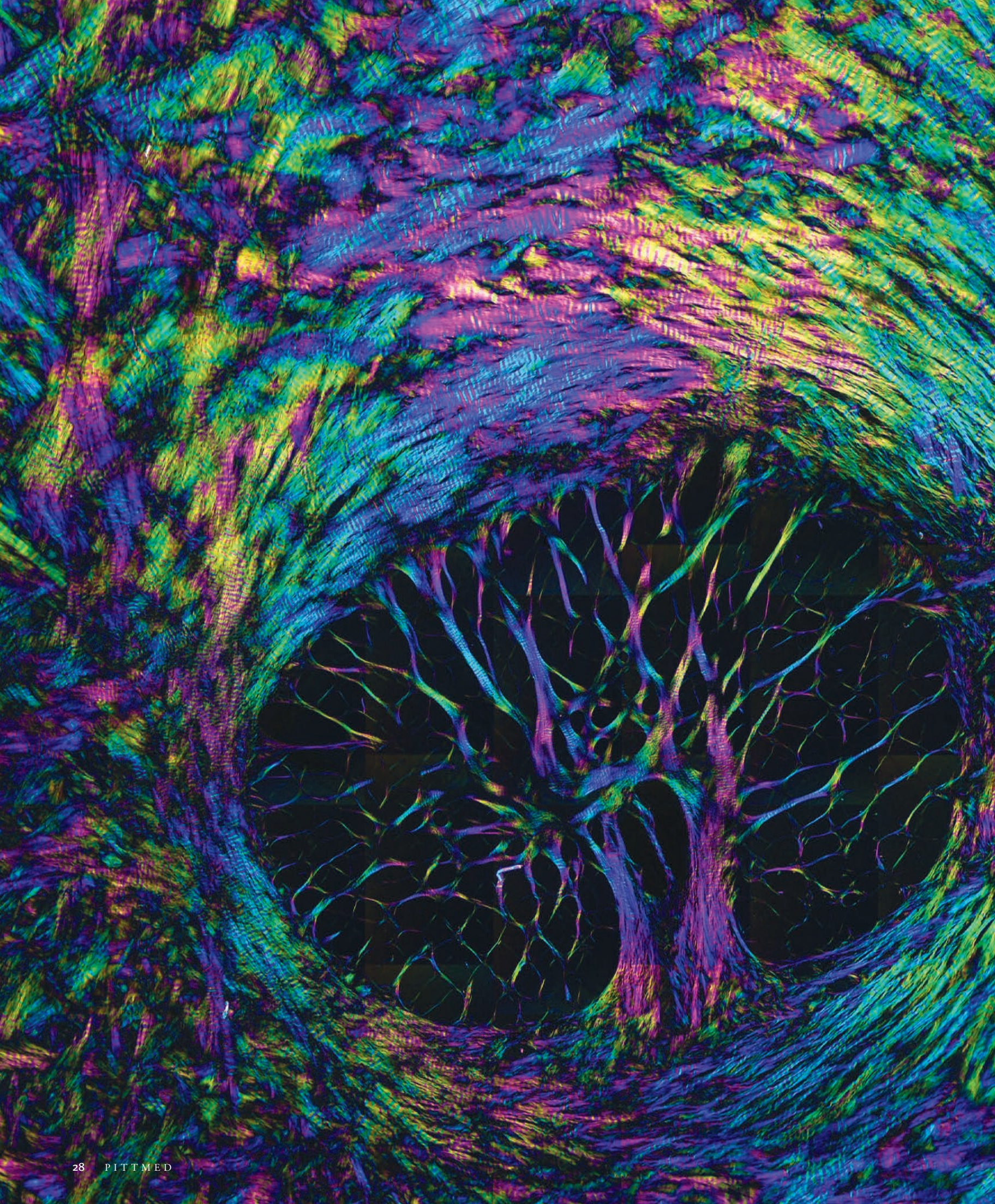
A close friend has been in prison for 51 years. Others Garland associated with in Philadelphia moved out of the city to escape gang life. Everyone else he knew from that crowd is dead.

**F**orsythe has so much experience informing family members that their loved one has died from gunshot wounds that she has a routine. First, she silences her pager and phone so that she's not disturbed while talking to the family. She checks her scrubs and shoes to make sure there's no blood on them. She takes the family to a quiet room, introduces herself, and then warns them she has bad news.

"It's important to use the word 'died.' It's clearer," Forsythe says.

"Some people get very quiet and internalize everything. Some people fall on the floor and cry and scream.

"You have to let people respond, and be silent—which is very hard because you want to jump in, and you want to comfort and soothe." ■



THE LANDSCAPE OF THE  
EYE IS EVER-CHANGING  
BY ELAINE VITONE

# THE FOREST, THE TREES, AND THE LEAVES

**W**hen Ian Sigal was a PhD student researching glaucoma—a group of disorders marked by damage to the optic nerve—he and his advisor homed in on those dying nerve fibers for their studies. But soon, they realized they couldn't understand what was going on there without also checking in on the optic nerve's nearby neighbors. So they widened their scope a tad.

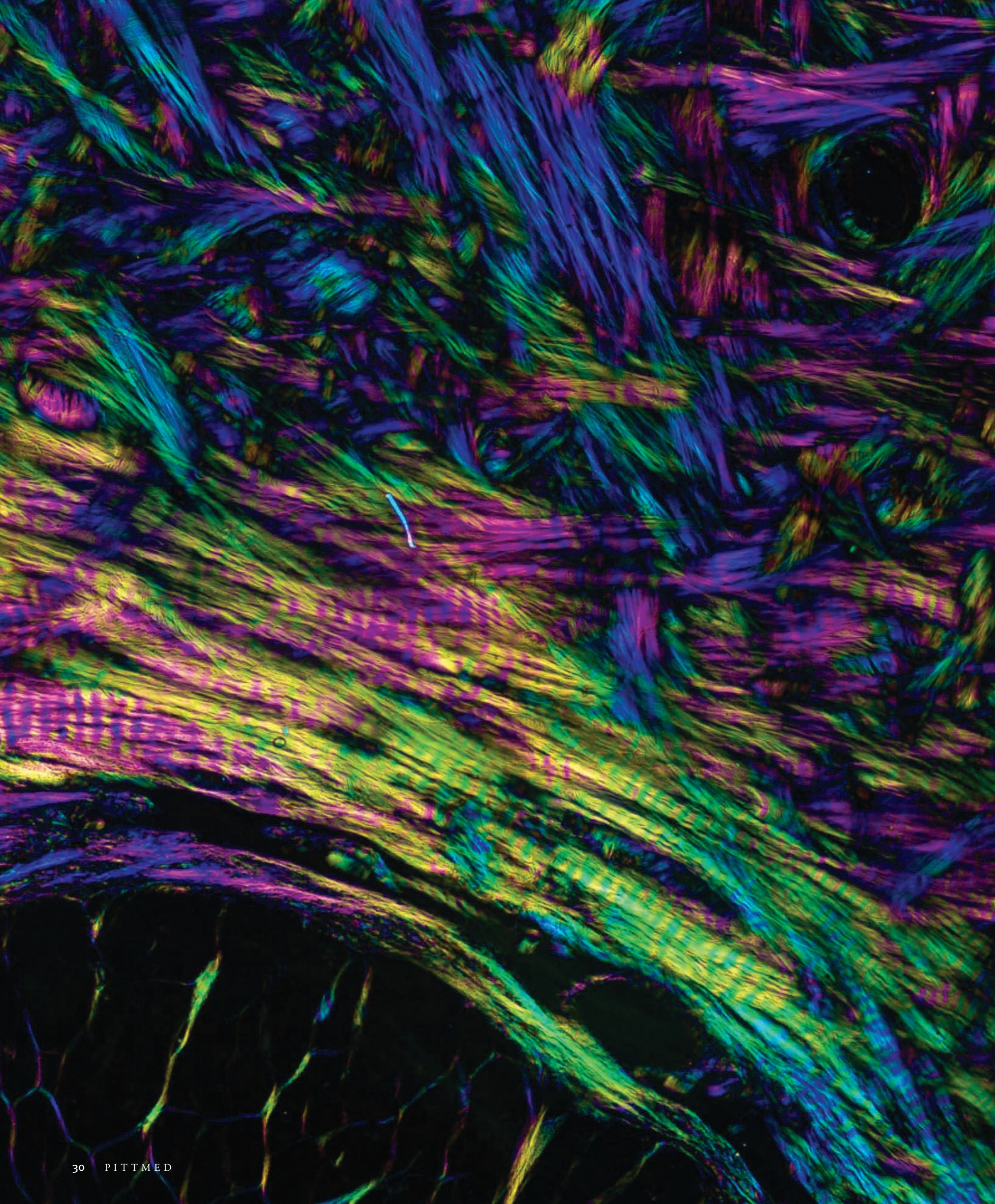
"Then we found, of course, that no, that's not enough," Sigal says. You have to look around that area, then you have to look around *that*. So they kept expanding their scope.

In time, he learned that changes within the eye don't happen in a vacuum. Hence, Sigal, founding director of the Laboratory of Ocular Biomechanics in the University of Pittsburgh Department of Ophthalmology, studies the whole enchilada—the dynamics of the complex organ in its entirety.

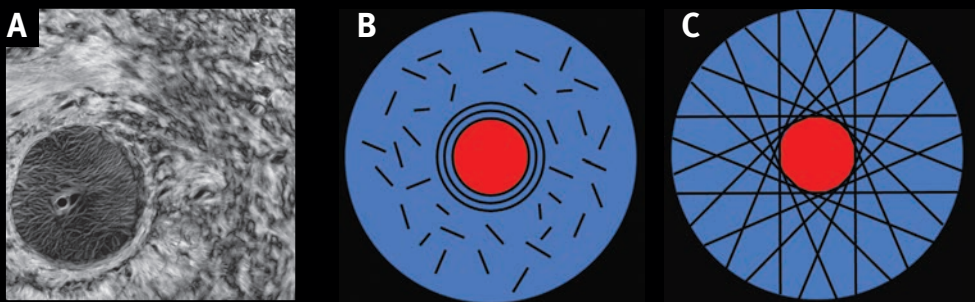
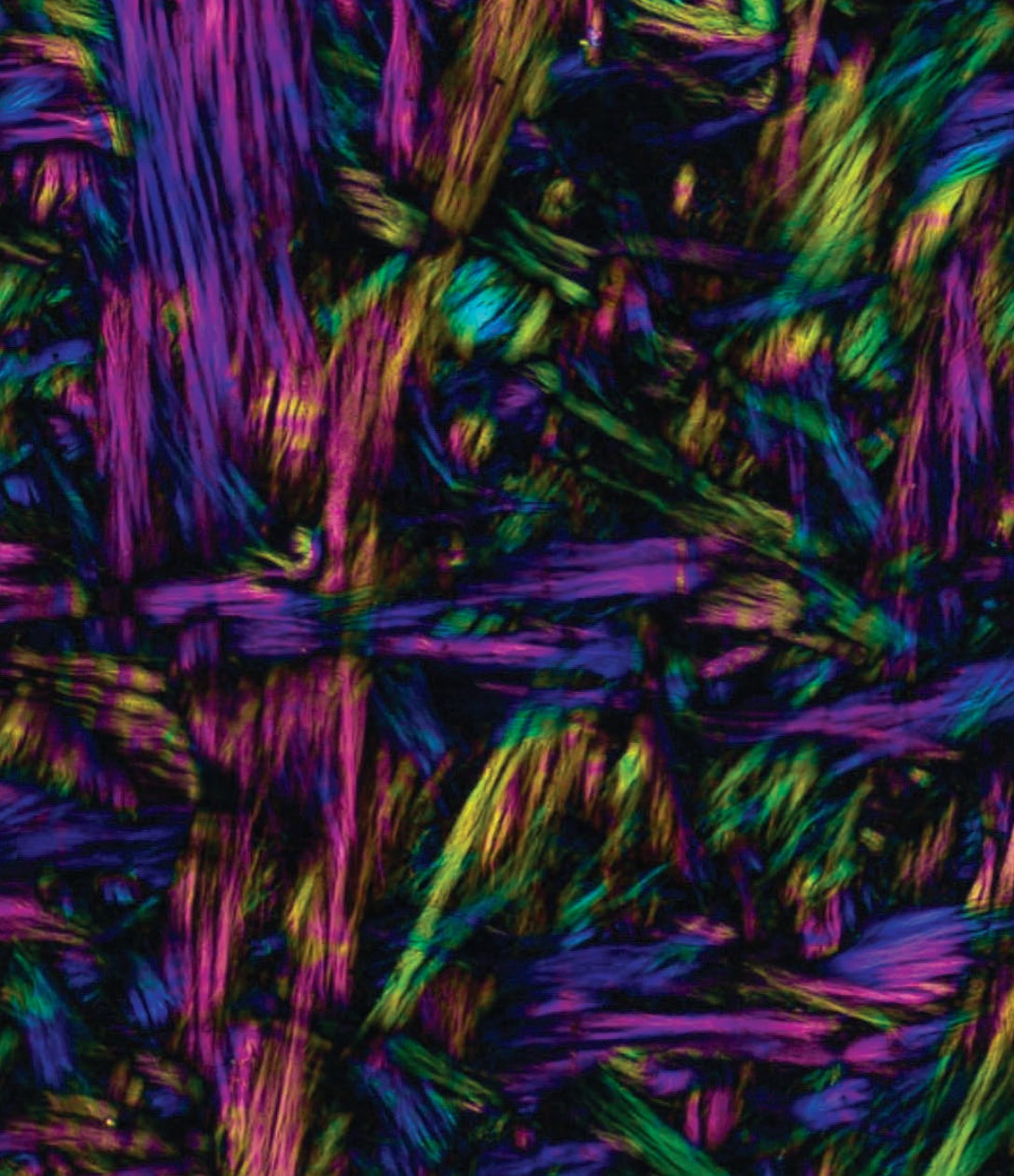
Traditional imaging methods used to make this difficult, he says. Imaging the delicate tissues in the back of the eye was slow going and very uncomfortable for patients. But in the last couple of decades, a 3-D imaging technology called optical coherence tomography, co-invented by Pitt's former ophthalmology chair Joel Schuman, "changed everything in ophthalmology," Sigal says. Or at least in how ophthalmology sees the eye, so to speak.

The eye is a biomechanical wonder. A delicate balance of forces is at work every time you focus on a word or follow a line of text across a page. Fluctuating pressure pounds on the back of the eye, where the optic nerve begins; and in some people, those nerve fibers deteriorate, causing vision loss (glaucoma). Yet a certain amount of pressure is necessary for the organ to maintain its shape and function. The eye is like a soccer ball, says Ian Sigal. "At some point, if it's too deflated, it just doesn't work. You can't play."

IMAGES COURTESY IAN SIGAL/LABORATORY OF OCULAR BIOMECHANICS, EXCEPT FOR PAGE 31







There's a lot going on in the back of the eye, at the portal where it plugs into the rest of your nervous system. It's essentially a hole, right in the middle of a pressure-burdened structure called the sclera. "And what did nature end up putting in that hole?" asks Sigal. "The axons—the most fragile part of the nerve fibers. Sounds crazy! That's one of the reasons we study this."

Conventional imaging (A) suggested a model wherein the hole is wrapped in rings of reinforcing collagen (B). But, as it turns out, those circular fibers were an optical illusion. Sigal's team designed a new technology, a modified form of polarized light microscopy, which revealed multitudes of crisscrossing lines (opposite page). In their new model, the fibers are arranged kind of like a basket weave (C).

The team learned there are lots of reasons why nature would choose this arrangement. A ring would mean one region determines the fate of the whole thing; but a weave spreads the burden more broadly. In Sigal's computational models, "the stresses were lower, the deformations were lower, it's much more robust" in the weave, he says. When damage befell the area around this all-important portal, the whole system shifted to relieve it. And "sometimes the biggest problems were actually far away from this region."

FIGURES B AND C REPRINTED FROM ACTA BIOMATERIALIA, VOLUME 79, A.P. VOORHEES ET AL, "PERIPAPILLARY SCLERA ARCHITECTURE REVISITED: A TANGENTIAL FIBER MODEL AND ITS BIOMECHANICAL IMPLICATIONS," PP. 113-122, © 2018, WITH PERMISSION FROM ELSEVIER.

Previously, imaging in this field was limited to either low-res views of the big picture or very hi-res views of cells and their components, and nothing in between. To make that sought-after middle ground possible, Sigal's lab has employed a technology of its own design—a variation of what's known as polarized light microscopy (PLM)—yielding new insights into the organ's inner workings.

On a recent afternoon, at his computer in the Eye and Ear Institute, he clicks through images of animal eye interiors, brilliantly rendered with stunning detail, like postcards from a dense, day-glow thicket.

"Now we can see the *leaves* and the forest," he says.

Sigal notes with a laugh that eyes are really, really complicated. They are full of fluid, and the amount of that fluid—and the pressure that its volume exerts—varies widely from person to person, as well as over the course of a lifetime, and even over the course of the day. The thinking, historically, was that glaucoma was the result of an excess of pressure pounding away year after year.

But as it turns out, research has revealed, plenty of healthy eyes have high pressure but never develop glaucoma.

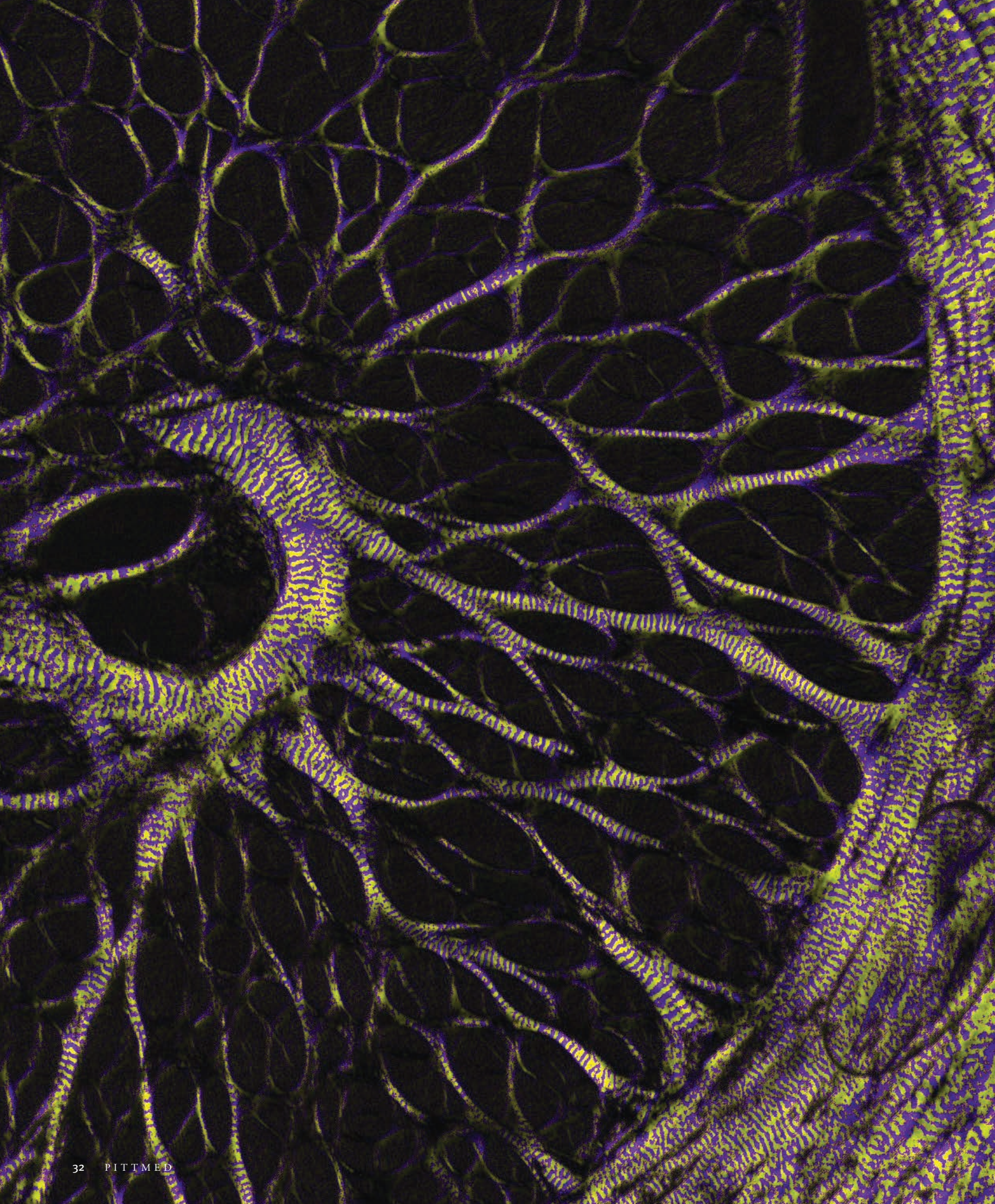
In computational and animal models, Sigal's team tested other possible explanations. For example, would shoring up the collagen—the supportive scaffolding of the eye—make the difference? And after careful study, the answer was: Nope, not necessarily. In fact, some eyes were even worse off for it.

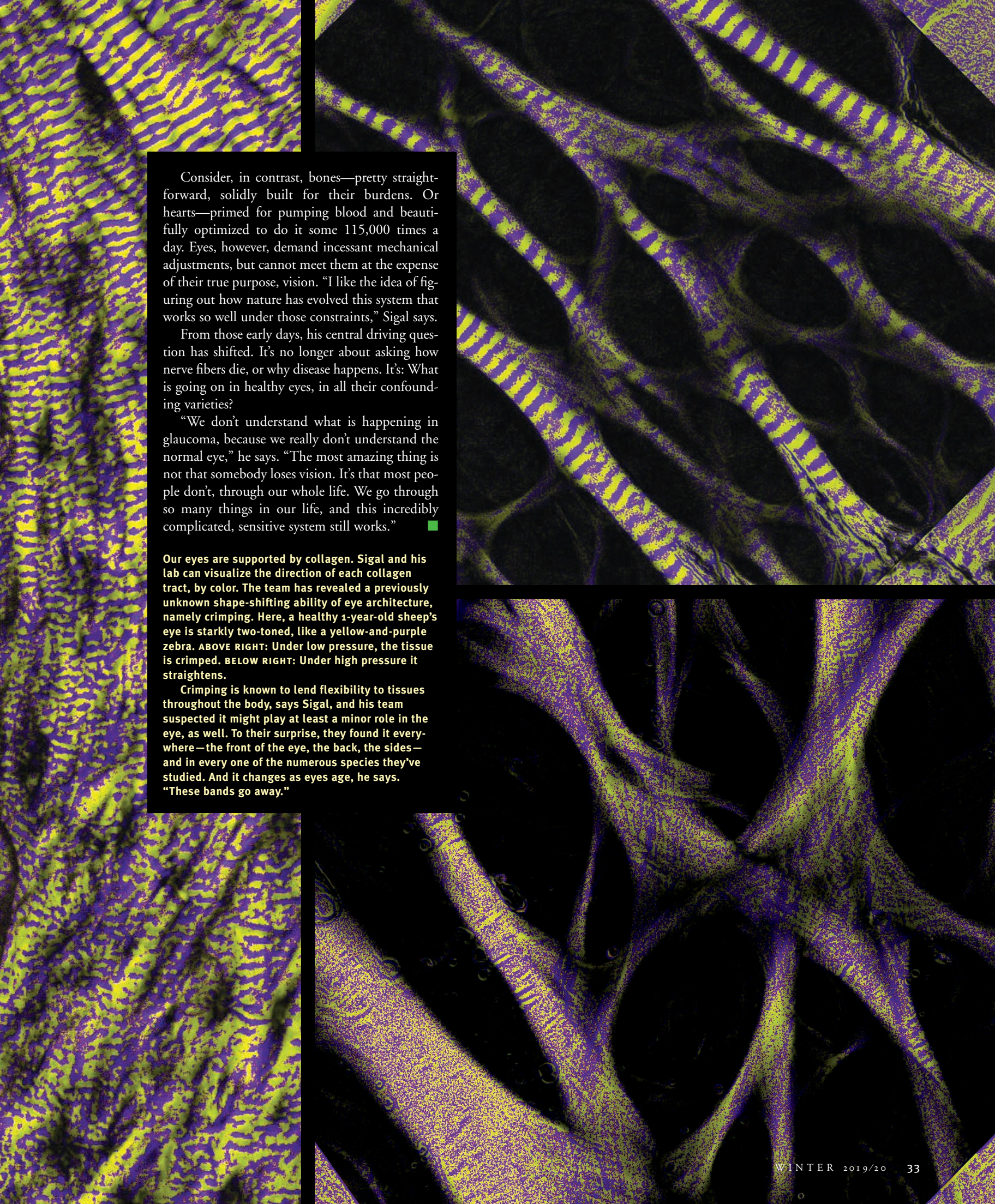
Over the years they've looked at lots of things that can go wrong with these structures: too stiff, too thin, too thick, too twisted, not twisted enough. No single factor seemed to serve as a measure of glaucoma risk. For just about every one of the structural varieties, there are people within the normal range who still got the disease.

The models grew increasingly complex over time, which made Sigal's job a lot harder, he says. But that was a good problem—and not just because he loves what he does. "Because when many things affect each other, you can have many ways for things to go wrong, and also many ways to fix them."

The eye tends to fix some things itself. For example, if the collagen becomes too stiff, it can decrease its thickness to balance things out. Or, if the lens or cornea in the front of the eye becomes too misshapen to properly focus the light, then the shape of the eye as a whole can lengthen out to compensate.







Consider, in contrast, bones—pretty straightforward, solidly built for their burdens. Or hearts—primed for pumping blood and beautifully optimized to do it some 115,000 times a day. Eyes, however, demand incessant mechanical adjustments, but cannot meet them at the expense of their true purpose, vision. “I like the idea of figuring out how nature has evolved this system that works so well under those constraints,” Sigal says.

From those early days, his central driving question has shifted. It’s no longer about asking how nerve fibers die, or why disease happens. It’s: What is going on in healthy eyes, in all their confounding varieties?

“We don’t understand what is happening in glaucoma, because we really don’t understand the normal eye,” he says. “The most amazing thing is not that somebody loses vision. It’s that most people don’t, through our whole life. We go through so many things in our life, and this incredibly complicated, sensitive system still works.” ■

**Our eyes are supported by collagen. Sigal and his lab can visualize the direction of each collagen tract, by color. The team has revealed a previously unknown shape-shifting ability of eye architecture, namely crimping. Here, a healthy 1-year-old sheep’s eye is starkly two-toned, like a yellow-and-purple zebra. ABOVE RIGHT: Under low pressure, the tissue is crimped. BELOW RIGHT: Under high pressure it straightens.**

Crimping is known to lend flexibility to tissues throughout the body, says Sigal, and his team suspected it might play at least a minor role in the eye, as well. To their surprise, they found it everywhere—the front of the eye, the back, the sides—and in every one of the numerous species they’ve studied. And it changes as eyes age, he says. “These bands go away.”

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



only part of his funding could be used for TPI research, the Borofkas decided to raise a million dollars for him. “We will do a fundraiser every weekend if we have to,” Tara Borofka says. So far, they have raised \$200,000 and channeled it to Palladino’s work through a fund set up for them by the University of Pittsburgh.

Palladino says the Borofkas have been especially effective parent advocates: “They are used to media and social media as professional anglers. And JT is currently healthy, so they are not consumed with his medical care, only worrying about his future.” JT, who is now more than a year old, is an exception because early genetic screening identified his condition before he showed neurological symptoms.

## THE RACE IS ON

### BUYING TIME FOR TPI RESEARCH

BY SARA WHITLOCK

**W**hen JT Borofka was 5 months old, he was diagnosed with a metabolic condition called triosephosphate isomerase (TPI) deficiency. Though his parents, Tara and Jason Borofka, had been taking him to doctors since he turned pale at 2 months old, the diagnosis was far from a relief. Tara Borofka remembers one doctor saying, “I would rather tell you that your child has cancer than tell you that your child has this.”

The triosephosphate isomerase enzyme is an essential part of glycolysis—a primary energy production pathway for our bodies. In TPI deficiency, the enzyme is destabilized by a mutation and degraded. Children with this condition have lifelong anemia and develop severe progressive neuromuscular degeneration. Most die by age 5.

JT’s doctors scoured the Internet to find Michael Palladino, professor of pharmacology and chemical biology at the University of Pittsburgh. “As far as I know, I’m the only one where TPI deficiency is a major focus in my lab,” Palladino says. He identified a mutant fruit fly that is the only animal model of TPI deficiency and is using it to find drug targets that could help the TPI enzyme continue to

NATE LANGER/UPMC



**Palladino with JT Borofka. JT’s family is supporting Palladino’s efforts to find a treatment for TPI.**

produce energy. Early identification has been promising, and, according to Palladino, “If we find any one of the 2,000 or so available FDA-approved drugs” to hit their targets, “a clinician could use one of those almost immediately.” However, money is an issue.

After JT’s diagnosis, the Borofkas flew from their home in Salinas, Calif., where they both are professional anglers, to Pittsburgh to meet Palladino. When they learned that

Now, he’s on a special diet—similar to the keto diet—that helps Palladino’s mutant fruit flies live longer; and so far, it’s slowing the progression of JT’s symptoms, too.

“He’s a happy kid,” Tara Borofka says. “Just being in one of our cars and holding the steering wheel makes him happy for like 30 minutes.” If Palladino’s team can find a drug that works, she says, maybe he’ll be a racecar driver someday. ■

## SOUND APPROACH

Private gifts can help researchers move an idea, or discovery, from the lab into the clinic. For instance, support from donors propelled Thanos Tzounopoulos's work forward to better understand tinnitus, an often maddening disease where people perceive an incessant

ringing noise. If everything proceeds as planned, patients may soon be able to try an experimental therapy. Pitt's Tzounopoulos is the UPMC Endowed Professor of Auditory Physiology and vice chair of research for otolaryngology.

### DOD STEPS UP

Gifts through the Eye & Ear Foundation, starting at \$50,000 and increasing to a total of nearly \$450,000, helped Tzounopoulos secure critical funding from the Department of Defense for tinnitus work—those increasing DOD amounts are shown here.

(His lab is also supported by the National Institutes of Health and National Science Foundation.)

\$919,700

\$1,196,980

\$1,957,555

SOURCE: EYE & EAR FOUNDATION. ADAPTED WITH PERMISSION FROM *SIGHT + SOUND*. BACKGROUND PHOTO: GETTY IMAGES

## 2009

Thanos Tzounopoulos develops an animal model of tinnitus.

## 2011

Tzounopoulos determines that the root of chronic tinnitus exists in a structure of the brain.

## 2013

The Tzounopoulos lab identifies a molecular target for correcting tinnitus. A potassium channel is not working properly.

## 2015

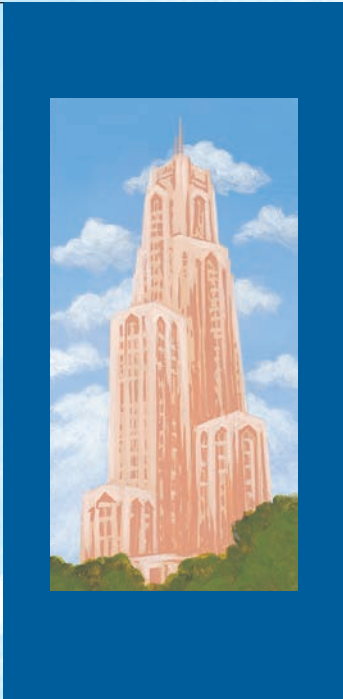
Pitt chemist Peter Wipf starts working with Tzounopoulos to modify an existing drug, a potassium channel activator, which has the potential to reduce or remove phantom sound.

## 2017

Work continues to more specifically target potassium channels and reduce other side effects to make a therapy safer for public consumption.

## 2019–2021

Preclinical testing begins to determine safety for human trials. An Investigational New Drug application will be submitted as a requirement for clinical trials to begin.



## CLASS NOTES

### '70s Gurmukh Singh

(PhD '77, Pathology Resident '78) holds the Walter Sheppard Chair in Clinical Pathology and is vice chair of pathology at Augusta University's Medical College of Georgia (MCG). Singh's laboratory investigates methods for diagnosing multiple myeloma, and its recent findings—that both urine and blood tests produce the most reliable results—were featured in the *Journal of Clinical Medicine Research*. He was honored in 2017 with MCG's Faculty Recognition Award in celebration of his passion for pathology education. "Pathology," he says, "is a little more like science than clinical medicine, which is more an art. It's a good fit for my personality."



Singh



Jaffee

Johns Hopkins University, where she also serves as deputy director of Hopkins's Sidney Kimmel Comprehensive Cancer Center. Her research focuses on developing vaccines to treat cancer, and she's currently researching a vaccine that "teaches" immune-system T cells to fight pancreatic cancer. "We're making a lot of progress" on the vaccine, she says—"it's quite an exciting time."

### '80s Elizabeth Jaffee

(Internal Medicine Resident '88) is the Dana and Albert "Cubby" Broccoli Professor of Oncology at

Jaffee was appointed chair of the National Cancer Advisory Board in 2013 by former President Barack Obama, a position she still holds today.

### '90s Theodore Delbridge

After 12 years as chair of emergency medicine at East Carolina University, Theodore Delbridge (Emergency Medicine Resident '92, Emergency Medicine Fellow '93) moved to Baltimore in 2018 to serve as executive director of the Maryland Institute for Emergency Medical Services Systems. This is a "one-of-a-kind job," he says; he oversees the state's emergency medical system—including ground and air transport and related policies—in a comprehensive system unlike that in any other state. Delbridge's love of EMS stretches back to high school.



Delbridge

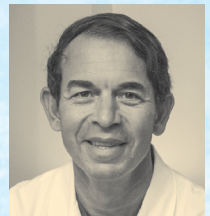
Anureet Bajaj (MD '96) started her private practice, Bajaj Plastic Surgery, in Oklahoma City in 2007. Her clinical repertoire includes the pioneering deep inferior epigastric perforator (DIEP) flap procedure for breast reconstruction, a vascular surgical method that reconstructs breasts with the patient's own tissue while also preserving their abdominal muscles. Until recently, says Bajaj, "I was essentially the only person in the state doing this procedure." She also serves on the editorial board for the journal *Plastic and Reconstructive Surgery*; her most



Bajaj

recent publication for them considers the best ethical-use practices for social media in plastic surgery.

At Columbia University, Selim M. Arcasoy (Pulmonary and Critical Care Medicine Fellow '98) serves as the Dickinson W. Richards Jr. Professor of Medicine (in pediatrics) and medical director of the Lung Transplantation Program. The program has grown to "one of the largest in the country," he says, performing more than 80 lung transplants a year. Arcasoy is a member of the Lung Working Group of the Organ Procurement and Transplantation Network, which is working on an allocation policy for continuous distribution of lungs, as opposed to geographic distribution—a system that will make organ transplants more accessible to underserved regions.



Arcasoy

### '00s Amy Hartman

(PhD '03) is an assistant professor of infectious diseases and microbiology at the University of Pittsburgh Graduate School of Public Health. Her research focuses on emerging viruses at the human-animal interface, particularly the mosquito-transmitted Rift Valley fever virus (RVFV): "a human and animal pathogen," says Hartman, "that presents a significant disease risk to people and livestock." RVFV causes serious disease in humans; Hartman works to develop vaccines and therapies to prevent infection; her research findings were published last December by *Science Advances*. "I find RVFV to be a fascinating virus," she says, "because of its complex ecology—it has implications for the environment, animals, and people."



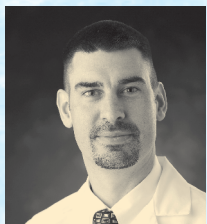
Hartman

KMarie Reid (General Surgery Resident '05) is a professor of surgery at Morehouse University, as well as director of quality, and the section chief for liver, pancreas, and foregut surgery. Since joining Morehouse in 2018, Reid has built a practice focused on hepatobiliary and pancreas surgery. She's on the board of the Society for Surgery of the Alimentary Tract and serves as a National Surgical Quality Improvement Program champion for Atlanta's Grady Memorial Hospital. "It's exciting," she says, "to have the opportunity to serve our patients and offer them multidisciplinary care in a field where they previously didn't have access."



Reid

**J. Scott VanEpps** (Bioengineering PhD '07, MD '09) is an assistant professor of emergency medicine at the University of Michigan, with additional appointments in biomedical engineering and macromolecular science and engineering. He practices in Michigan Medicine's



**VanEpps**

Emergency Medicine and Critical Care Center—a “one-of-a-kind-in-the-nation intensive care unit . . . in the emergency department,” says VanEpps. He also researches novel technologies for preventing and treating medical device infections. For this interdisciplinary research, VanEpps was named a Taubman Emerging Scholar in August. He says he's excited to “hang out” with these other scholars to find solutions to big problems.



**Prince**

**José Prince** (General Surgery Resident '08, Pediatric Surgery Fellow '10) is an associate professor of surgery and pediatrics at the Zucker School of Medicine at Hofstra/Northwell, where he also serves as director of the Laboratory of Pediatric

Injury and Inflammation and vice chair of surgery. In 2018, Prince was elected chair of the New York City Regional Trauma Advisory Committee, which oversees 20 NYC trauma centers. He attributes his career to his grandfather Manuel Beyra, a pediatrician in Cuba. “I didn't grow up around him because my parents left in exile,” says Prince. “But their stories about him influenced my decision to become a doctor and to take care of children.”

**'10s** **Juleen Rodakowski** (Clinical Research MS '14) is an assistant professor of occupational therapy at Pitt's School of Health and Rehabilitation Sciences; she also holds a secondary appointment in



**Rodakowski**

Pitt Med's Clinical and Translational Science Institute. Her research into quality-of-life enhancements for elder adults with minor cognitive decline was recognized recently with a \$3 million grant from the National Institute on Aging. “We have a growing issue here,” says Rodakowski about elder care and rehabilitation. “Our current strategy is watching and waiting—we could be

more proactive.” She's investigating early stage intervention strategies to empower seniors to increase their physical autonomy and agency. —*Rachel Mennies*

## MODJOROS

### CONSULT ON ADULT SITUATIONS

One evening, a man undressed his wife at the dinner table, while their meal was still warm. Skipping dinner and heading straight for intimacy was not their usual M.O. The husband—taking dopamine-enhancing drugs to treat Parkinson's disease—had become newly hypersexual, and his changed appetite coupled with a Parkinson's-characteristic decline in executive function had led the couple to this uncharted moment, says Melanie Modjoros (MD '05). “When you receive a new diagnosis,” she says, “doctors give you medicine, but there's not enough talk about how that's going to impact your sex life.”

An internist and certified sex counselor, Modjoros runs her Sexual Health Consultants clinic in the DC metro area, addressing the intersection of medical problems with sexuality and sexual experience. “Every patient has a sexual problem related to medicine—whether it's mental health, nausea, prescription side effects,” she says. For her Parkinson's patient and spouse, resolving issues like the dinner incident meant “setting rules and a schedule,” where both partners could feel comfortable and heard. They worked together over seven sessions, she says, “to figure out their new normal sex life.”

Modjoros's path to sex therapy began in residency, when a chronic back injury had her shift her focus from an ob/gyn residency into internal medicine with a women's health focus. After training, Modjoros worked as an office-based gynecologist, where “women would come in with pain or sex difficulty,” she says. Seeking solutions led her to sex medicine and, eventually, sex therapy. “I'm often teaching people what they never learned—sex positivity,” Modjoros says. “Sexuality is a part of [my patients'] health, theirs to own and enjoy.”

Modjoros is regularly interviewed for podcasts and gives grand rounds about the sexuality-illness intersection. She recommends sex therapy as a referral option for doctors who aren't able to fold much sex talk into their practice. “Your patients will have medical-related sexual dysfunctions that they will not tell you about—unless you ask,” she notes.

Getting, and staying, in touch with one's sexual self is far from simple, she recognizes. “If sex were so easy,” she jokes, “I wouldn't have a job!” —*RM*



PHOTO BY HASSAN MALIK. PHOTO ILLUSTRATION: ELENA CERRI

**Sexuality is part of our health, says Modjoros.**

## FREDERICK W. CROCK

FEB. 7, 1952–AUG. 16, 2019

**F**rederick Crock (Res '84), who was an echocardiologist and clinical assistant professor at the University of Pittsburgh, is remembered by his colleague Jenifer Lee as “Superman.” Lee, professor of medicine and director of medical student education in the Division of Cardiology, says: “The bottom line is, Fred was perfect.”

Crock, who died in August, taught second-year courses about individual organs. Students at all levels “really adored him,” Lee says.

She quoted a 2018 course evaluation that notes his “virtuosic mastery of his field and an infectious enthusiasm for both teaching and the subject matter.”

Cardiology trainees voted Crock outstanding teacher in 2005, 2010, and 2018; medical students chose him for that honor in 2010 and 2011; and medical residents did the same in 2012. The school's Alpha Omega Alpha Society awarded Crock its Charles Watson Teaching Award this year.

He also was part of a research team that Lee called instrumental in introducing percutaneous catheter-based treatments for valvular heart disease at UPMC Presbyterian. It's a substitute for traditional open-heart surgery, and “really in the vanguard to what we are doing nowadays,” she says. The pair worked together as noninvasive imaging cardiologists at UPMC, and she remembers him being last in the office, helping to close up. “He was one of those guys who really loved what he did.”

Crock was a fellow of the American College of Cardiology and the American Society of Echocardiography. He received his bachelor's degree from Pitt and MD from Temple University. He trained in internal medicine at Mercy Hospital and was chosen as a chief resident. He then completed a cardiovascular fellowship under Pitt's James Shaver before joining the teaching faculty at Mercy in 1984, when he also was appointed clinical assistant professor of medicine at Pitt. In 2004, he joined UPMC's Cardiovascular Institute.

—Marty Levine

© 2019 University Times. Reprinted with permission and adaptations.



Crock

## JOHN ROBERT DILLE

SEPT. 2, 1931–MAY 5, 2019

**G**raduating from Pitt Med, John Robert “Bob” Dille (MD '56) knew he'd be drafted into the Korean War. Certain he couldn't handle the physical demands of the Marine Corps, Dille went to an advisor, who suggested the U.S. Air Force (USAF).

Thus began a lifelong passion for Dille, who went on to become an authority on aerospace medicine. As a captain and flight surgeon at Loring Air Force Base in Maine, Dille signed up for hazard pay, accompanying flight crews on test runs.

“Most of the other doctors were stuck on the base,” says Dille's son, Paul. “Those milk runs gave my dad a great firsthand look at what the air crew was going through.”

Dille ultimately logged more than 250 hours in the air, kindling a passionate interest in the physical tolls of flight and ways to make flying safer. After completing studies at the USAF School of Aviation Medicine in 1957, Dille went to Harvard University to earn a master's degree in industrial health.

Dille continued to focus on these subjects as a civilian, serving as chief of the Federal Aviation Administration's Civil Aerospace Medical Institute in Oklahoma City from 1966 until his retirement in 1987.

A historian and writer, Dille published more than 200 research articles. He also traveled the world lecturing on pilot and aircraft safety. “He got sent to five continents, and he picked up the other two on his own,” Paul Dille says.

After retirement, Dille served as medical director for Oklahoma's department of corrections, traveling the state treating inmates. It was a fitting conclusion to Dille's career. Growing up in Waynesburg, Pa., during the Great Depression, he'd dreamed of working as a general physician.

“He was finally practicing medicine like he thought he would,” says Paul Dille. “That's what he envisioned growing up, and he finally got to do it.” —Adam Regier



Dille

## ROBERT KISILEVSKY

DEC. 19, 1937–JUNE 5, 2019

**I**n retirement, Robert “Bob” Kisilevsky (Biochemistry PhD '69, Res '69) biked 45 minutes each day to a local senior center where he spent hours pursuing a newfound passion for wood carving. Steadily improving his craft over time, Kisilevsky produced ornate pieces he gave to family members, walking sticks to help him cope with arthritis, and an intricate chess set for pursuing another serious hobby.

Kisilevsky's focus in these avocations would come as no surprise to colleagues. During a distinguished career as a researcher, Kisilevsky made foundational contributions to understanding the abnormal protein amyloid and the rare disease it causes, amyloidosis. He published more than 300 papers, abstracts, and book chapters on amyloid and on topics ranging from protein synthesis and cholesterol metabolism to malaria.

“In research you have to be creative; and when he retired, he turned his focus to another creative project, this time wood carving,” says his wife, Barbara Kisilevsky, professor emerita at Queen's University in Kingston, Ontario, where Kisilevsky was professor emeritus of pathology and biochemistry.

Kisilevsky's specialty was basic research, investigating the mechanisms and central functions of a disease, rather than working on diagnostic aids or translating prior findings into medical treatments.

“He was extraordinarily successful at coming up with plausible ideas of why people get a disease, and then what you might do about it,” recalls Paul Manley, a longtime colleague. “Once you knew that, then you had the possibility of intervening.”

A fellow of the Royal Society of Canada, Kisilevsky also founded two biotechnology companies aimed at addressing amyloidosis and atherosclerosis. As a department chair at Queen's, Kisilevsky was instrumental in establishing a doctoral program in research.

“He was open to a variety of ideas, and he wasn't afraid of challenging authority when appropriate,” Manley says. “He was quite wonderful.” —AR



Kisilevsky



## HE TOOK ON THE ESTABLISHMENT BERNARD FISHER: AUG. 23, 1918–OCT. 16, 2019

BY CARA MASSET AND JOE MIKSCH

**S**urgeons began performing radical mastectomies in the 1800s. Though the practice involved disfiguring removal of the breasts and nearby tissue, dogma held that this was the best approach for breast cancer patients. Less-invasive treatments were considered malpractice in some circles; both hubris and a lack of evidence for other treatment options played into that mindset.

A century later, surgeon-scientist Bernard Fisher challenged that dogma by conducting laboratory research on breast cancer biology and then pioneering large-scale, multi-institutional randomized clinical trials. Fisher, Distinguished Service Professor at the University of Pittsburgh who established a scientific approach to the study of breast cancer and shaped the landscape of cancer research more broadly, died Oct. 16 at the age of 101.

“Bernard Fisher was a titan. His research improved and extended the lives of untold numbers of women who suffered the scourge of breast cancer. His work overturned the dominant paradigm of cancer progression and, to the benefit of all, demonstrated the systemic nature of metastasis,” says Arthur S. Levine, the John and Gertrude Petersen Dean at Pitt Med and senior vice chancellor

for the health sciences.

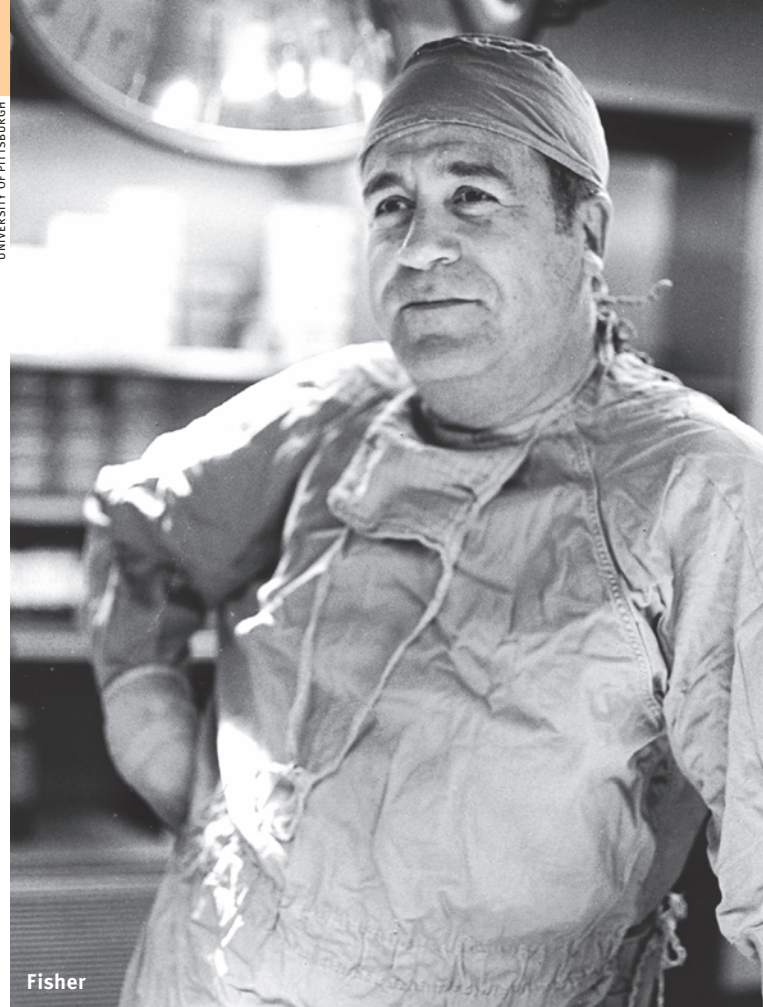
Born and raised in Pittsburgh, Fisher earned both his bachelor’s (’40) and MD (’43) from Pitt. Following his training as a surgeon, he joined Pitt’s Department of Surgery and established the University’s first Laboratory of Surgical Research.

“No clinical therapy should be determined by emotion or conviction—the determinant must be the scientific method,” Fisher said in 2009.

In 1958, Fisher attended an NIH meeting where he became a founding member and later chair (1967–1994) of the National Surgical Adjuvant Breast and Bowel Project (NSABP), a multi-institutional group that continues to conduct clinical trials on breast and colon cancers today. Fisher’s landmark clinical trials with the NSABP in the 1960s and ’70s provided a scientific basis for using less-extensive surgical treatments to effectively treat breast cancer.

“As a surgeon he was trying to reduce surgery—he always put the patient and the data first,” says Robert Ferris, director of the UPMC

UNIVERSITY OF PITTSBURGH



Fisher

Hillman Cancer Center.

“He delivered us from the age of tyranny when a single individual could dictate the therapy of a particular disease based on his own biased retrospective experience. All of oncology owes an enormous debt of gratitude,” says Norman Wolmark, director of the National Cancer Institute cooperative group on clinical trials, NSABP Foundation chair, and Pitt professor of surgery.

In the 1990s, Fisher demonstrated that the drug tamoxifen can prevent breast cancer in high-risk patients. That was the capstone of his career, he told *Pitt Med* in 2002. “Certainly, in 1958, when I began this journey, the idea of using an agent to try to prevent breast cancer was . . . science fiction,” he said.

Fisher received the Albert Lasker Award for Clinical Medical Research and the American Association for Cancer Research Award for Lifetime Achievement in Cancer Research. He served on the President’s Cancer Panel and the National Cancer Advisory Board.

“Bernard Fisher was one of the great medical pioneers of our time,” says Pitt Chancellor Patrick Gallagher.

Jeffrey A. Romoff, UPMC president and CEO, notes, “His advances are among the most important contributions ever made to women’s health.”

“The field of oncology has lost its noblest protagonist,” says Wolmark. ■

## IN MEMORIAM

### ’40s

**ROBERT L. BAKER**  
MD ’48  
OCT. 13, 2019

**ROBERT CHAMOVITZ**  
RES ’49, ’52  
AUG. 12, 2019

### ’50s

**THOMAS F. NEWCOMB**  
MD ’51  
SEPT. 23, 2019

**HAROLD R. HELLSTROM**  
MD ’52  
OCT. 19, 2019

**FRANK X. PAWLOSKY**  
MD ’53  
AUG. 21, 2019

**MARIO C. BATTIGELLI**  
FEL ’58  
SEPT. 27, 2019

**JOHN L. AMMER**  
MD ’59  
AUG. 17, 2019

### ’60s

**JOEL H. MERENSTEIN**  
MD ’60  
SEPT. 27, 2019

**HARVEY WEINTRAUB**  
RES ’64  
OCT. 14, 2019

**RONALD L. VINCENT**  
RES ’67, ’71  
OCT. 3, 2019

**ROBERT G. BRODOWS**  
MD ’68  
SEPT. 29, 2019

### ’70s

**JOHN DARYL KRISTOFIC**  
MD ’70  
SEPT. 26, 2019

**GARRET M. IHLER**  
MD ’76  
AUG. 30, 2019

### ’80s

**RICHARD L. LINDSEY JR.**  
RES ’80, FEL ’80  
AUG. 8, 2019

**LAWRENCE E. HERTZBERG**  
MD ’81  
AUG. 26, 2019

### FACULTY

**MICHAEL J. PAINTER**  
RES ’66, ’68  
OCT. 17, 2019

**JAN D. SMITH**  
FEL ’67, ’69, RES ’71  
SEPT. 6, 2019

**R. MARK WEBB**  
RES ’81, ’84, ’85,  
FEL ’85  
SEPT. 18, 2019

THE DEAN MACHINE

Leaders are made here. Several Pitt Med faculty members and alumni have gone on to run schools and universities elsewhere.



**Steven Kanter**  
President and CEO,  
Association of Academic Health  
Centers and AAHC International,  
Former dean, School of Medicine,  
University of Missouri–Kansas City.  
*Before that, Pitt Med vice dean.*



**Leon Haley Jr.**  
Dean, College of Medicine–  
Jacksonville,  
University of Florida  
CEO, UF Health Jacksonville  
*Pitt Med alum, MD '90.*



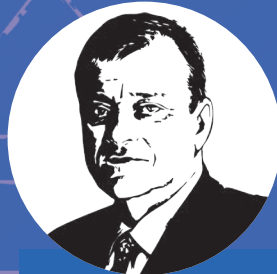
**Roberta Ness**  
Dean, School of Public Health,  
University of Texas  
*Former Pitt chair of epidemiology;  
also professor of medicine and of  
obstetrics and gynecology.*



**Henri Ford**  
Dean, Miller School of  
Medicine, University of Miami  
*Former Pitt chief of  
pediatric surgery.*



**David Perlmutter**  
George and Carol Bauer Dean,  
School of Medicine,  
Executive Vice Chancellor,  
Medical Affairs  
Washington University  
in St. Louis  
*Former Pitt chair of pediatrics.*



**John J. Reilly Jr.**  
Dean, School of Medicine,  
Vice Chancellor for  
Health Affairs,  
University of Colorado  
*Former Pitt chair of  
medicine.*



**Augustine M.K. Choi**  
Stephen and Suzanne Weiss Dean,  
Weill Cornell Medicine  
Provost for Medical Affairs,  
Cornell University  
*Former Pitt chief of pulmonary,  
allergy, and critical care medicine.*



**Rocky Tuan**  
Vice Chancellor and President,  
Chinese University of  
Hong Kong  
*Former Pitt professor of bio-  
engineering and mechanical  
engineering and materials  
science.*



**Vincent Verdile**  
Distinguished Dean,  
Albany Medical College  
Executive VP, Health Affairs,  
Albany Medical Center  
*Former Pitt professor of emer-  
gency medicine; alum, Res '87.*



**Steven Beering**  
President Emeritus,  
Purdue University,  
Former Dean,  
School of Medicine,  
Indiana University  
*Pitt Med alum, MD '58.*



**Brian Primack**  
Dean, College of Education  
and Health Professions,  
University of Arkansas  
*Former Pitt professor of medi-  
cine and dean of Pitt's Honors  
College. Pitt Med alum,  
Res '02, PhD '11.*



**Gerald S. Levey**  
Dean Emeritus, David  
Geffen School of Medicine,  
Former Vice Chancellor,  
Medical Sciences, UCLA  
*Former Pitt chair of  
medicine.*

You are getting sleepy.

## CALENDAR

FOR ALUMNI & FRIENDS

Unless otherwise noted,  
for information:  
Alexandra Rigby at  
412-648-9090 or  
amr276@pitt.edu

### 2020 WINTER ACADEMY FEBRUARY 14

Ritz-Carlton, Naples, Fla.  
“Headline News: Opioids, Violence,  
Drug Prices, and More”  
winteracademy.pitt.edu

### PITT DAY OF GIVING FEBRUARY 25

pittdayofgiving.com

### PITT HEALTH ACADEMY APRIL 30

Oakmont, Pa.

### MEDICAL ALUMNI WEEKEND SEPTEMBER 25-26

(Celebrating class years  
ending in 0 and 5.)

To find out what else is happening  
at the medical school,  
visit [health.pitt.edu](http://health.pitt.edu)  
and [maa.pitt.edu](http://maa.pitt.edu).

GETTY IMAGES



## FOR REAL! TWEEN SCIENCE

Like many kids, you might sleep with a favorite stuffed animal or soft blanket. These snuggly buddies are a huge comfort when you lie down to rest, and there are some likely scientific reasons for this:

Stuffed animals and blankets help you to relax. To fall asleep, your brain needs to feel safe and secure. Feeling Mr. Cuddles’s tail is probably enough to do the trick.

A stuffy can also train your brain to fall asleep. You see Mr. Cuddles as you get ready for bed, so your brain thinks of sleep whenever you look at and hold him. This is why comfort objects are called transitional objects. They let your brain know it’s time to rest and help you to switch from being awake to falling asleep.

Weighted blankets can help you relax, too. They are filled with beads or pellets, which makes them super heavy. To work, the blanket should weigh about 10 percent of what you weigh. Once you get under the heavy blankie, it will gently press on your body in a soothing way. Scientists aren’t sure, but they think people have a natural reflex that responds to this gentle pressure, which helps them to catch some z’s.

So next time you reach for that plush buddy, you can fall asleep knowing that comforting feeling isn’t all fluff! —Alyce Palko

*Thanks to Katherine Duggan, a psychology researcher at North Dakota State University who trained at Pitt, for the lowdown on the wind down.*

Is there a topic you’d like us to explore? Drop us a line: [medmag@pitt.edu](mailto:medmag@pitt.edu).

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

CHANGE SERVICE REQUESTED

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

ILLUSTRATION: FRANK HARRIS



## WHAT WAS LIFE LIKE BEFORE CHILDHOOD VACCINES?

On the latest episode of **Pitt Medcast**, hear from people who grew up in the shadow of a crippling disease—among them, “polio pioneers,” schoolkids from the clinical trials of the killed-virus vaccine.

[bit.ly/pittmedcast](https://bit.ly/pittmedcast)

