UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | WINTER 2024/25

PITTMED



FOUND IN SPACE

SCIENTISTS CAN MONITOR CANCER CELLS LIKE NEVER BEFORE.

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Winner, 2024 Press Club of Western Pennsylvania Golden Quill, Excellence in Written Journalism, Medical/Health (E. Lloyd, "Cultivating equanimity")

Finalists, 2024 Press Club of Western Pennsylvania Golden Quill, Excellence in Written Journalism, Medical/Health (M. Aubele, "A moving story" and A. Doerfler, "Outside influences")

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Right time, right place

"I've always been in the right place and time.
Of course, I steered myself there." —*Bob Hope*



AIMEE OBIDZINSKI/UNIVERSITY OF PITTSBURGH

Dear Pitt Med Readers,

It's not uncommon to hear successful people chalk up their achievements to being in the right place at the right time. Of course, most of them didn't end up in the "right place" by accident. Ambitious people seek out environments with the resources that will allow them to thrive. We're doing everything we can to make sure that the School of Medicine remains the right place for such innovators in the exciting times to come.

That means, in part, securing the best technology to move bold work toward new discoveries. You'll find a striking example of this in our cover story (page 26), about researchers applying "spatial omics" platforms. These tools analyze biological molecules in their native location within tissue, tracking molecular and cellular activity in ways that few could have imagined just a decade ago. The work is expected to point to new drug targets and therapies for cancer and other diseases.

More broadly, we're investing in a number of core facilities that centralize instrumentation and infrastructure for our research priorities, which span genomics, biomedical mass spectrometry and more. And we're listening to our faculty's ideas for what to build next.

Building the right environment for our people to succeed is not a new focus for the School of Medicine. As you can see on the map on page 4, our footprint in Pittsburgh has expanded greatly since this magazine launched 25 years ago. The facilities across this city speak to our commitment to making Pitt Med a place where researchers, educators, students and patients can flourish as medicine advances and evolves.

It's clear that those efforts have paid off. People of wide-ranging origins and pursuits have concluded that Pitt is the right place to make their aspirations a reality. Take José-Alain Sahel, the visionary vision-restoration scientist who recently received the prestigious Wolf Prize. José came to Pitt from the Sorbonne in 2016, and he's forged partnerships with leading institutions like Inserm, France's national medical research agency. (See page 10 to learn how those relationships have evolved.) Or consider our accomplished new chair of medicine, Anne Marie Lennon, formerly of Johns Hopkins University, who hails from Ireland (page 20).

In this issue, you'll also learn about Joon Lee and Nam Vo, who both overcame adversity during their life journeys and have since found a home in Pittsburgh, oceans from where they started (page 32). The new Bethel Musculoskeletal Research Center Biobank is just the latest example of our partners helping us make Pitt Med the right place for life-changing work. As ever, the right time is now. And the right place, Pittsburgh.

Anantha Shekhar, MD, PhD
Senior Vice Chancellor for the Health Sciences
John and Gertrude Petersen Dean, School of Medicine

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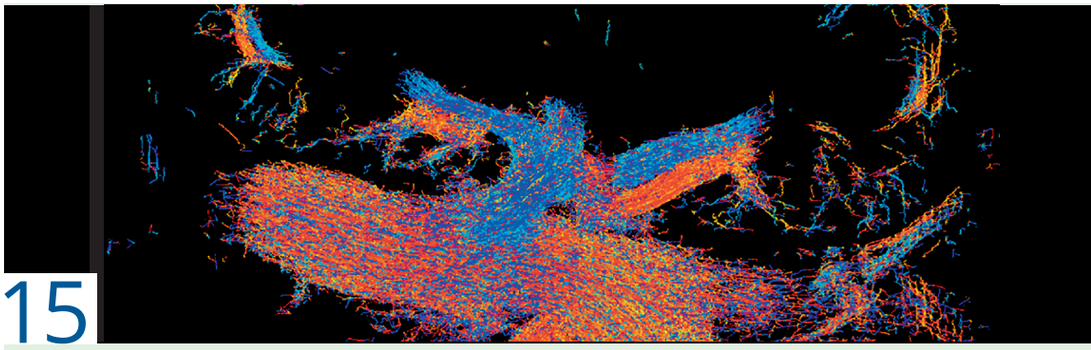
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A major contributor to shortened life expectancy in patients with sickle cell disease is chronic kidney disease.

THEN AND NOW 4
What a difference 25 years makes. Pitt Med's campus now extends throughout Pittsburgh.

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Mohamed Hagahmed's unbowed spirit.
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Sunny stuff.

University of Pittsburgh School of Medicine

Editor's note: School of Medicine faculty with clinical duties often have joint appointments with UPMC or the VA Pittsburgh Healthcare System, the University's clinical partners.

ABOUT THE COVER More than gee-whiz, spatial omics technologies are allowing scientists to see what's happening in cancer and other cells like never before. Scan: Courtesy Cytometry Facility at the UPMC Hillman Cancer Center, © 2024.

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20

"Whatever she envisioned, she made it happen," a Hopkins colleague says of Anne Marie Lennon.



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FEATURES

Coming of age **16**

At 25 years old, Pitt Med Magazine is the age of many med students. We take a look back at what was unfolding here at the school, as well as more broadly in medicine, as today's med students were growing up.

INFOGRAPHIC BY ERICA LLOYD AND MAGGIE NEGRETE

Undaunted **20**

Anne Marie Lennon finds a way to make it happen, whether she's detecting pancreatic cancer early or leading the Department of Medicine into the future.

BY SHARON TREGASKIS

Found in space **26**

An extraordinarily powerful emerging tech, spatial omics, lets scientists witness and monitor the activity of cells like never before.

COVER STORY BY MICHAEL AUBELE

CONTRIBUTORS

In 1999, **ERICA LLOYD**, editor in chief of this publication, was asked to start a magazine for the medical school. She soon recruited **ELENA GIALAMAS CERRI** as art director, and there's been no looking back since—errr, except for the times we do, like in this issue, as we mark a quarter century of publication. (See "All over the map" on page 4 and "Coming of age" on page 16.)

We are pretty sure that Cerri, as the child of a doctor and an artist, was born to art direct Pitt Med. She spent 10 years in New York City, where she lent her talents to J. Crew, Elle magazine and other pubs before returning to Pittsburgh. Lloyd, who has taken time off through the years to report for Radiolab, Wired and National Geographic News, finds working with Cerri and other colleagues here enormously rewarding: "I can't resist opening a file that Elena sends me. I love seeing what she's done with a piece."

Building a magazine that's worth spending time with is about process and discernment, not kismet, notes Cerri. "An exceptional editor in chief and great contributors, constant revision, rework, fact-checking and two trusting deans over the years have made the magazine successful," she says.

"Most importantly, we respect our readers," adds Lloyd.

All over the map

Pitt Med Magazine debuted 25 years ago, and the School of Medicine has indeed grown in that time. It only takes a drive through Pittsburgh to see it with your own eyes. With new facilities reaching from Lawrenceville to Greater Hazelwood to the South Side, Pitt Med's expanding footprint in the city reflects the breadth and depth of the work that faculty, staff, trainees and students are doing to improve medical education, research and care. A former Model T factory now assembling the latest cancer treatments, a hub for visual and physical rehabilitation and a new wing at the med school are just a few of the places where Pitt Med has made a mark on the local landscape.

Take a look at the map below to see several of the buildings where the School of Medicine has planted a flag in the past quarter-century—plus a few to come.

—Andrew Doerfler and Anvi Jain



LEGEND:

- ■ Now open
- ● Under construction

Research and innovation

Education

Research and clinical

(1) ■
UPMC Children's Hospital of Pittsburgh and John G. Rangos Sr. Research Center
Lawrenceville
Opened: 2008-09
The Richard King Mellon Foundation Institute for Pediatric Research and seven floors of lab space sit next door to top-notch clinical care and training opportunities.

(2) ■
The Assembly
Bloomfield
Opened: 2022
Formerly a Model T factory, the eight-story, 355,000-square-foot structure overlooking the Martin Luther King Jr. East Busway now buzzes with the activity of scientists pursuing cancer research and immunology, including Pitt investigators from the UPMC Hillman Cancer Center, the Department of Immunology and the Institute for Precision Medicine.

(3) ■
UPMC Hillman Cancer Center
Shadyside
Opened: 2002
Home to: Biobehavioral Cancer Control Program, Cancer Biology Program, Cancer Epidemiology and Prevention Program, Cancer Immunology and Immunotherapy Program, Cancer Therapeutics Program, Cancer Virology Program, Genome Stability Program, as well as cancer treatment and clinical services.

(4) ■
Alan Magee Scaife Hall West Wing
Oakland
Opened: 2023
The seven-story expansion to the School of Medicine's headquarters is designed for a modern medical education. The bright and airy West Wing features flexible learning spaces, a 600-seat auditorium, an anatomy lab incorporating both virtual and traditional learning experiences, an enhanced Falk Library of the Health Sciences, and plenty of spaces for med students to study, gather and unwind.

Original map design: Joe Petrina/Landesberg Design. Adapted by Elena Cerri.

Photography by Aimee Obidzinski and Rayni Shiring/ University of Pittsburgh and Wexford Science and Technology.
Renderings by HOK and HGA.

Lawrenceville



UPMC Children's Hospital of Pittsburgh and John G. Rangos Sr. Research Center

1

Oakland



Alan Magee Scaife Hall West Wing



UPMC Presbyterian Tower

4 5 6 7



The Assembly

2 3

Shadyside

10 9 8

Greater Hazelwood

13

11



Pitt BioForge

(5) ●
UPMC Presbyterian Tower
Oakland

Expected opening: 2026
With 636 private patient rooms for transplant, heart, vascular, neurological and other care as well as another 11 operating rooms, the tower will provide more opportunities for med students right in Oakland at the academic medical center's flagship hospital.

(6) ■
Biomedical Science Tower 3
Oakland

Opened: 2005
Home to: Departments of Structural Biology, Neurobiology and Computational and Systems Biology; Center for Integrative Organ Systems; Center for Vaccine Research;- Biomedical Mass Spectrometry Center; Pittsburgh Institute for Neurodegenerative Diseases.

(7) ■
Magee-Womens Research Institute
Oakland

Addition opened: 2007
Home to: Investigators studying reproductive biology and development, pregnancy, infectious diseases, fertility, cancer, pelvic health and wellness.

(8) ■
Bridgeside Point I
South Oakland

Opened: 2002
Home to: Aging Institute.

(9) ■
Riviera
South Oakland

Opened: 2021
Home to: Immunologic Monitoring and Cellular Products Laboratory.

(10) ■
Bridgeside Point II
South Oakland

Opened: 2009
Home to: McGowan Institute for Regenerative Medicine, the Department of Microbiology and Molecular Genetics.

(11) ●
Pitt BioForge
Greater Hazelwood

Expected opening: 2026
Pitt aims to drive biomanufacturing innovation with BioForge, which will help promising life sciences projects figure out how to successfully commercialize their work so that patients can benefit from precision biologic medicines. ElevateBio, a Massachusetts-based biomanufacturing company, will be an anchor tenant.

(12) ■
UPMC Mercy Pavilion
Uptown

Opened: 2023
The 410,000-square-foot Uptown facility is home to innovators in the UPMC Vision Institute, the Department of Ophthalmology and the Rehab Neural Engineering Labs, part of the Department of Physical Medicine and Rehabilitation. Putting visual and physical rehabilitation researchers with clinicians under one roof streamlines collaboration and translation. A quarter of the space is dedicated to research.

(13) ■
Rivertech
South Side Flats

First leased: 2007
Home to: Neuromuscular Research Laboratory, Biodynamics Laboratory.





AIMEE OBIDZINSKI/UNIVERSITY OF PITTSBURGH

Pennsylvania Gov. Josh Shapiro joined leaders from NVIDIA, Pitt and Carnegie Mellon to celebrate the announcement of an AI Tech Community in Pittsburgh.

NVIDIA collaboration powers AI ambitions

A developing collaboration between the University of Pittsburgh and the tech giant NVIDIA will accelerate medical research and enhance health care delivery in Pittsburgh and beyond.

The two will launch the NVIDIA Joint Center with the University of Pittsburgh for AI and Intelligent Systems to focus on computational opportunities across the health sciences, including applications of artificial intelligence (AI) in clinical medicine and biomanufacturing.

Pittsburgh will be the site of NVIDIA's inaugural AI Tech Community, bringing together academia, industry and public sector partners to drive progress in AI. Farnam Jahanian, Carnegie Mellon University president, Anthony Robbins, NVIDIA Federal vice president, Pennsylvania Gov. Josh Shapiro and Joan Gabel, University of Pittsburgh chancellor, (all pictured above) signed a ceremonial memorandum of understanding with NVIDIA on Oct. 14.

Pitt stands to strengthen its already impressive medical influence through access to the tech giant's hardware and software. NVIDIA chips power gaming systems, self-driving cars and data centers, but they also handle the accelerated computing that propels drug discovery, genomics and medical imaging through AI.

With access to AI capabilities that few other institutions have, Pitt medical researchers will be able to expedite their studies at a much faster pace. In pathology, for instance, this might include the use of AI for whole slide image assessment, which could accelerate and enhance the accuracy of certain cancer diagnoses.

Anantha Shekhar, Pitt's senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of the School of Medicine, says the collaboration will also enhance how the University carries out its mission as an educational leader.

"As a top-tier institution for the study of health sciences, it's imperative that we continually educate our entire academic community on the best ways to optimize AI for the equitable study, prevention and treatment of disease," Shekhar says.

Hooman Rashidi, an MD, MS who is Pitt Med's associate dean for AI in medicine, says the right hardware is crucial for the school's goals.

"That's where NVIDIA fits into all of this," he says. "They're the engine around all of the software tools we're developing." —*Michael Aubele*

TOM ALTANY/UNIVERSITY OF PITTSBURGH

FOOTNOTE

Want to guess who might win a Nobel Prize? You could do worse than picking from the list of past winners of the Dickson Prize in Medicine, Pitt Med's highest honor. That lineup now features 17 Nobel laureates with the addition this year of **Victor Ambros**, the Silverman Professor of Natural Sciences and professor of molecular medicine at the University of Massachusetts Chan Medical School.

Ambros, who won the Dickson Prize in 2009, earned the 2024 Nobel Prize in Physiology or Medicine for his codiscovery of microRNA, which help regulate gene expression. He shares the award with Gary B. Ruvkun, of Massachusetts General Hospital and Harvard Medical School.

Read our interview with 2024 Dickson Prize winner **Leslie Vosshall** on page 9.



Wallach



Hyderi



Trinh

New vice deans and urology chair named

Paul M. Wallach, an MD, has joined Pitt as executive vice dean for academic affairs at the School of Medicine and vice chancellor for health sciences education. He'll work with the provost's office to enhance academic activities and spearhead new opportunities in medical and graduate education, joint degrees and mentorship programs.

Wallach most recently served as executive associate dean at Indiana University School of Medicine, where he led efforts to enhance the curriculum and student support. He's also developed programs like point-of-care ultrasound (allowing quick interpretation of results at the bedside) and scholarly concentrations.

Abbas Hyderi, an MD, MPH, is the School of Medicine's new vice dean for education. In this position, Hyderi will oversee all aspects of medical education, including curriculum, student affairs, scholarships and financial assistance. He'll also serve as a professor of family medicine.

Hyderi comes to Pittsburgh from the Kaiser Permanente Bernard J. Tyson School of Medicine in California, where he served as the founding senior associate dean for medical education. He is nationally recognized for his work in medical education and in HIV and LGBTQ+ care and advocacy.

Quoc-Dien Trinh, an MD, MBA, has been named chair of the Department of Urology. He has also been recommended to hold the Dr. Frederic N. Schwentker Chair in Urological Surgery. A globally recognized urological surgeon and advocate for health equity, Trinh has made contributions to both clinical practice and research.

Trinh previously served as section chief of urology at Brigham and Women's Faulkner Hospital and codirector of the Prostate Cancer Program at Dana-Farber/Brigham and Women's Hospital. Trinh succeeds Joel B. Nelson, who led the department for 25 years. —*Staff reports*



The Greater Hazelwood community was well represented at a celebration for BioForge, where participants signed a beam that would soon complete the facility's frame.

A construction milestone for BioForge

Pitt's new hub for biomanufacturing innovation is taking shape along the Monongahela River.

University of Pittsburgh leaders, community members and representatives from foundations and industry gathered on Hazelwood Green in September to recognize a milestone for Pitt BioForge, a facility that promises to transform how precision biological medicines are made and drive life sciences advances in the region. Participants signed a beam that workers lifted the next day to complete BioForge's frame. The event's speakers included Pitt Chancellor Joan Gabel, Pitt Med Dean Anantha Shekhar, Pitt Board of Trustees Chair John Verbanac, BioForge CEO Ken Gabriel and Vikas Sinha, CFO of ElevateBio, BioForge's anchor tenant.

Lifelong Hazelwood resident Rev. Michael Murray Sr. expressed his hope that collaborations between residents and the University will continue to drive workforce development and community engagement. Hazelwood Green was home to Pittsburgh's last steel mill; and Murray noted how his father worked for the Jones and Laughlin Steel Corporation for 38 years.

"Together we are unlocking doors to future opportunities, emphasizing the vital role that innovation, education and partnership play in our collective success," Murray said. —*Patrick Monahan*

Faculty snapshots

Cancer survivors were once encouraged to avoid strenuous exercise. **Kathryn Schmitz**, a PhD, MPH professor of medicine, advises the opposite based on her more than 25 years of research in exercise oncology. She received a 2024 Lifetime Impact Award from the President's Council on Sports, Fitness and Nutrition for her findings on the value of physical activity programs as part of cancer treatment plans.



Schmitz



Owusu-Ansah

Sylvia Owusu-Ansah, associate vice chair of diversity, equity and inclusion and an MD, MPH associate professor of pediatrics and emergency medicine, is empowering women to take charge during health emergencies by leading initiatives to train Pitt's Division I athletes in CPR. Her efforts were recently recognized with the Health and Equity Leadership Award at the American Heart Association's Go Red for Women event.

José-Alain Sahel, an MD, received a major recognition for his efforts to transform patients' lives by restoring their vision. The Distinguished Professor, Eye and Ear Foundation Professor and chair of the Department of Ophthalmology was awarded the prestigious Wolf Prize in Medicine together with Botond Roska, an MD, PhD of the Institute of Molecular and Clinical Ophthalmology Basel. The Wolf Prize often heralds future honors—more than a third of past recipients have subsequently received a Nobel Prize.

Mehret Birru Talabi, an MD, PhD assistant professor of medicine in the Division of Rheumatology at the University of Pittsburgh, is a leader in the newly launched Equity in Maternal and Birthing Outcomes and Reproductive Health through Community Engagement Center. Funded by a $13 million NIH grant, the center aims to promote maternal health equity and reduce pregnancy-related complications, particularly within Black communities in Allegheny County.

Alexander Sorkin, chair of cell biology, ranked No. 2 in the world for his work in endocytosis by the ScholarGPS Highly Ranked Scholars classification, which recognizes the most productive authors whose works are of high impact and quality. Sorkin, a PhD, seeks to understand how endocytosis (in which surface membranes pouch inward and pinch off to form vesicles) regulates growth factor signaling within cells as well as dopamine neurotransmission. His lab pursues these questions in relation to both cancer and brain diseases like substance abuse. Sorkin is Pitt's Richard Beatty Mellon Professor of Cell Biology.

—Anvi Jain and Erica Lloyd



Sahel



Birru Talabi



Sorkin

From the courtroom back to the classroom

As a first-generation college student, **Brady Grano-Mickelsen** never felt bound by a fixed idea of what he could achieve. Now in his second year of medical school at Pitt with a JD and an MBA already in hand, he's forging a career that combines business, law and medicine.



RAYNI SHIRING/UNIVERSITY OF PITTSBURGH

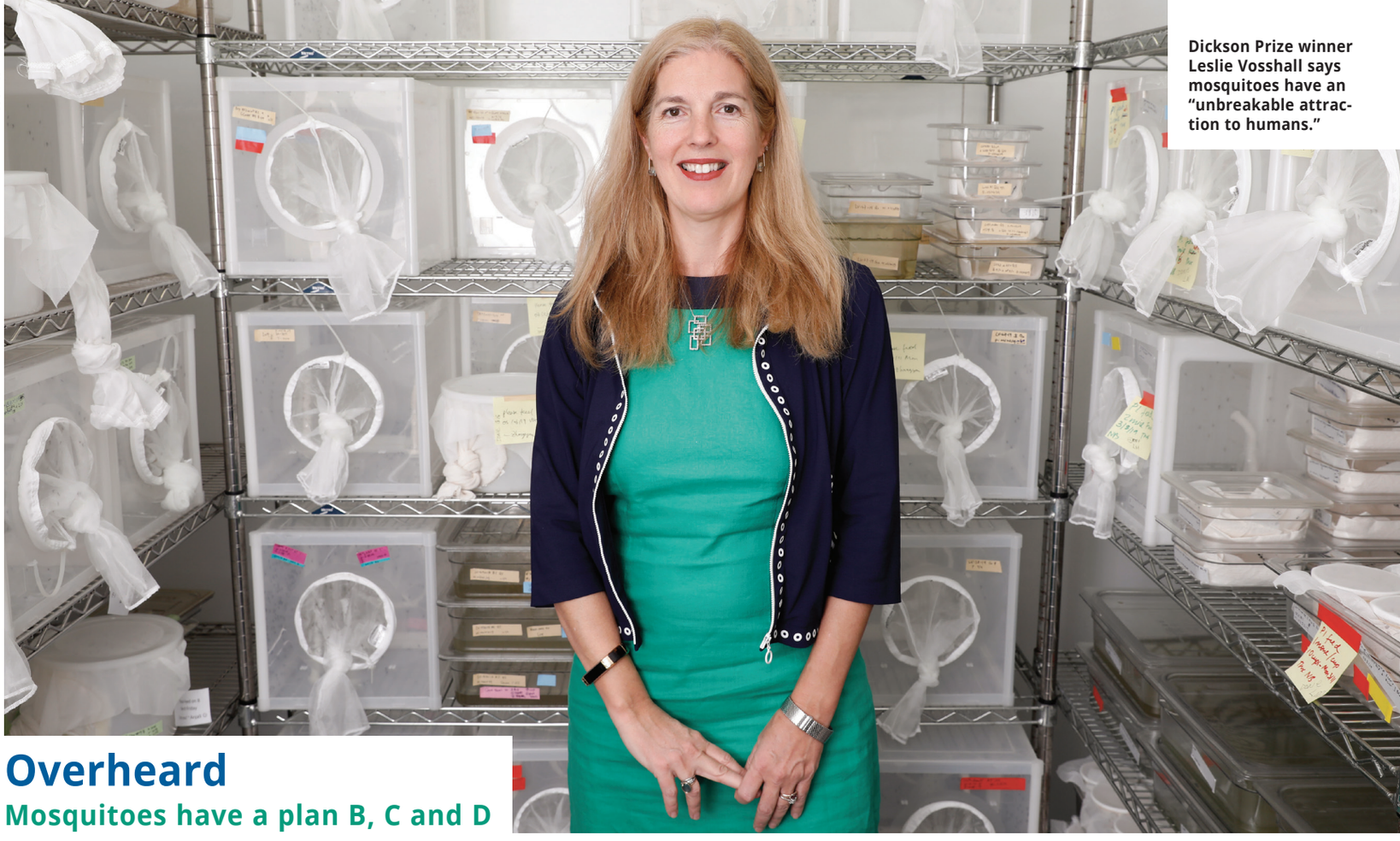
"At first I was joking," he says. "I think as a kid, I told my parents that I wanted to be a doctor and a lawyer. So that's kind of where it started."

Grano-Mickelsen has represented pharmaceutical and medical device manufacturers when they were investigated or criminally charged by the Food and Drug Administration (FDA) or the Department of Justice. His experience spans clinical and management positions for biologic research laboratories, along with regulatory compliance roles.

After earning his medical degree, Grano-Mickelsen aspires to work in policy on Capitol Hill while completing his residency and eventually seek a political appointment at the FDA.

Despite having plenty of postgraduate education, Grano-Mickelsen found that his shift from law to medicine was not as simple as he expected. "It took me a long time to build confidence in any type of scientific ability that I had," he says. The support and camaraderie among his class have eased the transition. Their outgoing nature, he says, has "made [Pittsburgh] feel more like home."

He also notes that many of his classmates intend to pursue advocacy work alongside medicine. Grano-Mickelsen appreciates Pitt's commitment to "expanding the traditional idea of medical education." By incorporating things like advocacy, he says, "[we're] making sure that we're aware of the society and the regulations and the laws that we're operating within." *—Amber Frantz*



COURTESY HHMI

Dickson Prize winner Leslie Vosshall says mosquitoes have an "unbreakable attraction to humans."

Overheard

Mosquitoes have a plan B, C and D

Leslie Vosshall is used to being the bearer of bad news.

In her work editing the genes of the mosquito species Aedes aegypti, the Robin Chemers Neustein Professor of Neurogenetics and Behavior at the Rockefeller University has continually found that the insects (actually, just the females) have backup plan after backup plan to find their preferred meal of human blood, which allows them to reproduce.

Their successful hunting leaves more than itchy welts in its wake. Aedes aegypti spreads viruses like dengue, yellow fever and Zika. Other mosquito species that carry malaria are responsible for hundreds of thousands of deaths every year.

Vosshall's findings on the genetic basis of chemosensory behavior in insects and humans earned her the 2024 Dickson Prize in Medicine, Pitt Med's highest honor. A PhD who is also vice president and chief scientific officer at the Howard Hughes Medical Institute, Vosshall gave her Dickson lecture on Sept. 27.

Just how strong is mosquitoes' attraction to humans?

Early on, we made mosquitoes that lacked one gene that allowed them to detect carbon dioxide. If you take a cage of normal mosquitoes, where the females have been hanging out, just chilling, and then you exhale into it, they immediately become super excited. The mutants that we made, they just kept sitting there and doing nothing.

But if you put them close to a human, they would still land and bite them. Carbon dioxide is just the beginning of the story that activates them. Right now, you're respiring, so you're giving off carbon dioxide. You're giving off heat. You're giving off smells. The mosquito uses all these sensors to find you.

If you take away one part of their olfactory system, we discovered completely by accident that they're much better at finding humans. They increase their acuity to heat—like a person who loses their sight becomes more acutely sensitive to touch or to hearing.

I am not here to give you a message of hope. Mosquitoes are always one step ahead of us.

What promising ways to repel mosquitoes are in the works?

A former fellow in my lab who now has a lab at Columbia University, Laura Duvall, made this really fundamental discovery. Mosquitoes go through this long-term satiety where, after they've taken a blood meal, for three to four days they just go back to hanging out on the ceiling. If you give them a human arm, they just don't care.

[Duvall] discovered a biochemical pathway for this and identified small molecules that would suppress their appetite. It's like Ozempic for mosquitoes. They feel like they've already had a meal.

What misconceptions about mosquitoes would you like to dispel?

There are all these myths about why some people are more attractive than others—that women are sweeter to mosquitoes, that it's blood type, that it's eating certain types of foods. It's not true. One thing that we could pinpoint with great certainty is that there are molecules—long-chain carboxylic acids belched out by the skin microbiome—that if they are present at higher levels on your skin, that makes you very vulnerable to being a mosquito magnet. It seems to impact people across age, race, gender and diet.

Another thing to dispel is that a lot of people are buying botanical [repellents]. I buy organic apples, but organic insect repellents are dangerous. They don't work. I would urge people to use repellents that work, where the ingredient is DEET or picaridin, not herbal lavender.

—Interview by Andrew Doerfler. The conversation has been condensed and edited for clarity.



Collaborations between vision leaders in Pittsburgh and Paris are blossoming.

COURTESY KELSEY MUCHNOK

Cross-Atlantic vision partnerships

World leaders in eye treatments and imaging came together in Pittsburgh to share advances in their disciplines at i2Eye, a conference hosted in September by the University of Pittsburgh Department of Ophthalmology, the UPMC Vision Institute and world-renowned institutions in Paris.

The sixth edition of the conference reinforced the relationship among vision innovators in Pittsburgh and Paris and laid the groundwork for further collaboration. It drew nearly 140 scientists, clinicians, engineers and trainees.

"These investigators coming from different fields rarely gather in this way," says José-Alain Sahel, Distinguished Professor, Eye and Ear Foundation Professor and ophthalmology chair. Sahel, an MD, is also the UPMC Vision Institute director and former founding director of Institut de la Vision in Paris.

His recruitment to Pitt in 2017 spurred Pitt's growing partnerships with Institut de la Vision, the Université Pierre et Marie Curie of the Sorbonne Universities in Paris, the Institut National de la Santé et de la Recherche Médicale (Inserm) and the Centre National de la Recherche Scientifique (CNRS).

The three-day i2Eye was held at UPMC Mercy Pavilion, which opened in 2023. The facility houses the new UPMC Vision Institute with research space for Pitt faculty in ophthalmology. (With clinicians and researchers under one roof, the Vision Institute allows for new, advanced treatments to reach patients with visual impairments more rapidly and seamlessly.)

In other cross-Atlantic news, Pitt and Inserm (France's primary national biomedical research agency) announced they will establish an International Vision Institute. It will be Inserm's first such partnership outside of Europe. Leaders from both institutions signed an agreement in October affirming their intent to collaborate on the project.

—Staff reports

$100 million renewal for trauma advances

In trauma care, every second counts, and even a slight delay can be fatal. "Trauma remains a leading cause of death in people younger than 45 years old," says Jason Sperry, an MD, MPH and the Andrew B. Peitzman Professor of Surgery at the School of Medicine. "It is also a leading cause of preventable death—which means that these people do not have to die."

Supported by an approximately $100 million renewal of funding from the U.S. Department of Defense, Pitt's schools of the health sciences will advance research to improve trauma outcomes through the Linking Investigations in Trauma and Emergency Services (LITES) network—a consortium of nearly 50 trauma centers across the United States and Canada.

Sperry is a coprincipal investigator, as are Stephen Wisniewski, a PhD and associate vice chancellor for clinical trials data coordination for the health sciences, and Francis Guyette, an MD, MS, MPH professor of emergency medicine. Leadership for the LITES network includes Pitt administrators Laura Vincent, Abby Cotton and Laurie Silfies.

The funding will support the network's 10th study, the Plasma Resuscitation Early for Evaluating Volume and Endotheliopathy of Thermal Injury (PREEVEnT) trial funding. Set to launch at UPMC Mercy—home to a top burn center—the study will explore whether giving plasma to burn patients earlier in their treatment leads to better outcomes. Around a dozen sites across North America will participate.

"Trauma patients are a difficult population in which to do research. Usually, there isn't time to enroll the patient in a clinical trial, and the transition from first responders and paramedics to doctors at the trauma center is fast and urgent," Guyette says. "You need a lot of infrastructure to ensure the trial is conducted in a way that both benefits the current patient and future patients. The LITES network brings those resources." *—Staff reports*

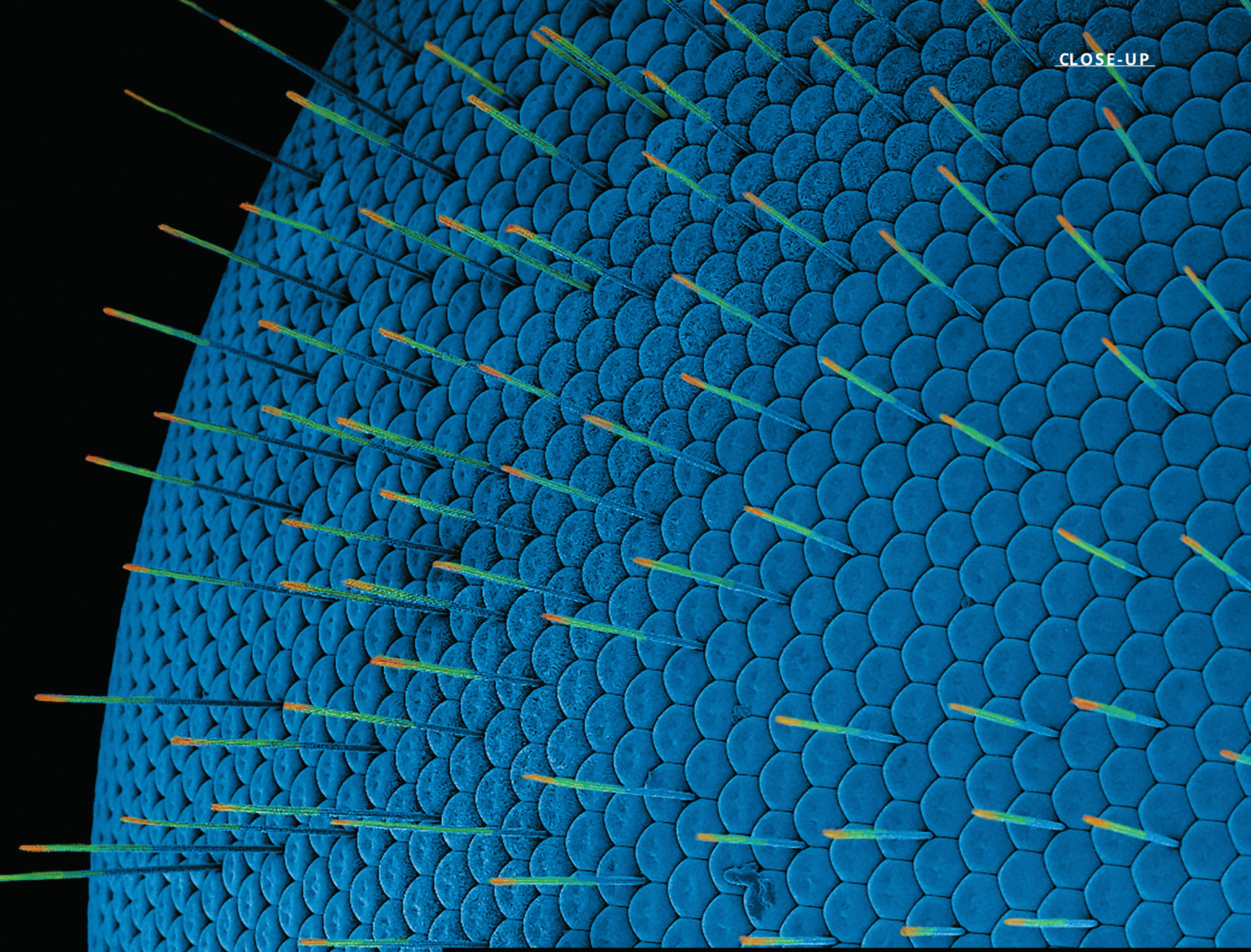
Major journal calls Pitt home

A team of physician-scientists at the University of Pittsburgh will serve as the editorial board of the American Society for Clinical Investigation journal JCI Insight for the next five years.

Leading the team is Oliver Eickelberg, Dorothy P. and Richard P. Simmons Professor of Pulmonary Research and executive vice chair for academic affairs in the Department of Medicine.

JCI Insight is known for publishing high-impact research that contributes to the understanding of the biology and treatment of disease, with an emphasis on clinically relevant basic and translational research. It is a sister journal to the Journal of Clinical Investigation, or JCI. Both are owned and published by ASCI, a nonprofit honorary scientific society of which about 75% of the scientists on Pitt's editorial board are members.

"It is the preeminent honorific scientific society of our day in medicine," says Eickelberg. *—Staff reports*



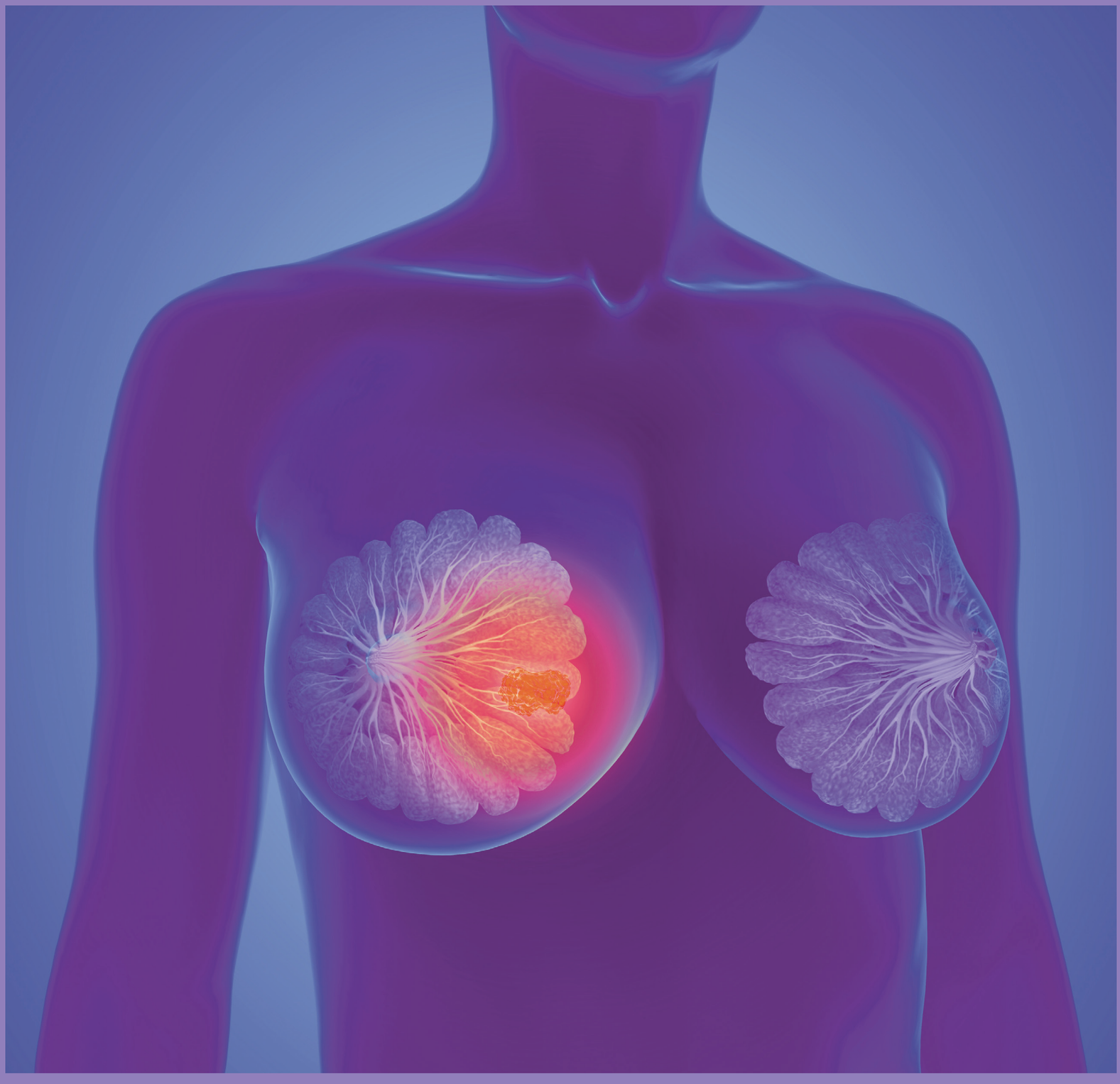
It's the little things

When **Donna Beer Stolz** looks through the microscope at human cells or insect body parts, she might see the makings of a holiday card, a collage or the centerpiece of an art exhibition.

Stolz, a PhD associate director of Pitt's Center for Biologic Imaging and a professor of cell biology and pathology, has been an author on more than 350 papers; her collaborators often rely on her transmission- and scanning-electron microscopy acumen. The scientist has also enhanced our understanding of cell signaling during liver regeneration and developed methods for isolating proteins and cells.

Microscopists and artists alike know her for capturing the beauty of life in vivid detail, demonstrating that little things really do mean a lot. Stolz, who is retiring in December after 33 years at Pitt, leaves a portfolio packed with striking images like the 250-times magnified moth eye seen here at micron resolution. (Her team adds color to many images like the above.) Two examples of her work have placed in the top 20 of the Nikon Small World photomicrography competition, which receives about 2,000 entries per year. That includes a second-place finish in 2011; the same year, the journal Nature named another shot among their "Images of the Year."

Stolz has curated several cell-centric art shows (including one honoring the famed HeLa cell line), provided the covers for numerous journals and books and, yes, adorned many a page in Pitt Med Magazine over the years. We wish her well. *—AD*



Researchers worried nitro fatty acids would accelerate tumor growth. Instead, the team found they could help treat one of the most aggressive and drug-resistant breast cancers.

POSITIVE FINDINGS

ABOUT TRIPLE-NEGATIVE CANCER

ANTI-INFLAMMATORY MOLECULES ALSO INHIBIT CANCER'S DNA REPAIR.

BY ANDREW DOERFLER

Not long after Carola Neumann arrived at the University of Pittsburgh in 2012 as an associate professor of pharmacology and chemical biology, Bruce Freeman approached her about a potential collaboration.

Freeman, the department chair, had been working to translate molecules called nitro fatty acids, which he and collaborators had found to have anti-inflammatory effects, into drugs for a variety of conditions. But a potential drawback concerned him: "We had to evaluate whether these anti-inflammatory molecules, which were entering into human safety studies, might accelerate tumor cell growth," recalls Freeman, a PhD and the Irwin Fridovich Professor and Distinguished Professor in the Department of Pharmacology and Chemical Biology.

Neumann, a cancer biologist, was a good fit for the project. Her lab was studying how amino acids called cysteines drive cancer cell growth, and she had questions about the interaction between cysteines and nitro fatty acids. At the recommendation of Nancy Davidson, then the director of UPMC Hillman Cancer Center, the team focused on triple-negative breast cancer, one of the most aggressive cancers and among the hardest to treat.

What the team found was that nitro fatty acids, far from accelerating tumor growth, instead were a possible therapy for patients of this brutal disease.

Neumann's team previously had found that a cysteine is important to the function of RAD51, a protein integral to several aggressive cancers.

"Nitro fatty acids often react with cysteines," Neumann says. "We thought, why don't we try to see if the nitro fatty acid interacts with that cysteine, and boom—it did."

The interaction inhibited the function of RAD51, hindering the DNA repair pathway that allows the cancer to resist therapies that try to kill it.

RAD51 is important to the health of all living cells, yet it is also "part of a machinery unique to certain cancers, meaning that those cancer cells depend very much on the DNA repair pathway that is functioning to keep the cancer cell alive," Neumann says.

The important interactions were identified by four graduate students—Chen-Shan Woodcock, Alparslan Asan, Dennis Braden and Lisa Hong—as well as John Skoko and Stacy Gelhaus, both PhD faculty members in pharmacology and chemical biology.

Crucially, the team also found no toxicity to normal cells, because they interact differently with the nitro fatty acids. After finding such promise in the first nitro fatty acid molecule they tried, they screened a library of 55 similar molecules. The first new candidate didn't work at all in a mouse model, a discouraging development.

"So we pulled ourselves up and identified another candidate," Neumann says. That one, they were pleased to find, effectively inhibited RAD51 and triple-negative breast cancer growth in the model.

Finding new treatment options for triple-negative breast cancer is urgent. The cancer's name comes from the fact that it lacks three receptors that are typical targets for some of the most effective therapies for other breast cancers. Patients are often left with radiation treatment or toxic chemotherapies, all of which have risks and severe side effects.

"The thing that Carola and the team have seen is that when you add in a nitro fatty acid that inhibits DNA repair, triple-negative breast cancer is highly sensitive to radiation treatment and DNA-targeting therapy," says Freeman. The effect is not just additive, Freeman says, it's synergistic—that is, the effect is more than the sum of their parts.



Freeman



Neumann

This could also mean less of the current treatments goes a longer way, cutting down on toxic side effects. Their drug, CP-8, would be a once-a-day oral pill that wouldn't add to the burden of onerous treatments patients are already taking on.

Their findings have been published in studies over the last several years in the Journal of Biological Chemistry and Redox Biology. The team expects what they've learned will be relevant to other cancers—such as ovarian, prostate, pancreatic—that are similarly sensitive to DNA-damaging therapies. (Mutations to the BRCA genes are the most well-known cause of this genomic instability, but there are others.)

The team has started a company, Creegh Pharmaceuticals, to move their work toward clinical trials, and CP-8 is currently going through the Food and Drug Administration's Investigational New Drug process to test its safety. It will be about three years, they expect, before the drug is available to patients.

"Our mission is to give new optimism to patients with little hope," Freeman says. ■

Nitro fatty acids may lead to new treatments for a range of diseases. Read about another on the next page.

LARS NEUMANN/GETTY IMAGES

HEADS AND TAILS

STITCHING TOGETHER A BETTER SICKLE CELL DRUG

BY MICHAEL AUBELE



POCO BW/GETTY IMAGES



Straub



Chowdhury



Wood



Xu

You might say that rather than heads or tails, a team of University of Pittsburgh researchers is playing heads *and* tails with a drug candidate called CP-50. Only it's not a game; they're testing its potential to treat sickle cell disease better than other drugs.

CP-50 has what researchers describe as a dual warhead effect. Its quinone "head" and nitro fatty acid "tail" each address different complications from the disease. As a heat-stable oral drug, it would be useful in areas lacking the resources, access and infrastructure for treatments that require intravenous delivery or gene therapy; the developers are anxious to get it to patients in sub-Saharan Africa, where the disease is most prominent.

Adam Straub, a PhD professor of pharmacology and chemical biology and principal investigator on the project, says that while there are other oral medications that address obstructed blood flow and pain, CP-50 has the potential to treat more hallmarks of the disease.

"There's still a great need to develop new small molecules that have multiple different targets to limit the pathologies of this complex disease," he says.

In sickle cell disease, red blood cells are misshapen due to a genetic mutation that affects hemoglobin, the protein they contain that carries oxygen. Usually, red blood cells are disc-shaped, flexible and move easily through blood vessels. But when they sickle, or become crescent-shaped, they don't bend or move easily, and they obstruct blood flow. As a result, people can experience pain, infections, organ damage, stroke and other health problems. Upward of 400,000 people are born each year with sickle cell, including about 100,000 in the United States. But the majority are in sub-Saharan Africa.

Katherine Wood and Fabliha Chowdhury, PhD researchers in Straub's lab, discovered that hydroxyurea, a common therapy for sickle cell disease, is less effective at keeping red blood cells round and flexible in patients who carry a high-frequency genetic mutation. The finding was published in Blood Advances and highlights the need for new therapies.

A Redox Biology report penned by Chowdhury discusses how CP-50 may be an answer. Its head-and-tail composition has the potential to benefit many sickle cell patients.

Its head has an antioxidant effect that acts as a sponge to limit the accumulation of damaging molecules, while its tail fights inflammation and other oxidative stress. The buildup of harmful molecules and not enough defenses to stop them causes organ damage and disease.

CP-50 provides protective actions on hallmark pathology of sickle cell disease, says Straub: Vascular function is improved when hemolysis (red blood cell destruction) is inhibited, and anemia (lack of red blood cells) is reversed.

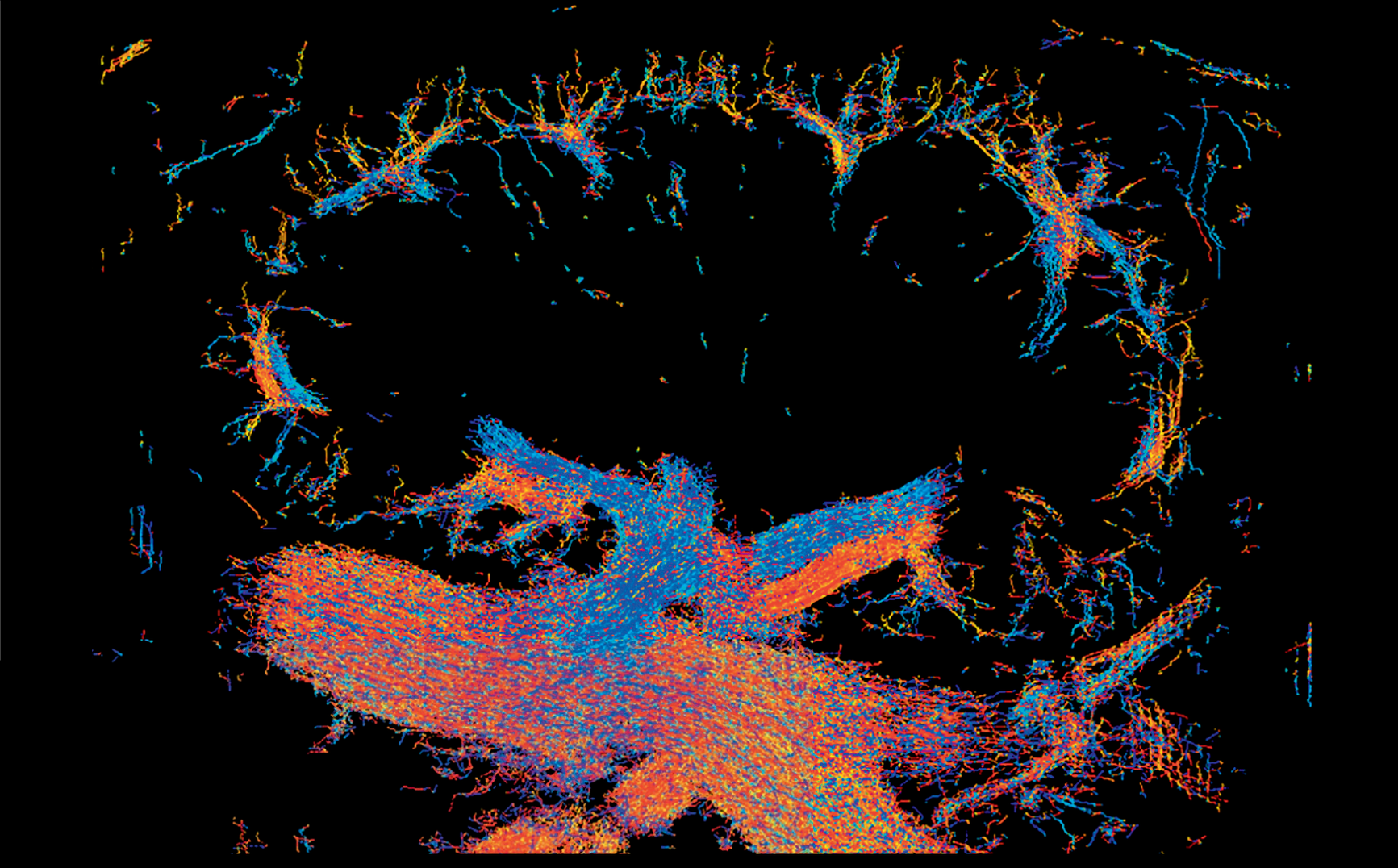
"While many drug companies focus on creating highly targeted treatments, sickle cell patients often receive multiple therapies at once—a 'polypharmacy approach.' We took a different tack and developed an orally available, single [hybrid] molecule that targets multiple pathways, offering a wide range of benefits. With just a few chemical reaction steps, we successfully 'stitched together' a quinone and nitro fatty acid to create this potent, multifunctional drug."

Straub says that colleagues Bruce Freeman, a PhD and the Irwin Fridovich Professor and Chair of the Department of Pharmacology and Chemical Biology, and Francisco Schopfer, a PhD professor of pharmacology and chemical biology, discovered years ago that nitro fatty acid molecules inhibit tissue damage and inflammation.

"They discovered the mechanisms by which they work, but we developed a hybrid, multitarget molecule by adding the naturally occurring quinone," Straub says.

Straub and his team are partnering with Julia Xu, an MD assistant professor of medicine who specializes in sickle cell, as a clinical expert. They're hoping to move CP-50 to clinical trials and expect doing so will go smoothly because nitro fatty acids are already being tested in trials for other diseases.

"We're hoping to translate this from bench to bedside within the next few years," Xu says. ■



LETTING OFF HEME

HOW SICKLE CELL DISORDERS MAY DRIVE CHRONIC KIDNEY DISEASE

BY ASHER JONES AND ANVI JAIN

Super-resolution ultrasound imaging shows how repeated exposure to heme leads to extensive loss of small blood vessels in the kidneys of mice with sickle cell disease. (Image courtesy Qiyang Chen and Kang Kim.)

While the average American can expect to live around 78 years, those with sickle cell disease have their life expectancy reduced by about two decades, with many patients only living into their 50s. A major contributor to that bleak outlook is chronic kidney disease, which affects more than half of patients with sickle cell.

A study from Pitt researchers published in August in the journal Blood suggests that this serious complication may be driven by the oxygen-binding molecule heme, which is released from the fragile red blood cells of sickle cell patients.

"When heme is inside red blood cells, it's essential for carrying oxygen to different tissues around the body," explains senior author Samit Ghosh, a PhD assistant professor of medicine and member of the Vascular Medicine Institute. "But when heme is released out of the cell via hemolysis, it's toxic to organs and tissues."

To learn about the connection between hemolysis and kidney disease, the team infused mice with repeated heme exposure. They found it led to damage of the renovascular endothelium, the layer of cells lining the kidney's blood vessels, and renal failure. (The super-resolution ultrasound image above shows damage in the vessels of mice.)



Ghosh

Their findings not only suggest that ongoing hemolysis drives chronic kidney disease but also showed an increase of an endothelial protein called EPCR in the bloodstream of the heme-infused mice, which mirrors elevated levels in sickle cell patients with chronic kidney disease.

"Our findings suggest that blood levels of EPCR could act as a potential biomarker of chronic kidney disease in patients with sickle cell disease," said Ghosh. "If we can predict who is at greater risk for kidney disease, we could treat these patients earlier to help prevent disease progression." ■

COMING OF AGE

BY ERICA LLOYD

ILLUSTRATION BY MAGGIE NEGRETE



At 25 years old, Pitt Med Magazine is the age of many med students.

We invite you to take a walk down memory lane with us to see what was unfolding here at the School of Medicine, as well as more broadly in medicine, during that quarter century. On these pages, we offer highlights of that story alongside one of an imagined med student (we'll call her Violet) as she comes into her own.

Fall 1999

First issue of magazine

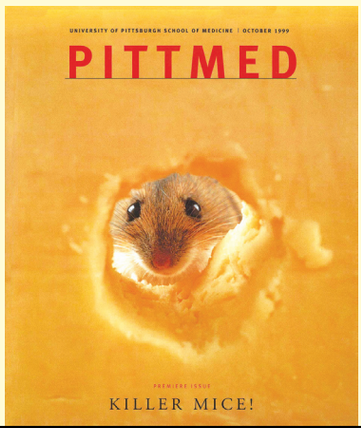
Around the time our med-student-to-be, Violet, was born, her parents were worried about whether their computers would work after Y2K, and the Human Genome Project had nearly completed a detailed account of the human genome. Among the news items in the first issue of the magazine: A Pitt infectious disease expert's hypothesis that viral load played a huge role in determining an HIV patient's prognosis had gained acceptance. Faculty members in the Department of Surgery were welcoming dexterous robotic systems as part of the OR teams. A cardiology faculty member, referring to how genes were now "knocked out" in mouse models to study disease, said, "Gene therapy, in some distant, future world, might actually correct such defects."

2000–2010

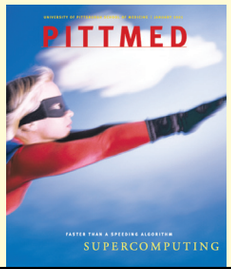
As Violet started to crawl and then toddle, the med school dean and senior vice chancellor for the health sciences, Arthur S. Levine, who had been recruited in 1998, was making moves of his own. He was determined, for instance, that Pitt would lead the way in educating a new generation of physician-scientists, so the school began requiring every med student to complete a scholarly research project through their four years here. (Eventually, leaders at other top schools would take notice of how well-prepared Pitt Med graduates were and began to adopt similar programs.)

Just as Violet's parents began enforcing bedtimes, the Accreditation Council for Graduate Medical Education was

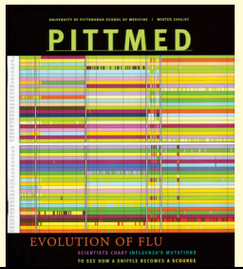
Our first cover story, "Killer mice!" described how molecular changes can bring about dramatic behavior changes. Other cover stories from the first decade of publication (this page, left to right) reported on supercomputing supercharging discovery, tracking virus evolution and what we were learning about cancer.



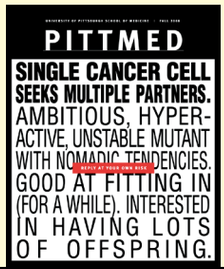
Fall 1999



Winter 2001



Winter 2006–07



Fall 2008



enforcing new standards for resident and fellow work hours, hoping to combat exhaustion among these fledgling doctors. A 2002 Pitt Med cover feature reported that graduate medical trainees would be constrained to working no more than 80 hours a week on average.

Cover stories highlighted the school's bursting onto the scene in the basic sciences. For instance, in "Dark arts," we got a glimpse of structural biologists exploring the natural world beyond visible light; in "Biology reloaded," systems biology recruits argued for studying organisms holistically rather than one component at a time. Pitt researchers had discovered one of seven known cancer-causing viruses (Merkel cell polyomavirus); these same investigators had already identified another. (They'd informed the world that Kaposi sarcoma is brought on by a herpes virus.)

Meanwhile, studies from a range of fields were demonstrating more differences between the sexes than we'd ever imagined, even at the cellular level, portending huge implications for medical research and care.

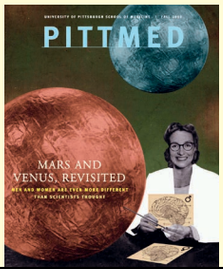
2011–2019

Violet gradually became less interested in playing Mario Kart with her brother and more interested in playing jazz with her friends. A summer volunteering in a neuroscience lab piqued a desire to go into medicine.

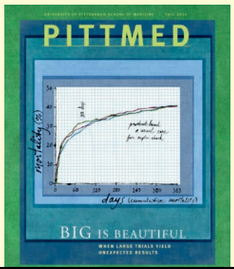
During this time, Pitt immunologists and transplant doctors were finding ways to teach the body to accept new organs. A computational biology researcher was letting us know that junk DNA was not so junky. And thanks to insights gleaned from neurobiology studies here, patients with paraplegia were able to move a robotic hand just by thinking about it. That breakthrough resulted in a fist bump photo-op with then-President Barack Obama.

By this time, biomedical researchers were rubbing their hands with delight as they looked to the combined power of genomics, big data and the latest computational tools to determine why some patients respond to therapies or develop certain conditions when others don't. Pitt, in fact, established an institute for precision medicine, as well as centers devoted to aging, vision, drug discovery and other areas where it was positioning itself to make a difference.

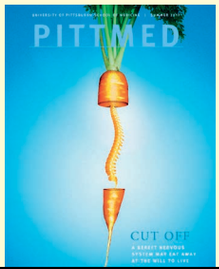
In the first two decades of Violet's life, the school added another 10 departments and several graduate programs (some in conjunction with Carnegie Mellon University).



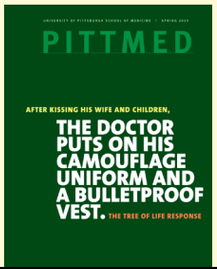
Fall 2010



Fall 2014



Summer 2017

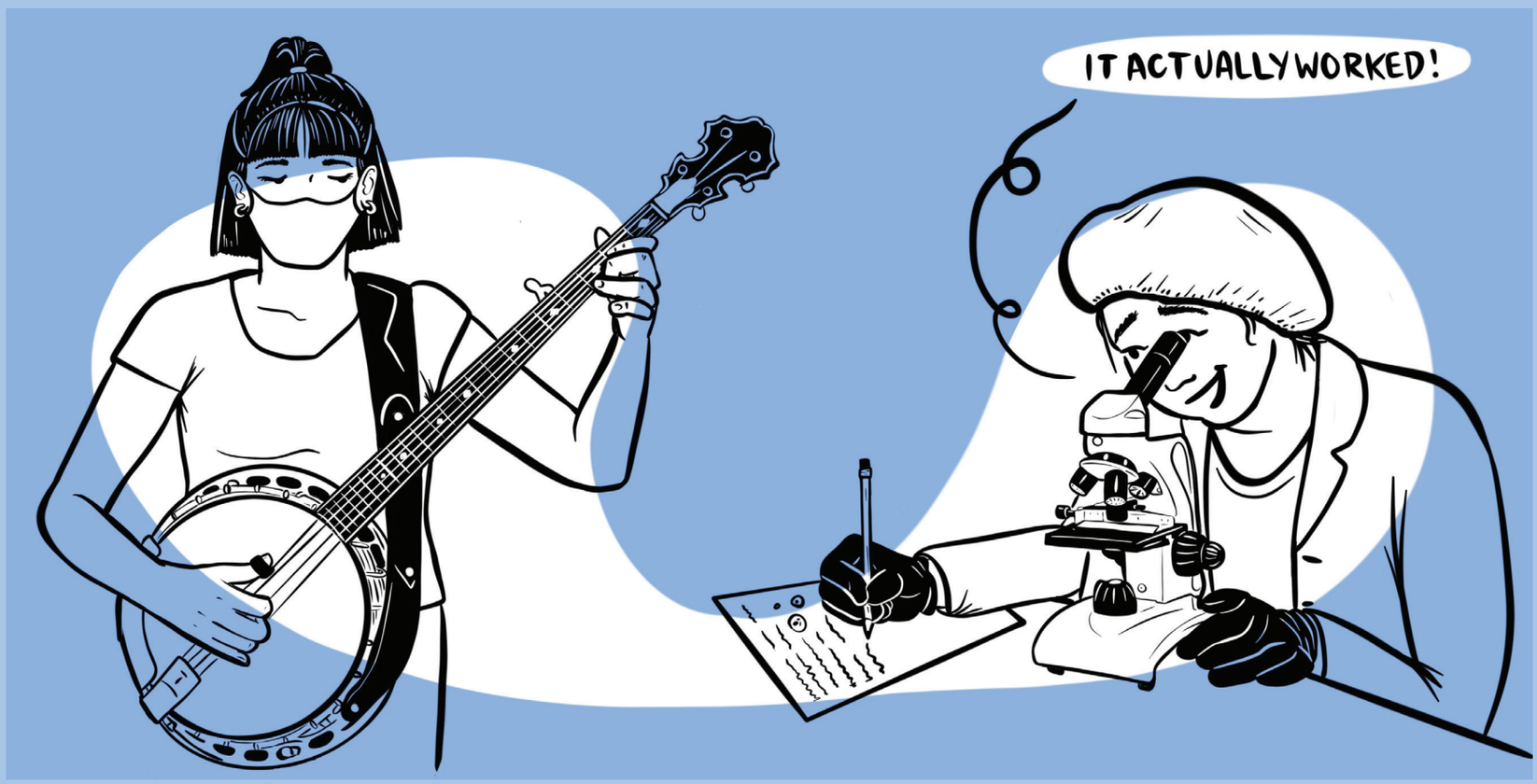


Spring 2019



Summer 2019

Among the many topics explored in the next decade (left to right, this page): how women are not small men, large clinical trials reveal unexpected results, metabolic deficiencies eat away at the will to live, physicians called to action during the Tree of Life massacre and new ways to build tolerance among organ recipients.



2020–2024

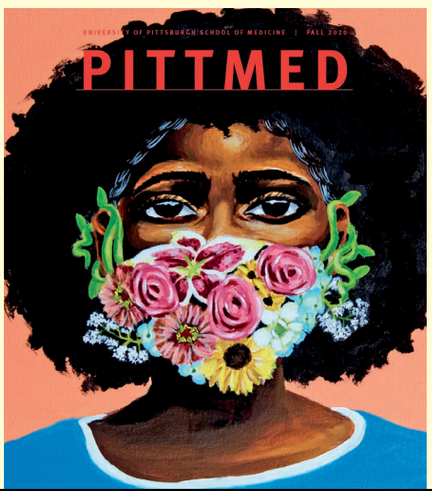
Pitt had become a powerhouse in health sciences, ranking in the top 9 for National Institutes of Health funding for most of the past two decades. Under Anantha Shekhar, the new John and Gertrude Petersen Dean and senior vice chancellor for the health sciences who took the helm in 2020, the University would soon rise even higher, to No. 3 in NIH funding.

Violet was further inspired to become a doctor as the COVID-19 pandemic shined a light on dramatic health inequities in our country. In the midst of the pandemic, the School of Medicine reassessed how it taught and studied medicine and disease. New emphasis was placed on understanding the environmental and societal circumstances that influence a person's health. And as researchers approached their neighbors to investigate the conditions that plagued them, increasingly, they saw them anew as partners (studying "with" them, rather than conducting studies "on" them).

Among the top schools for psychiatry and other fields that intrigued Violet? Pitt Med. Attracted by the school's research heft, as well as its focus on community-engaged scholarship, she applied (as did 7,177 others that year) and was accepted.

Violet donned her short white coat just as the School of Medicine finalized its Three Rivers Curriculum, which reshaped medical education in favor of small group and case-based learning. In fall 2023, Violet and her classmates made themselves at home in Alan Magee Scaife Hall's beautiful new West Wing, a long-awaited expansion for the school. (See page 4 for the many more facilities added since 1999.)

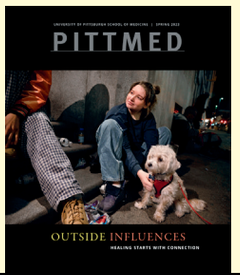
There's been plenty of good fodder for the magazine of late: Our "Let there be sight" cover story highlighted how an international collaboration among ophthalmologists and engineers is partially restoring vision to people blinded by retinitis pigmentosa. "Steel Valley to become Bio Valley" reported on a Pitt and Richard King Mellon Foundation–led effort to create a life sciences sector in the city, with a biomanufacturing innovation facility at its heart. In "AI for all" we learn how Pitt Med grads will be savvy about artificial intelligence applications in medicine.



Fall 2020



Summer 2022



Spring 2023

During the pandemic, issues of equity rose to front and center, and we reexamined the idea of race as a risk factor. Other cover stories shown: serving Plain People and health sciences students on street rounds.



What's next?

Of course, we don't really know what we will report on in the years to come, but we can lay some bets that align with Dean Shekhar's vision for the health sciences.

Students will glean a richer understanding of how health conditions affect underrepresented groups as they get to know a local organization as part of the Community Alliance Program. (This program is in addition to the ongoing requirement of a longitudinal research project, so Pitt Med grads will be exceptionally prepared to find health solutions.)

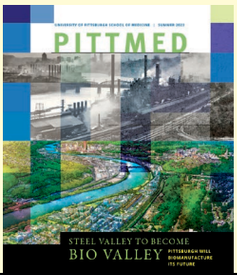
As interprofessionalism is baked into the curriculum, students will have a better understanding of what other health professionals bring to the table.

Pitt people will invent and bring even more new therapeutic interventions to patients as manufacturing, commercialization and clinical trial processes here are strengthened.

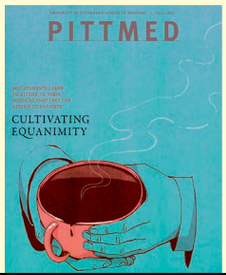
Pitt scientists will continue to tap into, and shape, the latest and greatest tools, such as spatial omics (see this issue's cover story), CRISPR and machine learning. We can't wait to see what they discover as they do. ■

HEALTHY OUTLOOK

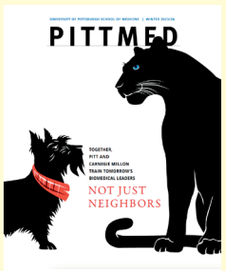
And what's on the horizon for Violet? Soon, she'll graduate from one of the top tier schools of medicine with a great deal of curiosity and compassion, as well as a strong work ethic. She'll find her way.



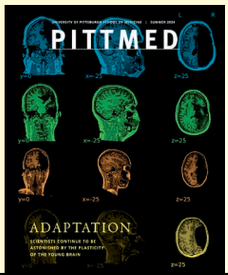
Summer 2023



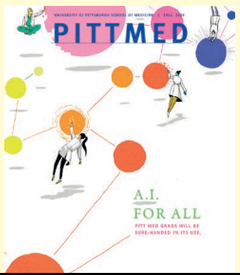
Fall 2023



Winter 2023–24



Summer 2024



Fall 2024

Covers in recent years (this page, left to right): "Steel Valley to become Bio Valley," "Cultivating equanimity," "Not just neighbors" (Pitt and Carnegie Mellon, that is), "Adaptation" (the young brain is more astonishing than we thought) and "AI for all."



UN

DAUNTED

ANNE MARIE LENNON WILL FIND A WAY.

BY SHARON TREGASKIS

PORTRAIT BY RAYNI SHIRING UNIVERSITY OF PITTSBURGH

Pancreatic cancer kills. And because it's often detected only after the disease has advanced well beyond the abdominal gland in which it originates, death comes fast. Around 70% of people with the disease die within 12 months of diagnosis; just 13% are still alive at the 5-year mark. By 2030, pancreatic cancer is projected to surpass colon cancer to become the second leading cause of cancer deaths in the United States.

The University of Pittsburgh's new chair of medicine, gastroenterologist Anne Marie Lennon, has dedicated her career to understanding the origins of the disease and detecting it early, when her patients have their best chance for extended survival with treatment. In 2017, that work yielded a blood test that was engineered to detect the earliest signs of eight different types of cancer, even before symptoms manifest.

To evaluate the test's merits, Lennon and her colleagues designed DETECT-A, the first large, prospective, interventional clinical trial of its kind. They enrolled about 10,000 women between the ages of 65 and 75 with no prior history of cancer. The cohort they had in mind would be old enough to have a higher risk of the types of cancer the test might detect—including ovarian and breast—and not so old that the benefits of earlier treatment would be obscured by the other forms of mortality that increase as we age.

Before they could start recruiting participants, Lennon and her collaborators needed the go-ahead from two institutional review boards—committees overseeing the ethics and regulatory compliance of studies involving human subjects.

The IRB members had a lot of questions. As one of the more strident critics put it, "Why would you want to detect pancreatic cancer? Everyone dies."

Colleagues credit Lennon with engaging deeply with those concerns. She and her team compiled and shared the body of evidence that supports early diagnosis and treatment to extend survival for people with pancreatic cancer, as well as the other cancers the test detects.

They didn't stop there. The team significantly expanded and refined the DETECT protocol. They proposed cross-checks to replicate blood test results, both positive and negative, as well as surveys to learn more about participants' experiences of anxiety or stress related to testing and its results. They also proposed tracking participants' adherence to recommendations for mammogram, colonoscopy and other established cancer screening tests throughout the study period.

They also invited the IRB members who voiced the greatest concerns to join the study's advisory committee—to take a formal and ongoing role on the project.

"I think we all want the same thing—the best for patients," says Lennon, the lilt of her upbringing in Dublin softening her vowels. "We all want to detect cancer earlier and cure it. So how can we come together, find solutions and protect patients?"

In 2020, Science published findings from the resulting clinical trial, with Lennon as first author.

"We found that the test worked in real life," she says. "We were able to detect cancers early and advanced, and of the 10,000 women, just three people went to surgery that didn't have cancer," she says. "Two had high-grade dysplasia and one had a huge mass that was not cancerous." Ongoing studies are laying the groundwork for FDA review.

Thousands of people facing pancreatic disease have already benefited from Lennon's dedication and drive, and now the University of Pittsburgh and the communities it serves across Pennsylvania and beyond will as well.

This year, Lennon became the first woman to head Pitt's Department of Medicine. She oversees more than 1,000 faculty members with combined clinical and research revenues of nearly $600 million.

"She's an extraordinarily positive force of nature," says Ralph Hruban, who directs the Department of Pathology at Johns Hopkins University and has worked closely with Lennon since 2008.

"She has positive energy that she brings to everything that gives you a can-do feel, and at the same time she's humble and selfless and confident."

Consider, for example, Lennon's first foray into leadership, which laid the groundwork for DETECT. During a two-year fellowship at Hopkins in advanced endoscopy, Lennon focused on endoscopic ultrasound and a diagnostic and treatment technique called endoscopic retrograde cholangiopancreatography. And as she made the transition from fellow to assistant professor, she hatched a plan to use her advanced skills to do better by people with pancreatic cysts.

Though often benign, pancreatic cysts can—rarely—become cancerous. When Lennon was a trainee, clinicians lacked prognostic tools to distinguish which cysts could be monitored and which must be removed. For most patients, surgery was the standard of care. Yet retrospective analyses showed that most of those patients could have done without those operations, which themselves carry a risk of long-term complications and even death.

Lennon pitched her supervisors, including Hruban, on the creation of a multidisciplinary clinic whose experts would review individual cases akin to an approach Hopkins was already using to personalize care for people with pancreatic cancer.

"My boss said, 'You're out of your mind,'" Lennon recalls. "He said, 'No one will come, but you can do it.'"

Hruban and another mentor, however, urged Lennon to barrel ahead.

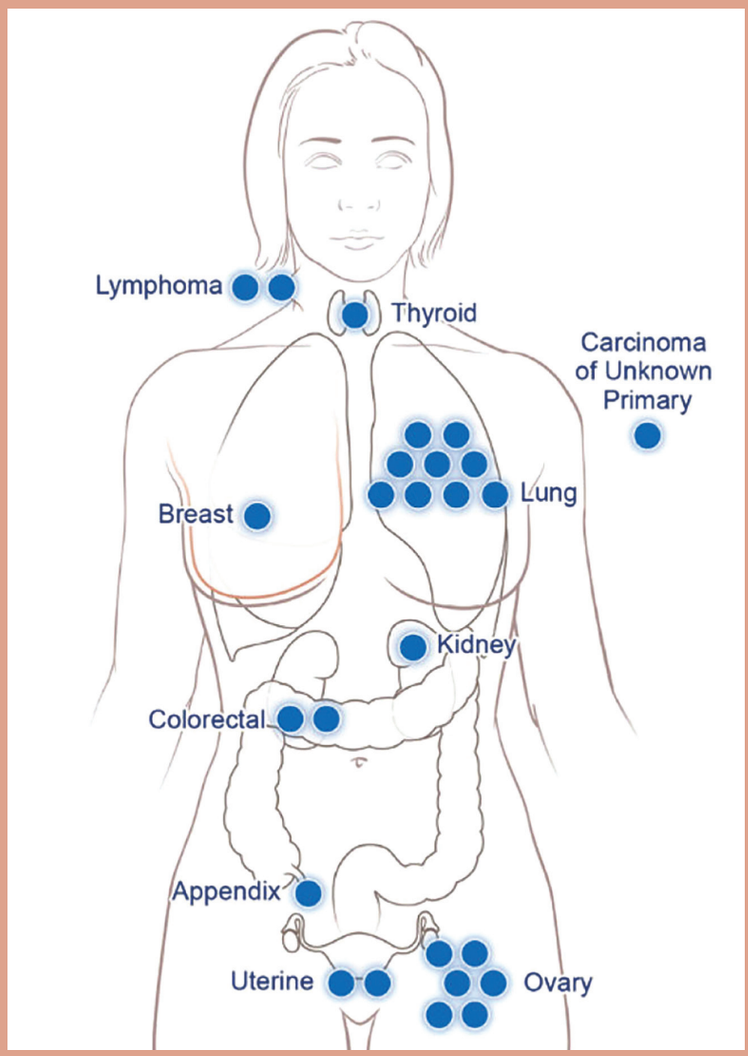
As founding director of the new clinic, Lennon had a fancy title, though no salary bump and no budget. That first year, the team was just Lennon, Hruban and a surgeon. As their patient population grew, Lennon cast an ever-widening net of experts. A radiologist, more surgeons, a nurse practitioner, a physician assistant and trainees in pathology and radiology joined the team. "She was always interested in what was best for the patient," says Hruban, who notes that Lennon was meticulous about eliciting input from everyone on the team.

"My boss said, 'You're out of your mind,'" Lennon recalls. "He said, 'No one will come, but you can do it.'"

The multidisciplinary review process altered the management of 30% of their cases, laying a foundation for clinical guidelines adopted by the American College of Gastroenterology and the International Association of Pancreatology.

Still, postoperative analyses showed that a stubborn fraction of cases referred to surgery by the Hopkins clinic could have been treated less invasively. A trio of Hopkins scientists had been developing methods to isolate molecular markers of cancer. Lennon saw promise in tailoring the approach for people with cysts and reached out to Bert Vogelstein, Ken Kinzler and Nick Papadopoulos. Already, they had cracked the

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The DETECT-A trial showed that blood tests could reveal previously undetected cancers, with hardly any false positives. "We were able to detect cancers early and advanced, and of the 10,000 women [enrolled in the trial], just three people went to surgery that didn't have cancer," says Lennon. The DETECT blood test found 26 cancers in 10 organs (blue dots). Standard treatment detected an additional 24 and another 46 were found by other means.

code on a blood test for cervical cancer. With Lennon, they turned their attention to the pancreas.

When Vogelstein, Kinzler and Papadopoulos asked for more patient samples to examine, Lennon picked up the phone: "I called all my friends and said, 'We want to find cancer earlier. This is what we're doing, do you want to be part of it?'"

The resulting report identified a panel of molecular markers and clinical features for the accurate classification of cystic neoplasms. Published in 2015 by Gastroenterology, the paper credited coauthors from 18 centers in Belgium, Ireland, Italy, Japan, Korea, the Netherlands, Portugal and across the United States.

"It's one little example, but it illustrates the general concept of bringing people together for a bigger picture," says Lennon, who highlights the hundreds of patients worldwide who signed onto the project. "We would explain, 'This is where we are. This is where we hope to be. Would you give us blood, cyst fluid, to share with scientists?'"

One of those scientists was Aatur Singhi, a chief resident in pathology at Hopkins when he started working with the multidisciplinary clinic in 2011.

The work Lennon led was foundational, says Singhi, an MD, PhD who joined the Pitt faculty in 2012 and is now an associate professor and director of anatomic pathology research.

"She focused on answering the big questions for patients: What type of cyst are you dealing with? Could it turn into cancer or is it benign?" The key was in the fluid biopsies Lennon was able to collect deep within pancreatic cysts through minimally invasive endoscopy. "She showed that she could diagnose a pancreatic cyst based on the molecular profile and predict whether it would turn into cancer during the patient's lifetime."

The findings reported in 2015 also laid the molecular foundation for an even more ambitious approach to presymptomatic cancer detection.

Like the stardust in Earth's atmosphere, our blood is awash in molecular debris, including—among people with even early stage tumors—DNA and protein fragments shed by dying cancer cells. The Hopkins team set to work designing a single blood test powerful enough to detect that cancerous detritus and localize the organs in which the associated tumors had originated. They dubbed it CancerSeek.

Their goal was a screening test both specific enough to minimize false positives and sensitive enough to accurately identify the unique combinations of markers associated with eight types of cancer: breast, colorectal, esophageal, liver, lung, ovarian, pancreatic and stomach. Combined, they account for more than 60% of cancer fatalities.

While the basic scientists refined the test parameters, Lennon laid the groundwork for a series of trials. The first, reported in 2018 in Science, provided proof of concept. CancerSeek achieved 99% specificity—only 7 of the 812 healthy controls received false positive test results. Meanwhile, sensitivity of the test—its accuracy zeroing in on the types of cancer among the 1,005 participants who had already been diagnosed—was promising. Among the five types of cancer for which no presymptomatic screening exists for average-risk adults—ovarian, liver, stomach, pancreas and esophageal—CancerSeek had sensitivities ranging from 69% to 98%.

The next step was DETECT-A. "Anne Marie was involved from the beginning," says Papadopoulos, who credits Lennon's work ethic and "Irish calm" for keeping the project on track with both health care systems involved in recruiting study participants.

"Anne Marie first tries to understand the issues, then tries to offer a first solution," he says. "You can tell that she's worried, but the voice stays the same, the smile stays the same, and she goes to work."

What motivates her? "I hate telling people

that they have cancer, that it's not curable," says Lennon. "One of my passions is to not have to do that. I'm bringing teams together and helping them remember the direction we're going, which is to try to change the lives of our patients—not to fight over first and last author."

Joanna Law, an MD, trained with Lennon as an endoscopic fellow from 2012 to 2014. "I'm still mindful of the way she taught," says Law, now a therapeutic gastroenterologist at Virginia Mason Franciscan Health in Seattle. "Expect the unexpected." The principle wasn't limited to the complex procedures in the OR.

"She takes that approach to life in general," says Law.

As a physician-scientist who earned her MD and PhD in her native Ireland, Lennon faced a Heller-esque Catch-22 to medical licensure in the United States in 2010, as she transitioned from fellow to assistant professor. In the decade since she had taken the first two levels of the U.S. Medical Licensing Exam (as a resident at the Cleveland Clinic in the late 1990s), USMLE had instituted a third exam. After she passed it in 2009, state officials informed her that all three steps had to have been passed within seven years for licensure in Maryland. To retake exams she had already passed, however, required a series of requests, rejections and appeals involving both USMLE and the state licensing authority, and ultimately a return to Ireland.

"I sold everything, had no money, moved in with my parents in my 30s, re-sat all of the exams," says Lennon. "We're talking Krebs cycle, basic surgery.

"I think if you're really passionate about something, you'll do what you need to do to get there."

At Hopkins, she knew her division had the capacity to generate breakthroughs to improve care, so she put institutional structures in place to sustain translational research. Lennon allocated division funds for research that connected basic and clinical scientists, achieved salary increases for faculty, launched a suite of programs to guide junior scientists through the grant writing process and established a dedicated clinical translational research unit within the division that offers project management, research coordinators and IRB support. The unit now boasts close to 100 ongoing projects that have collectively tapped funding from a range of sources, unlocking a flood of discovery.

"Whatever she envisioned," says Hopkins colleague Elham Afghani, an MD, MPH, "she made it happen."

Since coming to Pitt, Lennon has turned her attention to the system-level challenges facing patients and their providers. Her priorities include supercharging the path from basic discovery to clinical care, enhancing access to clinical trials for the 350,000 patients the department sees every year and promoting job satisfaction and staving off provider burnout.

As she's been getting acquainted with Pitt, she's had some big questions: What about marginalized communities? How are we doing in our own backyard, the Hill District, a part of the section of Pittsburgh where the legacy of redlining and economic disenfranchisement combine for the region's highest infant and maternal mortality rates and lowest lifespans? And for rural people living several hours' drive from Pittsburgh, how can technology affordably enhance access to specialists across the commonwealth and beyond? And how do we address the burgeoning health care needs of an aging population facing a shortage of geriatricians?

"What gets me out of bed is having an impact on a larger level," says Lennon, noting the unique potential in Pitt's integration of six schools of the health sciences and hefty clinical partnerships. "We've got brilliant clinicians and scientists, an enterprise treating 5 million, plus an incredible VA group.

"[Pitt] has incredible people, and when you have incredible people, you can do incredible things."

It's here that her longtime collaborator Aatur Singhi further developed a diagnostic panel based on the work he started with Lennon and Hruban in 2011. It took scientists at Hopkins five years to convert their research lab protocol to a test that meets the federal government's quality standards for clinical use; Singhi accomplished the same in just one at Pitt. "Aatur brings novel ideas into clinical practice and makes them available for patients at UPMC, across the U.S. and around the world," she says.

Lennon intends to cultivate such efforts across the Department of Medicine. "You can have great ideas, show they work," she says. "But we have to show that it's cost-effective and convince payers that it's worth their while to pay for it, or that great idea never gets into clinical practice."

Toren Finkel, head of Pitt's Aging Institute, says that Lennon cultivates the creativity necessary to surmount entrenched challenges in medicine.

"Academics tend to think—as does the NIH and others—along these hierarchies of organ systems: kidney, lung, heart. But obviously the body is integrated, and there are processes, like aging, that affect all of these organs. If you think differently, you can reap insights by seeing what's common across medical domains," says Finkel, the G. Nicholas Beckwith III and Dorothy B. Beckwith Professor of Translational Medicine.

Just a few months into her role, he says, that expansive approach has spurred new connections among Aging Institute faculty and

"What gets me out of bed is having an impact on a larger level," says Lennon, noting the unique potential in the integration of Pitt's six schools of the health sciences and hefty clinical partnerships.

COURTESY A. LENNON



Lennon at the helm passing glaciers in the Southern Ocean.

people with relevant interests throughout the Department of Medicine.

"She's been incredibly effective at getting things done, but she does it in such a delightful and cheery spirit—she's always smiling," says Finkel. "She doesn't seem to be flustered by the usual incoming fire. She sees the important things and lets the little things dissipate."

When Pitt's search committee invited Lennon to give a job talk in her bid for the post as chair of medicine, she started with slides about her own family history—her admiration for her father, himself an academic gastroenterologist honored by the Irish Society of Gastroenterology, and her mother, who instilled in her eldest daughter a commitment to facing adversity and finding solutions, and her younger sisters, each of whom has also earned a PhD.

Through her slides, she introduced her husband, Scotland-native Robert Bunch, and her love of ocean sailing. With the move from Baltimore to Pittsburgh, the couple has berthed Frantic, their 46-year-old, 33-foot monohull, in Lake Erie. Says Lennon: "I've become very good at learning about diesel engine repair."

Multiple colleagues report Lennon logging on to video conferences from the high seas, clad in a life vest.

Among the revelations about herself that Lennon offered in that introductory presentation was how, when Bunch was in a motorcycle crash in 2022 that broke both of his arms and pelvis, leaving him in a wheelchair for months, she added the role of primary caregiver throughout his six-month recovery to her duties as division chief.

"We all face challenges, and it's good to acknowledge how hard it is, try to support each other," says Lennon.

As an administrator, Lennon has made it her mission to eliminate structural barriers to success. As a member of the governing board of the American Society for Gastrointestinal Endoscopy, she helped develop the society's five-year strategic plan and cochaired its Women's Task Force.

Law, who opted not to prioritize translational research in her own career, credits Lennon with playing to her trainees' strengths. "If you hate broccoli, Anne Marie's not going to make you eat it every day," says Law. "She'll offer it, but it won't be the main course."

Elham Afghani left a clinical career in Los Angeles to train with Lennon and took over from her mentor as director of the pancreatic cyst clinic when Lennon ascended to division director of Gastroenterology and Hepatology at Hopkins. Afghani credits Lennon with regularly referring opportunities that have boosted the younger scientist's profile, including an international fellowship.

Afghani, who has ongoing projects with senior scientists to whom Lennon furnished introductions, says, "Anne Marie really just opened these doors."

Most days, Lennon commutes by electric bike from her home (a World War I–era fixer-upper that's had its share of leaks) in leafy Squirrel Hill. As she rides through Oakland to Cardiac Hill, Lennon pedals past the Cathedral of Learning and several construction cranes. Symbols of aspiration.

"There are wonderful opportunities here," says Lennon.

As evidence, she points to ID Connect, a telemedicine initiative launched by the Division of Infectious Diseases that helps rural and urban patients alike access the care they need from providers who are themselves geographically dispersed. She sees similar promise in using artificial intelligence to transcribe patient visits, freeing providers to focus fully on their patients and reduce burnout.

"I love being part of pushing the boundaries to change the way we care for patients, to provide better care," she says.

In 2010, when Lennon accepted her first faculty appointment, the U.S. government issued her an O-1 visa as an "alien of extraordinary ability." ("I felt like I should have two heads," Lennon quips.)

The visa was consigned to the dustbin of history in 2019 when Lennon became an U.S. citizen. Her extraordinary ability, however, remains evident. ■



CLUES TO THE MOST LETHAL FORM OF OVARIAN CANCER

Bruno

Here you see a TLS, or tertiary lymphoid structure, from a woman with ovarian cancer. In October 2024, Tullia Bruno and colleagues reported in the journal Cancer Cell their surprising findings on TLS formation and activity in the most lethal form of ovarian cancer. Among their discoveries, says Bruno: "TLS formation is markedly different depending on the site of cancer. Specifically, fallopian tube and omental tumors have increased TLS formation and activity compared to ovarian tumors. Another important finding was that B cells, the white blood cells that make antibodies, from ovarian tumors didn't multiply well and made less effective antibodies than B cells from fallopian tube and omental tumors."

Spatial omics reveals immune markers in this image—CD20 (white, B cells), CD4 (yellow, T cells), PNAd (red, tiny vessels to bring in B cells and T cells) and CD21 (blue, follicular dendritic cells to support B cells and high-affinity antibodies to target the tumor).

COURTESY IAN MACFAWN/DEPARTMENT OF IMMUNOLOGY



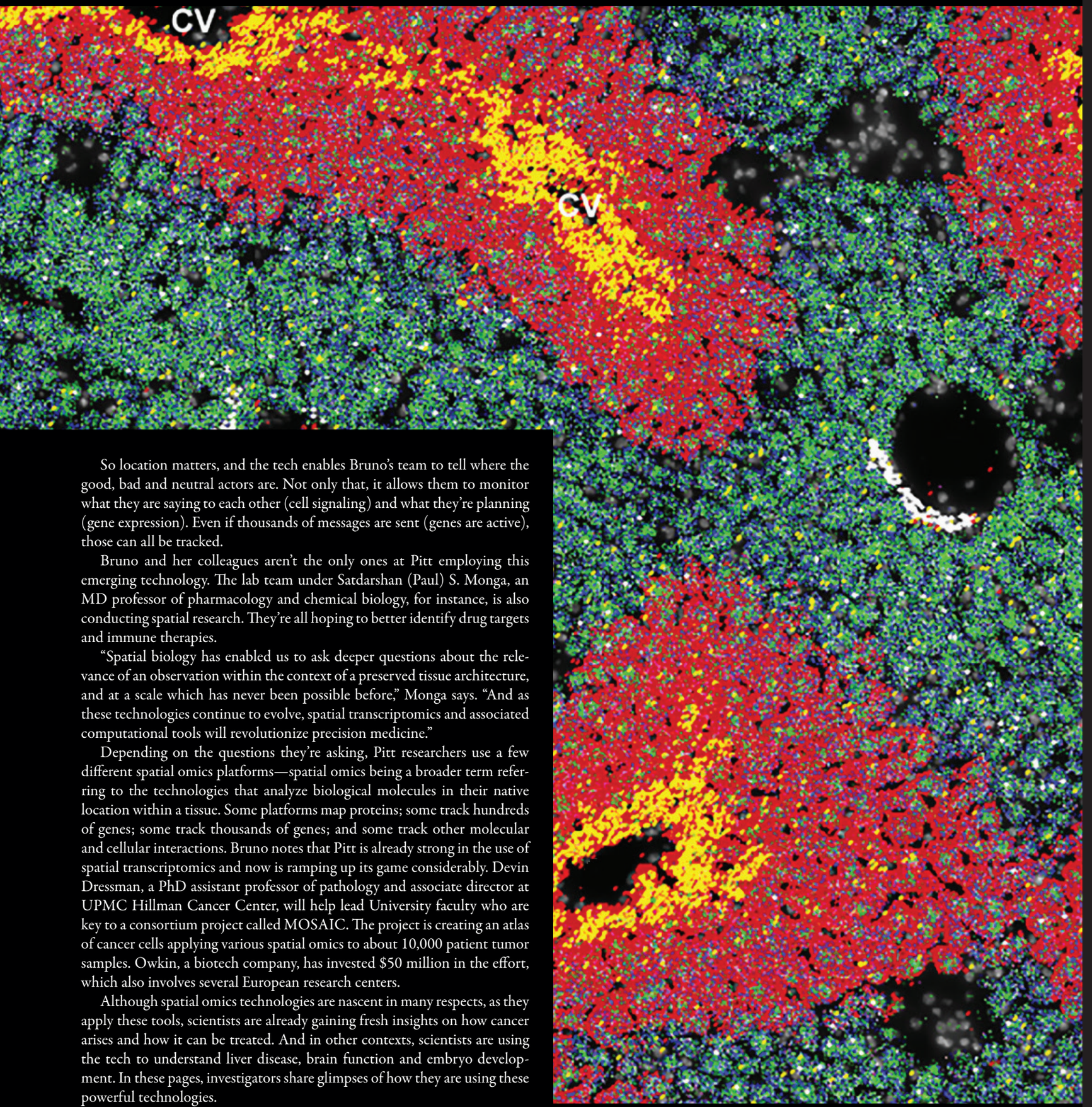
FOUND IN SPACE

AN EXTRAORDINARILY POWERFUL EMERGING TECH LETS SCIENTISTS WITNESS AND MONITOR CANCER AND OTHER CELLULAR ACTIVITY LIKE NEVER BEFORE.

BY MICHAEL AUBELE

Gotham City is a nasty place, always gray, dirty, seemingly one big red-light district with some bad dudes and their henchmen lurking. But somewhere in this superhero world where the likes of Joker, Riddler and Penguin vie for control, you'll find the Batcave, and inside, Batman and Robin, the city's dynamic crime-fighting duo. A tumor can be thought of the same way: a dense, seedy environment rife with bad actors (cancer cells). In it, though, you can find a haven for cancer fighters, tertiary lymphoid structures (TLSs). These command centers orchestrate immune cell function and are associated with better patient outcomes and responses to immune therapy.

But just as not all cities have a caped crusader and his sidekick working out of a Batcave, not all cancers have their B cells and T cells working out of a TLS. One of the cancers where TLS formation is less common is high-grade serous ovarian cancer—about 15% of patients with this form, the deadliest, have these, whereas the formation is about 40% in other solid tumors. Tullia Bruno, a PhD assistant professor of immunology, and fellow University of Pittsburgh researchers wanted to learn more about why TLSs develop less frequently in these tumors. To investigate, they used emerging technology that Batman would be jealous of. Through spatial imaging and transcriptomics, they peered into the cancer tissue to visualize and analyze how the cells interact with one another, and in doing so came to a better understanding of how TLSs form. They also discovered that TLS formation often depends on the site of the cancer.



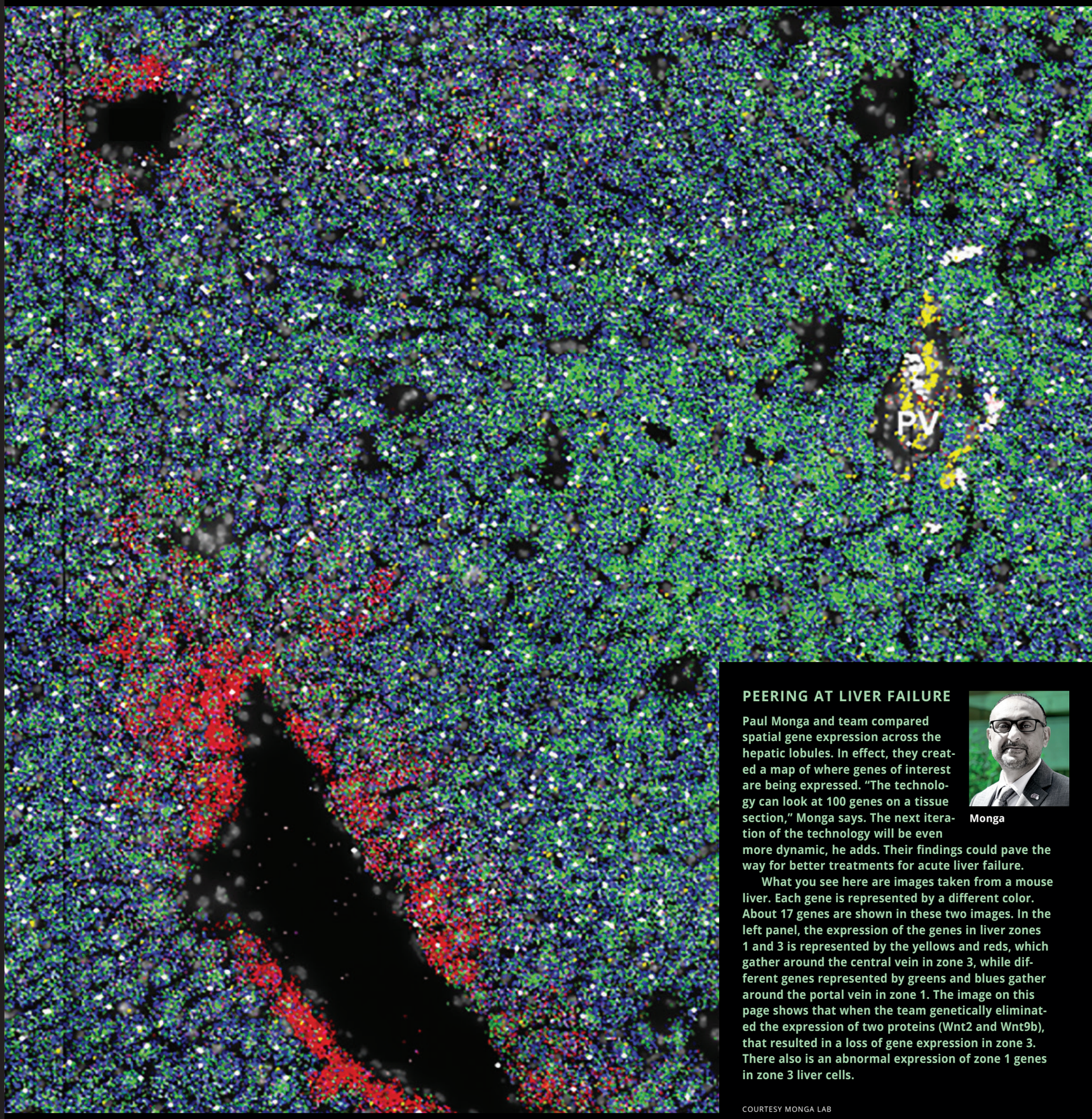
So location matters, and the tech enables Bruno's team to tell where the good, bad and neutral actors are. Not only that, it allows them to monitor what they are saying to each other (cell signaling) and what they're planning (gene expression). Even if thousands of messages are sent (genes are active), those can all be tracked.

Bruno and her colleagues aren't the only ones at Pitt employing this emerging technology. The lab team under Satdarshan (Paul) S. Monga, an MD professor of pharmacology and chemical biology, for instance, is also conducting spatial research. They're all hoping to better identify drug targets and immune therapies.

"Spatial biology has enabled us to ask deeper questions about the relevance of an observation within the context of a preserved tissue architecture, and at a scale which has never been possible before," Monga says. "And as these technologies continue to evolve, spatial transcriptomics and associated computational tools will revolutionize precision medicine."

Depending on the questions they're asking, Pitt researchers use a few different spatial omics platforms—spatial omics being a broader term referring to the technologies that analyze biological molecules in their native location within a tissue. Some platforms map proteins; some track hundreds of genes; some track thousands of genes; and some track other molecular and cellular interactions. Bruno notes that Pitt is already strong in the use of spatial transcriptomics and now is ramping up its game considerably. Devin Dressman, a PhD assistant professor of pathology and associate director at UPMC Hillman Cancer Center, will help lead University faculty who are key to a consortium project called MOSAIC. The project is creating an atlas of cancer cells applying various spatial omics to about 10,000 patient tumor samples. Owkin, a biotech company, has invested $50 million in the effort, which also involves several European research centers.

Although spatial omics technologies are nascent in many respects, as they apply these tools, scientists are already gaining fresh insights on how cancer arises and how it can be treated. And in other contexts, scientists are using the tech to understand liver disease, brain function and embryo development. In these pages, investigators share glimpses of how they are using these powerful technologies.



PEERING AT LIVER FAILURE

Monga

Paul Monga and team compared spatial gene expression across the hepatic lobules. In effect, they created a map of where genes of interest are being expressed. "The technology can look at 100 genes on a tissue section," Monga says. The next iteration of the technology will be even more dynamic, he adds. Their findings could pave the way for better treatments for acute liver failure.

What you see here are images taken from a mouse liver. Each gene is represented by a different color. About 17 genes are shown in these two images. In the left panel, the expression of the genes in liver zones 1 and 3 is represented by the yellows and reds, which gather around the central vein in zone 3, while different genes represented by greens and blues gather around the portal vein in zone 1. The image on this page shows that when the team genetically eliminated the expression of two proteins (Wnt2 and Wnt9b), that resulted in a loss of gene expression in zone 3. There also is an abnormal expression of zone 1 genes in zone 3 liver cells.

COURTESY MONGA LAB

18,000 GENES, EVERYWHERE, ALL AT ONCE

In this tissue sample from a muscle invasive bladder cancer, each multicolored spot is approximately 55 micrometers—about the width of a human hair—and contains, on average, one to 10 cells. Pitt's Devin Dressman helps lead a team of researchers on the MOSAIC project to capture images like this.



Dressman

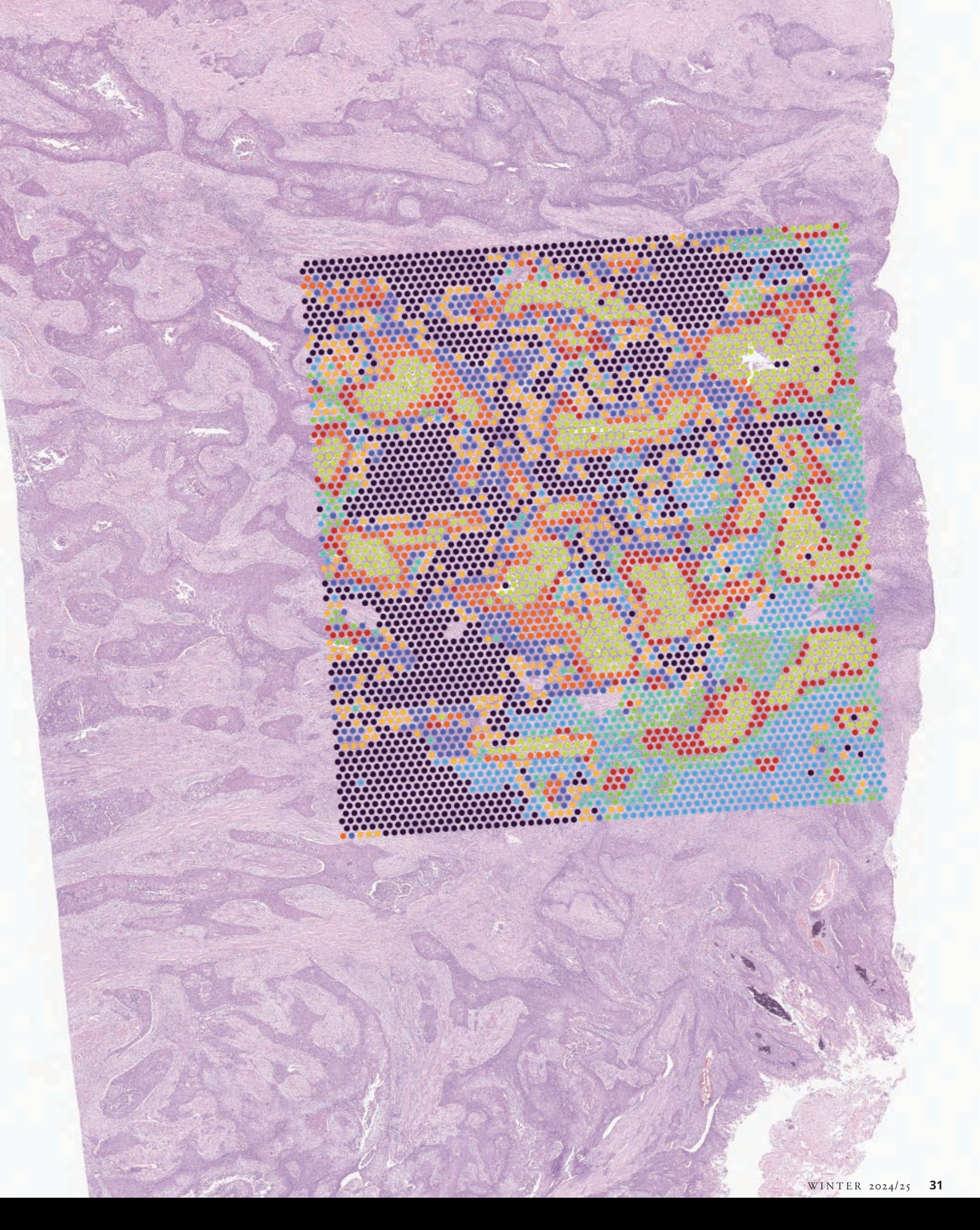
"The research represented here gives scientists some of the first insights into how the same or different cell types respond to a specific environment and how that environment influences gene expression," Dressman says. "Until recently, scientists could only look at a few genes at a time, but now with this technology and this project, Pitt researchers will be able to look at the expression of over 18,000 genes in their spatial context."

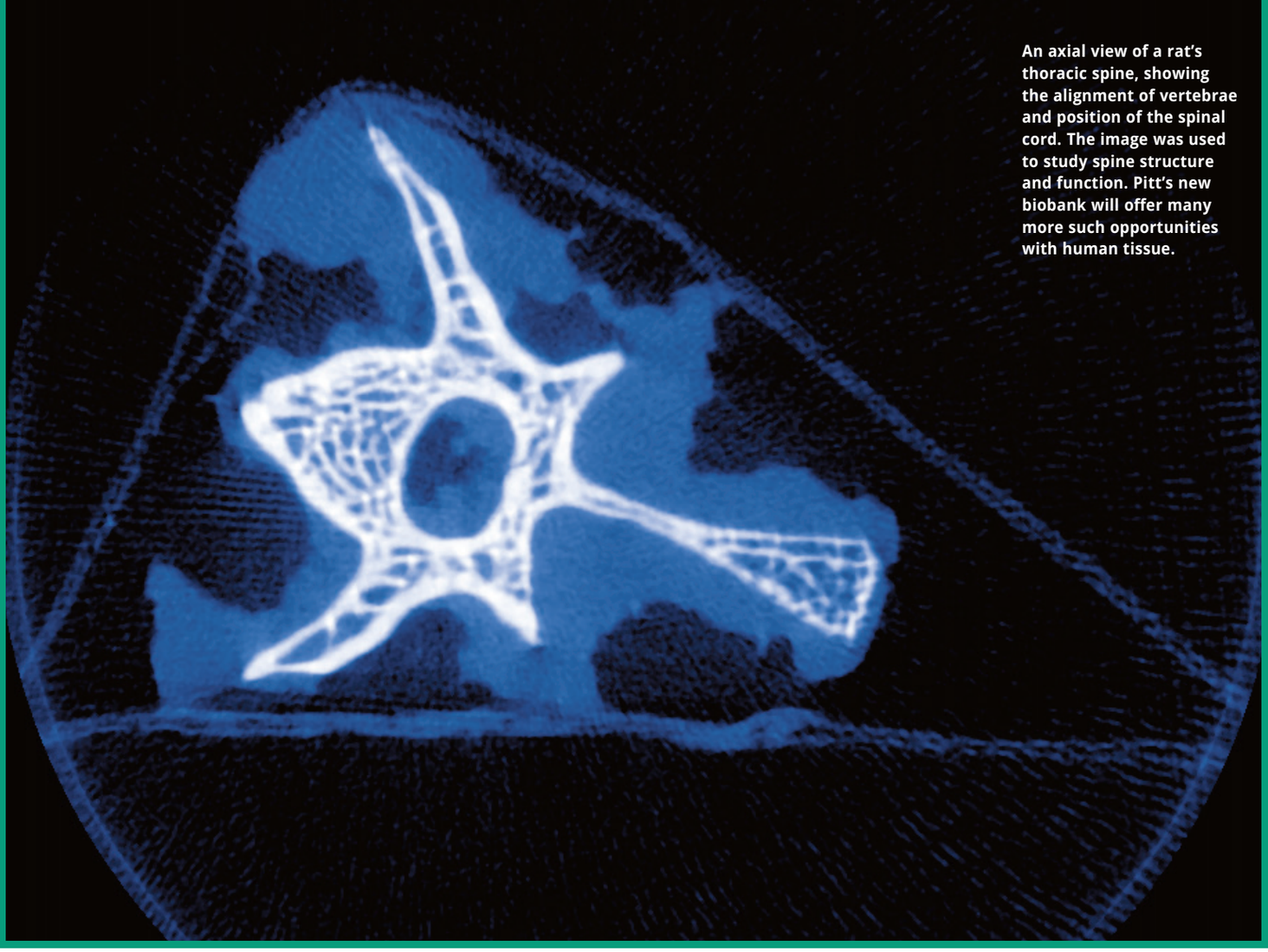
Vascular endothelial growth factor A (VEGFA) is shown on this page by light or dark red dots indicating its level of gene expression. A cytokine, VEGFA can stimulate blood vessel formation in cancers. Not all the cells are expressing this gene the same way in this tumor, which gives scientists insight into how to better target VEGFA for therapies.

The software Dressman and team are using to analyze the 18,000 genes can do so in several ways. The image on the opposite page shows the expression of cell clusters and links them by color to what is most closely related by gene expression. "With this technology," Dressman says, "scientists can identify different types of cell clusters that are either related to each other by expression or are completely different yet living directly next to each other. This should lead to new biomarkers for either diagnostics or therapies for cancer. Methods previously used without the spatial context would have not been able to identify so many different expressing cell clusters in the same tumor.

"The technology we have gained access to gives us insight into the cancer microenvironment at a scale we didn't think possible a decade ago. While we are only just beginning to get MOSAIC off the ground, the Pitt team is tremendously excited about the potential for what we can learn about cancer and how we can use what we discover to change patients' lives."

COURTESY DEVIN DRESSMAN/DATA GENERATED BY THE MOSAIC CONSORTIUM (OWKIN, CHARITÉ-UNIVERSITÄTSMEDIZIN BERLIN, LAUSANNE UNIVERSITY HOSPITAL-CHUV, ERLANGEN HOSPITAL, GUSTAVE ROUSSY INSTITUTE, UNIVERSITY OF PITTSBURGH)





An axial view of a rat's thoracic spine, showing the alignment of vertebrae and position of the spinal cord. The image was used to study spine structure and function. Pitt's new biobank will offer many more such opportunities with human tissue.

FERGUSON LAB, BETHEL MUSCULOSKELETAL RESEARCH CENTER

MOUNTAINS TO CLIMB

A NEW BIOBANK, AND A STRONG KINSHIP, PROMISE TO ADVANCE ORTHOPAEDIC RESEARCH.

BY MICHAEL AUBELE

Orland Bethel says the story behind his overwhelming generosity to the University of Pittsburgh, which now includes an $18.5 million gift to create a biobank, bears repeating.

Suffering from spinal stenosis nearly a decade ago, he sought surgical care from Joon Lee, an MD professor of orthopaedic surgery. About two years later, Lee operated on Bethel's neck to relieve pain so severe it forced him to use a wheelchair. The procedures improved his life to a degree that prompted Bethel to "really do something that could make a difference."



UNIVERSITY OF PITTSBURGH



Above, Orland Bethel is flanked by Gwen Sowa and Nam Vo during a reception celebrating Bethel's philanthropy, which has made it possible to create the BMRC and its biobank. Bethel and his surgeon Joon Lee, right, have developed a strong kinship.

Through his foundation, he committed $25 million to the University last year, which Pitt matched, to create the Orland Bethel Family Musculoskeletal Research Center. He previously gave $2 million to endow the Orland Bethel Professorship in Spine Surgery that Lee holds. All told, he has pledged more than $45 million to Pitt through the Orland Bethel Family Foundation.

His most recent gift will be used to create one of the few comprehensive musculoskeletal biobanks outside of Europe.

Lee says that he and colleague Nam Vo, a PhD professor of orthopaedic surgery, talked for years about the potential to create a biobank in Pittsburgh. They believed that collecting, housing and properly distributing tissue specimens would shed light on disorders such as arthritis, osteoporosis and a range of spinal conditions that diminish the quality of life for millions of people and lead to billions in health care costs.

But their conversations normally ended with the recognition that they were hamstrung by a lack of funding—until Bethel stepped in. He recognized the pair "had a mountain to climb."

"I wanted to rectify that," Bethel says.

The Orland Bethel Family Musculoskeletal Research Center Biobank will create modern storage, processing and access systems and leverage the existing infrastructure within Pitt Med to collect tissue and process large datasets. Using these resources, it will acquire and store high-quality biospecimens including bone, muscle, ligament, tendon, cartilage, stool and whole blood samples. Large biological data will then be determined from these biospecimens through advanced research assays.

Pitt will also seek new sources of funding to ensure the long-term health of the operation.

"We hope to establish a first-in-kind encyclopedic and accurate data repository that will foster cross-institutional collaboration," says Anantha Shekhar, the John and Gertrude Petersen Dean of the School of Medicine and senior vice chancellor for the health sciences at Pitt. "Once the biobank database is established, we can explore the use of artificial intelligence and machine learning data analysis for more accurate treatment of musculoskeletal diseases."

Surmounted

As Bethel has said, the gifts he's made to Pitt come from a great appreciation, as much for Lee himself as for the healing procedures he completed. Bethel comes from humble beginnings and says that when Lee shared his backstory, he felt a kinship with the physician.

Bethel was driving a coal truck for a living in 1958 in Ohio when he took a job with an egg company. He noticed the potential for the business and borrowed $4,000 from his parents and in-laws to buy it. He recounts working 18-hour days, driving a truck to pick up eggs to resell. When he expanded into Pittsburgh, he says, he would get into the city at about 3 a.m., work all day, sleep at a YMCA and then head back to Ohio. It was a gritty lifestyle, much like Lee's early days.

Although no one in his family spoke English, Lee's parents moved them from South Korea to the United States in the early '80s. "Our story is not unique to our family, but to many other immigrants to the U.S. We moved [here] for a better economic opportunity, and education to us was not a luxury but a necessity for a better future."

Lee's family of five, which had lived in a one-room home outside Seoul (where, at one point, a coal heating system poisoned them with carbon monoxide), was able to settle in a good school district near Los Angeles. Because the cost of living was high, Lee's parents took on multiple jobs, working on food trucks, selling sneakers at swap meets and the like. (To this day, Lee won't buy sneakers at full price, knowing what his dad paid for them at wholesale.) Lee's own hard work took him to the University of California, Berkeley, and then to Yale University School of Medicine.

Vo's origin story is particularly inspiring. He was born in South Vietnam to a wealthy family, but after the Vietnam War, Vo, then 10, and one of his brothers escaped Communist rule from the North by boat—a vessel that was about 20 feet long and 5 feet wide, carrying 18 people. After two weeks at sea with little food and water, they ran out of fuel. Fortunately, a Taiwanese fishing boat rescued them in the Pacific. From there, Vo and his brother were taken to a refugee camp in Taiwan. That was in 1980.

Landing in the LA area two years later, thanks to the support of a Vietnamese couple, Vo eventually reunited with his family. They lived in a two-bedroom apartment with eight other family members. Growing up, Vo worked odd jobs—collecting cans to recycle, passing out flyers for landscaping companies, washing cars.

Like Lee, Vo didn't speak English when he arrived but picked it up quickly. The two crossed paths at Berkeley: Vo was a graduate student in a biochemistry lab that Lee worked in as an undergraduate. Fast forward to 2006 when Lee recruited Vo to Pitt Med. "I studied nucleic acids, to which Lee said, 'You can apply nucleic acids biochemistry on studying the spine and low back pain!'" Vo says with a laugh.

During their tenure together, the pair discovered that unrepaired DNA damage promotes cellular senescence in the intervertebral disc, which drives age-related intervertebral disc degeneration and low back pain. And in collaboration with Gwen Sowa, the MD, PhD chair of physical medicine and rehabilitation, they performed deep phenotyping of patients with chronic low back pain to determine the right therapy.

Now they are eager to see how the biobank will offer new insights to their work.

They often reminisce about how far their lives have come, Vo says. "A lot of times, when we get together, we trade stories."



BUILDING WHOLE DOCTORS, AND WHOLE PEOPLE

PITT MED'S COACHING PROGRAM

BY RACHEL MENNIES

"No one in my immediate family," says Lauren Kaseman, a second-year medical student, "has ever been to medical school or any other health graduate school." Upon arriving at Pitt Med, she faced not only the academic challenges that all medical students face; she also had to contend with the "hidden curriculum," she says, of the skills and knowledge bases often assumed known but not taught formally, like boards preparation, financial literacy or networking skills. These areas underpin a medical education but often go unstated at many medical schools, leaving students in the dark who don't have experienced peers or family members to help them navigate.

Kaseman is far from alone. So with the 2023-24 school year, Pitt Med introduced a comprehensive program to bring this hidden curriculum into the light. Known as Pitt Med's Coaching Program, the formal effort also helps build the connective tissue between a medical student's academic pursuits, professional goals and personal life.

Introduced as part of the school's new curriculum, the program pairs each first-year student with a Pitt Med faculty member coach for monthly meetings and as-needed check-ins for all four years of medical school. "Our purpose," says Julia Meade, MD assistant professor of pediatrics, director of the Pediatric Cancer Predisposition Program at Children's Hospital of UPMC and coach, "is to help the student identify their goals, their values and how they want to live their life—and to then support that student, often through probing questions and giving the space to open up about these sometimes-difficult questions in a supportive and nonjudgmental way."

Coaching sessions are now a focused, regular component of the curriculum. For Karensa Tjoa, whose coach is Deborah DiNardo, MD associate professor of medicine and women's health medical director for the VA Pittsburgh Healthcare System, this stability makes coaching easy to include in her schedule. "I think that the [30-minute] monthly check-ins were helpful in developing the relationship."

Previously, students were matched with coaches only if it seemed the student might be struggling or at risk of struggling, says Suzanne Templer, DO associate professor of medicine and assistant dean for student affairs, who directs the program. Beginning in fall 2023, the program has included every incoming med student, regardless of achievement level or perceived need. This change has been welcomed by many coaching faculty, including Yui Sugiura, DO assistant professor of family medicine, associate program director for UPMC McKeesport Family Medicine Residency Program and coach.

"I think it's even better," she says, "because even if you're doing amazing, there's going to be barriers and boundaries. And you still have that someone to navigate you through this really tough educational process."

Students—like Ivy Yip, a second-year student and part of the program's inaugural class—have also welcomed the change. Having a coach, Yip says, "takes away barriers, including internal barriers, for seeking help."

Through coaching, students might develop study schedules, connect with other faculty in specialties of interest for residency and strategize about ways to integrate their hobbies and interests with their academic expectations.

One of the most challenging aspects of medical school is finding balance, especially in the face of burnout or overwhelm. Kaseman, whose coach is Ankur Doshi, an MD associate professor of emergency medicine, says, "I sing at my church. So Dr. Doshi said, 'If that is something you love, let's make a goal to keep doing that once a month.'"

Tjoa credits DiNardo with helping her to "step into this new identity of being a medical student, while finding balance and perspective." And Yip, whose coach is also Doshi, worked with him on integrating training for a 70.3-mile triathlon into her schedule. To Yip, it seemed "unheard of" that a professor would encourage her to focus on anything but academics.

Coaches suggest strategies like reflection, journaling and other planning tools to help students stay on track with their goals.

"There is a lot of insecurity and a lot of rumors that permeate medical education," says Meade. The coaches help students address these insecurities directly, as well as to develop savvy around that "hidden curriculum."

"Is there something above and beyond the curriculum and studying that I should be preparing for? How should I be building my resume for residency?" Kaseman wondered before working with Doshi.

The confidence needed to achieve in a high-pressure environment, especially one with historically unspoken rules or guidelines, can be hard to maintain.

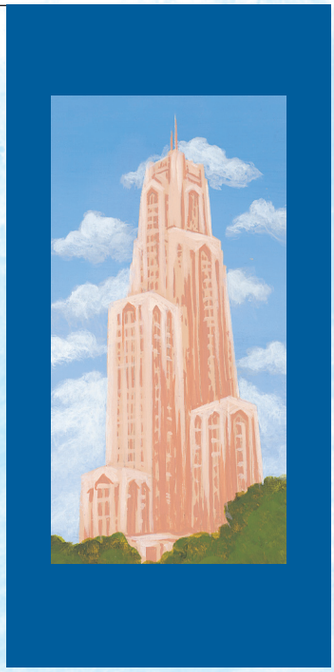
She's grateful to have someone to help her navigate this hidden curriculum and its timelines, she says.

Meade often reminds her students, "They are incredible people who are in a place where somebody thought that they were good enough to be a doctor." Still, even high-achieving young people may find it hard to maintain the confidence needed to achieve in a high-pressure environment, especially one with historically unspoken rules or guidelines. Developing and maintaining this confidence in students is a primary goal for coaches.

"I wish that I had had this [program] when I was a medical student," says Meade. "Because many times if you weren't having any issues, you weren't necessarily in a place where somebody was looking to help you shine either."

But coaches now provide an essential component of Pitt Med's core offerings: helping students grow as whole people, not just as future clinicians. ■

PHOTO ILLUSTRATION: ELENA CERRI/PHOTOS: CANVA





Meltzer, now dean at Keck, is drawn to servant leadership as well as imaging.



WE KNEW YOU WHEN: CAROLYN MELTZER

Drawn here by Pitt's positron emission tomography (PET) opportunities, **Carolyn Meltzer** came to Pitt Med in 1996 as an MD assistant professor of radiology and psychiatry under what she describes as somewhat atypical circumstances.

"When I was brought in," she says, "it was unusual for the Department of Radiology to invest in early career physician-scientists."

During her early tenure, up to 75% of Meltzer's focus was on research, rather than clinical work, but "that investment was a good one," and it was one she enjoyed.

Her mentors here—among them Charles F. "Chip" Reynolds III, an MD who retired in 2017 as a Distinguished Professor of Psychiatry and the UPMC Professor of Geriatric Psychiatry, and Richard Baron, an MD and former chair of Radiology who died in 2017—saw potential in her beyond clinician and scientist. "I started taking on administrative positions along with my clinical and research duties—or rather I was getting thrown into administrative positions," she says with a smile. "And that happened well earlier than one might have planned, but it really taught me how much I enjoy leadership, servant leadership."

In 2003, Pitt sponsored Meltzer for the Hedwig van Ameringen Executive Leadership in Academic Medicine (ELAM) Program, which is designed to increase the number of women in leadership positions in medical and dental schools; and she has thrived as a leader since. She moved to Emory University in 2005 and spent more than 15 years there as the William P. Timmie Professor and Chair, Department of Radiology and Imaging Sciences, and as an executive associate dean and chief diversity and inclusion officer. Today, she is dean of the Keck School of Medicine of USC, the May S. and John H. Hooval Dean's Chair in Medicine and a professor of radiology, having assumed those appointments in 2022.

Most of Meltzer's daylight hours are spent on her deanly duties, yet she still pursues some neurodegenerative disease research.

On her own time, she remains drawn to imaging—but through more of a fine art lens. Her longtime interest has been in nature photography. More recently, she's ventured into street photography, having drawn inspiration from the #MeToo and Black Lives Matter movements and other social issues. Photography, she says, "is something I've done since childhood."

—Michael Aubele

SPOTLIGHT: SETH HAWKINS



Hawkins

When he was pursuing anthropology at Yale University, Seth C. Hawkins, then an EMT, quickly realized that it was "more fun to help people than to study them," he says.

"I took a sudden left-hand screaming turn out of anthropology and into medicine my senior year in college."

More recently, working with the North Carolina State Park Service made him want a greater understanding of population-based care, so he's back in school.

Hawkins (Res '03), an emergency medicine and wilderness medicine physician, is in the dual degree MA-MPH program at UNC Charlotte. The MD is finding his undergraduate education in applied anthropology to be helpful, in addition to his expertise as medical director of North Carolina State Parks and local emergency medical advisor for all U.S. Forests in North Carolina, as well as the National Park Service Outer Banks.

Practical applications of the knowledge he's gaining include determining how best to maximize resources and available personnel when both are limited during a large-scale emergency.

Hawkins also serves as an emergency medicine physician within the Catawba Valley Health System, as well as associate professor of emergency medicine at Wake Forest University. On a contract basis, he provides medical advice and direction for a number of outlets, including Recreational Equipment Incorporated (REI) and Landmark Learning. (He's also worked as a ski instructor and rafting guide.)

His diverse out-of-the-clinic career continues to be influenced by the time Hawkins spent as a resident here, he says. "I think what really was special for me [in Pittsburgh] that continues to kind of influence my work now was the Jeep rotations." The UPMC emergency medicine program allows residents to spend time practicing street medicine from the back of a Jeep or other vehicle. The field experience was foundational to his career as mentor and physician, he says.

Hawkins encourages students and young physicians to be comfortable with failure and to be open minded to opportunities.

"Be a stem cell as long as possible," he says. "I think being open to the possibility that the universe is going to tell you that you're good at something you didn't realize or that you wanted to do something that you hadn't expected is very important." Hawkins lives by the principle, "Be undifferentiated until you aren't." *—Amber Frantz*

STEP UP: PITT MED TRIVIA



GETTY IMAGES/CAMPWILLOWLAKE

Can you answer these without going online?

(We encourage you to call doctors-in-the-know for consults.)

1. Named Wally, this Massachusetts farm animal made headlines in 2020 for its contributions to COVID research at Pitt. What type of animal was it?
   - A. Llama
   - B. Donkey
   - C. Pig

2. Pitt researchers announced a "whole" new game in concussion testing earlier this year when they released news that a blood test they codeveloped could diagnose the injury within:
   - A. 15 minutes
   - B. 15 hours

3. We're wondering how closely you've been reading this issue. Who became Pitt Med's chair of medicine in 2024?

4. Neal ElAttrache, an orthopaedic surgeon and Pitt Med resident alum, has operated on A-list actors, top athletes and Average Joes alike. Who from the list below has he treated? (Choose all that apply.)
   - A. Aaron Rodgers
   - B. Leonardo DiCaprio
   - C. Tom Brady
   - D. Andrew Doerfler

Done? Now, check our inside back cover to find out if you aced this one. And if you have an idea for a Pitt Med-related trivia question, send it our way; we're all ears: medmag@pitt.edu.







THEY TOOK THE CHALLENGE
At the Pitt Alumni Weekend this fall, a few brave alumni took the Pitt Med Trivia Challenge, including Allan Sulzer (MD '64), Lynsey Brandt (MD '04) and William Cleveland (MD '74). See how well they and others did: pi.tt/livetrivia24

OBITUARY

ROLF JACOB

DEC. 12, 1942–AUG. 7, 2024



Jacob

While working on the psychiatry consultation-liaison service at UPMC Western Psychiatric Hospital, Rolf Jacob, an MD, was known for embracing the old with the new.

"He would send emojis and text messages like none other. I remember him encouraging trainees to use Google Maps Street View to really get a good feel for patients' lives. He was ahead of the curve when considering social determinants of health," says Priya Gopalan, an MD associate professor of psychiatry and obstetrics, gynecology and reproductive sciences at the University of Pittsburgh.

Jacob joined Pitt in 1979 where he became a professor of psychiatry and otolaryngology. In addition to his work with UPMC's psychiatry consultation-liaison service, he studied anxiety disorders and vestibular disorder and treated patients.

He earned his medical degree from the Karolinska Institute in Sweden in 1971. He then went on to complete psychiatry and behavioral medicine training at UCLA and Stanford Medicine. He was board certified in geriatric psychiatry.

"He was deeply committed to the well-being of his patients, and deeply committed to the importance of psychotherapy as a component of treatment in psychiatry," says Jackie Dunbar-Jacob, a PhD Distinguished Service Professor and dean emeritus of the Pitt School of Nursing, whom Jacob married in 1989.

Loren Roth, an MD, MPH Distinguished Professor Emeritus of Psychiatry at Pitt, worked alongside Jacob for many years. "He was an excellent, experienced psychiatrist with wonderful judgment. I believe he enjoyed his work to the core," he says.

He was known for always being willing to collaborate and share knowledge.

"On several occasions over many years, when I had great challenges in managing a potentially violent patient, I turned to Rolf. He assisted me with his opinion and next steps in management—to my great relief!" recalls Roth.

Colleagues also emphasized his interest in preparing future generations.

"He had a profound impact on me and my entire residency class and remained a powerful educational force for years after I graduated. I still routinely see my residency classmates, and it's a rare conversation where his name is not brought up with a fond smile," says Gopalan.

"He will be missed by his family—our three children and myself," says Dunbar-Jacob. —*Shannon Turgeon*

IN MEMORIAM

'40s

CLYDE LAMP JR., MD '45
NOV. 4, 2024

'50s

ROBERT BADWEY, MD '59
NOV. 4, 2024

IRWIN SCHAFER, MD '53
AUG. 28, 2024

'60s

BARRY BRENNER, MD '62
AUG. 6, 2024

JAMES BRESS, MD '62
AUG. 11, 2024

PAUL CHERVENICK, MD '61, RES '64
OCT. 4, 2024

PETER COHEN, MD '63, RES '68
NOV. 28, 2024

IRVIN HIRSHFIELD, PHD '66
OCT. 27, 2024

EDMUND PETRILLI, MD '69, RES '72
SEPT. 30, 2024

SAMUEL WOODINGS, MD '60
AUG. 26, 2024

'70s

RICHARD KASDAN, MD '72, RES '76
NOV. 1, 2024

ROBERT STANGER, MD, RES '70
AUG. 21, 2024

MOHAMED HAGAHMED: REFUGEE THEN PHYSICIAN TO OLYMPIANS

By Michael Aubele



COURTESY FIGS

Hagahmed provided treatment for Olympians before the Paris Games.

In 2020, Mohamed Hagahmed posted a short opinion piece about the potential benefits of using tranexamic acid to treat patients with traumatic brain injury. He drafted it for CriticalCareNow, an online medical publication he wrote for as a senior editor.

The furthest thing from his mind when he put it together was the 2024 Summer Olympics, though he says it played a critical role in getting him on the team of health care professionals who treated U.S. Olympians leading up to the Paris Games.

Later, a recruiter from the scrubs company FIGS uncovered the paper and some of his medically themed social media posts and reached out to gauge his interest in becoming a brand ambassador. FIGS was launching its campaign as the official outfitter for the Olympics medical team and pulled in Hagahmed (Res '18), an MD and Pitt assistant professor of emergency medicine, to be part of it.

Leading up to Paris, FIGS featured Hagahmed in a promotional video filmed at a training facility in Colorado Springs, where you catch him rushing to assist a javelin thrower after her leg injury forces her to the ground writhing in pain.

"Dr. Hagahmed has always used his public platform to advance health care, and we knew we wanted him to be part of our FIGS community," says Anum Hashmani, FIGS director of community.

From getting the recruiter's phone call to treating elite athletes and starring in the video, Hagahmed was enjoying the thrill of a lifetime. But there turned out to be a wrinkle: He wouldn't be able to join the medical team in Paris after all.

"I wasn't there," he says. "But I wanted to be. With some of the clinical commitments I had here, and on relatively short notice, it was impossible for me to go."

You really don't get a frown out of Hagahmed, but talking about the lost opportunity almost produces one. His next train of thought turns to the 2028 Games in Los Angeles, where he hopes to serve as part of the United States Olympic and Paralympic Committee sports medicine division, and a smile returns. "I'm applying to be a part of that team," he says.

Hagahmed is used to twists and turns. He was forced to flee with his family from war-torn Sudan as a kid. His family moved to the United Arab Emirates, where he completed high school in Abu Dhabi. Before finally settling in Pittsburgh, he lived in several countries in the Middle East, Africa and Europe; he earned an undergraduate degree at the RWTH Aachen University, Germany, where he also attended medical school.

Once in Pittsburgh, Hagahmed worked as a paramedic in the city and earned a bachelor's at Pitt. After that, he attended medical school at Drexel University.

"I'm not shy in talking about it," he says of what he's gone through. He appreciates opportunities to share that, in becoming a physician, he had to overcome imposter syndrome—a common but powerful potential setback for med students.

"I almost drowned in it. I mean, I came here as a refugee. I was really nothing. The first couple years, I was on temporary protected status. So, every year I had to renew my visa. I did all these odd jobs. I was bouncing at a bar in Shadyside at one point.

"I actually think," he says after a pause, "that people should know that humble beginnings—they provide you with this sense of humility. And then when you get to a certain position, you appreciate it more." ■

ROBERT WARNER, MD '76
AUG. 20, 2024

'90s

DAVID META, MD '93
SEPT. 19, 2024

JOHN JEFFREY RICH, MD, FEL '93
AUG. 5, 2024

FACULTY

ROLF JACOB, MD
AUG. 7, 2024

RON STEWART, MD
OCT. 21, 2024

Please send In Memoriam notices to mia97@pitt.edu.



Soak up some sunshine.

GETTY IMAGES

FOR REAL! TWEEN SCIENCE



In the summer, your parents might have told you to play outside to "get some vitamin D." But what does it mean to "get" vitamin D—and what does it do, anyway?

It turns out that while some of our vitamin D comes from food, we mostly make it ourselves. A chemical reaction in our skin makes molecules that our liver and kidneys turn into vitamin D.

The reaction can only happen with the help of heat from ultraviolet B rays, which are a part of sunlight. That's why we make the most vitamin D in the summer, when ultraviolet light is the most intense. We also make a lot around noon, when the sun's rays hit Earth at more direct angles. But when you're indoors, you aren't directly exposed to sunlight, so you don't benefit from this clear-sky chemistry—not even if you're sitting by a window.

So, what's the big deal about vitamin D? Its main role is to help our bodies absorb calcium, which strengthens our bones. That process keeps your bones healthy; and that's especially important when you're still growing.

In fact, before scientists knew about this job of our solar sidekick, a disease called rickets was much more common. Rickets causes bones to be softer, which could lead them to slightly bend or grow out of their usual alignment in the body. When people found out how important vitamin D is, we started adding it to certain foods. Now, rickets is rare in the United States.

The vitamin also helps us feel better in other ways—it's important for mental health. So now that you know the lowdown on D, maybe you'll catch some rays on the next sunny day. *—Sarah Lindley*

A special thanks to Kumaravel Rajakumar, an MBBS (MS '10) professor of pediatrics at Pitt Med and physician at UPMC Children's Hospital of Pittsburgh, for shining some (sun) light on the importance of vitamin D.

CALENDAR

VANSCOY WINTER ACADEMY
FEBRUARY 13, 2025
Healthy Aging: Live Long, Live Well.
Naples, Florida

HEALTH ACADEMY
MARCH 6, 2025
Featuring: Hooman Rashidi, MD, MS
The State of AI in Pitt's School of Medicine
Beverly Hills, California

MATCH DAY
MARCH 21, 2025
Petersen Events Center

For more information, contact Alex Rigby at +1-412-789-5866 or hsalumni@pitt.edu. To find out what else is happening at the medical school, visit health.pitt.edu and maa.pitt.edu.



Pitt Med Trivia *(from page 37)*

Trivia answers:
1. A—Llama
2. A—15 minutes
3. Anne Marie Lennon
4. A, B and C

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Fuhrman won his department's teaching award so many times that they named it for him.

NIKHIL B. AMESUR/PHOTO ILLUSTRATION: ELENA CERRI

Teach, Train, Treasure.

When Uncle Carl stopped by family gatherings, he took a keen interest in what his nieces and nephews were learning at school. He was proud that all five of them earned graduate degrees as they grew into adulthood. But he was humble about his own academic pedigree and career. At the weddings of his nieces and nephews, Uncle Carl responded humbly when guests inquired about what he did for a living. "Oh, I work in health care," he would say.

His eldest sister, Barbara Pugel, said her brother never let on that he was a nationally recognized University of Pittsburgh professor and chief of thoracic radiology who won the radiology department's teaching award so many times it was renamed the Carl R. Fuhrman Excellence in Teaching Award. Pugel, a retired nurse, says the field of radiology was a perfect fit for her inquisitive little brother: "There's always a mystery, and always a problem to solve."

Fuhrman died in 2020. At his memorial celebration, Pugel was particularly touched when fellow profs told stories about how he uplifted students. "He always wanted his students to shine," Pugel recalled them saying.

In June, Pugel and the families of her two sisters pooled together a $100,000 philanthropic gift for the Carl Fuhrman Radiology Education Fund—the largest single gift in the department's history.

"Carl still serves as the role model for the educator physicians in our department," says Jules Sumkin, professor and chair of radiology, noting that today's residents listen to Fuhrman's recorded lectures. The department is grateful for the family's generosity and contributions of other donors to the fund, he says.

"We are planning to use some of the funds to create an interactive teaching file with his saved cases," Sumkin says, adding that the fund has already been used to support student teams at imaging competitions and trainees teaching medical care abroad.

To make a gift to the medical school:
giveto.pitt.edu/medmaggive
Or contact Jen Gabler: +1-412-864-5547