

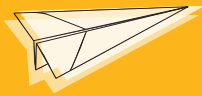
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | SUMMER 2022

PITTMED



HIDDEN IN PLAIN SIGHT

UNWELCOME INHERITANCES



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CREATE NEW MEMORIES

Health Sciences Alumni Weekend Sept. 16-18, 2022

It's class reunion time. Don't miss this opportunity to reconnect with Pitt Med classmates and mingle with peers across the health sciences. Tour old and new spaces, see the acclaimed documentary "Burden of Genius" about the great Thomas E. Starzl, learn about promising research by our faculty and students, and more. Graduate alumni are invited to take part in a ceremony for new PhD students, welcoming them to the community of biomedical scientists.

For schedules, accommodation options
and registration: alumni.pitt.edu/hsreunion



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**“Wherever the art of
medicine is loved, there is
also a love of humanity.”**

—Hippocrates



AIIMEE OBIDZINSKI/UNIVERSITY OF PITTSBURGH

Dear Pitt Med Readers,

One of the most instructive relationships an academic medical center can enter into is with the community it serves. We are lucky to have so many good neighbors. Western Pennsylvanians are diverse and less transitory than patients served by other leading health centers. This means that when they raise their hands to help guide or participate in academic activities and medical research, the results are likely to be more meaningful.

The partnerships and reach of UPMC, our academic medical center, are impressive, reaching across the state and beyond. UPMC integrates 40 hospitals, and 800 doctors' offices and outpatient sites, with roughly 4 million annual patient visits; and it provides health insurance to more than 4 million people.

This is part of what attracted me to Pittsburgh: Pitt, with hundreds of thousands of community partners and six top-tier health sciences schools, along with UPMC, is uniquely suited to make important discoveries and find solutions to barriers to good health.

Pitt scientists can tap into a treasure trove of patient data and employ the latest artificial intelligence, 'omics and other technologies. Yet equally important for human health are the relationships they build: in clinics, in churches, on front porches.

I encourage you to read this issue's cover story, "Hidden in Plain Sight." You'll learn how a medical genetics team at UPMC Children's Hospital of Pittsburgh discovered dangerous genetic variants within Northwestern Pennsylvania Amish and Mennonite communities. What they've learned promises to save lives in those communities and elsewhere. The team created a clinic in Mercer County that offers ongoing support and care to these families.

This example of clinical outreach is instructive for health research of various stripes. We've learned that "parachuting into" an area to further a research agenda is not adequate. When we're most effective, we show up as listeners and partners, incorporating the wisdom of the people we want to help—in ways that value their time and culture.

Another example is the University's research participant registry, Pitt+Me, which has enrolled over 250,000 participants, supporting 318 research studies for 300 conditions. Because the University of Pittsburgh is positioned so well, the National Institutes of Health's All of Us program, which aims to sequence the genomes of 1 million people, trusted us to enroll the first participants.

As we continue to build mutually respectful and beneficial relationships with our communities, this story will unfold further. I hope you'll stay tuned.

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

PITTMED

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University of
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The Class
of 2022's
impressive
match.

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Hangry? Here's what's actually
happening to you.

ABOUT THE COVER Families in the Plain Community of Western Pennsylvania are at risk for dangerous genetic diseases that present in ways rarely seen. There are some bright lights: These folks have partnered with Pitt people to help their communities and help patients elsewhere.

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FEATURES

Southern Exposure

A Magee Prize-winning effort shines light on the importance of vaginal health.

BY MICHELE DULA BAUM

Problem at the Pump

Working with clinicians at Children's Hospital, Cecilia Lo's team discovered that in the worst cases of hypoplastic left heart syndrome, the cell's energy source fails.

BY CRISTINA ROUVALIS

This family carried a rare mutation that should have been lethal. What was keeping them alive?

Doctors were flummoxed by cardiac cases in a family from Amity, Pennsylvania.

Again, they turned to Cecilia Lo's team to figure it out.

BY ERIC BOODMAN (COURTESY STAT NEWS)

Hidden in Plain Sight

Genetic conditions among Western Pennsylvania Amish and Mennonites are not well understood. Lina Ghaloul Gonzalez and colleagues are changing that and saving lives.

COVER STORY BY MAUREEN PASSMORE

Your Health Care Team Will See You Now

Pharmacists could help with chronic conditions.

BY MICHELE DULA BAUM AND ATHENA CURRIER

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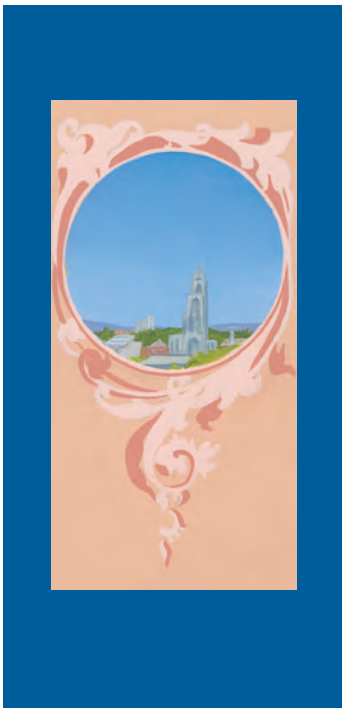
CONTRIBUTORS

ATHENA CURRIER'S ["Your Health Care Team Will See You Now"] publishing career began by folding and stapling her own mini-comics. The cartoonist, designer and illustrator has been in the book-making business for more than a decade now. And her extensive portfolio includes book covers, interiors, magazine illustrations, hand-lettered board games and posters, and more. Educational and political work are of particular interest to Currier, a Minneapolis resident, who earned an MFA in sequential art from the Savannah College of Art and Design.

MAUREEN PASSMORE ["Hidden in Plain Sight" and other stories] wrote our cover story, which is also her first feature for the magazine. "I grew up in a town much closer in proximity to Plain communities, so it was nice to write about people I used to encounter more often," she notes. A senior writer and project manager in the Office of the Senior Vice Chancellor for the Health Sciences, Maureen has worked for Pitt for 16 years. She earned a bachelor's in English (plus a minor in Ukrainian) prior to a master's in English education and MFA in poetry. Her chapbook, "Stranger Truths," was published by the Kent State University Press, and her poems have been published in numerous journals.

OF NOTE

*Devoted to noteworthy happenings
at the medical school*



People with Parkinson's can have temporary returns to function.

GETTY IMAGES

Placebos Shed Light on Parkinson's

In a memorable video, a man with the stooped posture, shuffling gait and hand tremors characteristic of Parkinson's gets on a bicycle. Somehow, he effortlessly pedals around a parking lot. As soon as he hops off the bike, however, the man's movement challenges reappear.

"This is an example of paradoxical kinesia," says Peter Strick, "or the remarkable return of apparently normal motor function that can occur for some Parkinson's patients under special circumstances, such as the ability to quickly respond to a fire alarm."

Strick is chair of neurobiology and scientific director of the Brain Institute at the University of Pittsburgh. He and his collaborators believe they may know why paradoxical kinesia happens.

"For some patients, placebos can be surprisingly effective in treating the movement disorders associated with the disease," says Strick, a PhD.

"We think there is brain circuitry that makes this possible, so we plan to define it and explore its potential impact on Parkinson's."

Strick is leading an expedition to explore this little-known brain region, which may point the way toward new therapies for Parkinson's disease. The inter-institutional team is funded over three years by a \$12 million Aligning Science Across Parkinson's (ASAP) initiative. ASAP's implementation partner, the Michael J. Fox Foundation for Parkinson's Research, issued the grant.

Other Pitt PhD investigators include Robert Turner and William Stauffer, of neurobiology, and Helen Schwerdt, of bioengineering. They are joined by Scott Grafton, an MD, of the University of California Santa Barbara. —Anita Srikameswaran

FOOTNOTE

National Institutes of Health funding for faculty of Pitt's School of Medicine totaled more than \$476 million during federal fiscal year 2021. The entire University faculty garnered more than \$596 million from NIH. (That total does not include \$44 million in NIH WARP Speed funding subawarded to Pitt.)



Skinner



Zevallos



Seybert

Appointed this Summer

Skinner Leads Radiation Oncology

Heath Skinner, an MD, PhD, is now chair of Pitt Med's Department of Radiation Oncology, as of July 1. He succeeds Joel Greenberger, an MD, who served Pitt for almost 30 years.

Greenberger's contributions to basic science and cancer care can be seen in the more than 500 publications and books he has written from 1973 until today. The National Institutes of Health has continuously funded his lab for 40-plus years; and his team lays claim to 44 patents and counting. Among their breakthroughs: preclinical models of the use of a lead compound to ameliorate irradiation toxicity in patients with head, neck and esophageal cancer.

Skinner most recently served as an associate professor of radiation oncology at Pitt and as an investigator at UPMC Hillman Cancer Center. Skinner specializes in the study and treatment of head and neck and lung cancers. As a physician-scientist, he maintains an active translational research laboratory focused on identifying novel, clinically targetable biomarkers of resistance to radiation.

Skinner has multiple currently funded NIH grants, has completed several randomized trials as principal investigator and is a member of the American Society for Clinical Investigation.

In his new role, he'll focus on further elevating the department's reputation for excellence in academic radiation oncology and training the next generation of radiation oncologists. Clinically, he will focus on advancing UPMC Hillman's radiation oncology services nationally and enhancing access to care.

Zevallos New Chair of Otolaryngology

José P. Zevallos, an MD, MPH, will be the Eugene N. Myers Professor and chair of otolaryngology, effective August 1.

Zevallos comes to Pitt from Washington University in St. Louis, where he serves as chief of the Division of Head and Neck Surgical Oncology. He's also the Joseph Kimbrough Professor of Head and Neck Surgery and director of the head and neck surgical oncology and microvascular reconstruction fellowship.

Building on the tradition established by Eugene Myers and Jonas Johnson, Zevallos will continue to invest in clinical and translational research, define new paradigms of clinical care and enhance the department's already excellent educational and training programs.

The list of Zevallos' research interests and clinical specialties is too long to cover fully here but includes head and neck squamous cell carcinoma, human papillomavirus head and neck cancers, oropharyngeal cancers, salivary gland tumors and head and neck skin cancer.

Throughout the course of his physician-scientist career, Zevallos has been an investigator on multiple research grants, published widely and remained dedicated to mentoring junior faculty and fellows. He is the founder and chair of the board of an early stage liquid biopsy company focused on early detection of minimal residual disease after cancer surgery.

Zevallos succeeds Johnson, an MD, who led the department for 17 years. Johnson will remain clinically active in the UPMC Head and Neck Cancer Survivorship Clinic, which he founded in collaboration with nursing colleague Marci Nilsen, a PhD, RN, and considers one of the highlights of his career.

Seybert Now Dean of Pharmacy

Amy Lynn Seybert, who has served the past 12 years as chair of Pitt's Department of Pharmacy and Therapeutics, has been named the dean of its School of Pharmacy.

On July 1, Seybert succeeded Patricia Kroboth, a PhD, who led the school for two decades.

Seybert takes the helm of a school that's ranked number five in research funding by the American Association of Colleges of Pharmacy.

"Dr. Seybert has a long track record of outstanding leadership in pharmacy education and research," says Anantha Shekhar, senior vice chancellor for the health sciences. "I look forward to working closely with her to advance interprofessional education and transdisciplinary research in the health sciences, and I am deeply grateful to Dr. Kroboth for her service and her leadership over the past two decades."

Seybert, a PharmD, is recognized as an international leader in simulation education in pharmacy and pioneered the use of human patient simulation to advance pharmacotherapy knowledge, clinical decision-making and medication safety skills in health care professionals. Her research in cardiovascular and critical care pharmacy practice and medication safety has led to substantial advances in patient care.

"The University of Pittsburgh School of Pharmacy has a phenomenal foundation and culture," says Seybert. "I am excited to build on the strengths of our research, education and clinical practice programs to maximize our impact." —*Staff reports*



Hard Stop on Hospital Infections

Pitt Med clinical scientists, with partners at Carnegie Mellon University, have found that machine learning and whole genome sequencing surveillance can stop in-hospital infections in their tracks.

They published their findings in fall 2021 in *Clinical Infectious Diseases*. UPMC Presbyterian is now implementing their system, designed to save lives and cut costs, in real time.

Senior author on the study Lee Harrison is an MD professor of medicine at the School of Medicine and of epidemiology at the School of Public Health; he leads the team using the Enhanced Detection System for Healthcare-Associated Transmission (EDS-HAT). EDS-HAT couples genomic sequencing with computer algorithms connected to the vast trove of data in electronic health records. When sequencing detects that two or more patients have near-identical strains of an infection, machine learning quickly mines those patients' electronic health records for commonalities; it then alerts infection preventionists to investigate and halt further transmission.

Alexander Sundermann is a clinical research coordinator and a recently minted DrPH and assistant professor of medicine. He says the typical model hospitals use for detection is labor-intensive and often dependent on busy health care workers noticing a shared infection between patients. "These practices haven't changed significantly in over a century," adds Harrison.

From 2016 to 2018, UPMC Presbyterian ran EDS-HAT with a six-month lag (so as not to interfere with normal clinical practice) for several infectious pathogens often associated with health care-acquired infections. EDS-HAT detected 99 clusters of similar infections in that period and identified at least one potential transmission route in 65% of those clusters. During the same period, infection prevention used whole genome sequencing to aid in the investigation of 15 suspected outbreaks, two of which revealed genetically related infections.

If EDS-HAT had been running in real time, the team estimates as many as 63 transmissions of an infectious disease from one patient to another could have been prevented. It also would have saved the hospital up to \$692,000.

Harrison says the current real-time implementation has detected one bronchoscopy-associated cluster and multiple nursing unit-based clusters. Hospital staff members were able to intervene for all of those. —*Michael Aubele*

PRESBY EXPANSION

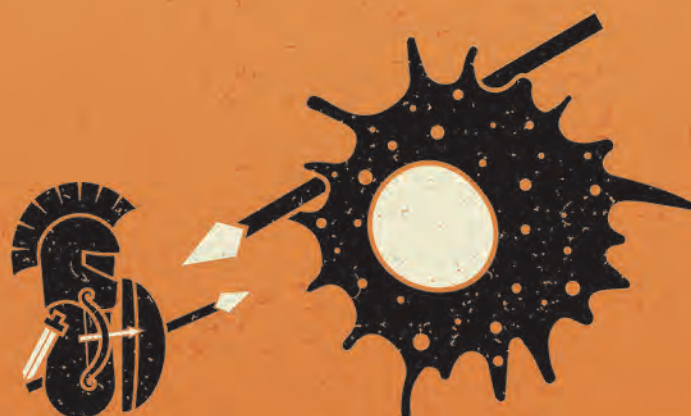
In June, UPMC broke ground on a 17-story addition to Presbyterian hospital that will transform the landscape of the Oakland campus, how care is delivered in Southwestern Pennsylvania and how medical education looks at Pitt.

The new building will make UPMC Presbyterian the largest academic hospital in the region. For Pitt Med students, the addition will translate to more learning and training opportunities in the heart of Oakland.

Twelve new operating rooms and 636 private patient rooms—many of them "acuity adaptable"—will create more spaces for specialized care and easier opportunities to keep patients in place, rather than transferring them to another unit or hospital as their condition changes. Teams will be able to ramp up support more seamlessly as needed in this patient- and family-centered care environment.

The new facility opens in late 2026. —*Micaela Fox Corn*

ASIDE



Bacteria battles, by Rachel Keeney.



"That example of collaboration, I think, is just emblematic of the region, and one of the reasons I love living in Allegheny County."

TOM ALTANY/UNIVERSITY OF PITTSBURGH

Overheard

Debra Bogen on leading a county health department through a pandemic

Debra Bogen, an MD, completed her training in pediatrics at Johns Hopkins in the '90s and then joined the faculty at Pitt in 1998. Through the years, she'd grown interested in moving into health policy and community-level programming. She proved to be a quick study as she took the reins as Allegheny County's top public health official just as the pandemic was taking shape.

Bogen assumed leadership of the Allegheny County Health Department two months ahead of schedule, shortly after the first cases of COVID-19 were reported in the United States, in mid-March 2020. She maintains ties to Pitt as adjunct professor of pediatrics with secondary appointments in psychiatry, in clinical and translational science and in health policy and management—and also as a community partner.

How did the county health department approach the pandemic?

The pandemic was really a test in endurance and flexibility, because it never stopped changing.

We needed to continually respond and adapt—from information sharing, testing, case investigation, data analytics, to vaccinations. Usually, the department has a significant regulatory role and a smaller clinical role, but during the pandemic we ramped up clinical services and provided more than 100,000 vaccinations. We partnered with numerous organizations and agencies and also brought resources to partners. We adapted to meet the needs facing residents throughout the pandemic.

What surprised you about stepping into the role?

What really amazed me was how willing people were to step up.

I had been on a call with the Allegheny Conference, and the CEO of Argo AI said, "Anything you need, let me know." A month or so later, I

called him and said, "There are two things I need help with. One is logistics. If I give you a list of all these locations where the federally qualified health centers are doing testing, can you figure out how efficiently we could pick up those tests and get them to our county lab to be packaged and sent for analysis in California? The second is: Would your self-driving cars be willing to do the pickup?" And he said, "Yes and yes." That was on a Friday at 4 p.m., and by early the next week, he and his team were ready with a plan. It was an incredible coalescing of resources and collaboration. The results were as we had hoped, to increase access to testing in higher risk, historically excluded communities.

Another example of collaboration was that the chief medical officers from the region's health systems had weekly meetings to share protocols, strategies, ideas and challenges—and they always invited me to the table. That example of collaboration, I think, is just emblematic of the region, and one of the reasons I love living in Allegheny County. The CMO collaboration persists today, which is terrific.

How did your background in pediatrics influence you?

I was worried about the impact of the pandemic on children's social and emotional growth and development—and on families, in general. I saw disparities every day as a pediatrician. For example, I often thought about a family I cared for and wondered how they were managing. The mother worked in health care. She had a long commute on a couple of buses—with a stop to bring her two young children to childcare early in the morning. What was she doing with many childcare programs closed and limitations on public transportation? These issues of health equity and access and who was at higher risk of COVID-19 were always on my mind. Community organizations stepped forward to try to address many of the issues in ways that I hope will endure. I hope we don't backslide in our efforts to address these inequities. At the health department, we continue to keep this a major focus of our work.

—Interview by Micaela Fox Corn

Third year students had a do-over of their virtual White Coat Ceremony—this time in person.



JOHN ALTDOERFER

Rites of Passage, Remixed

Two coats of white

Pitt Med's Class of 2024 matriculated like no other. They came to school at the height of the pandemic, in summer 2020. If it had been a more typical time, they would have marked their entry into medical training surrounded by family and welcomed by their instructors in a "coating" ceremony. Instead, they communed on Zoom and their white coats were delivered directly to wherever they were living at the time.

The tone of the nation wasn't one of pageantry. That simmering summer, just a few months after the killings of George Floyd, Breonna Taylor and Ahmaud Arbery, Pitt Med deans challenged the incoming class to write its own Oath of Professionalism. Their final draft recognized and pledged to address structural racism plaguing the United States, among other inequities. For their efforts to modernize what it means for physicians to "do no harm," the class garnered national media attention from outlets such as CNN and NPR, even before starting coursework. Now, every incoming med student class at Pitt drafts its own oath—those too have stressed the importance of advocating for others.

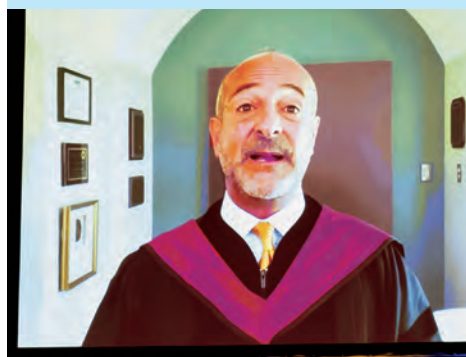
The Class of 2024 is not afraid to speak up for itself, either. This past year, as they embarked on their clinical rotations, the students asked for a do-over of their White Coat Ceremony, this time in person. School leaders happily complied, combining a formal reissuing of the coats with the traditional pinning ceremony for third-years. The big day was May 6.

Jim Withers of Operation Safety Net, which offers street medicine to people experiencing homelessness, delivered the keynote. And Varun Mandi, of the MD/PhD program, won the Sally Miller Award for the medically underserved.

Nicolás M. Kass, president of the Class of 2024, acknowledged the imposter syndrome many of them felt going into rotations. But, he said, "I would argue that our class has a unique skillset based on all we've been through for the past two years."

Alda Maria Gonzaga, MD associate dean for student affairs, offered these words of wisdom:

"Comparison is the thief of joy. And imposter syndrome doesn't make doctors; we make doctors. Pitt Med makes doctors. And we make excellent ones. We are proud of you." —MFC



Clockwise from top: keynote speaker Joseph Betancourt; professor of surgery Giselle Hamad hoods Michelle Zhang; Dean Shekhar.



Together Again

Class of 2022 Send Off

School of Medicine graduates and their friends and loved ones came together at Carnegie Music Hall on May 23 to celebrate the first in-person School of Medicine Diploma Day since the COVID-19 pandemic began. Keynote speaker, Harvard's Joseph Betancourt, who joined virtually, advised students to show grace with their patients. See the "Difficult Patient" story on the right to learn about his case in point.

Dean Anantha Shekhar, Provost Ann E. Cudd and Chancellor Patrick Gallagher also spoke at the ceremony, praising the 2022 graduates' resilience and grit as the pandemic disrupted their lives in the middle of their studies.

FREYBERG AND SPERRY HONORED

Zachary Freyberg, an MD, PhD, and **Jason Sperry**, an MD, MPH, of Pitt's School of Medicine are among 95 newly elected members of the American Society for Clinical Investigation (ASCI).

ASCI, founded in 1908, is one of the most esteemed honor societies of physician-scientists. Membership recognizes a researcher's significant contributions, at a relatively young age, to the understanding of human disease.

Freyberg, assistant professor of psychiatry and of cell biology, focuses on improving our understanding of the mechanisms associated with disorders such as addiction, schizophrenia and Parkinson's disease.

Sperry, professor of surgery and of critical care medicine, focuses on prehospital trauma care and sex-based outcome differences following injury or surgery.

They were formally inducted in April. —Staff reports



“People don’t get a manual on how to interact with health care.”

Joseph Betancourt’s Difficult Patient

Years ago, internist Joseph Betancourt was prepping for an appointment with a Latina patient whose chart had a large red sticky note on it, characterizing her as “difficult.” “She always wants to be seen early,” his colleague told him. Betancourt managed to see the patient a little sooner than scheduled. He braced himself for the encounter, speaking to the patient in Spanish, and found her to be lovely—not at all difficult as the red note indicated. He asked the scheduler to arrange for her to get the earliest appointment next time. “Sure,” he was told; the woman was given a 9 a.m. slot.

When the day came for the woman’s next appointment, he learned she had been outside waiting when the clinic was unlocked at 5 a.m.

Betancourt had to ask her, “Why do you arrive so early?” During a subsequent visit, she took a photo out to illustrate her answer. It showed a rural community health center in her native country in the early morning, with what must have been 100 people lined up at the entrance. He realized that she was used to overwhelmed first-come, first-served clinics, where she was expected to wait hours in line. The woman didn’t want to be seen early; but she did want to get in to see the doctor. That was not guaranteed in her previous health care experience.

She was not at all difficult. But because of language and cultural barriers, she was thought to be a prima donna.

Betancourt, senior vice president for equity and community health at

Massachusetts General Hospital and associate professor of medicine at Harvard, shared this story at Pitt’s School of Medicine Diploma Day in May. His lesson for graduates: Keep an open mind. Don’t let assumptions or unconscious bias get in the way of your patient interactions. They can lead to unequal or inaccurate treatment.

Betancourt is an internationally recognized expert in health policy who’s served on several Institute of Medicine committees producing landmark reports about addressing health care disparities and diversifying the health care workforce. Because he grew up in Puerto Rico in a bilingual, bicultural household, the difficulties of achieving health equity are also a personal matter for him:

“The challenges I tackle today are the ones I, my family, my community faced as I was growing up—discrimination, racism, the social determinants of health and language barriers in health care. These are things I’m intimately familiar with.”

During his address, he asked the future physicians in the audience to show grace. He reminded them that people “don’t get a manual on how to interact with health care,” and that curiosity, empathy and respect are critical to caring for patients effectively.

“Listening takes time,” he said, “but not listening can take more time and lead to poorer outcomes.”

—Maureen Passmore

—Photo illustration: Elena Cerri



The surgical team that transplanted a genetically engineered pig heart into a man in January 2022 included Pitt's David Kaczorowski. The procedure took place at the University of Maryland Medical Center.

Xenotransplantation was an interest of Pitt transplant giant Thomas Starzl, who conducted studies in transgenic pigs in the years before his death in 2017.

IMPLICATIONS

OF THE FIRST PIG-TO-HUMAN TRANSPLANTS

**XENOTRANSPLANTATION
COULD SHORTEN THE WAITLIST**
BY DAVID KACZOROWSKI

Demand for life-saving organ transplantation is at an all-time high. Last year, a record 41,000-plus organ transplants were performed in the United States, with top numbers for kidney, liver and heart transplants.

But a limited supply of donor organs continues to be a problem. Currently, transplant waitlists in this country exceed 100,000, with many patients unable to get on the list because of eligibility requirements and racial disparities in access.

As a cardiac transplant surgeon, I've witnessed the tragedy of this donor-organ shortage. But I'm also aware of a solution: xenotransplantation, which is transplantation of organs from one species into another.

In September 2021, researchers transplanted two genetically engineered pig kidneys into a brain-dead patient. And, in January 2022, I was part of the surgical team, with Bartley Griffith (Res '81), that conducted the first pig-to-human heart transplant in a living patient at the University of Maryland Medical Center. I worked with members of the team at Maryland to perform the donor portion of the operation. Sadly, the patient died two months later; but the initial success of the procedure shows how far science has come toward making species-to-species transplants a reality.

Animal-to-human transplants aren't new. In the 1960s, Keith Reemtsma, at Tulane University, performed 12 kidney transplants using chimpanzees as donors. While most of the transplanted organs—and ultimately the patients—survived for only a few weeks, one patient survived for nine months. Infection

was the major issue in half of the patients, while irreversible organ rejection occurred in the other half.

Around that time, Thomas Starzl, then at the University of Colorado, also performed similar animal-to-human kidney transplants using baboons as donors, with the organs surviving up to two months. He's most known for his liver transplants, with three attempts using chimpanzee livers from 1966 to 1974 that lasted from 24 hours to about two weeks. In the early 1990s, his two baboon-liver transplanted patients lasted for 26 and 70 days. Although one of the baboon livers functioned well, that patient died from infection.

Doctors have also made attempts to transplant animal hearts, the first of which predated the first human-to-human heart transplant. In 1964, a chimpanzee heart transplanted by James Hardy, at the University of Mississippi Medical Center, survived for a few hours.

Len Bailey's 1983 attempt, at Loma Linda Health, at transplanting a baboon heart into an infant known as Baby Fae prolonged her life for 20 days, a record at the time.

While these early results may seem poor at first glance, a number of these transplants actually lasted longer than many early human-to-human kidney transplants. The first patient to receive a donated human kidney lasted for only four days in 1933, and later attempts in the 1940s and 1950s yielded similar results. Also, immunosuppressing drugs that prevent the immune system from attacking donor organs weren't available during the early attempts at xenotransplantation.

Certainly, transplanting organs across spe-

cies faces obstacles, the most integral being evolution. As species grow apart, increasing differences in their molecular makeup can result in incompatibilities that make cross-species transplant difficult or impossible. Among the most problematic are differences in immunity, inflammation and blood clotting that damage both the transplanted organs and the host's body.

So, while pig-to-human transplants had been attempted in the past, 80 million years of evolution stood in the way. Pigs have molecules on the surfaces of their cells that humans don't. If these molecules are introduced into a person's body, the human immune system will register them as foreign and mount an attack. This process, hyperacute rejection, is a central reason many transplanted animal organs fail.

There have been advances in thwarting hyperacute rejection, such as using genetically engineered pigs that don't carry the genes that produce the foreign molecules triggering rejection. The pig heart my team transplanted this year was genetically engineered, as were the pig kidneys from late 2021. There have also been improvements in medications that suppress the immune system of the recipient so it's less likely the organ is attacked.

With more of these kinds of medical advances, I'm optimistic xenotransplantation will become a sensible option for all who need an organ. ■

Editor's Note: David Kaczorowski (Res '10) is a Pitt associate professor of cardiothoracic surgery. A longer version of this essay appeared in The Conversation.



The Hemolung gained FDA clearance earlier this year. It was developed by ALung, a Pitt spin-off that's been acquired by LivaNova.

PHOTO COURTESY LIVANOVA

DEEP BREATHS

RESPIRATORY TREATMENT FROM PITT SPIN-OFF
GETS FDA OK | BY MICHAEL AUBELE

In 1997, when few people were worried about a pandemic, ALung spun out of the University of Pittsburgh. The startup's cofounders—William Federspiel, the John A. Swanson Professor in Bioengineering, and the late Brack Hattler, surgery professor—had set their sights on developing artificial lung technology.

A quarter century later, COVID-19 has accentuated the need for treating patients with acute respiratory failure. And, in those 25 years, ALung Technologies has created a platform designed for such cases with its Hemolung Respiratory Assist System.

The ALung device Federspiel, a PhD, and Hattler, an MD, initially developed was designed to be implanted into the body. Alternatively, the Hemolung uses a small catheter to circulate blood outside the patient and efficiently remove carbon dioxide before the blood returns to the patient. It allows the lungs to rest and heal.

The system can keep patients off mechanical ventilation or wean them off through its low-flow extracorporeal (outside the body) carbon dioxide removal (ECCO2R) technologies. Last fall, the Hemolung System became the first and only ECCO2R device

cleared by the FDA.

"Patients with COPD [chronic obstructive pulmonary disease], emphysema—these patients oftentimes will experience acute exacerbation and will need to be on nasal oxygen," says Federspiel.

"A lung infection can put them over the edge to the point at which they can't breathe effectively. The carbon dioxide builds up in the lungs, and the Hemolung brings their CO₂ levels back down to a manageable level."

When the pandemic hit, the ALung team recognized that its technology could offer benefits to patients with acute respiratory failure caused by COVID-19; they thought its use might preempt the need for a mechanical ventilator, which often causes added lung damage. The company quickly received FDA emergency approval to treat COVID patients.

(ALung received its first FDA emergency use approval for the Hemolung in 2014 to treat a patient with cystic fibrosis who was waiting for a lung transplant at UPMC Presbyterian.)

The device's success treating COVID-19 patients helped build a convincing case for its use. The company submitted data to the FDA from more than 1,000 Hemolung patient

treatments on clinical safety and more than 230 patient treatments on clinical performance outcomes, which convinced the agency to give its approval.

"The Hemolung will be an important new treatment modality for acute respiratory failure to avoid or mitigate the harms from invasive mechanical ventilation," says Steven Conrad, medical director at ALung and professor of medicine at Louisiana State University Health Sciences Center.

"FDA clearance of the Hemolung is a game-changer for the treatment of these critically ill patients and will usher in a new era of extracorporeal lung support."

The London-based medical technology company LivaNova evidently agrees, because it recently acquired the company for \$10 million, according to LivaNova's 2022 first-quarter earnings report.

Paul Buckman, president of LivaNova's Advanced Circulatory Support Division reports that ALung will become part of the ACS division that also includes Pittsburgh-based TandemLife, a 1996 cardiopulmonary startup spun out of Pitt and acquired by LivaNova in 2018. ALung's 26 employees, like those of TandemLife, will remain in Pittsburgh.

The FDA clearance is even broader than what the company had been seeking through its COPD trial. The device can now be marketed for use in severe asthma, cystic fibrosis, as a bridge to transplant and for any condition requiring CO₂ removal directly from the blood.

Buckman says plans for ALung now include scaling up manufacturing and commercial field capacity. ■



GETTY IMAGES/SMARTBOY10

AGE, FAT, DNA

NEWLY UNVEILED LINKS TO GERIATRIC DISEASES

BY ASHER JONES

Older adults are highly prone to frailty, cardiovascular disease, cancer, arthritis, neurodegeneration and other maladies. Exactly why age makes people more susceptible to these disorders isn't yet clear, but findings by Pitt's Aditi Gurkar, an assistant professor of medicine, may explain how shedding pounds with age can lead to development of these types of diseases.

"People typically think that aging is linked with putting on fat, which is true, but there's a tipping point when weight gain switches to weight loss. People seem to lose weight about nine to 10 years before they develop age-related diseases," explains Gurkar, a PhD who is a member of the University of Pittsburgh/UPMC's Aging Institute.

"However," she adds, "there hasn't been a mechanistic understanding of the connection."

At least not until now. Gurkar and her research team may have found that connection. Their findings were recently published in *Science Advances*.

They used a grain-of-sand-size worm, *Caenorhabditis elegans*, to show that DNA damage—a hallmark of aging—rewires metabolism, triggering the breakdown of fat deposits and production of inflammatory compounds that drive age-related disorders.

"DNA damage happens to all of us, all of the time," says Gurkar. "Even sitting in the sun or eating that burger last night generates compounds that damage DNA. But with age, our

DNA repair pathways become less efficient and damage accumulates."

To understand how persistent DNA damage drives aging, Gurkar and her team used *C. elegans*. The worm's 20-day lifespan allows scientists to study aging without gaining too many gray hairs themselves. *C. elegans* shares many cellular features and molecular pathways with mammals, making insights potentially relevant to humans.

The researchers compared normal *C. elegans* to mutants that lacked key DNA repair genes. Unable to fix DNA lesions, the mutants accumulate damage faster than usual and experience premature aging and shortened lifespans.

By nematode "middle age," the mutant worms had elevated expression of genes involved in lipid breakdown and depleted fat stores compared with their normal peers. When the researchers did the same experiments in "young adults," they didn't observe these differences. These results indicate that accumulation of DNA damage with age rewires cellular metabolism to break down fat deposits.

Looking more closely, the researchers found that lipid breakdown led to elevated levels of omega-6 polyunsaturated fatty acids in the mutant *C. elegans*. These fatty acids are precursors for compounds called lipid mediators, which promote inflammation, a known driver of age-related diseases.

Gurkar says that the findings, in addition to possibly explaining how shedding pounds with

age can lead to development of disease, may also reveal that DNA damage is more than just a consequence of getting old—it may actually drive aging.

"When cells recognize DNA damage, they sound an alarm, and if the damage isn't resolved, the siren never shuts off. It's not the damage itself, but the noise that seems to be driving aging," she says.

When the researchers reduced fatty acid oxidation in mutant worms, they no longer lost fat stores and normal lifespan was restored.


"We can inhibit inflammation and excessive fat loss," says Gurkar. "It's about calming the cell down so it's no longer screaming SOS all the time."

Lipid metabolism pathways in *C. elegans* are shared by mice and humans, suggesting that the findings could help identify therapeutic targets for age-related diseases and accelerated aging disorders. The research could also explain why people who were treated successfully with chemotherapy or radiotherapy for pediatric cancer as children often become frail and have accelerated aging by their mid-40s.

"We plan to partner with pediatric doctors to follow chemotherapy patients over time," says Gurkar. "By measuring their DNA repair proteins, we hope to identify patients who might be more susceptible to frailty and age-related disorders later in life. This could inform tailored, or precision medicine, approaches to chemotherapy dose." ■



The latest Magee Prize
shines a light on the need
for better options for
vaginal wellness.



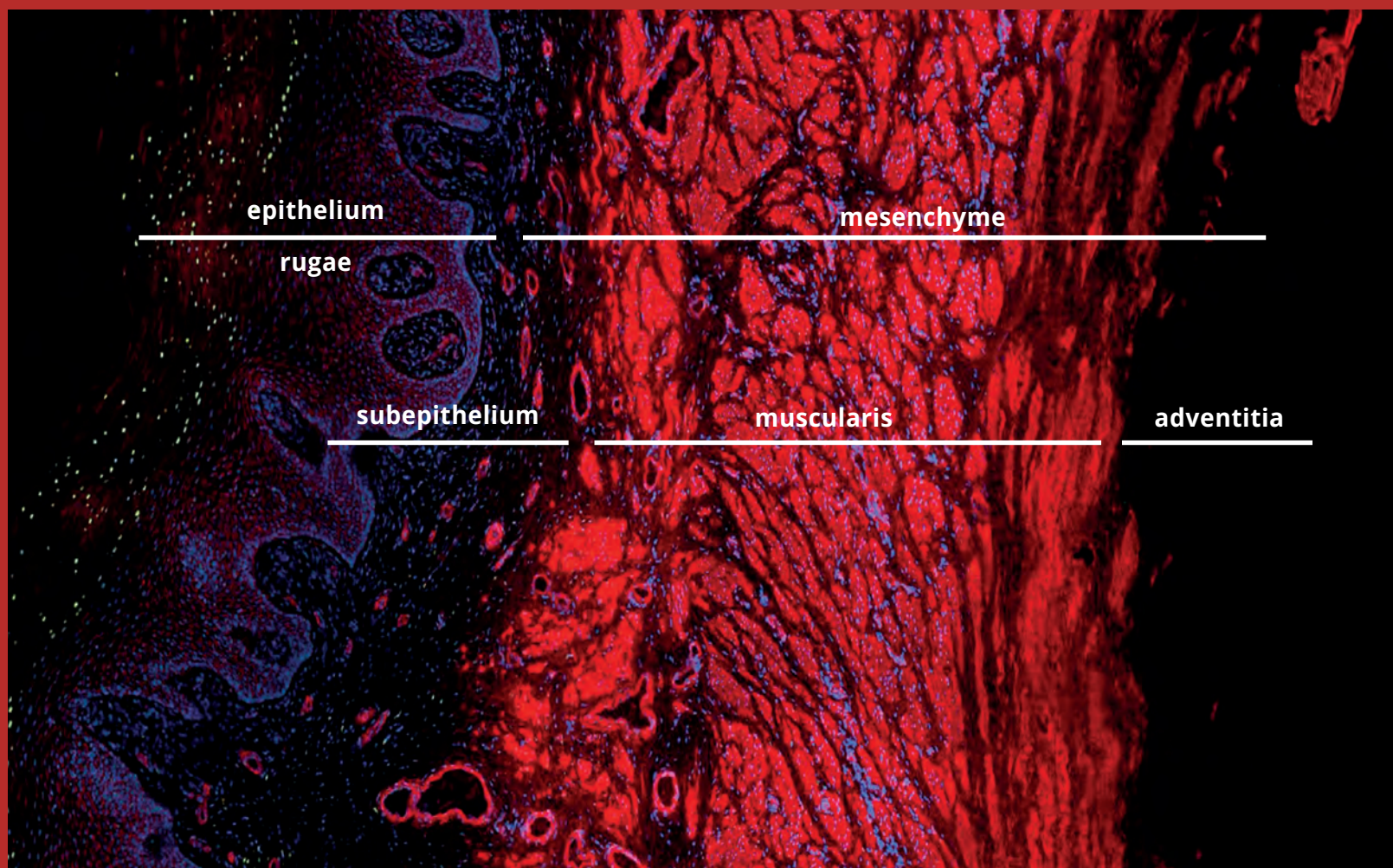
DESIGNS ON STEM-CELL BASED
"NEOVAGINA" TAKE \$1 MILLION MAGEE PRIZE
BY MICHELE DULA BAUM
ILLUSTRATIONS | ELENA CERRI (THIS PAGE)
AND SHANIEL BOWEN (PAGE 17)

SOUTHERN EXPOSURE

Apparently, even people who've dedicated their careers to women's health research can get fussy about the "V" word. Pamela Moalli gave a presentation recently on her work and chuckles at the recollection. "Initially, we were asked to tone down our talk and just refer to it as 'the female organ,' and I said, 'Well, which one?'"

Moalli, University of Pittsburgh professor of obstetrics, gynecology and reproductive sciences, leads a team that won the \$1 million Magee Prize in November 2021. The prize, awarded to an international team, was created to promote knowledge and enhance the health and wellness of women and infants worldwide; it's sponsored by the Richard King Mellon Foundation.

To build a vagina from stem cells, scientists need to better understand cellular composition and function.



Though many women and girls struggle with vaginal wellness—“It’s just not talked about openly,” notes Kyle Orwig, Pitt professor of obstetrics, gynecology and reproductive sciences who is a project coinvestigator.

Orwig, a PhD, and Moalli, an MD, PhD, are both members of the Magee-Womens Research Institute. Caroline Gargett, a PhD from Monash University in Australia, has joined them in their studies of vaginal stem cell populations as a possible basis for regenerative medicine solutions. Krystyna Rytel, an undergraduate at Pitt, is also on the team.

The group will use the prize funds to develop new biomaterials for repairing tissue loss in women with compromised vaginal structure and function. If successful, the work could have sizeable therapeutic potential:

CONGENITAL DEFECTS

Each year, one in 5,000 girls in the United States is born without a vagina. Current reconstruction techniques involve grafts of skin or intestinal tissue. In terms of sensation and function, both are problematic.

CANCER TREATMENT

Surgical treatment of genital, bladder, breast, colorectal and ovarian cancers, as well as chemotherapy and radiation treatment, can result in structural and functional damage. That damage can affect hormones (leading to abrupt menopause) and impair self-image, relationships and normal activities of daily living. Each year, hundreds of thousands of women are diagnosed with these cancers.

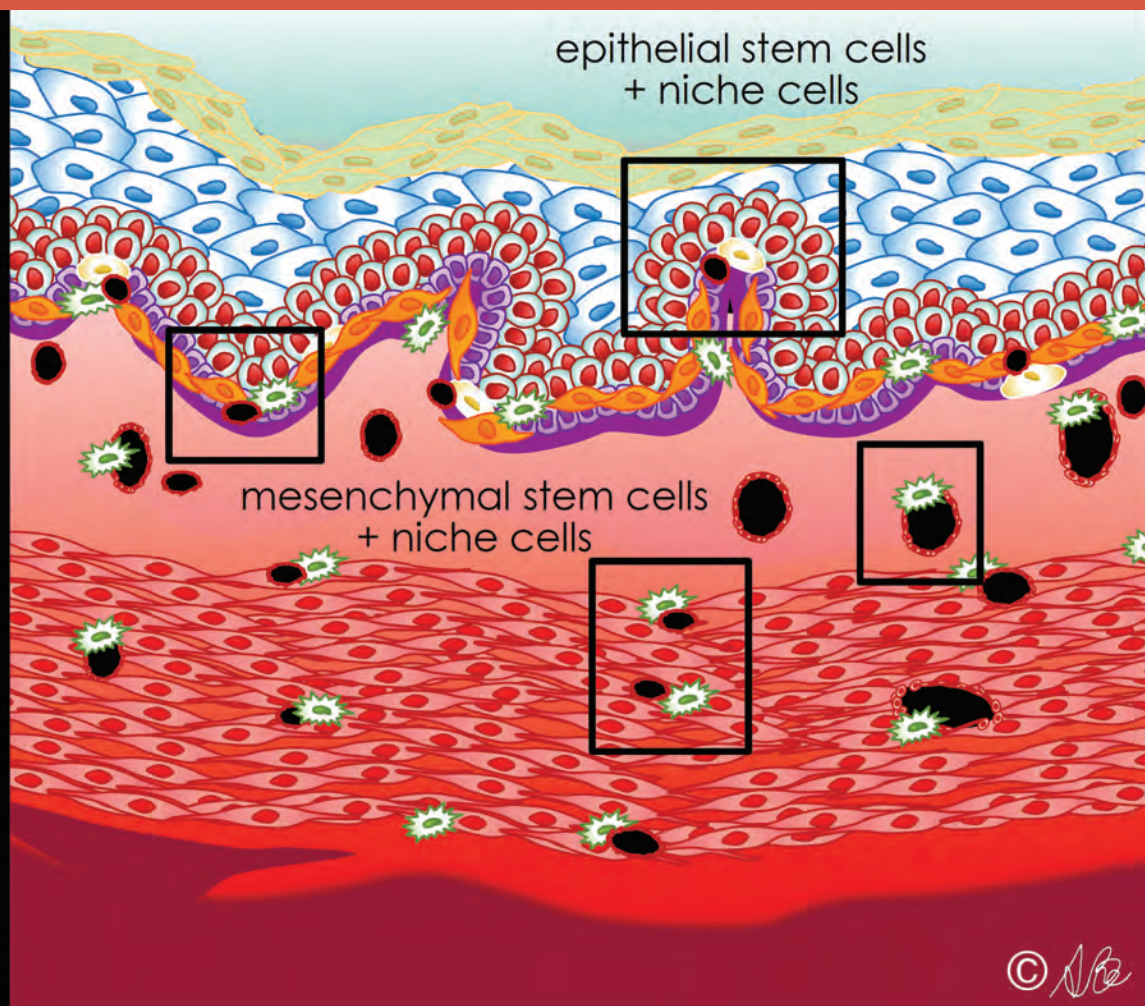
AGING AND MENOPAUSE

Today’s long-term solutions to vaginal dryness and other age-related changes pose issues. Hormone supplements, even when used locally, are contraindicated in women with serious blood clotting disorders and those with certain hormone-responsive cancers.

Lubricants might enhance sexual function, but the results are transitory. Laser treatments are painful, and they can be toxic to vaginal cells.

The bottom line, so to speak? Current therapies to restore vaginal anatomy, structure and function don’t work well enough. That’s where Moalli and colleagues’ neovagina comes into the picture.

The right environment is key.



Niche cells make up a stem cell's neighborhood. They also signal stem cells, telling them to stay idle, multiply or differentiate into specific cell types. The vagina has distinct layers, each with multiple cell populations that work together to maintain function. All of these cells, however, begin as epithelial or mesenchymal stem cells. The Moalli team expects to locate these key cells at the intersections of tissue layers and deeper blood vessels. The team will analyze human vaginal biopsies to determine each cell's genetic profile to build a blueprint of specific cell layers. In turn, these "instructions" will inform the biofabrication of a neovagina with authentic structural and functional properties.

IT STARTS WITH STEM CELLS

Vaginal changes throughout the life cycle—during menstruation, for instance—are “pretty strong evidence the vagina is dependent on a population of stem cells,” says Orwig. The team wants to tap into this natural reservoir.

Other studies often neglect what are known as niche cells, which form the environment in which stem cells form, says Moalli. “They are the soil which allows the stem cells to engraft and proliferate. Without the correct soil or niche, stem cells do not survive.”

For one study, the team will acquire samples from healthy women, as well as from women with vaginal malformations or cancer survivors—patients like those Moalli sees in the clinic.

In preclinical studies, mice will be subjected to chemotherapies routinely used to treat cancers of the breast and reproductive tract. These regimens deplete local stem cell populations, including those that maintain vaginal health. The researchers will then transplant vaginal stem cells and their niche cells into these stem cell-depleted mice to determine exactly what's needed for engraftment.

The team is already making progress and may be the first to characterize stem cell populations found within the full thickness of vaginal tissues.

In time, Moalli hopes to use their findings to improve on existing therapies by growing neovaginas. So, how would they do this?

First, they'd reprogram stem cells and their niche cells (from the patient), then graft these neovagina seeds back into the patient. This could happen either by injecting masses of new vaginal stem cells directly into the patient (preclinical experiments indicate some stem cells can begin to build new organ structures on their own) or by placing the stem cells onto a scaffold made from donor vaginal tissue.

This method might be extended to transwomen for gender-confirming surgeries. For survivors of hormone-dependent cancers, the team aims to understand how to activate remaining stem cell populations to restore hormonal function.

“The vagina has tremendous regenerative potential,” says Moalli, explaining that even severe childbirth injuries can often heal with little, if any, scarring. “If we can biofabricate kidneys and livers, we most certainly can make vaginas.

“It's really hard to sit across from these people who are hurting and say, “We don't have any options for you.” ■



An energy shortage in the cells causes the heart to pump poorly.






PROBLEM AT THE PUMP


NEW HOPE FOR A DANGEROUS
CHILDHOOD HEART CONDITION

BY CRISTINA ROUVALIS

ILLUSTRATION BY MICHAEL HIRSHON



For biologist Cecilia Lo, every day at work revolves around medical mysteries. But there was one particular diagnosis that was so confounding and devastating, she couldn't rest until she figured it out. In the United States, an average of one-third of babies born with hypoplastic left heart syndrome (HLHS) die before their first birthday. What made the condition fatal for some, while others grew up to live fairly normal lives?



Lo, Distinguished Professor and F. Sargent Cheever Professor, who chairs developmental biology at the University of Pittsburgh, has spent four years trying to pinpoint the mechanism that leads to cardiac failure in certain babies born without a functional left ventricle, the heart chamber responsible for pumping oxygenated blood to the rest of the body. Some children struggle even after major surgery to reconfigure the organ—in which a surgeon creates a one-chamber heart that allows the right ventricle to pick up the slack—and even when the operation is technically successful.



Although outcomes are better at UPMC Children's Hospital of Pittsburgh and are improving generally with advances in surgical options and medical approaches, for a subset of children with HLHS—"It's heartbreaking," says Lo. "There is interest to see if we can rescue these babies and to develop therapies to treat them if they go into acute heart failure."

Many speculated that the poor outcomes were because the surgically enhanced right ventricle becomes overworked to the point that it just gives out.

But based on a study of the condition in mice, Lo theorized the problem was at the cellular level. If she could prove her hypothesis, it might allow doctors to identify the highest-risk patients and move them to the top of the long waiting list for a heart transplant. "If we don't understand what causes the heart failure, there is no way to identify who is at risk."

Medical researchers expect surprises—behind many medical breakthroughs are hypotheses that don't exactly pan out and force scientists down a new path. But when Lo peered into the microscope to examine the heart cells, she tingled with excitement. The surprise was that there were no surprises. Her theory held up—the mitochondria of people with severe HLHS were damaged.

"It was very gratifying, very exciting. What we predicted actually happened in a very clear-cut fashion. A lot of the time your hypothesis doesn't necessarily go exactly the way you think. But this just came out beautifully."

She likens the heart to a car and mitochondria to the gasoline that fuels it—if the mitochondria are defective, the car won't move.

To test her hypothesis, Lo and her team started with research on mice, looking for genetic mutations that cause congenital heart disease. "We proved that you could get HLHS in mice." And by studying the animals, they discovered the problem was the mitochondria in the diseased mouse cells.

To test the theory on humans, they collected fibroblast cells (which build connective tissue) from three healthy children and 10 with HLHS. They divided the HLHS cells into two groups—those from patients with severe HLHS who either died or had a transplant before their first birthday and those

from a mildly affected group of patients who had lived past age 5 without a transplant.

They converted the fibroblast cells into pluripotent stem cells, which have the capacity to develop into any kind of cell in the body. By adding a specific mixture of nutrients and growth factors, the researchers were able to turn the stem cells into human heart cells that actually beat in the dish.

Just as a heart pulsates as it pumps blood, so do individual heart cells. (See them in motion at pi.tt/LoFindings.)

Peering at the heart cells through a microscope at the John G. Rangos Sr. Research Center, Lo noticed differences between the two study groups immediately. The heart cells of the healthy patient pulsated robustly. The heart cells of patients who had mild HLHS were similar to the healthy heart cells, pumping a little slower but still steadily. In contrast, the cells from patients with severe HLHS pumped slowly, their labored movement similar to what doctors saw in the hearts of the sickest patients.

Lo discovered that both groups of HLHS cells had defective mitochondria, but the damage was more significant in the group with severe disease. These cells were also unable to use natural defenses to compensate for the damaged mitochondria. The languid pumping could be fatal for a baby, even after a procedure to reroute the anatomy of the underdeveloped heart. At the root of this energy shortage in HLHS is a process known as oxidative stress.

Typically, when the body works as it's supposed to, mitochondria produce the energy required for cells to function. This happens through a series of steps in which electrons are passed along by protein molecules and then accepted by oxygen. But when there's oxidative damage, the electrons get lost before they reach the oxygen molecule, holding up the energy production process. The result is damage to the mitochondria, resulting in damage to the cell's ability to function and, ultimately, a severely damaged organ. "The heart is not going to work very well if you have cells that die and can't pump blood," says Lo. Her team uncovered a metabolic marker that may one day be accessed with a simple blood test.

"There's a lot of data that shows that these patients also have poor neurodevelopmental outcomes such as autism or cognitive impairment. The genes that regulate heart development also regulate brain development."

Having figured out what caused the problem, Lo and her team set out to test various drugs in search of potential therapies to remedy the mitochondrial defect. They found two promising candidates—sildenafil, which is commonly known by the brand name Viagra, a drug that increases blood flow. The other one is a supplement called TUDCA, a "molecular chaperone" that restores the folded structure of protein molecules that have fallen apart because of oxidative stress. Xinxu "Cindy" Xu was a lead author on a May 2022 Cell Stem Cell paper that described the findings.

Both of these drugs are already known to be safe in adult humans and won't have to go through a lengthy approval process. "We don't have to do safety studies like you would if the drug had never been used clinically." TUDCA is sold over the counter in health food stores and is often used by body builders. Whether either would be safe and effective for babies with HLHS, we don't yet know.

First, clinical studies have to be conducted in this patient population. But that's difficult with a relatively rare condition. "Any one medical center might not have enough patients," says Lo. "You might only get 10 or 15 a year." So clinical trials would require multiple centers to participate, which would require more funding.

Nationally HLHS affects about 1,000 babies born each year.

Mary Sanderson (not her real name), a new mother in Harrisburg, had never heard of HLHS until she was pregnant with her first child and had a prenatal screening.

The first doctor she saw told her that surgery wouldn't be an option and that her baby wouldn't survive. That was agonizing.

Then a second doctor, a cardiologist, referred her and her husband to UPMC Children's Hospital, which has some of the best HLHS patient outcomes in the country. Children's cardiology and surgery teams

are led by Jacqueline Kreutzer, professor of pediatrics who is the Peter and Ada Rossin Professor of Pediatric Cardiology, and Victor Morell, surgeon-in-chief who is the Eugene S. Wiener Professor of Cardiothoracic Surgery.

Sanderson's baby boy was born on May 7 and had his first major operation on the 12th. "He is recovering well," she says.

Sanderson says the condition made the entire birth process incredibly stressful: "I couldn't enjoy any part of the pregnancy. I was always worried. I went into labor in Harrisburg, and I worried I wouldn't get to Pittsburgh on time."

She is relieved that doctors at Children's could do surgery—"Science is amazing," she says—and gladly allowed researchers in Lo's lab to take cell and blood samples from her son. "It is so important that they learn different ways to treat it."

"Despite major advances in pediatric cardiology over the last few decades, there continue to be major challenges and unsolved life threatening conditions that affect children with congenital heart disease," says Kreutzer. "Dr. Lo's groundbreaking research is critical to improve their quality of life and shift traditional care approaches to a new level."

Even if all goes smoothly with Lo's studies, it's difficult to predict how long it will take to finish them and get approval for treatment. Lo and her team plan to test other drugs, as well, to see if they can reverse the effects of mitochondrial damage safely.

A biomarker might come sooner, perhaps within five years, if funding is available. Her research opens the possibility of a simple blood test that will let doctors know which babies are at the highest risk of going into cardiac failure, bumping them to the top of



Two major breakthroughs from Cecilia Lo's lab this year are likely to save the lives of children with heart conditions.

the long transplant list. "There aren't enough to go around," Lo says.

"This will tell us who should have priority to get the transplant." ■

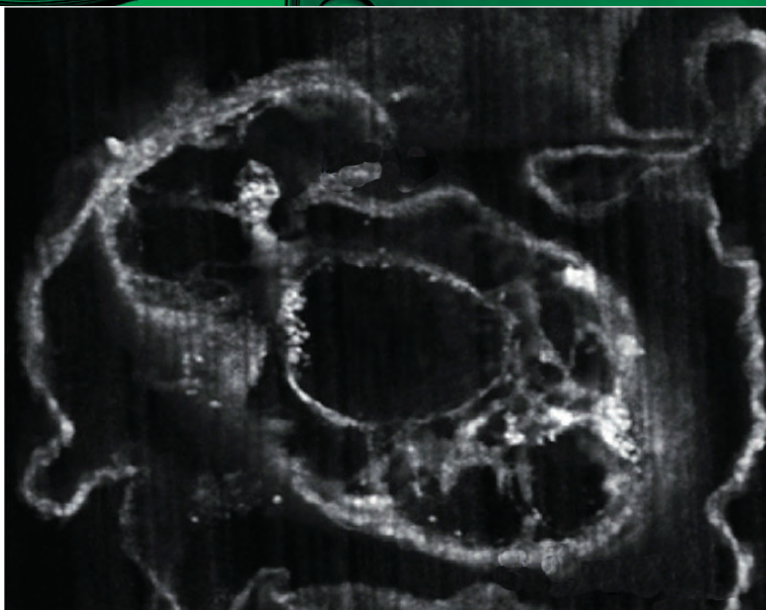
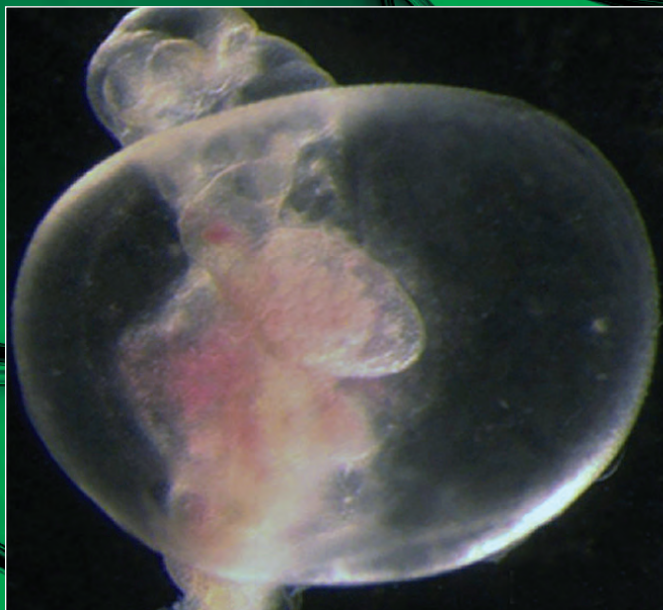
THIS FAMILY CARRIED A RARE
MUTATION THAT SHOULD
HAVE BEEN LETHAL.

WHAT WAS KEEPING
THEM ALIVE?

BY ERIC BOODMAN
FROM STAT NEWS.

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The result didn't make sense. The researcher kept scanning the mouse's pregnant belly, back and forth, back and forth. They could see the embryos on the ultrasound screen, cocoon-like, in grayscale—but there were no heartbeats. It should've been visible by now, at eight and a half days, a rhythmic flashing, a clue that the organ was on its way. Instead, each outline was utterly still, dead before it had come to life.



After the lethal mutation was edited into mouse eggs using CRISPR, the early stage mouse hearts developed severe abnormalities, as shown here.

Image: Cell Reports Medicine

That couldn't be right. These mice carried the exact same genetic mutation as a family who lived about an hour away, in the county outside Pittsburgh, near the West Virginia line. The humans definitely had beating hearts. Nicole Burns worked at an assisted living facility, hoisting residents in and out of bed, guiding them as they shuffled to dinner with a firm hand on the back. Her daughter Peyton loved hunting. Her son Cameron loved playing basketball. Their genome couldn't contain something so lethal: They were all very much alive.

The researchers tried again, inserting the family's genetic variant into the DNA of a mouse egg, injecting that into the coils of a mother's oviduct. The same thing kept happening, sound waves bouncing back and revealing [mouse] embryos dead in the womb.

"This is basically not a survivable mutation," said Cecilia Lo, chair of developmental biology at the University of Pittsburgh, who led the research. "If you have it, you're pretty much dead."

So how had Burns and her relatives survived? Lo wondered if, against all odds, they'd inherited not just one but two ultra-rare mutations, the second shielding them from the deadly effects of the first. It seemed stunningly improbable—but that is, in fact, what she, postdoctoral researcher Xinxiu Xu and their colleagues showed in a paper [published in February in *Cell Reports Medicine*].

The idea wasn't new. In 2016, some geneticists had hypothesized that people were walking around with this sort of good-gene, bad-gene drama going undetected on their chromosomes. The researchers had combed through over half a million genomes, looking for patients who should have inherited a severe

childhood disease but hadn't gotten any serious symptoms. As Stephen Friend, now a visiting professor at the University of Oxford, put it, "Clinicians would say, 'If anyone with that mutation were alive, I wouldn't believe it.'"

Out of 589,306 people, 13 were medically unbelievable. But the data were anonymized; there was no way for them to go back to those patients and find the protective variants they suspected were lurking in their cells.

Now, almost by accident, Lo found herself analyzing eight genomes that seemed to tell the story Friend had been speculating about. Her team dove back into the code, searching for the mutation that might be responsible for the rescue. There were a handful of other variants shared by all eight relatives—but only one of those genes was called into action in the heart. Bingo. Sure enough, when the researchers bred new genetically modified mice, this time with both variants, the [mouse] embryos survived. Some also showed the same heart defect as Burns and her kids. In other words, imperfect as it was, the second variant was protective.

It felt like a scientific triumph. Often, the narrative arc in biomedicine is a quest for disease-causing genes. Understand harmful alterations, the thinking goes, and you can hopefully reverse them—and there are reams and reams of papers about these "bad genes." There are "good gene" storylines, too. In 1996, a genetic variant was described that could stymie HIV—an observation that became a class of drugs. But Lo's paper was genre-bending, in a way. The "good gene" they'd pinpointed wasn't safeguarding against something extraneous, like a virus; it was softening the damage of another gene. "That's the untold story of human genetics," she said.

To Friend, the paper could provide a road

map to look for other, similar instances. But it was also a technical feat. "It's almost like, 'Here's what you could do today that you couldn't do 10 years ago.' It's like, whoa! Just beautiful," he said.

But that wasn't exactly how Burns felt about what was going on inside her genome.

Nicole Burns lives in her great-grandfather's house, in Amity, Pennsylvania, about an hour south of Pittsburgh. He'd had over 100 acres of rolling Appalachian foothills, with sheep, horses, cows, pigs, though some of the land has since been sold off. What's left from the farm is mostly scrap, a rusted plough, an old wheel sitting at the edge of the yard where it fades wearily into woods. ...

The land wasn't the only thing he'd passed down. Her other less appealing birthright was a hole in the heart. For her, actually, it was several, the biggest the size of a quarter. Normally, blood would pass from the heart's right side to the lungs, from the lungs to the left side and from the left side to the rest of the body. But these openings allowed some to burble backward, oxygen-rich blood leaking from left to right, to get resent to the lung. Sometimes, those holes close up on their own. If they don't, the inefficiency can slowly, over decades, stretch out the tissue, changing the heart's shape, potentially shifting its rhythm. In some cases, a doctor can thread a patch in through an artery or vein, but that doesn't always work.

In her family, heart surgery is a kind of ritual, a rite of passage. Her great-grandfather was the exception, diagnosed too late to operate, and he died of a massive heart attack. After that, everyone ended up under the knife. Her grandfather, a metallurgist at a steel mill, got surgery as an adult. Her mom, aunt and uncle all got it around their teens. She and her sister got it, both her kids had to have it, and it seemed like

if they were to have children themselves, they'd be destined to need heart surgery, too.

But it only came to a geneticist's attention because of Burns' son Cameron. He was born six and a half weeks early, by C-section. "I knew something was wrong, because they wheeled me down in the bed so I would be able to see him," she said. He was already hooked up to too many machines for her to hold him. A minute later, they rushed him to the children's hospital.

She discharged herself early Cameron's team kept calling her in her hospital room His body kept filling up with fluid. This wasn't because of a hole. His heart just wasn't pumping right.

The cardiologist said she had a choice to make. They could take him off all the machines and medications—nothing seemed to be working anyway—and see if he could pull through. Or they could try ... inserting a drain tube, to see if they could siphon away some of his swelling. She chose the drain. "It was selfish on my part, because I was thinking, you know, any time I can get with him—God forbid, before something happens—that's what I want," she said.

It worked. But during those discussions, the cardiologist also heard something that intrigued him. Often, inheritance patterns of congenital heart defects were murkier, weirder, harder to predict. "Like, not everybody in the family has it. That's what struck me," said Brian Feingold, director of the pediatric heart failure center at University of Pittsburgh Medical Center. "That's why I said to Dr. Lo, 'You have the expertise to help unravel what's going on here; there's something different than what we typically see going on in this family.'"

The researchers drove out on a snowy day in 2011. Four generations of the family were there: Eight biological relatives who had holes in their hearts and three relatives by marriage who didn't. The kitchen became a makeshift lab for swabbing noses and collecting blood. Burns' grandmother had bought pop and a tray of sandwiches. The snow was picking up. Once they had their samples, the scientists didn't linger. After they left, the house quieted. Burns was glad that part was done. Now, she thought, maybe they'll be able to start figuring out some of these mysteries. ...

For Friend and his colleagues, the idea of

looking for mutations that suppress bad counterparts began with lab animals. Experiments in the classic creatures of genetics—yeast and roundworms, for instance—showed how much interplay there was between different parts of DNA. A complex choreography of many genes is often the backstory to a particular trait.

That gave them an idea. So much of the search for drugs involved looking for disease-causing variants. Repairing the damage is often tough—and Friend wondered if there might be cases where toying with a different gene could make it easier to stop some of the first one's troublemaking. Imagine a broken machine on an assembly line, twisting a piece unusably out of shape. Getting that device back to normal is an intricate fix. But if there were another, earlier point on the conveyor belt where you could reroute around that station, maybe you could save some of the damage and keep things rolling. ...

[One] challenge is finding the people who have unidentified protective variants. "They're not going to be coming into clinics, because they're not sick," explained Friend. "They're not under the microscope, so to speak."

Even if they are sick, they're exceedingly rare. ...

The rarity itself can create a methodological problem. ... As [Eric Minikel, a grad student at the Broad Institute] explained, "... So if you look at a person who has supposedly-lethal mutation X but is mysteriously alive, there's no quick way to know which, if any, of their rare genetic variants kept them alive."

In the case of Burns' family, it seemed possible, but slow. At the time, sequencing whole genomes was prohibitively expensive. The team could read only short snippets of DNA and then try to piece together the part of the code that contained instructions for making proteins—a technique in which tiny alterations might be missed.

They were looking for a mutation shared by the eight affected relatives that might explain their heart issues. They found nothing. Years passed. Burns wondered whatever happened to the blood and saliva she'd given away. Her doctors had no news when she asked. Her mom died. Then her aunt. Both

had heart attacks.

But, by five years ago or so, sequencing methods had become fast, accurate and cheap enough for the team to go back into the freezer and get out the family's vials. When they found mutations, they had CRISPR gene-editing tools, allowing them to easily and quickly insert the alterations into mice. When they took bits from a family member's samples and chemically coaxed them into heart muscle cells, they saw only a mild structural defect, and the cells could still beat, could still help generate a pulse.

When they spliced the first, lethal variant into African clawed frogs, another common lab animal, the embryos had a heartbeat that was reduced but not eliminated. And there were questions the study didn't answer. How exactly this pair of mutations was giving rise to the strange set of symptoms in Burns' family remains unclear. The first gene was already known to play an important role in the growth of heart tissue. But why would this combo so insistently give rise to heart holes?

... For now, the idea [of developing a therapy from the Burns' case] retains an aura of what-if, a garden of forking paths that is the germ of all research, at once captivating and dismaying. [This winter], Lo called Burns to share what she'd found in the family's genomes. "I told them, 'You know, you're actually very blessed,'" Lo recalled. "Think about it. None of you would have been born if you didn't have the second mutation."

... When [Burns] finally heard about the results from Lo, she felt ... conflicted. On the one hand, it felt good, to have some sort of closure, some kind of answer. On the other, she wished her grandfather and mother and aunt could have been alive to hear it. It was cool to know you were so scientifically unique. She'd told some of her friends at work. "They just kind of look at you like, holy cow. Really?"

But there were also downsides to being such a mystery. She knew there wouldn't be a therapy anytime soon. The biggest change was that the cardiologist would want to follow up more, to keep an eye on their hearts, powering them through work shifts and classes and basketball games and hunting trips, all normal but utterly improbable. ■

HIDDEN IN PLAIN SIGHT

GENETIC CONDITIONS IN WESTERN
PENNSYLVANIA AMISH AND MENNONITES
ARE AMONG THE LEAST STUDIED. PITT PEOPLE
ARE CHANGING THAT AND SAVING LIVES.

BY MAUREEN PASSMORE

PHOTOGRAPHY | MARTHA RIAL, EXCEPT WHERE NOTED







A huge swath of rural Northwestern Pennsylvania is the very definition of verdant in the summertime. Lush forests of oak, red maple and spruce carpet both the mountains and the valleys—the wash of green broken only by patches of farmland and the occasional line of a narrow road. In pockets of this remote area, fields of wheat, barley or hay surround solitary houses or maybe a one-room school, and cars share the road with horse-drawn buggies.

Among the nine counties in this corner of the commonwealth, approximately 13,000 members of Old-Order Amish and Mennonite groups (collectively known as the Plain community) live in a way that has remained relatively unchanged for several hundred years.

This brings us to the story of 15-year-old Sarah (not her real name); she's Amish and, like most in the Plain community, is a descendant of Anabaptists who came to the United States in the 18th century to escape religious persecution. Plain community members live intentionally separate from mainstream culture, so the world for them hasn't changed much over the centuries. They don't use public utilities or other modern conveniences; they dress unadorned in muted colors and speak Pennsylvania Dutch. Formal education typically ends at eighth grade; and men and women adhere to conventional gender roles. They value humility and obedience, community and tradition, and they reject anything that draws attention to the individual (hence their preference not to be photographed).

This is Sarah's world; but it hasn't always been tranquil. After a long walk one summer day in 2010, she started to have trouble seeing. She found herself vomiting. Seizures came on.

Because of her alarming condition, she ended up in another corner of the commonwealth for some 21st century health care—in the emergency room of UPMC Children's Hospital of Pittsburgh. Sarah was seen by Jerry Vockley, an MD/PhD professor of pediatrics, who leads the Division of Genetic and Genomic Medicine in the University of Pittsburgh Department of Pediatrics and Children's Center for Rare Disease Therapy, and Amy Goldstein, a pediatric neurologist (now an attending physician at Children's Hospital of Philadelphia).

A blood test revealed a significant buildup of lactic acid. An MRI confirmed the teenager was having a metabolic stroke. The two physicians recognized the symptoms and made sure the patient was seen by the hospital's medical genetics service for appropriate testing.

Vockley looked over the genetic evaluation with his team—including Cate Walsh Vockley,

a genetic counselor at UPMC Children's, and Lina Ghaloul Gonzalez, an MD (Res 12, Fel '13), who was then a trainee and is now a professor of pediatrics in the Division of Genetic and Genomic Medicine. They were able to pinpoint the cause of the illness. Sarah had a mutation associated with MELAS syndrome—short for mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes—one of the most common mitochondrial disorders. She was immediately put on a treatment plan of various medications to slow the progression of the disorder and prevent strokes, as well as anticonvulsant medications to prevent seizures.

But the team—having identified Sarah's as the first known MELAS case in the Plain community—knew their work was far from done. They knew that other members of Sarah's family could also have MELAS, even if they weren't showing symptoms. MELAS is a mutation in mitochondrial DNA, which is inherited maternally.

Centuries of living culturally, socially and geographically apart from the larger population has led to limited genetic diversity among

Plain people. Researchers have documented a significant number of genetic diseases—mostly autosomal recessive disorders—in the Plain communities, and in the Eastern Pennsylvania area in particular. Suitable treatment exists for serious conditions, like maple sugar urine disease and glutaric aciduria type 1, and they are well managed with early diagnosis and intervention.

But genetic diseases in the Western Pennsylvania Plain community had not been well documented. (It's the least studied population of Plain people.) And detection of mitochondrial DNA mutations in the Plain community was concerning. If undiagnosed and untreated, these are potentially fatal conditions.

"We knew we had to test Sarah's other family members because a diagnosis could get them appropriate treatment—hopefully before anyone else had severe symptoms," like Sarah, says Ghaloul Gonzalez.

The case studies would present opportunities to learn more about mitochondrial mutations that would be helpful for the general



Lina Ghaloul Gonzalez (left) and Cate Walsh Vockley

population, too. The mitochondrial respiratory chain requires hundreds of proteins for normal assembly and function, explains Walsh Vockley, and mutations in the proteins' genes can lead to a wide range of diseases. Cells have hundreds to thousands of mitochondria, energy-producing organelles, each with its own DNA. However, in a disease like MELAS, not all mitochondria in the cell have a mutation. The ratio of altered to normal mitochondria dictates the severity of the disease symptoms, which means that some disease phenotypes vary from person to person.

So there are hundreds of possible mutations in mitochondria and different ways they manifest. This makes the work of linking diseases to mitochondrial mutations tricky in many cases. Genetic researchers are often looking for the proverbial needle in the haystack. Sarah's family gave them threads to follow.

People with MELAS might end up with any or all of these conditions: Stroke, dementia, epilepsy, recurrent headaches, short stature, infertility, organ failure, progressive weakness (myopathy), dangerous lactic acid build-up, intestinal dysmotility (difficulty defecating that can lead to nutritional issues), maternally inherited diabetes and deafness.

MELAS is not curable; treatment involves medications to alleviate or help with symptoms. About 10% of people who carry the mutation have severe symptoms and the same percentage are asymptomatic. People who fall between those two extremes experience a variety of possible conditions.

Identifying MELAS in a Plain community opened the possibility that people could be

treated and lives could be saved. In 2015, Ghaloul Gonzalez and Walsh Vockley and their team traveled to Sarah's community to sit down with about 30 of her family members for what would not be a routine consent conversation.

In general, Plain people seek natural remedies and chiropractic care and only engage with conventional health care when those familiar options are exhausted. Also, few Plain community members in Western Pennsylvania live close to medical facilities—nor do they drive cars. When families in the region need care, they often pay an “English” person (a term for someone outside the Plain community) for a car ride, which can be expensive.

Sarah's extended family listened intently to the team's description of MELAS. They learned what was at stake for them and why the medical professionals wanted to work with them.

“We explained that because Sarah had MELAS it was likely other family members did, too,” recalls Walsh Vockley. “No one thought they had it; but, as we were talking to them, it became clear that many of them had undergone major medical interventions without a genetics evaluation, without knowing that there could be an underlying cause.”

Sure enough, Sarah's family history uncovered that Sarah's mother had reported having migraines and hearing loss, symptoms of MELAS syndrome. Other family members had already experienced symptoms severe enough for conventional care, including organ transplants and hearing aids. By the end of the

conversation, most of the family consented to genetic evaluation.

After testing the family's blood and urine samples, the team was not surprised to find that all participating at-risk adults and two children carried the mutation and none of the control group (unrelated spouses of maternal relatives) did. This discovery led to transformative care for Sarah and her family. It was now clear that the carriers' previous health issues were related to their mitochondrial DNA mutation.

It was also clear to Ghaloul Gonzalez and Walsh Vockley that Sarah's family was probably

If doctors had known of John's diagnosis sooner, his life might have been saved.

just one of many in the Western Pennsylvania Plain community with undiagnosed hereditary disorders. They knew they could help by identifying underlying genetic diseases in this population. So, in addition to providing genetic services at UPMC Children's Hospital of Pittsburgh, Ghaloul Gonzalez and Walsh Vockley developed the Plain Community Translational Medicine Program at UPMC Children's, the Plain Community Outreach Clinic in Mercer County and a research registry to discover new genetic disorders among Plain people of Western Pennsylvania.

As a part of the translational program, Ghaloul Gonzalez and Walsh Vockley work to increase in-hospital referrals of Plain community members to their genetic



consulting services. In 2016, after a year-long review of medical records of 303 Plain patients at outpatient clinics and at UPMC Children's, their team found that 102 patients had a clinical presentation that suggested a genetic disorder; however, only 32 of the 102 patients had been evaluated by the Division of Genetic and Genomic Medicine.

"We don't know why this is," says Ghaloul Gonzalez. "Maybe the physicians offer a genetics referral and families decline. Or, physicians know that families often have limited resources and can't pay for testing, so they don't call us. Now, every day, Cate gets a list of Amish and Mennonite patients who are in UPMC Children's. We have permission to look at their records and determine whether they need genetic evaluation. Then we approach the attending physicians about talking to the family."

Some Plain community families are fine with genetic evaluation. Some are hesitant—often for financial reasons. They usually don't have private insurance, so leaders or bishops

in the community typically negotiate with UPMC to pay a certain percentage for services. To offer families services closer to their homes, the two women travel to Mercer County, to the Plain Community Outreach Clinic, once a month.

"We used to place ads in Amish newspapers about our services," says Walsh Vockley. "We went to a health fair at a fire station once to reach families. Families have now heard of us and are more willing to go to the clinic."

Ghaloul Gonzalez targets testing for certain diseases based on symptoms and will screen for founder mutations, i.e., genetic variations that are more common among Plain people. If targeted testing does not reveal anything, she will try gene panel testing or whole-exome testing, which identify variations in any gene.

As a genetic counselor, Walsh Vockley collects a family history, interprets and discusses test results with patients, and, if patients need to see a specialist, coordinates their care. Because whole-exome testing is expensive, Walsh Vockley searches for ways to get fami-

lies low-cost or free testing.

"If we're critically concerned about a child's health issue, we do our darndest to find ways to get answers," says Walsh Vockley. "Some testing companies will help with costs, but we can also get families free testing when they participate in research"—like the research registry they started.

The registry for the Western Pennsylvania Plain community is much like one that exists for Eastern Pennsylvania communities through the Clinic for Special Children (which refers some patients to UPMC/Pitt transplant surgeons). The little-studied Western Pennsylvania population has mutations common in all Plain communities, but, as Ghaloul Gonzalez discovered with MELAS in Sarah's family, its members also have unique genetic disorders and mutations.

Ghaloul Gonzalez and colleagues identified a Mennonite patient with a gene variant (of *GUCY2C*), which causes chronic diarrhea and other issues that can lead to life-threatening symptoms. The team studied an



“What we’re learning from the Plain community doesn’t just go back to that community,” says Ghaloul Gonzalez. The findings are likely to save lives in the larger population, as well.

experimental drug for diarrhea, but it’s not available for patient use. They hope their work will inspire other research for therapies.

“What we’re learning from the Plain community doesn’t just go back to that community,” says Ghaloul Gonzalez. “We have learned more about diseases and mutations—in which populations they are inherited, who should be tested for which genetic disease and new ways these diseases present in people.”

As for Sarah, since her original diagnosis after that walk several years ago, she has had other health setbacks, as expected with her disease. When doctors have the ability to help manage an illness early on, outcomes tend to be better, notes Ghaloul Gonzalez. She and Walsh Vockley can’t stress enough the importance of early diagnosis of a genetic condition.

Take the case of a young Amish boy, John (not his real name), who was enrolled in the Ghaloul Gonzalez team’s studies after physicians had ruled out any known causes of his immune deficiency. John started having

serious health issues—severe infection, sepsis and pneumonia—when he was 10 months old. Throughout the next five years, John was treated for neutropenia (a low white blood cell count), as well as recurrent lung and blood infections before undergoing a transplantation of stem cells of the blood and bone marrow.

He didn’t make it to his sixth birthday; John died after complications from a second stem-cell transplantation. It turned out that John had reticular dysgenesis, a severe immunodeficiency disease. It’s caused by what’s known as adenylate kinase 2 (AK2) deficiency. Diseases related to AK2 deficiency usually present during early infancy. Children born with reticular dysgenesis are likely to die within days or a few months after birth if not treated.

Because John had a less severe and delayed presentation of reticular dysgenesis, he did not meet the clinical criteria for the disorder and was not flagged for genetic testing of an AK2 mutation. (The child had tested negative for known founder mutations among Plain

people.) Through whole-exome sequencing, Ghaloul Gonzalez and her colleagues found that John did, indeed, have an AK2 mutation.

This discovery suggested that other people with combined immunodeficiency who don’t seem to meet the clinical criteria for “classical” reticular dysgenesis should be tested for AK2 mutations—not just those within the Plain community.

Recognition of reticular dysgenesis before a transplant is crucial; conditioning regimens can lead to better outcomes.

If doctors had known of John’s diagnosis sooner, his life might have been saved.

John’s parents agreed to be tested for the mutation and were found to be carriers, though they do not have the disease. (That’s typical for most autosomal recessive disorders.)

The couple now has another child who was screened a few hours after birth. A few days later, the results came in. He was found to be a carrier like his parents; but, to their great relief, he’s not expected to be affected. He continues to do well at 4 years of age. ■

Your Health Care Team Will See You Now

Pharmacists could help with chronic conditions

KYLE MCCORMICK, a PharmD (Pharmacy '14), owner, Blueberry Pharmacy, West View, Pa., a borough north of Pittsburgh

A Somerset native who completed a residency in Indiana, Pa., before opening his own shop in West View

WE SEE EVERY CONDITION, BASICALLY. WE CAN BE THERE AT FIRST DIAGNOSIS TO HELP PEOPLE UNDERSTAND THEIR CONDITION, MONITOR THEIR PROGRESS AND MAKE SURE THEY'RE TAKING THEIR MEDICATION PROPERLY.

WRITTEN BY MICHELE D. BAUM


DRAWN BY ATHENA CURRIER

IS THE CONDITION WELL CONTROLLED? WE CAN FOLLOW UP WITH THE DOCTOR TO HELP THEM MAKE CHANGES.

BASED ON A MEMBERSHIP MODEL, BLUEBERRY PHARMACY ACCEPTS NO INSURANCE. FOR ABOUT \$60 A YEAR, PATIENTS CAN EXPECT PERSONALIZED SERVICE AND LOWER DRUG PRICES. NONMEMBERS ALSO CAN BENEFIT FROM LOWER OVERALL DRUG PRICES.



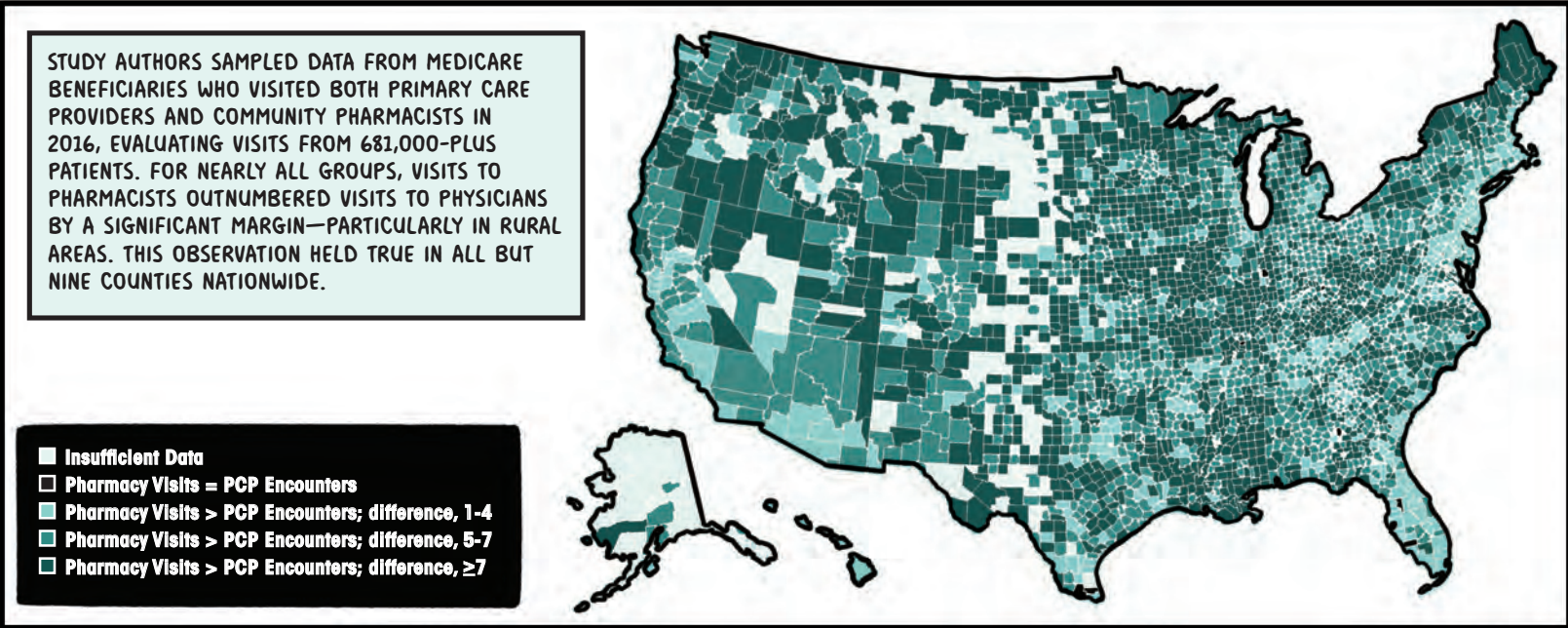
PEOPLE WITH MEDICARE VISIT COMMUNITY PHARMACIES ALMOST TWICE AS OFTEN AS THEY DO THEIR FAMILY DOCTOR OR PRIMARY CARE PHYSICIAN.



LUCAS BERENBROK, a PharmD (Pharmacy 13), MS, associate professor of pharmacy and therapeutics, School of Pharmacy

Coauthor of a JAMA Network Open study that calls these visits out as opportunities for greater collaboration among health care providers

THEY ARE ACCESSIBLE. YOU CAN JUST WALK IN OR GET THEM ON THE PHONE.



IN COLLABORATION WITH PHYSICIANS, PHARMACISTS CAN DO MORE THAN DISPENSE MEDICATIONS—THEY CAN BE VALUABLE PARTNERS IN HELPING PATIENTS MANAGE DIABETES, HIGH BLOOD PRESSURE OR OTHER CHRONIC CONDITIONS.




IN THE MARVEL UNIVERSE, IT TAKES THE COMBINED EFFORTS OF 10 AVENGERS, A PAIR OF SORCERERS, THE WARRIORS OF WAKANDA AND A RAGTAG LOT OF SPACE ALIENS TO DEFEAT A WORLD-DESTROYING SUPERVILLAIN. IN THE REAL WORLD, TOO, A CAPABLE TEAM IS THE BEST DEFENSE AGAINST THE FORCES THAT THREATEN WELL-BEING.

COMMUNITY PHARMACISTS ARE IN PLACES WHERE PEOPLE LIVE AND WORK. EACH PHARMACY VISIT IS AN OPPORTUNITY FOR ENGAGEMENT.




STEPHANIE MCGRATH, a PharmD (Pharmacy '07), executive director, Pennsylvania Pharmacists Care Network

PENNSYLVANIA PHARMACISTS CARE NETWORK (PPCN) IS A STATEWIDE ASSOCIATION OF 175 MOSTLY INDEPENDENTLY OWNED COMMUNITY PHARMACIES.



PPCN SUPPORTS COLLABORATION AMONG CLINICIANS, PHARMACISTS, PATIENTS AND FAMILIES TO DEVELOP SUSTAINABLE MODELS OF CARE AND IMPROVE PATIENT OUTCOMES.



WHAT DOES MCGRATH MEAN BY ENGAGEMENT? WELL, PHARMACISTS CAN FACILITATE CONNECTIONS WITH CARE-MANAGEMENT SERVICES OR SUGGEST APPROPRIATE LOCAL RESOURCES.



RIGHT NOW, COMMUNITY PHARMACISTS REPRESENT AN UNTAPPED OPPORTUNITY FOR THE PROVISION OF TEAM-BASED CARE.



REGULATORY ISSUES NEED TO BE RESOLVED AND AGREEMENTS REACHED ON REIMBURSEMENT BEFORE YOUR PHARMACY NEXT DOOR CAN PLAY A LARGER ROLE.



STILL, THERE HAVE BEEN STEPS FORWARD. MANY PHARMACIES OFFER COVID-19, INFLUENZA AND OTHER VACCINES ON SITE.



TRACEY CONTI SAYS THAT BERENBROK'S STUDY FINDINGS MAY POINT TO AN OPPORTUNITY, YET SHE CAUTIONS THAT NUMBERS OF VISITS MAY NOT TELL THE WHOLE STORY. THERE'S A DIFFERENCE BETWEEN STOPPING TO PICK UP A PRESCRIPTION AND HAVING A CONVERSATION ABOUT A QUESTION OR CONCERN, SHE NOTES. EVEN SO, CONTI WELCOMES THE OPPORTUNITY TO COLLABORATE.

TRACEY CONTI, an MD, associate professor and chair of Pitt's Department of Family Medicine

WORKING AS PART OF A TEAM, PARTICULARLY AS WE GO FURTHER OUT FROM AN ACADEMIC CENTER, IS ESSENTIAL.

MULTIDISCIPLINARY TEAMS CAN BE AN ESPECIALLY EFFECTIVE TOOL TO REDUCE HEALTH DISPARITIES, SHE SAYS.

PITT HELD ITS 13TH ANNUAL INTERPROFESSIONAL FORUM IN OCTOBER. THE FORUM IS MANDATORY FOR ALL FIRST-YEAR STUDENTS IN PITT'S SIX HEALTH SCIENCES SCHOOLS AND THE SCHOOL OF SOCIAL WORK.



DURING THE FORUM, SMALL INTERDISCIPLINARY GROUPS OF STUDENTS WORK TOGETHER ON SIMULATED PATIENT CASES AND TAKE PART IN EXERCISES DESIGNED TO ILLUSTRATE THE WAYS IN WHICH POVERTY, DISCRIMINATION AND OTHER SOCIOECONOMIC FACTORS AFFECT HEALTH.



WHEN I WAS TRAINING, PHARMACISTS WERE SEEN AS SOMETHING EXTERNAL. NOW, WE NEED TO HAVE EVERYBODY AT THE TABLE WHEN TRYING TO MANAGE CHRONIC DISEASE.

IN CARING FOR A PATIENT WITH DIABETES, FOR EXAMPLE, EXPERTISE IN PODIATRY, OPHTHALMOLOGY AND BEHAVIOR CAN PLAY IMPORTANT ROLES, SHE SAYS.

I LOVE WHAT I DO, SEEING PEOPLE FROM BIRTH TO DEATH, BUT THERE'S NO WAY I COULD DO THAT BY MYSELF.



MATCH RESULTS

CLASS OF 2022

ANESTHESIOLOGY

Anglin, Elaina
UPMC/University of Pittsburgh, Pa.

Armann, Kody
Johns Hopkins Hospital, Md.

Brisbin, Alyssa
University of California San Francisco, Calif.

Dayananda, Sanjana
McGaw Medical Center of Northwestern University, Ill.

Gupta, Niharika
McGaw Medical Center of Northwestern University, Ill.

Kennedy, Niki
Beth Israel Deaconess Medical Center/
Harvard University, Mass.

Worku, Hermoon
Brigham & Women's Hospital/
Harvard University, Mass.

Yeker, Richard
University of Chicago Medical Center, Ill.

DERMATOLOGY

Harper, Kamran
UPMC/University of Pittsburgh, Pa.

Mizes, Alicia
Strong Memorial Hospital/
University of Rochester, N.Y.

Ortiz, Camila
NYU Grossman School of Medicine, N.Y.

Patel, Bansri
Penn State Milton S. Hershey Medical Center, Pa.

Wack, Sarah
UPMC/University of Pittsburgh, Pa.

EMERGENCY MEDICINE

Berrin, Lily
Alameda Health System-Highland Hospital, Calif.

Galli, Gabriela
New York-Presbyterian/Columbia and
Cornell universities, N.Y.

Ma, Henry
UPMC Hamot/University of Pittsburgh, Pa.

Murphy, Carolyn
Denver Health Medical Center, Colo.

Pusateri, Alexandra
Rhode Island Hospital/Brown University, R.I.

Snyder, Oliver
Mercy Health Program, Mich.

Stern, Harrison
UPMC/University of Pittsburgh, Pa.

FAMILY MEDICINE

Cox, Abigail
University of Wisconsin, Wisc.

Gilbert, Nicholas
Fort Belvoir Community Hospital, Va.

Hu, Allen
UPMC St. Margaret/University of Pittsburgh, Pa.

McMillan, Calvin
Kent Hospital/Brown University, R.I.

Quam, Steven
Allina Health, Minn.

Weinhold, Jonathan
UPMC McKeesport, Pa.

INTERNAL MEDICINE

Brown, Rebecca
University of Virginia Health System, Va.

Crymes, Anthony
LAC+USC Medical Center/
University of Southern California, Calif.

Culley, Miranda
University of California San Francisco, Calif.

Curtis, Brett
University of Michigan Hospitals, Mich.

Doenier, Emma
St. Louis Children's Hospital-Barnes Jewish Hospital/
Washington University in St. Louis, Mo.

Dooley, Sean
Beth Israel Deaconess Medical Center/
Harvard University, Mass.

Ewing, Caroline
University of Wisconsin, Wisc.

Huang, Joanne
UPMC/University of Pittsburgh, Pa.

Kagalwalla, Sana
University of Minnesota Medical Center, Minn.

Kang, Heejae
UPMC/University of Pittsburgh, Pa.

Kassir, Zachary
Johns Hopkins Bayview Medical Center, Md.

Kettering, Caroline
UPMC/University of Pittsburgh, Pa.

Kocak, Brian
St. Louis Children's Hospital-Barnes Jewish Hospital/
Washington University in St. Louis, Mo.

Kumar, Deepak
UPMC/University of Pittsburgh, Pa.

Kusztos, Amanda
University of Washington Medical Center, Wash.

Lin, Lauren
University of Washington Medical Center, Wash.

Madill, Martine
Ronald Reagan UCLA Medical Center, Calif.

Meltzer, Avery
Yale-New Haven Medical Center, Conn.

Moon, Mackenzie
Johns Hopkins Hospital, Md.

Murphy, Joseph
UPMC/University of Pittsburgh, Pa.

Murray, Vanessa
University of Pennsylvania Health System, Pa.

Nanni, Michelle
Icahn School of Medicine Affiliated Hospitals, N.Y.

Nelson, Mackenzie
Walter Reed National Military Medical Center, Md.

Newhouse, David
UPMC/University of Pittsburgh, Pa.

Nguyen, Vi
Ronald Reagan UCLA Medical Center, Calif.

Oh, Loreanne
University of Michigan Hospitals, Mich.

Park, Sanghoon
University of Texas Southwestern, Texas

Rokaw, Sarah
Beth Israel Deaconess Medical Center/
Harvard University, Mass.

Seabolt, Liliana
MedStar Georgetown University Hospital,
Washington, D.C.

Sun, Aaron
Johns Hopkins Hospital, Md.

Tucker, Laura
University of Minnesota Medical Center, Minn.

INTERVENTIONAL RADIOLOGY

Martinez Garcia, Ricardo
Emory University, Ga.

Tublin, Joshua
Beth Israel Deaconess Medical Center/
Harvard University, Mass.

NEUROLOGICAL SURGERY

Jaman, Emade
University of Miami/Jackson Health System, Fla.

Luy, Diego
Loyola University Medical Center, Ill.

Nturibi, Eric
UPMC/University of Pittsburgh, Pa.

NEUROLOGY

Lamade, Andrew
Cleveland Clinic Foundation, Ohio

Mitzner, Jackson
UPMC/University of Pittsburgh, Pa.

Moehl, Keelin
University of Utah Health, Utah

Olawaiye, Lydia
Boston University Medical Center, Mass.

Opeyemi, Sinmi
Brigham & Women's Hospital/
Harvard University, Mass.

Perkins, Jonathan
Hospital of the University of Pennsylvania, Pa.

OBSTETRICS AND GYNECOLOGY

Bunde, Sophia
Temple University Hospital, Pa.

Garland, Ayanna
University of North Carolina Hospitals, N.C.

Goldfeld, Ester
University of Virginia Health System, Va.

Levine, Melanie
Temple University Hospital, Pa.

McDonnell, Jill
Swedish Medical Center, Wash.

Moreno, Alexa
Mount Sinai Medical Center of Florida, Fla.

Pifer, Benjamin
Yale-New Haven Medical Center, Conn.

Rajprohat, Swati
Women and Infants Hospital of Rhode Island/
Brown University, R.I.

Tessmer, Matthew
UPMC Magee-Womens Hospital/
University of Pittsburgh, Pa.

Warshafsky, Meryl
UPMC Magee-Womens Hospital/
University of Pittsburgh, Pa.

OPHTHALMOLOGY

Beale, Oliver
UPMC/University of Pittsburgh, Pa.

Davis, Amani
UPMC/University of Pittsburgh, Pa.

Dmitriev, Aidan
UPMC/University of Pittsburgh, Pa.

Melachuri, Samyuktha
UPMC/University of Pittsburgh, Pa.

Ong, Joshua
University of Michigan Medical Center, Mich.

Williamson, Ryan
UPMC/University of Pittsburgh, Pa.



The Class of '22 celebrated residency matches—live and in person!—in March.

Yadav, Sanya
West Virginia University School of Medicine Hospital
Affiliates, W.Va.

Yan, Annie
Medical University of South Carolina, S.C.

ORTHOPAEDIC SURGERY

Ahrendt, Gillian
UPMC/University of Pittsburgh (Research), Pa.

Como, Christopher
UPMC/University of Pittsburgh (Research), Pa.

Drain, Nicholas
UPMC/University of Pittsburgh, Pa.

Ernst, Jennafrir
West Virginia University School of Medicine Hospital
Affiliates, W.Va.

Evashwick-Rogler, Thomas
Icahn School of Medicine Affiliated Hospitals, N.Y.

Onyeukwu, Chukwudi
UPMC/University of Pittsburgh, Pa.

Schulz, William
Mayo Clinic, Minn.

Talentino, Spencer
Ohio State University Hospital, Ohio

OTOLARYNGOLOGY

Kacin, Alexa
Beth Israel Deaconess Medical Center/
Harvard University, Mass.

Konanur, Anisha
University of Washington Medical Center, Wash.

Olonisakin, Tolani
Johns Hopkins Hospital, Md.

Sim, Edward
Massachusetts Eye and Ear Infirmary/Harvard
University (Research), Mass.

Smith, Brandon
UPMC/University of Pittsburgh, Pa.

Tarfa, Rahilla
University of Washington Medical Center (Research),
Wash.

PEDIATRICS

Burton, Danielle
Children's Hospital Los Angeles, Calif.

Ehrenberg, Sarah
Johns Hopkins Hospital, Md.

Gregory, Jessica
Boston Children's Hospital/Boston Combined
Residency Program, Mass.

Khetarpal, Susheel
NewYork-Presbyterian Hospital/
Columbia University, N.Y.

Li, Yu
UPMC Children's Hospital of Pittsburgh/
University of Pittsburgh, Pa.

Lim, Chae Hee
Massachusetts General Hospital/
Harvard University, Mass.

Miller, Tyler
Primary Children's Medical Center/
University of Utah, Utah

Newton, James
University of North Carolina Hospitals, N.C.

Prochownik, Katherine
Yale-New Haven Children's Hospital, Conn.

Tumuluru, Priya
Ann & Robert H. Lurie Children's Hospital of Chicago/
Northwestern University, Ill.

Westbrook, Kevin
Walter Reed National Military Medical Center, Md.

Wolfe, Rachel
Duke University Medical Center (Research), N.C.

PLASTIC SURGERY (INTEGRATED)

Roy, Eva
Brigham & Women's Hospital/
Harvard University, Mass.

PSYCHIATRY

Adebiyi, Ololade
Langley Porter Psychiatric Hospitals and Clinics/
University of California San Francisco, Calif.

Bertolini, Dominique
Emory University School of Medicine Hospital
Affiliates, Ga.

Gorraiz, Gregory
LAC + USC Medical Center/
University of Southern California, Calif.

Grimes Webster, Tinsley
University Hospitals Cleveland Medical Center/Case
Western Reserve University, Ohio

Hensler, Christopher
University of Illinois Medical Center at Chicago, Ill.

Hilal, Jad
Brigham and Women's Hospital (Child)/
Harvard University, Mass.

Kopelman, Jared
University of California San Diego Medical Center
(Research), Calif.

Meltzer, Amelie
Langley Porter Psychiatric Hospitals and Clinics/
University of California San Francisco, Calif.

Rosen, Miriam
UPMC/UPMC Western Psychiatric Hospital, Pa.

RADIOLOGY—DIAGNOSTIC

Eichar, Bradley
Mallinckrodt Institute of Radiology/
Washington University in St. Louis, Mo.

Hampton, Erica
University of Colorado Anschutz Medical Campus,
Colo.

Kowalski, Aneta
UPMC/University of Pittsburgh, Pa.

Ly, Maria
Mallinckrodt Institute of Radiology/
Washington University in St. Louis, Mo.

Murphy, Hannah
Creighton University School of Medicine, Ariz.

Oommen, Kevin
University of Washington Medical Center, Wash.

Yu, Gary
Mallinckrodt Institute of Radiology/
Washington University in St. Louis, Mo.

Zhang, Alexander
Sidney Kimmel Medical College at Thomas Jefferson
University, Pa.

SURGERY—GENERAL

Adams, Eric
UPMC/University of Pittsburgh, Pa.

Campwala, Insiyah
UPMC/University of Pittsburgh, Pa.

Fongod, Edna
UPMC/University of Pittsburgh, Pa.

Hier, Zachary
University of Louisville School of Medicine, Ky.

James, Nia
University of Tennessee Health Science Center, Tenn.

Larkin, Timothy
LAC+USC Medical Center/University of Southern
California, Calif.

Plautz, William
University of Virginia Medical Center, Va.

Sivagnalingam, Umayal
UPMC/University of Pittsburgh, Pa.

Sundaram, Niteesh
Crozer-Chester Medical Center, Pa.

Williams, Abraham
University of Minnesota Medical Center, Minn.

Zhang, Michelle
NewYork-Presbyterian Hospital/
Columbia University, N.Y.

THORACIC SURGERY

Christie, Ian
UPMC/University of Pittsburgh, Pa.

Haskett, Darren
University of Maryland Medical Center, Md.

UROLOGY

Anyaechie, Ifunanya
Emory University Hospital Affiliates, Ga.

Bowers, Levi
Vanderbilt University Medical Center, Tenn.

Hacker, Emily
Mission Bay Medical Center/University of California
San Francisco, Calif.

Islam, Raeesa
Rutgers Robert Wood Johnson University Hospital, N.J.

Mihalo, Jennifer
West Virginia University School of Medicine Hospital
Affiliates, W.Va.

VASCULAR SURGERY

Mosher, Emily
UPMC/University of Pittsburgh, Pa.

Reinert, Nathan
Cleveland Clinic Foundation, Ohio



CLASS NOTES

'70s

In a career that has spanned more than four decades, **Joseph Briggman** (Human Anatomy and Cell Biology PhD '78) has invented multiple patent-protected methods for the detection and treatment of cancer, especially carcinomas, urinary, bladder and prostate cancer. In his years of human anatomy and cell biology research, he's made numerous contributions to the discovery of novel cancer biomarkers. Among his honors, he was the Boehringer Ingelheim Visiting Professor at the University of Heidelberg and four other German universities in the 1990s. Today, he is a biotechnology commercialization consultant in the Boston area.

'80s

With clinical and research interests that focus on hand conditions (arthritis, tendinitis, nerve compression, tumors), hand injuries, congenital hand anomalies and complex hand and extremity reconstruction, **Gene Deune** (MD '89) says he finds particular enjoyment in working with children: "The reconstruction you do of their fingers/hands will change the quality of their life by making their hands more functional," he told a reporter at the University of North Carolina, where he was on the faculty before becoming a professor of surgery at Boston University. Deune is on the editorial board for the Journal of

Orthoplastic Surgery, which serves the needs of surgeons from around the world whose primary focus is on limb salvage and reconstruction.

'90s

Yolonda Colson (Immunology PhD '89, Surgery Resident '98) is already recognized for an outstanding body of research, having been the recipient of numerous grants from the National



Colson

Institutes of Health (NIH), notably the National Cancer Institute. And now Colson—chief of thoracic surgery at Massachusetts General Hospital and professor of surgery at Harvard Medical School—will become the first woman to be president of the American Association for Thoracic Surgery, an international organization whose members are renowned for their contributions to the care and treatment of cardiothoracic disease.

'00s

About 37 million U.S. adults have chronic kidney disease (CKD) and many of them spend

hours a week in medical settings, whether receiving dialysis, attending check-ups or recovering from surgery. Improving their quality of life is the focal point of the research by **Khaled Abdel-Kader** (Internal Medicine Resident '05, Nephrology Fellow '08, MS '09). Abdel-Kader, an assistant professor of medicine at Vanderbilt University, is one of two principal investigators leading the NIH-funded Kidney Coordinated Health Management Partnership study, which examines whether an electronic health record-based population health management approach can improve care for CKD patients—especially in primary care settings.

The career of **J. Nadine Gracia** (MD '02, Pediatrics Resident '05) has spanned the White House to the C-suite. She served in the Obama Administration as a White House fellow, the deputy assistant secretary for minority health and director of the Office of Minority Health at the U.S. Department of Health and Human Services—where she provided leadership on the Affordable Care Act and advised First Lady Michelle Obama's Let's Move initiative. Today, she is president and CEO of Trust for America's Health, a nonpartisan public health policy, research and advocacy organization. In her leadership role, Gracia works to advance policies that promote optimal health and advance health equity.



Gracia

"Believing in and advocating for my residents" is what **Julie B. McCausland** (Outcomes Research Fellow '03) says

is the heart of her educational career. With that approach, it's no surprise that McCausland—Pitt associate professor of emergency medicine and program director of the Transitional Year Residency—received the 2021 Parker J. Palmer Courage to Teach Award from the Accreditation Council for Graduate Medical Education, which oversees the accreditation of residency and fellowship programs in the United States. "It has been my personal mission," says McCausland, "to offer a supportive first year where residents can become the best physician and person they can be."

Having specialized in bleeding disorders since 2005, **Adam Giermasz** (Internal Medicine Resident '08) stresses the importance of patients receiving routine care, following treatment plans, maintaining



McCausland

a healthy lifestyle and learning how to lower the risk of complications. Giermasz codirects the Hemophilia Treatment Center at the University of California Davis. Among his career honors is a Top 10 Clinical Research Achievement Award for his coauthored “Hemophilia B Gene Therapy,” published in 2019 in the New England Journal of Medicine.

'10s **Cyrus Raji** (MD, PhD '10), an assistant professor of radiology at Washington University in St. Louis, has long been interested

in brain health. COVID-19 gave his work another level of complexity. He recently coauthored a study exploring how anosmia, stroke, paralysis, cranial nerve deficits, encephalopathy, delirium, meningitis and seizures are some of the neurological complications in COVID-19 patients. He proposes a “NeuroCovid” classification scheme for the virus’s short- and long-term neurological consequences. In 2021, he received an NIH grant to further his studies of brain health. For his earlier work, he was recognized with the 2016 Radiological Society of North America’s Roentgen Research Award and a 2017 American Society of Neuroradiology Boerger award.

Pitt Med first spoke with

Jean-Claude Rwigema

(MD '11) when he was a first-year medical student and somewhat new to America; he and his family were survivors of the Rwandan genocide. Eleven years later, Rwigema is on the vanguard of cancer treatment research—specifically focusing on proton therapies and their applications for treating head, neck and genitourinary cancers—as a consultant and associate professor of radiation oncology at Mayo Clinic Arizona. In 2007, he said he had a “responsibility to serve.” That commitment appears to be steadfast as he pursues this vital line of research.

—Emily Liu and Rachel Mennies



On Life and Practice: Lisa Maddox

When Lisa Maddox trained at the MedStar National Rehabilitation Hospital in Washington, D.C., they had a motto, “adding life to years,” she says. This is what her medical specialty—physical medicine and rehabilitation (or PM&R)—is all about. It’s not the injury, but how you live after it. “We make people’s quality of life better,” she says.

In 2006, Maddox (MD '95) came to know PM&R from the patient’s perspective, as well, when her leg was amputated after a years-long struggle with a condition known as complex regional pain syndrome.

“When your patients realize that you have something going on, too, it’s encouraging for them to see that their life isn’t gonna end,” she says.

Maddox herself is a lifelong athlete. She fell in love with wheelchair tennis—a few years ago, she was ranked first in a United States Tennis Association wheelchair tennis division.

Sometimes the way she talks about tennis sounds like instructions for living wisely: “We can’t move laterally in the chair.

“There are just some balls you’re not gonna get to. But that’s the same way in able-bodied tennis. And so you just practice; you practice, you play. Just like anybody else.”

Before med school, she attended the United States Military Academy West Point as part of the school’s ninth-ever class of women.

Maddox, former director of Augusta Polytrauma Network at the Charlie Norwood VA Medical Center in her hometown of Augusta, Georgia, retired in 2019. As COVID restrictions have been lifting, she’s been thrilled to get back out there.

“I’m actually doing a lot of wheelchair curling now.” —Elaine Vitone

WE KNEW YOU WHEN

William Marchl: The Doctor of Feelings

“It’s good to say the things we mean. Of all we’ve seen and heard and felt for and wished and knelt for.... It’s good to talk, don’t you think?” asks X the Owl, in episode 15 of the beloved children’s show *Mister Rogers’ Neighborhood*.

“Sure,” answers **William Marchl** (MD ’64, Res ’67), smiling from under his dark-rimmed glasses in the 1968 *Neighborhood of Make-Believe*.



Marchl

His answer wasn’t meant to be make believe, though. For Marchl—who provided lessons on physical and emotional health to a vast cast of puppet-characters during his appearances as the Doctor of Feelings in *Mister Rogers’ Neighborhood*—the role allowed him to reach real children worldwide.

Marchl died in 2020 at the age of 82; he spent much of his career practicing psychiatry in Pittsburgh. But his practice transcended the city and time. On the show, he helps characters with complexities like dealing with

embarrassment, developing friendships and trying to understand dreams. His cameos are earnest, skillful and profoundly kind.

“My husband was the most gentle person you could have ever spoken with,” recalls Mary Anne Marchl, who met her husband at Pitt-Johnstown, where they were both undergraduates.

For his U.S. Public Health Service assignment, Marchl was a staff psychiatrist for the U.S. Federal Bureau of Prisons in Denver, where he worked with adolescents. He later served as director of Head Start Child Development Center, director of the preadolescent inpatient unit at St. Francis Hospital, medical director of Craig House-Technoma, and as a consultant at the Speech Clinic at UPMC Children’s Hospital of Pittsburgh as well as at the Western Pennsylvania School for the Blind and the Western Pennsylvania School for the Deaf. He maintained a private practice in Shadyside. —Rachel Mennies



COURTESY FRED ROGERS PRODUCTIONS

OBITUARY

JACK PARADISE

SEPT. 1, 1925—DEC. 20, 2021

The intern watches intently as the attending pediatrician prepares to perform an earwax removal procedure. The physician, Jack Paradise, instructs the child’s parent to have the youngster lie down. Then the doctor pulls out a custom otoscope head—which he invented and named, appropriately enough, the Paradise. The device combines a magnifying glass and a small loop for wax removal.



Paradise

John Williams, the intern, marvels at the ease of the ensuing procedure: “He made it look effortless and with minimal discomfort for the child. I thought to myself, ‘That’s the gold. That’s my standard.’”

Throughout Williams’ internship at UPMC Children’s Hospital of Pittsburgh (1994-1995), he says he learned much by observing Paradise, a Pitt professor of pediatrics and of otolaryngology.

“He was a model of patience and just a marvelous clinical teacher,” recalls Williams, who today is professor of pediatrics and of microbiology and molecular genetics at Pitt and director, Institute for Infection, Inflammation, and Immunity in Children. “He taught me how to do ear examinations and remove ear wax,” which, says Williams, “sounds simple but is actually difficult to do without tormenting the child.”

Patient care and teaching were just two aspects of an internationally renowned career in pediatrics for Paradise, who—at 96—died peacefully in his home last December.

When he joined Pitt’s faculty in 1970 and became director of the Children’s Hospital outpatient department, he began

decades-long studies—first examining a question he encountered during his practice: Did severe throat infections lead to future illness and necessitate tonsillectomies or adenoidectomies? Paradise’s results, finding no need for such widespread operations, led to a nearly 80 percent reduction in pediatric tonsillectomies nationally.

Paradise then undertook another study—whether tympanostomy-tube placement was necessary in children with persistent ear infections involving fluid accumulation. Those ear tubes had been used with the intention of preventing impairments in speech, cognitive and psychosocial development. But Paradise found no significant differences between ear-tube recipients and nonrecipients, prompting pediatric associations to recommend alternative interventions.

After his 2006 retirement, Paradise remained active in three studies: use of antibiotics in children with acute ear infections, length of therapy for that condition and use of tympanostomy tubes when that condition recurred. All were published in the *New England Journal of Medicine*, most recently in May 2021.

“A lot of our current trainees are benefiting from his impact,” notes Williams. “He is a big part of our history here in Pittsburgh and in pediatrics.”

—Marty Levine

Adapted from the University Times,
© December 2021.

IN

'50s

GEORGE GILMORE, MD '52
FEB. 4, 2022

THOMAS GUSTIN, MD '59
JAN. 13, 2022

ROBERT HORSCH, MD '59
APRIL 19, 2022

MARTIN JONES, MD '55
DEC. 17, 2021

GEORGE MCCOLLUM, MD '57
FEB. 19, 2022

DONALD MEISTER, MD '54
APRIL 13, 2022

DAVID SCHAUB, MD '53
APRIL 10, 2022

HAROLD THOMAS JR., MD '54
MARCH 9, 2022

THE FORCE IS WITH HER MELINA KIBBE

BY MICHAEL AUBELE

Katharine McGinigle watches the auction's emcee waive a lighted wand around as he addresses the crowd, and her 5-year-old comes to mind. "Wow, if my son could have a lightsaber like that one—" McGinigle whispers to her friend. "It's just like Luke Skywalker's!"

The two women, both surgery professors at the University of North Carolina, chuckle at the thought. Then, as the gala benefit nears its end, McGinigle's friend bids on an item and says, "I'll double it if I can have that lightsaber for her son."

It was a few years ago that Melina Kibbe (Res '02) paid for that lightsaber. The proceeds for the 2019 gala helped fund a scholarship for students pursuing vascular surgery. And the lightsaber knighted a young Jedi.

In fall 2021, Kibbe left UNC, where she was surgery department chair, to become the 17th dean of the University of Virginia School

of Medicine. She is also chief health affairs officer for UVA Health.

The auction bid wasn't out of character for Kibbe, says McGinigle, who points out that Kibbe's interest in supporting others as they pursue their dreams sets her apart from the pack.

"She fundamentally cares for and finds pride in the successes of the people she leads."

Kibbe looks back fondly at her time in Pittsburgh, where she spent eight years (1994-2002) completing her residency and research fellowship and where she trained with the likes of Edith Tzeng, UPMC Professor of

Surgery, and Timothy Billiar, chair and the George Vance Foster Professor. Even as dean at UVA, she still maintains a clinical practice and NIH-funded research portfolio for developing novel therapies for patients with vascular disease (including nitric oxide therapies). She holds 13 patents or provisional patents. In 2009, President Obama recognized her with the Presidential Early Career Award for Scientists and Engineers. She's past president of the Association for Academic Surgery and the Association of VA Surgeons and is editor-in-chief of the journal JAMA

Surgery.

Kibbe's captaining tendencies surfaced early on. She recalls organizing dodge ball and Marco Polo games as a kid. "I was always leading groups of people," she says with a laugh. Later as a young professional at Pitt and UPMC, she took it upon herself to organize resident rotation schedules and work with trainees and faculty to make sure everyone's needs were addressed.

Becoming a med school dean became a career aspiration for Kibbe. What better way to help young people as they strive to become the best doctors they can be?

Allan Tsung (Res '08) got to know Kibbe during their residencies here. In June, he joined her at UVA—leaving Ohio State's College of Medicine, where he was chief of the surgical oncology division—to become UVA's chair of surgery.

Tsung says he welcomed the opportunity to associate professionally with Kibbe again, in part because of her extraordinary capacities as a surgeon-scientist. Generally, he says, surgeon-scientists excel more in either research or clinical practice, but Kibbe "straddles both realms well." And she leads by example, he notes.

When Kibbe became UNC's surgery chair in 2016, she recognized that her stature had national ramifications: Only about 6 percent of chairs of surgery at U.S. medical schools are women. About 18 percent of med school deans are women.

She hopes the route she's taken will make leadership paths in medicine seem less daunting to women:

"You can't be what you can't see." ■

COURTESY UNIVERSITY OF VIRGINIA



Kibbe is dean at the University of Virginia and editor in chief of JAMA Surgery.

MEMORIAM

ROBERT URBAN, MD '56
JAN. 23, 2022

JOHN WARD, MD '57
FEB. 17, 2022

A. LEONARD ZIMMERMAN, MD '58
JAN. 13, 2022

'60s
RONALD AMALONG, MD '61
FEB. 20, 2022

BARRY BERKEY, MD '61
APRIL 12, 2022

JAMES GARRETTSON, MD '65
DEC. 18, 2021

JAMES HOUSTON, MD '62
MARCH 4, 2022

DAVID KRAUS, MD '65
APRIL 7, 2022

STANLEY RABINOWITZ, MD '66
JAN. 1, 2022

JANET TITUS, MD '67
DEC. 9, 2021

'70s
MICHAEL MALLINGER, MD '74
APRIL 23, 2022

LAWRENCE NELSON, MD '70
APRIL 15, 2022

'90s
ERIN SABO, MD '90
FEB. 12, 2022

'10s
ALICIA SAUNDERS, MD '10
DEC. 13, 2021



FOR REAL! TWEEN SCIENCE



"Hangry" happens. But why?

Babies cry for the breast or bottle. Toddlers have meltdowns that can only be quieted with food. Growth-spurting teens ravage the pantry daily after school; standing in their way is not advised. We are all born to be "hangry" (hungry plus angry). So, what's actually happening inside our bodies when that irritability comes on and snowballs so quickly? What's the cause and effect? Why do some people get hangrier than others? Is there a quick fix?

First things first: Hangry is a real thing, biologically speaking.

Our bodies need fuel in the form of food to keep running. When we go too long without eating, our blood sugar drops and the stomach and intestines send signals to the brain, saying, "Feed me." That's the feeling of hunger. The main messenger here is a hormone called ghrelin—sounds like growlin', as in, the sound your stomach makes. (The scientific term for that growl is borborygmi.)

Ghrelin gets released when your stomach is empty and shuts off when your stomach is full. For most people, the timing clicks along with sleep-wake cycles and eating routines.

In addition, stress or intense emotions can actually lead to more ghrelin production and hunger. Stress-eating is a cousin of hangriness.

So, in other words: Sometimes an empty stomach can make you feel distressed. And sometimes distress can make you feel hungry.

In response to ghrelin, the brain releases other hormones that help drive the desire to go find something to eat. (Not all stress is bad!) But of course, each of us has a different emotional relationship to food. And what's happening around us can also influence behavior, sometimes complicating the calculus of when, why and what we eat.

A quick fix? A quick snack. Even better: Get off the mood-altering cycle by eating well and regularly. —Micaela Fox Corn

Thanks to David Levinthal, a Pitt Med brain-body-tummy expert (neurogastroenterologist), for helping us make hangry more palatable, at least for this article.

CALENDAR

FOR ALUMNI & FRIENDS

For information:
Alex Rigby at hsalumni@pitt.edu

WHITE COAT CEREMONY

AUG 7

Carnegie Music Hall

HEALTH SCIENCES

ALUMNI WEEKEND

SEPT 16-18

PITT HOMECOMING

OCT 8

PITT HEALTH ACADEMY, ERIE

OCT 11

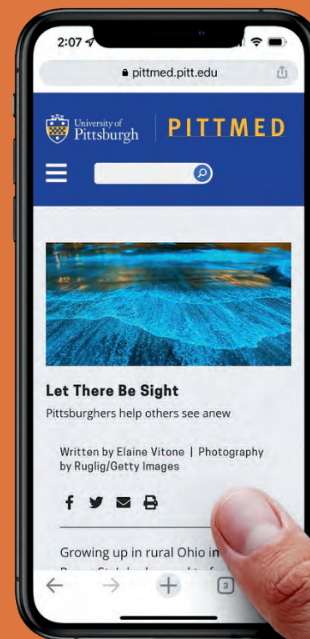
VIRTUAL PITT HEALTH ACADEMY

OCT 18

WINTER ACADEMY

FEB 17, 2023

Naples, Fla.



TAKE IT TO GO

Not too long ago, QR codes were kinda, well, square. But our takeout lifestyle of late gave them a new lease on life.

Say, have you thumbed through our menu on Pitt Med's new website? (Talk about a cool retool!)

Scan the code below. If it pleases your palate, tell your friends! Our fabulous feast of features is more phone friendly.

www.pittmed.pitt.edu



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@pitt_med_magazine



A new annual bike race in Pittsburgh, Rush to Crush Cancer, will raise money for cancer research at Hillman.

Personal. Powerful.

Brian Shanahan is dealing with pancreatic cancer and not naïve to long odds. He also knows the biblical reference to the cheerful giver, which he wholeheartedly embraces. With gratitude for his ongoing treatment at UPMC Hillman Cancer Center, the fintech entrepreneur and real estate developer and his wife, Karen, donated \$3 million to the center that will fund research now and into the future. "Giving is living," says Shanahan, who frames his generosity around his Christian faith.

Diagnosed in August 2020, Shanahan was immediately confronted with a disheartening statistic—pancreatic cancer is terminal in 93% of patients.

"Brian had a pretty advanced cancer—a tumor that was wrapped around critical blood vessels and was large," says Amer Zureikat, professor of surgery and chief of surgical oncology at Pitt Med, as well as director of surgical oncology at Hillman. "But because he had a specific genetic mutation, we were able to tailor specific chemotherapy to the mutation and shrink the tumor to be operable."

Zureikat will lead the Hillman arm of a trial the Shanahan gift will support. The study will investigate the use of a biomarker to identify the most effective chemotherapy for patients during the preoperative period. It will also investigate how a patient's tumor genetics influence survival. That research will employ whole genomic sequencing, transcriptomics, radiomics and microbiomics.

The Shanahans' other \$1.5 million donation to Hillman will serve as seed money for an annual Rush to Crush Cancer bike race, the first of which will be held in spring 2023; it will be managed by the same organization that runs the Pittsburgh marathon. "Brian is so generous of his time and as a supporter," says Zureikat.

Shanahan says the clinicians who treated him when he was most vulnerable, and who continue to treat him, have become like family.

He's struggled through a few setbacks and remains on medication. To manage the fears he faces, he tells himself that like everyone else, he's only got a lease on life: "I think what most people don't always realize is that life truly is a gift, not a right."



The Shanahans

COURTESY SHANAHAN

To make a gift to the medical school: [Giveto.pitt.edu/shanahan](https://giveto.pitt.edu/shanahan)
To learn about the race: rushtocrushcancer.org