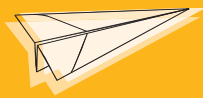


PITTMED



WHAT DOES THE PATIENT
REALLY NEED?



INSPIRATIONAL ENERGY

I was thrilled to see the article [“Hidden in plain sight” by Maureen Passmore] about the work being done in Western Pennsylvania on genetic diseases in Amish and Mennonite communities, greatly expanded by Lina Ghaloul Gonzalez and Cate Walsh Vockley. I’m grateful that I had the opportunity to take care of the MELAS [mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes] patient referred to as “Sarah” in the article, as well

as other Amish and Mennonite patients with the genetics team at UPMC Children’s Hospital of Pittsburgh. Going to their community in Grove City to provide education, counseling and clinical testing was one of the highlights of my career and inspired me to move to Philadelphia to work further on treatments and cures for mitochondrial disorders at Children’s Hospital of Philadelphia.

Amy Goldstein (MD ’96, Res ’99)
Children’s Hospital of Philadelphia

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“Making the complicated simple—awesomely simple—that’s creativity.”

— excerpted from *Charles Mingus*

AIMEE OBIDZINSKI/UNIVERSITY OF PITTSBURGH



Dear Pitt Med Reader,

It’s easy to get caught up in the scientific promise of the latest biomedical technology. And for good reason: Applications of genomics, CRISPR, deep learning and the like will be saving lives as they come of age. This is truly an exciting time in medicine.

However, for patients facing a majority of common medical conditions, the barriers to better outcomes may often be paradoxically simple. Maybe what’s needed is regular transportation to the clinic or help from a trusted caregiver to navigate health care or social needs. In most clinical encounters, we tend to overlook such interventions. Our health care model incentivizes hospital-based care, advanced diagnostic testing and high-tech solutions. It is less likely to reimburse activities of providers who carefully explore what would be most helpful to improve outcomes for an individual patient.

How do we change our current system and create a new type of health care? One that honors significant, yet often simple, needs of patients? Part of the answer may be found in successful population health models that have focused on basic principles of individualized patient care in countries with limited access to technologies or sophisticated tertiary hospitals. In other words, we can learn a great deal from what works in resource-limited countries—such approaches save thousands of lives every day.

Let me share some examples: In western Kenya, for instance, a community worker–driven program called AMPATH has provided testing and counseling to more than 1 million patients with HIV/AIDS and helped save the lives of thousands of children with HIV by increasing access to and compliance with treatments. In Harare, Zimbabwe, a person in distress can sit on a “friendship bench” to get counseling and access to other resources.

Here in the United States, a similar innovative program prepared trusted women from local communities to work on reducing infant mortality in inner-city Indianapolis. As is the case in many inner-city neighborhoods in this country, infant mortality rates in these areas were shockingly high. The community workers gained trust, provided education, coordinated basic prenatal services and were the implementation arm as obstetricians and medical leaders ran the project. By taking most of the care to the pregnant person’s neighborhood or home, disruptions to work schedules, family obligations or school attendance (yes, unfortunately many of the pregnant subjects were young girls) were minimized while care and compliance were improved. These services, combined with a negotiated extension of state Medicaid support for new mothers, improved infant and maternal health significantly in these neighborhoods within two years of instituting the program. The approach saved many infants while saving money—complex childbirth, which was previously the norm in these areas, comes at a high price in terms of dollars and lives.

What is best for patients is not necessarily a medically sophisticated approach with bells and whistles. “High touch for most and high tech for some” is often what’s needed—as demonstrated in our cover story in this issue. I encourage you to read that feature to learn about a breast cancer doula program led by our colleague in nursing, Margaret Rosenzweig, as well as another thoughtful initiative, in perioperative care, that helps patients coming in for surgeries get the best care.

Creative innovations needed to change our poor health outcomes can be elegantly simple.

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

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His legs were thin as wires having / outrun lions pinned in the end / by tumors

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How about a good scare?

ABOUT THE COVER We can help stop patients from slipping through the cracks. High-touch and high-tech approaches in cancer and perioperative care are yielding rewards. Illustration: Carolina Moscoso © 2022.

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“Machine learning is very good at predicting features” of biological processes but “not able to interpret those features. For that, we still need human intelligence.”

FEATURES

A summer to understand lifetimes

What’s life really like for people our students will treat and devote research careers to?

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First Model Ts, now CAR Ts—a former Ford factory is a hub for the next generation of cancer treatments.

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What does the patient really need?

Sometimes a patient just needs a ride to the clinic, or help getting through the day, not an expensive test. Multipronged approaches to care help people from slipping through the cracks.

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CAROLINA MOSCOSO’s [Cover story illustration] career story began in Portugal, where she earned a degree in architecture from the University of Lisbon. After moving to New York City in 2010 for an illustration residency at the School of Visual Arts, Moscoso shifted her focus from designing domestic spaces to using them as her muse. Today, her illustrations focus on the aftermath of those interiors, once they’ve been lived in and untied. “I like noticing the meaningless and mundane moments that are full of poetry,” she notes. The Brooklyn-based architect and illustrator has worked for Adidas, Nike, Bloomberg and many other notable clients.

MARK ROTH [“The Assembly”] was an editor and reporter at the Pittsburgh Post-Gazette for more than 30 years. He spent the decade before his 2015 retirement covering scientific innovation. Until recently, the longtime East End resident had no idea that the eight-story building at Baum Boulevard and Morewood Avenue was connecting Pittsburgh’s industrial past to its research and technology-driven future. His first feature for Pitt Med gave him a chance to talk to innovators powering that shift. “They’re not afraid to fail and often learn as much from their misses as from their successes,” he says.

OF NOTE

*Devoted to noteworthy happenings
at the medical school*



**MaCalus Hogan at the unveiling
of the bronze bust of his mentor
and colleague, Freddie Fu.**



Hogan chairs orthopaedic surgery

It was Freddie Fu who recruited MaCalus V. Hogan to Pitt Med in 2013, recognizing his talents in surgery and research. Hogan now will continue the standard of excellence that Fu helped create here in orthopaedic care.

Appointed in September as the David Silver Professor and chair of the Department of Orthopaedic Surgery at Pitt and chair of orthopaedic surgery at UPMC, Hogan will build on the department's tradition of groundbreaking research as well as its identity as a destination for clinical training that has produced leaders in orthopaedics at medical centers throughout the world.

"Dr. Hogan's commitment to building a diverse environment at Pitt/UPMC and growing the academic excellence in musculoskeletal research made him the ideal next chair," says Anantha Shekhar, an MD, PhD, senior vice chancellor for the health sciences and John and Gertrude Petersen Dean, School of Medicine.

Hogan told the Pittsburgh Post-Gazette that after injuring his ankle playing football in high school, a surgeon planted the seed that he should consider a career in orthopaedics. Hogan shadowed that surgeon and is now a prominent foot and ankle expert and consultant to a number of collegiate teams, as well as the Pittsburgh Ballet Theatre.

Hogan, an MD, MBA (BUS '19), most recently served as professor of orthopaedic surgery at Pitt, with secondary appointments in bioengineering, clinical and translational science, and business. He was also residency director and vice chair of education for orthopaedic surgery at UPMC, chief of its Division of Foot and Ankle Surgery and medical director of outcomes with the UPMC Wolff Center for quality, safety and innovation.

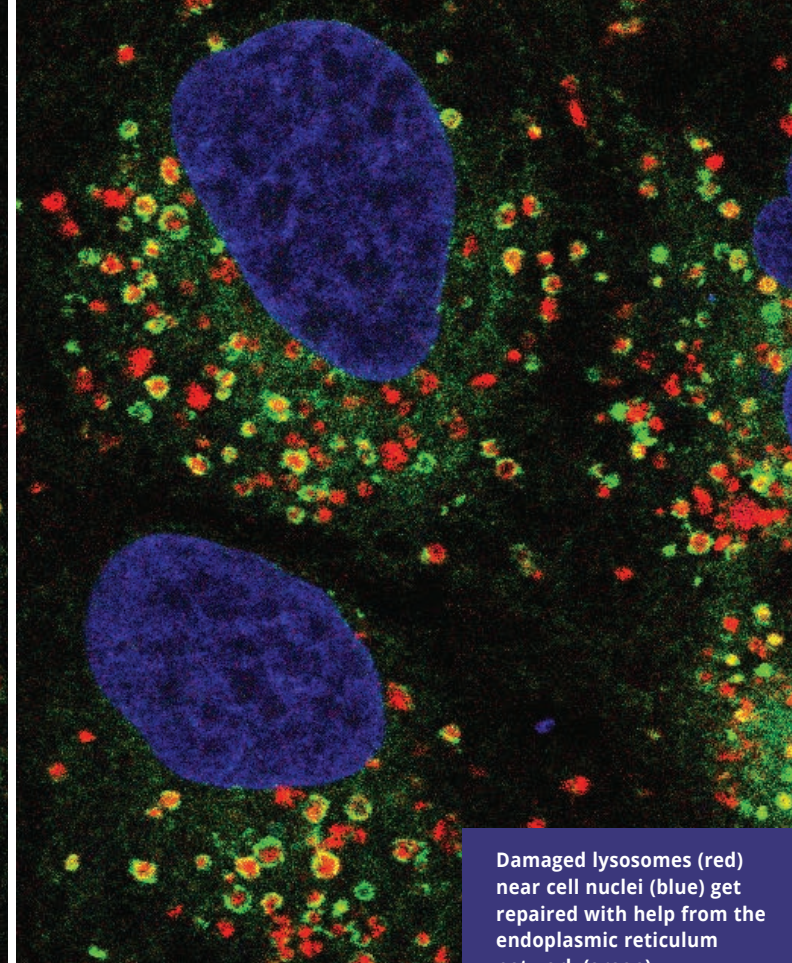
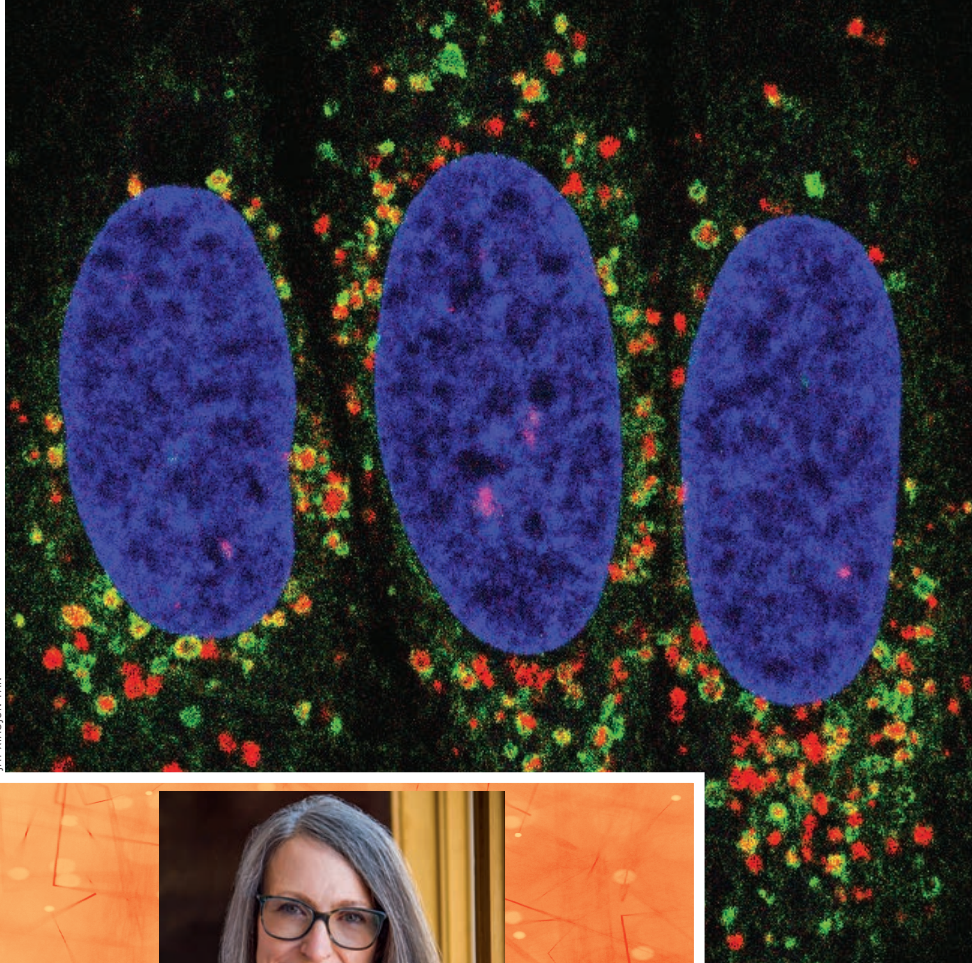
Hogan is the recipient of a number of awards, including the American Academy of Orthopaedic Surgeons' Influencers Award and two American Orthopaedic Foot & Ankle Society J. Leonard Goldner Awards for Best Basic Science Research. In 2018, he was selected as one of Modern Healthcare's Top 15 Up and Comers as an emerging national leader in health care. —Staff reports

FU IS STILL WITH US

A bronze bust of the late Freddie Fu (MD '77, Res '82) was unveiled at the UPMC Freddie Fu Sports Medicine Center on Sept. 30, honoring Pitt's long-time chair of orthopaedic surgery.

Parker B. Donaldson, son of past interim chair William Donaldson, sculpted the piece.

In addition, the University of Pittsburgh Library System recently announced it has acquired the Fu papers; the collection includes presentations and treatment overviews documenting advancements Fu made in orthopaedic surgery, particularly in anterior cruciate ligament reconstruction.



Damaged lysosomes (red) near cell nuclei (blue) get repaired with help from the endoplasmic reticulum network (green).

PITT fix

A how-to guide for patching cell leaks

A leaky lysosome can spell trouble inside a cell, but usually the repair process is quick and easy.

In healthy people, cells undergo needed maintenance without a hitch. But disease and aging can put this process in jeopardy.

Now, Pitt Med researchers have created a how-to guide for the fix, describing for the first time the pathway that cells take to mend the leaks. Published in the journal *Nature* in September, their findings could help scientists understand and treat age-related diseases like Alzheimer's.

Considered the cell's recycling system, lysosomes contain digestive enzymes that break down molecular waste. A membrane around the lysosome normally keeps those enzymes from damaging other parts of the cell, but leaks do sometimes appear.

To see how the repair process springs into action, Jay Xiaojun Tan, a PhD and the study's lead author, experimentally damaged lysosomes in lab-grown cells. He found that an enzyme quickly accumulated on the injured organelles and generated high levels of a signaling molecule that Tan compared to a "red flag."

"It tells the cell, 'Hey, we have a problem here,'" says Tan, assistant professor of cell biology and member of the Pitt/UPMC Aging Institute. "This alert system then recruits another group of proteins, called ORPs." The ORPs tether the lysosome to the cell's endoplasmic reticulum, which allows lipids and proteins to reach and patch the leaks. The researchers named the sequence of steps the "PITT pathway." (PITT, in this case, stands for phosphoinositide-initiated membrane tethering and lipid transport.)

When age or disease causes major damage or compromises the pathway, the leaks can mount and lead to further problems. Leaks of misfolded proteins (specifically, tau fibrils), for example, spur the progression of Alzheimer's disease.

Tan collaborated on the study with senior author Toren Finkel, an MD, PhD, director of the Aging Institute and Distinguished Professor of Medicine. In the future, the researchers plan to investigate whether manipulating this pathway can protect mice from developing Alzheimer's. —Staff reports

Kasper named nursing dean

Christine E. Kasper, a PhD and RN, who served the past four years as dean of the University of New Mexico's College of Nursing, has been named the new dean of Pitt's School of Nursing. On Jan. 1, 2023, Kasper will replace Jacqueline Dunbar-Jacob, a PhD and RN, dean and Distinguished Service Professor of Nursing.

Before joining UNM, Kasper served as a senior nurse executive in the U.S. Department of Veterans Affairs, Office of Nursing Services. In that post, she advised the chief nursing officer on academics, research and policy and was a professor in the Daniel K. Inouye Graduate School of Nursing at Uniformed Services University of the Health Sciences in Bethesda, Maryland.

Kasper is the editor of the *Annual Review of Nursing Research* and was the founding editor of *Biological Research for Nursing*. She was elected a fellow of the American Academy of Nurses in 1994, a fellow of the American College of Sports Medicine in 1995 and to the International Nurse Researcher Hall of Fame, Sigma Theta Tau International, in 2015.

She has more than 200 national and international peer-reviewed and invited publications, books and presentations to her credit. —Staff reports

New Pitt Med students visited city neighborhoods as part of orientation this summer. Shown here, impromptu line dancing at a Homewood health fair. The students also met representatives from the Hill District, East Liberty, Hazelwood and McKeesport to hear about health challenges, assets and resources in those communities.



PHOTO: COURTESY THUY BUI

Who's new in '22?

The medical school's incoming class is 227 people strong, including 153 medical students and 74 PhD students.

Of the med students matriculating this fall:

- **22** (or **14%**) are underrepresented in medicine, including 11 who identify as Black.

- **7** (or **4.5%**) are first-generation college students.

- Their average age is **24** (that's typical).

- **65%** are women and **34%** are men.

- **27%** of the class comes from Pennsylvania; the next most represented states are New Jersey and California (each at **9%**). Overall, they represent **80** undergraduate schools from **25** different states.

- **13** are Medical Scientist Training Program students, who will pursue both a PhD and an MD.

- **9** are Physician Scientist Training Program students.

Of the graduate students entering the School of Medicine this fall:

- **51%** identify as women, **45%** as men and **4%** as unreported/non-binary gender.

- **9%** are underrepresented minority students.

- The average age is **26**.

- They come from **43** U.S. schools, including **11** in Pennsylvania; as well as **14** schools in **9** other countries.

- **67%** are U.S. citizens.

- **16** are in programs jointly operated between Pitt's School of Medicine and Dietrich School of Arts & Sciences and with CMU.

FOOTNOTE

Did you know Pittsburgh once had a Chinatown? Occupational therapy student Lydia Ott caught a glimpse of what life was like for her family when they settled there in the 1930s; she shares their story in the documentary "Pittsburgh's Lost Chinatown." "It's really important as we train here, at the University of Pittsburgh, to see people who aren't being seen," Ott notes in the short film, which you can catch here: pi.tt/chinatown



"The findings are actually shocking and straightforward," says Behrmann, shown left. Granovetter is shown right.

Overheard The brains of kids are astonishingly plastic, it turns out.

Despite scientists' best efforts to inject nuance into the idea, there remains a certain dogged determination in the general public to describe people as "left-brained" or "right-brained," to squeeze personality and inclinations into discrete sections of the noggin. *Are you more analytical? You must be left-brain dominant, the thinking goes. Creative? That's coming from the right side.*

And, to some extent, scientists do tie function to brain hemispheres.

Adults who've suffered significant brain trauma—stroke or traumatic brain injury, for instance—can experience a profound loss of ability to recognize words or faces, depending on where the lesion happens.

New research out of Pitt and Carnegie Mellon, however, suggests that for children, each hemisphere is plastic and capable of mimicking the other when necessary.

The work will shed new light on how brains work and develop.

In an article published online in October in PNAS, **Marlene Behrmann**, PhD professor of ophthalmology who recently joined Pitt from CMU, and **Michael Granovetter**, a PhD and med student in Pitt's Medical Scientist Training Program, showed that younger patients with just one hemisphere were able to perform surprisingly well on tasks typically associated with the opposite hemisphere.

What's the context of your research?

Marlene Behrmann: We wondered, what can one brain hemisphere do? And does it matter if your one hemisphere is just the left hemisphere or just the right hemisphere?

The thinking was, that as the brain matured, and function was already assigned to particular regions, those functions became more consolidated. There was no brain area that was lying fallow, that could take over a new function. You couldn't recruit anything. Everything already had a job.

We do know now, and prior to the study, that the left hemisphere has some superiority in recognizing words, and the right hemisphere has some superiority in recognizing faces.

We examined children with only a single hemisphere, when the other hemisphere had been removed surgically because it was giving rise to very frequent epileptic seizures. [The mean age of children having the proce-

cedure was 5 and a half.] They all basically grew up with one hemisphere.

What were some of the key findings in your study?

MB: Here we've got kids that don't have just a small lesion, they've got a walloping lesion—the whole hemisphere is gone. If it were the case that the hemispheres were kind of preprogrammed, then you might expect that if the left hemisphere is missing, these kids would never learn to read words. And if the right hemisphere was missing, they'd never learn to recognize faces.

The findings are actually shocking and straightforward: It doesn't matter if the preserved hemisphere is the left one or the right one. When we test the face and word recognition abilities of these patients, they score at about 80% accuracy for both words and faces, in a single hemisphere, and it doesn't matter which hemisphere. This is the shocking part: If you've only got 50% of your brain, you still perform at roughly 80% accuracy.

What are some of the clinical implications?

Michael Granovetter: At the surface of it, you can imagine it being a very shocking and difficult conversation to tell the parents of a 2-year-old child that one of their options for treatment is to remove a large portion, if not the entire hemisphere, of their child's brain. There's a lot of questions that clearly come to mind.

We know that these surgeries very often are curative of children's seizures. You could be on medications for many, many years and continue to have seizures, whereas we know that surgery can in many cases—not all—alleviate patients of these seizures such that they can live a healthy, happy childhood. So the question is less about seizure-freedom when it comes to these procedures, but the question any parent would want to know, and that the medical team takes into very careful consideration, is cognitive outcomes, and quality-of-life outcomes.

This study doesn't answer those questions definitively, but it does attest to a certain amount of plasticity of the child brain to move us one step forward to provide clearer reassurance to families going through this very difficult decision in their child's life. —Evan Bowen-Gaddy



ANNE OBIDZINSKI/UNIVERSITY OF PITTSBURGH

Dickson winner nabs Nobel

“As a physicist, I marvel at how we managed to bend space and time to get three eminent scientists here on the same day,” said University of Pittsburgh Chancellor Patrick Gallagher on July 19 at the University Club during his welcoming remarks on Dickson Prize Day.

Less than three months later, one of those scientists would win the Nobel Prize in Chemistry.

Carolyn Bertozzi, the winner of this year’s Dickson Prize in Medicine, which is Pitt Med’s highest honor, learned in early October that she would share a Nobel Prize with Morten Meldal, professor at the University of Copenhagen, and K. Barry Sharpless, W.M. Keck Professor of Chemistry at Scripps Research, “for the development of click chemistry and bioorthogonal chemistry.”

Bertozzi is the 16th Dickson Prize winner to become a Nobelist.

Recognized for her foundational work in bioorthogonal chemistry, Bertozzi is the Anne T. and Robert M. Bass Professor at Stanford University. Her research on how sugar molecules on cell surfaces can be modified by chemical reactions within a living system led her to identify new approaches to treating cancer, inflammation and bacterial infections.

Two other esteemed biomedical researchers also came to campus in July to receive the Dickson Prize. The pandemic delayed presenting the honor to the 2020 and 2021 winners until this summer.

Cynthia Kenyon, the 2021 winner, vice president of aging research at Calico Life Sciences and an emeritus professor of biochemistry and biophysics at the University of California, San Francisco, overturned the longstanding notion that aging does not have a genetic basis but is simply a result of progressive decline.

The 2020 winner, **James Collins**, who is the Termeer Professor of Medical Engineering and Science at the Massachusetts Institute of Technology, has engineered artificial living systems for combatting rare metabolic and inflammatory diseases and cancer. His team has also built systems that can rapidly detect infectious threats—like masks incorporating COVID-19 diagnostics.

Several Pitt scientists also shared their work with the guests, giving talks on topics related to the keynotes, like synthetic biology for next-generation medical robotics by Warren Ruder, an associate professor of bioengineering, and weight loss and disease in aging by Aditi Gurkar, an assistant professor of medicine.

Gurkar posted on Twitter, “I got to spend the day with some amazing scientists, and I feel so inspired! This is why I love science.” —*Asher Jones and Anastasia Gorelova*

MEET THEM WHERE THEY ARE

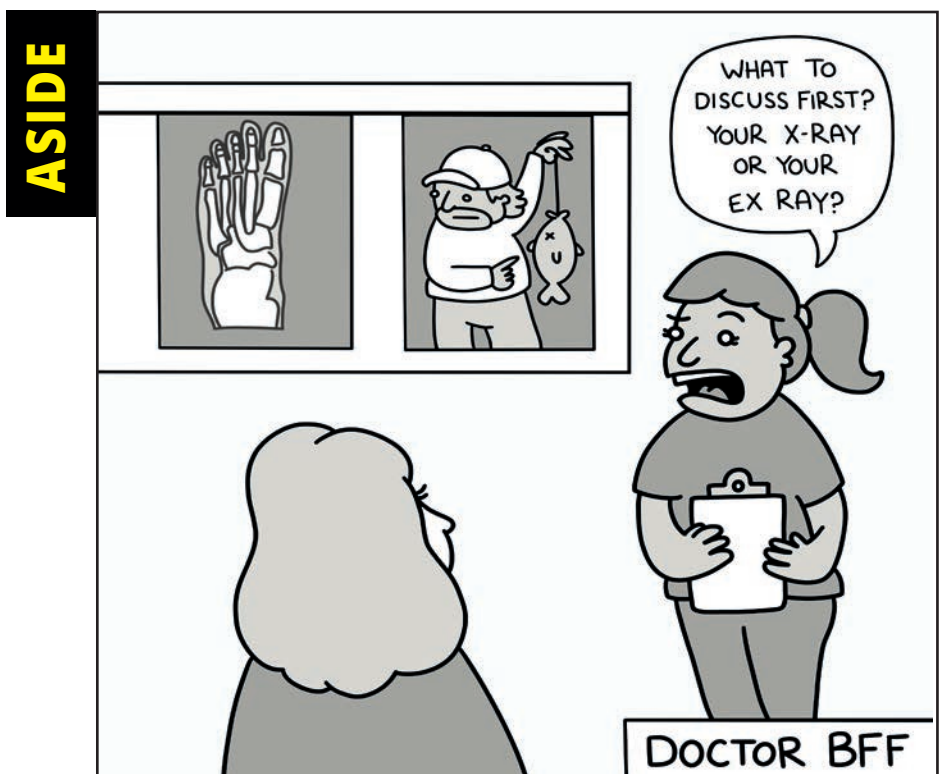
Altoona is a small city in central Pennsylvania—a company town founded by the Pennsylvania Railroad. In late May, residents and faculty from all eight UPMC family medicine residency programs across the state gathered at a conference center there for a scholarship day. Pitt family medicine chair Tracey Conti, an MD, gushed about the 33 research presentations she was taking in.

“If we just stay in the academic center, we’re missing so much,” Conti said. “Think about the cascade of care and the small percentage of patients that actually hit the academic center. If we only learn from patients from there, we’re really not doing the scholarship and providing good clinical advancements for the majority of the population. Working across the system and collaborating outside allows you so much more growth.”

John Maier, an MD, PhD assistant professor of family medicine and the department’s director of innovation and strategic initiatives, says discovering and implementing new solutions from family medicine in a timely manner will require greater investments in electronic health records, artificial intelligence and machine learning.

In response to a call from Dean Anantha Shekhar and in collaboration with Shyam Visweswaran from the Department of Biomedical Informatics, Maier introduced the entire Class of 2025 to these topics in the spring. The school’s longer-term goal: Require all students to learn about AI and machine learning in enough depth to responsibly use them to care for patients and carry out research.

Maier’s introduction for the class sent the message that AI and machine learning aren’t only the purview of the biomedical informatics or computational biology departments. —*Cara Masset*



by Tara Kaloz



PAGE FROM HADAMAR INSTITUTE'S DEATH REGISTER; WIKI COMMONS; PHOTOS OF GIRL AND MAN; GETTY IMAGES.

Normal Human Variation 2.0

A teenage boy on the autism spectrum who aged out of pediatric care was referred to the Progressive Evaluation and Referral Center (PERC) at UPMC Montefiore but kept missing appointments. When Kristen Ann Ehrenberger, the center's director, noticed the pattern, she called the young man's mother to find out why.

"When I got his mom on the phone, it turned out that she wasn't used to seeing him as needing attention for complex medical needs," Ehrenberger (Res '20) says. "She saw her son as a healthy teen who happened to have autism."

Ehrenberger, an MD, PhD assistant professor of medicine and pediatrics, believes the mother was also trying to shelter her son from stigma that people with physical and mental challenges face.

Having earned her PhD in the history of medicine with a focus on nutrition and public health, Ehrenberger looks closely at how people with disabilities have been stigmatized through time. For instance, when researching post-World War I nutrition in Germany, the historian discovered that some institutions, like mental asylums, were left out of the country's rationing program. The idea that it was OK to neglect the "impaired" was gaining momentum. Jurist Karl Binding and psychiatrist Alfred Hoche wrote arguments in favor of the "destruction of life unworthy of life"—meaning those who experienced mental or physical disabilities. (Eugenics had its proponents in the United States, as well.) Those ideas helped shape the century's tragic and monstrous history.

Ehrenberger's insight on such ideologies, and their modern remnants, informs how she practices medicine and works not only to advance care for those with complex medical needs but also to change the narrative thread.

"What's a common label for people who use wheelchairs?" she asks.

"People who are 'confined to a wheelchair.'" But she argues, "You're confined to a house. You use a wheelchair to move around."

She prefers thinking of disability in a more social way. Bodies are diverse, she says. Some people communicate with words, others use signs. Some people walk on two feet while others use wheelchairs.

Ehrenberger wants to broaden this message to eliminate stigmas people with mental and physical challenges face. She says it's not just a matter of semantics—such as simply replacing "retarded" or "crippled" with "disabled" or "handicapped." Using different adjectives doesn't go far enough; she wants to alter perceptions.

At PERC, center staff—including Reed Van Deusen (MS and Fel '08), associate professor of medicine, and clinic founder Alda Maria Gonzaga (MD '00, Res '04, MS '06), associate dean for student affairs and professor of medicine and pediatrics—are trained in both pediatrics and adult medicine. Founded by Gonzaga in 2008, the clinic accepts those with complex medical needs ranging from autism spectrum disorder to cerebral palsy to rare genetic disorders. PERC serves more than 300 patients. Most transition to the clinic between 18 and 26 years old.

Ehrenberger has learned that while labels are harmful in most instances, there are situations in which they are useful. She points out that autistic people tend to prefer diagnosis-first language to person-first language—that is, saying "an autistic person" rather than "a person with autism." They are likely to say that neurodiversity is an integral part of who they are, and that they cannot be understood without it. However, people with other disabilities often prefer person-first language.

To Ehrenberger's chagrin, "The disability medical model is that there's something wrong with the mind or body," she says. "[People with disabilities] exist on a spectrum of normal human variation, not as a group that's easy to separate from 'normal' or 'healthy' patients."

—Michael Aubele

—Photo illustration by Elena Cerri

INVESTIGATIONS

Explorations and revelations



Queen naked mole-rats seem ageless and can reproduce throughout their lifetimes.

SECRETS OF THE NAKED MOLE-RAT

STRANGE RODENTS MAY HOLD THE KEY TO
BETTER FERTILITY AND ANTI-AGING PROPERTIES
IN HUMANS. | BY JASON BITTEL

With wrinkly pink skin, beady black eyes and a hellish set of chompers, the naked mole-rat is not the kind of creature many people gravitate toward. But increasingly, researchers have been drawn to this subterranean animal as a potential model for reversing human infertility and avoiding the typical effects of aging.

Sounds far-fetched, right?

“It sounds really far,” says Miguel Brieño-Enriquez, an MD, PhD assistant professor of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh. “But it’s not that far.”

Here’s why. Although lab mice usually die after around 2 years of age, the naked mole-rat, which is native to East Africa, can live more than 30 years. That’s a long lifespan for a mammal that weighs less than a Snickers bar. What’s more, naked mole-rat queens never appear to go through menopause, successfully reproducing all the way up until their deaths.

And this has made scientists like Brieño-Enriquez wonder if there aren’t components of the naked mole-rat’s physiology that can be borrowed to create treatments for humans. After all, scientists developed life-saving insulin from dogs and then cattle, he says. And that’s just one example among many medicinal loans from elsewhere in the animal kingdom.

Doctors routinely prescribe: a drug derived from Gila monster saliva to diabetes patients, another drug that comes from cone snail venom for those suffering from chronic pain

and a heart-attack prevention drug from the venom of southern pygmy rattlesnakes. So there’s nothing particularly strange about looking to the naked mole-rat for a little inspiration.

To start chipping away at how the wrinkly critters continue to reproduce well into what should be their golden years, Brieño-Enriquez designed a series of experiments to test three hypotheses about how naked mole-rat ovaries work.

The first experiment investigated whether naked mole-rat females at birth simply have more germ cells, or eggs, as opposed to mice or people. They do. The second looked at whether the animals lose fewer egg cells as they age. They do. And the third sought to determine whether the naked mole-rats can create new germ cells after birth. They do.

(By the way, whether humans can create new germ cells after birth is a contentious topic in fertility, stem cell and aging research circles.)

At first blush, you might think the findings would be bad news for women experiencing problems with infertility. After all, the findings suggest that the naked mole-rat’s ovaries are just way too different from those of humans. But here’s the rub.

Naked mole-rat colonies are eusocial, which means they are led by a single queen who does all the breeding. All the other females in the colony are subordinate, and, by some mechanism scientists are still trying to understand, unable to breed. However, if you take a subordinate female out of the colony,

something shifts in her physiology and allows her reproductive organs to flip the switch into the on position.

In essence, the subordinate becomes a queen.

“What it seems like is that when you are a naked mole-rat, and you transform to a queen, somehow, you start to age slower,” says Brieño-Enriquez. “And the only thing that is different is that the ovary is actually working.”

Now Brieño-Enriquez and his team are mimicking the on switch found in naked mole-rat ovaries and producing some of the same results in genetically modified laboratory mice.

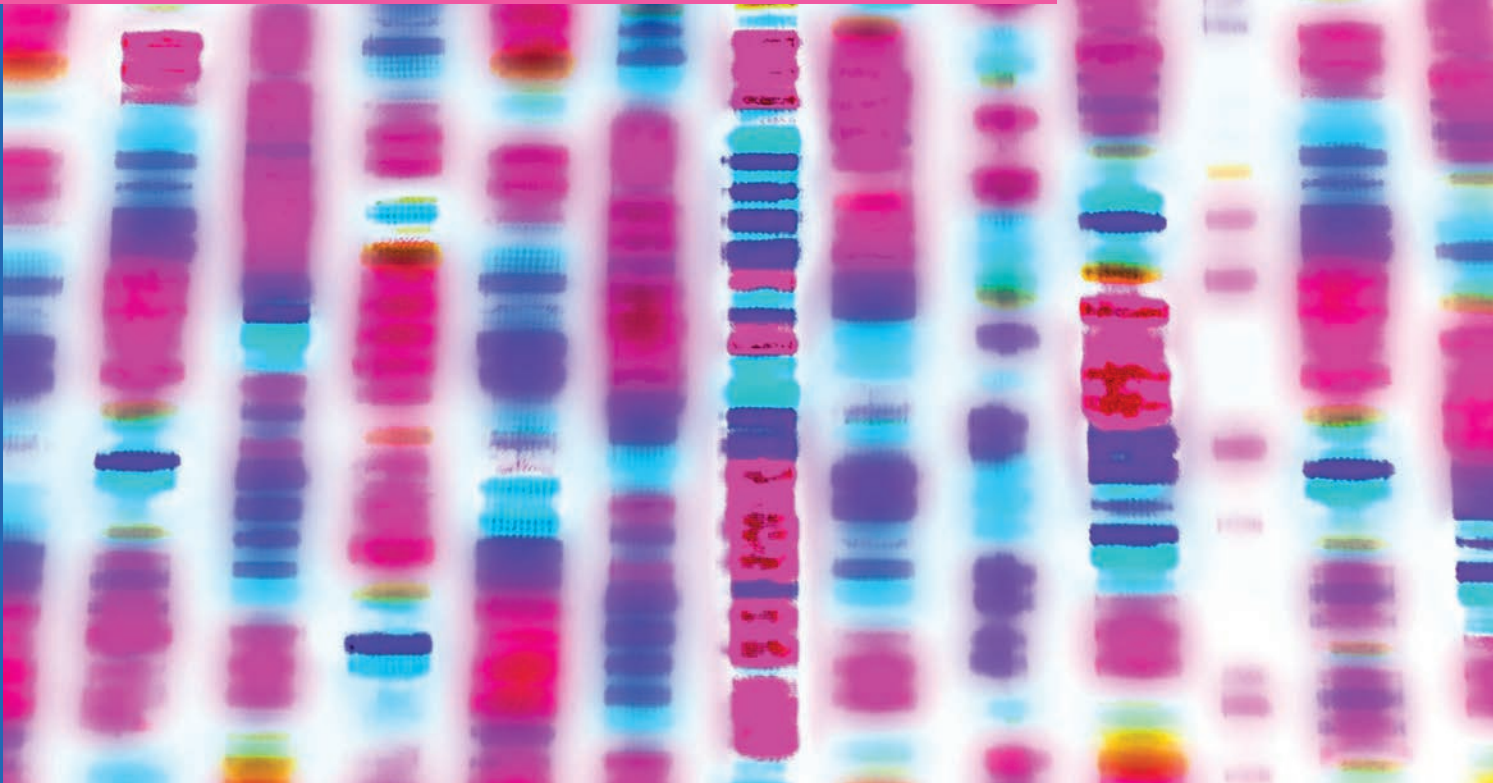
“The potential for this research is huge,” he says.

Clearly, a derived drug that could make women produce more eggs or keep the ones they have would give in vitro fertilization clinics more material to work with, which could result in higher baby-making success rates. But the aging aspects are important, too, he says. For both men and women, aging is associated with increased risks of cardiovascular disease, mental health diseases and cancer.

“If we cannot turn back time, perhaps we can at least slow the speed of aging, which would mean that people will be in better shape for longer,” says Brieño-Enriquez. “So it’s not just reproduction or just aging; I think it’s the marriage of the two.”

And to think, we could owe it all to a gnarly little mammal that spends its whole life in a hole in the ground. ■

College students discover and “adopt” proto-genes through a new Pitt program. RIGHT: Representation of a DNA sequence.



ORIGIN STORIES

UNDERGRADS WITNESS NEW GENES

ARISING | BY JENNY BLAIR

Brandon Garcia, a student at Florida’s Rollins College, hadn’t had any particular plans to visit Pittsburgh until a professor told him about an unusual opportunity. The marine biology major wound up spending the summer of a lifetime at Pitt, advancing new discoveries about evolution.

Garcia and Pitt undergraduate Aaron Zhang, a pre-med, were the first students to benefit from a prestigious CAREER Award from the National Science Foundation (NSF) granted to Anne-Ruxandra Carvunis in January 2022. The five-year grant enables the pioneering evolutionary biologist to loop gifted undergraduates into her research. Carvunis is an associate professor of computational and systems biology in Pitt’s School of Medicine. Earlier this year, she was one of the recipients of a Chancellor’s Distinguished Research Award.

The students studied proto-genes—sequences of genetic material that arise from “dark matter” in the genome and encode sim-

ple proteins. Proto-genes may sometimes give birth to novel genes that let organisms adapt quickly to changing conditions. Of thousands of these mysterious sequences, very few are understood.

“I basically, selfishly, don’t want to be the only person interested in this question,” says Carvunis, with a laugh. “I want many young people to bring their bright minds and help me solve this.”

She says her quest to understand the origins of new genes started with an original hypothesis, published in *Nature* in 2012, according to which the birth of brand-new (de novo) genes “involves the existence and translation of transitory genetic elements called proto-genes.”

Carvunis’ NSF-funded Adopt a Proto-Gene initiative aims to get young researchers interested in proto-genes, improve evolutionary literacy and encourage STEM careers. Part of the idea is to empower them with the experience of making the very first discovery about an unstudied proto-gene.

One portion of the grant funds training for college educators in virtual and in-person workshops that introduce them to experimental techniques with proto-genes in yeast. Armed with those skills, the instructors, in turn, teach them to students at their home institutions. Then undergrads can “adopt” a proto-gene and study it in their college labs, generating useful data for the burgeoning field.

And every summer, two students will get to do it in the Carvunis lab.

Garcia and Zhang explored the lab’s vast collection of genes and proto-genes. And, as the rising seniors investigated how proto-genes influence the functioning of yeast, they designed and executed a research experiment requiring them to use bioinformatics and practice various wet-lab techniques that incorporate cloning, microbial phenotyping and high-throughput robotics.

When they ultimately presented their work to the Carvunis lab team, they were thrilled by the enthusiastic response.

“It was just super satisfying and super rewarding to see that our efforts actually meant something. Dr. Carvunis was so visibly excited,” recalls Zhang. “It was hard not to smile.”

Garcia was smiling too. He says it’s rewarding to know that all the data they managed to compile and gather in just a couple of months will be useful to the lab: “It’s a very good feeling. I don’t think it’s a feeling that I will forget.” ■

MUTANT SUMMER

High school students and their teachers witness evolution in action. The program uses bacterial colonies.

EVOLUTION UP CLOSE, ALL WET AND SQUISHY | BY JENNY BLAIR

Picture two lab dishes inches apart, each containing a layer of gel studded with cream-colored bumps. On one dish, the bumps are shiny circular domes. On the other, they look very different—wrinkly and ruffly like lace.

The bumps are colonies of bacteria from the same species. The simple colonies are ancestors; the elaborate ones have evolved to function differently. That change took place in one week.

“Seeing evolution happen in real time is just so captivating,” says Vaughn Cooper, a professor of microbiology and molecular genetics at Pitt Med. In an interview with Pittsburgh’s NPR news station, WESA, he recalled that “the first time I saw, as a graduate student, bacteria evolving in real time, I knew that this had to be the way that we learn about evolution.”

That realization led to him found the nonprofit EvolvingSTEM, which provides high school students with that same “captivating” learning experience.

The microbiology experiment is the centerpiece of EvolvingSTEM’s curriculum. “Learning by doing works. We know this,” says Cooper. “But the life sciences have lagged well behind in learning-by-doing relative to, say, computer science, math, engineering, physics. You can kit that and distribute that remotely, but life sciences requires squishy things. Wet things.”

Wet and squishy is about right. In the experiment, students squirt a solution of harmless, genetically identical bacteria into a test tube that

contains a plastic bead. After letting the bacteria multiply for about 24 hours, they fish the bead out and transfer it to a fresh tube that contains a clean bead. Then they wait again.

In the initial generation, most or all of the bacteria float indifferently around the bead. But as they divide and multiply, some develop random genetic mutations that allow them to form a sticky slime, or biofilm, and adhere to the beads.

With each bead transfer, cells whose genes favor that knack for stickiness are selected. Riding the bead out of one tube and into the next one, they pass the trait to the next generation. The bacteria go through about six generations a day.

Early in the experiment and again after a few transfers, students spread a solution of bacteria over a gel-filled Petri dish. There, each individual bacterium gradually gives rise to a single colony.

Bacterial colonies from mutants that are good at forming biofilms look wrinkled, unlike their ancestors’ smooth, round colonies. It’s clear evidence of evolution. And it’s relevant to medical science: Bacteria that cause chronic infection are often excellent biofilm formers, and the mutations that get them there are the same ones causing these changes in the classroom.

Currently, students attending 15 high schools in eight states participate in EvolvingSTEM; many of them come from

communities traditionally underrepresented in STEM careers. “If we can offer the experience in the freshman and sophomore years, that’s when you get the broadest, least discriminated population,” says Cooper. “You have the greatest chance of hooking a diverse pool of people who wind up considering careers in STEM.”

For years, Cooper used discretionary funds to purchase supplies and pay instructors to bring the module to classrooms. But the School of Medicine has stepped in with a three-year, \$90,000 annual commitment to sponsor EvolvingSTEM during the academic year. And in early 2022, a nearly \$600,000 three-year grant from the National Science Foundation began funding a new eight-week summer program on Pitt’s Oakland campus. There, middle and high school teachers gather for training, stock up on supplies and fan out to their classrooms to take students through the experiment.

In a 2019 paper published in *Evolution: Education and Outreach*, Cooper and his coauthors documented that EvolvingSTEM students learn about 50% better on a common assessment of knowledge about evolution and heredity.

“Doing science is the best way to make scientists,” says Cooper, whose lab focuses on the evolution of infectious disease and evolutionary processes in microbial populations. When he reflects further on EvolvingSTEM, he adds: “It’s the most important work that we do.” ■



A SUMMER TO UNDERSTAND LIFETIMES

WHAT'S LIFE REALLY LIKE FOR
PEOPLE OUR STUDENTS WILL TREAT?

BY CRISTINA ROVALIS

ILLUSTRATIONS | ATHENA CURRIER



Through a new summer enrichment program, med students are learning from community mentors. As part of her project, Taylor Williams participated in a festival focused on children with autism.

Susan Burke had long suspected something was different about her son when he was 6, but she couldn't put her finger on it. She marveled at how Jack (not his real name) could memorize scene after scene in movies, so she knew he was intelligent. But he also spent much of his time seemingly in his own fantasyland; and when he would play in the vicinity of other children, he wouldn't really engage with them. His mom just couldn't figure out why.

When she and her husband sent him off to first grade, Jack's behavior became more concerning after he and a classmate had a physical altercation. To get to the root of his misbehavior, he was referred to a school psychologist, which ultimately explained a lot. Jack was later diagnosed with autism.

The earlier intervention begins, Burke learned, the more dramatic a difference it can make for developing social skills and maximizing learning potential for youngsters like her son.

The Burkes did everything they could to get Jack services. In elementary school, he received an IEP (Individualized Education Plan), which outlines personalized educational goals and services for children with disabilities. He also attended a special summer camp for children with autism. In these group-based therapy settings, one thing always stood out.

“We were the only Black people there,” recalls Burke.

That was often the case back when she was trying to get services in the 1990s. Jack is in his 20s now.

Historically, Black and Hispanic children have been diagnosed with autism at lower rates than white children. A 2017 study based

physical conditions in which people are born, grow, live, work and age—has been a priority for Anantha Shekhar, senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of the School of Medicine at the University of Pittsburgh.

When he began his leadership positions, he made it clear that the School of Medicine was committed to advancing medical education and research that promotes health equity. He was right in line with many students at Pitt Med. During the 2020 summer of civil unrest, students lobbied the University to teach through the lens of social justice, recalls Noble A-W Maseru, director of social justice, racial equity and faculty engagement for the health sciences.

As a response, school leaders created a summer SDoH enrichment opportunity for first-year med students; 2022 was the second pilot year of the program.

When a physician addresses the issues through a lens of health equity, Maseru says, studies show it’s more likely patients will not return with the same issues over and over.

Taylor Williams (Class of ’25) is a second-year med student who completed what’s called the dean’s summer research project after her first year. Students who opt to do this project receive a summer stipend to devote 40 hours a week to conducting research in collaboration with a faculty research mentor. That’s nothing new at the school. It’s often the first foray into a required longitudinal research project that students pursue through graduation, typically offering opportunities to publish papers and give scientific presentations.

But the med students now have the option to spend an additional 16 hours that first summer on an enrichment component, which has them talking to real people about real barriers to good health. The SDoH project gets them

“The conventional thinking is that medicine—the diagnostic intervention—is the silver bullet, but the science proves otherwise.”

on CDC data showed that white children were 19 percent more likely than Black children and 65 percent more likely than Hispanic children to be diagnosed with autism between 2002 and 2010.

While the disparity has narrowed significantly according to 2018 data, some are still falling through the cracks. Fewer Black children are screened by the recommended age of 36 months. And more can be done to identify Hispanic children on the spectrum in some communities.

Lu Randall, president of Autism Connection of Pennsylvania, isn’t surprised by what the Burkes experienced. Randall says that too often children from underrepresented groups still aren’t diagnosed properly until there is a behavior problem in elementary school or later—years after the ideal time for a diagnosis.

The delay in diagnosing Burke’s son demonstrates how a life can be impacted by the social determinants of health (SDoH). Addressing SDoH—the social, economic and

Maseru, who codirects the program with Leslie Hausmann, assistant dean for medical student research, says understanding socioeconomic factors leads to better outcomes for children like Jack. He cites a CDC study showing that life expectancy in the United States increased from 47 years in 1900 to 77 years in 1999. Of the 30-year increase, 25 were attributed to improvements in SDoH, such as safer cars, safer workplaces and safer and healthier foods and homes. Also key: a living wage, less racism and a healthier social environment.

“The conventional thinking is that medicine—the diagnostic intervention—is the silver bullet,” Maseru says, “but the science proves otherwise.”

A doctor should look at the person in the context of their environment, he adds: “Maybe the person doesn’t get exercise, which is attributable to the community where they live not being walkable. Or if they are malnourished, it may be because they live in a food desert.”

out of the bubble of med school, where they spend the first year buried under books, memorizing bones, muscles and glands and immersing themselves in genetics, immunology and neuroscience.

“Students are very focused on learning the body systems and how to recognize problems and what to do about those problems,” says Hausmann.

“There is so much biology that needs to be learned, and the community piece hasn’t historically been baked into the medical training. So this is an opportunity to expose students early on and get them out of the University and into the community. They can see the different issues that people may be facing and grappling with as they engage with the health care system.”

Williams, like other med students taking part in the dean’s summer research SDoH project, was paired with a mentor in the community. Pitt compensates these professionals for their expertise and time, notes Maseru.

Autism Connection’s Randall mentored



Some kids are expected to prepare meals for younger siblings when they themselves are quite young. Lucy Cheng ran a cooking class with those youngsters in mind.

Williams, who decided to help spread the word about the importance of early detection of autism to families with Black and other under-represented children.

Williams came into the program knowing that the medical establishment sometimes fails to diagnose children of color with autism. Lu Randall encouraged her to find out why parents might not seek out a diagnosis. The student learned that some view a child's atypical social interactions as part of their personality. And some sense stigma about disabilities.

In recent years, significant progress has been made in closing the diagnosis gaps, yet disparities persist in certain subgroups, including Black kids with autism who do not also have an intellectual disability. Many of these students aren't receiving special education services in school, which might lead to problems making friends and self-regulation in the classroom.

"It's so important for doctors to recognize this, and there's often a lack of focus on this in med schools," says Randall.

Williams has a personal connection to the topic. Her younger brother is on the spectrum, and she saw firsthand how early intervention helped him reach his potential. She says he's a "super-social" high school student who is a member of the marching band and plays dek

hockey.

For her dean's summer research project, Williams focused on how having a disability limits access to care. A patient may have issues with transportation, or a doctor's office might not accommodate a patient's physical or sensory needs. When Williams met with Randall, they discussed ways to equip physicians at community health centers to diagnose kids on the spectrum and to encourage Black parents with concerns to seek a diagnosis.

In their meeting, Williams learned that Randall and a young man on the spectrum had talked about creating brochures to distribute at community health centers. They decided that Williams would write a plain-language brochure telling parents about signs of autism in children of different ages.

From the pamphlet, parents will learn that younger children might not respond to their name or avoid eye contact, while older children might find it hard to say how they feel.

Williams also touched on the stigma of autism in some communities.

She notes that the lack of diagnosis can become problematic when children are expected to follow specific school routines and social cues.

"This can cause issues adapting and look

like purposeful behavioral disturbances when truly it's caused by being overwhelmed or overstimulated."

Williams also helped Randall plan ways to connect with people during an event called Autistic Urban Connections Fun Days in the Pittsburgh neighborhood of Hazelwood.

That Sunday in late summer, Williams met with families and used sensory-friendly toys as tools to start conversations. She engaged in games with the kids and their families, spending time learning about them as they played.

She says the kids ranged from very verbal to nonverbal, including one child who didn't say anything but lined up candies methodically. "Everyone communicated in their own way," Williams recalls.

She talked to a mother who was well-informed about autism but had never heard of a developmental pediatrician (a doctor who specializes in diagnosing developmental disabilities in children). It made Williams realize that even some parents who are tuned into the autism world may not be aware of all the resources available.

And now, after her experience this summer, Williams is even more inclined to explore a career as a developmental pediatrician—perhaps specializing in autism spectrum disorder

and ADHD: “I want to focus on helping a child have the proper tools growing up.”

When driving through the streets of Braddock, just east of Pittsburgh, Lucy Cheng (Class of '25) can't help but notice the lack of grocery stores. Despite the food pantries and community gardens, she sees how difficult it is for residents to get fresh and healthy food in what was once a bustling steel town.

But good nutrition is not just a matter of accessibility.

Cheng now knows that some of the youngsters she drives past are tasked with taking on a lot of responsibilities for children of their age.

Elementary and middle school kids are often expected to prepare meals for them-

He shrugged.

She convinced him to take a bite. He did and shrugged again. “Thank you for trying it,” she told him.

That's the point of the program—to expose kids to healthy foods, as well as teach basic nutrition and cooking skills.

The summer project is an offshoot of Cheng's clinical research project on pediatric facial fractures, often caused by falls and motor-vehicle accidents. Given the importance of nutrition in the healing process, Cheng decided to look more broadly at pediatric nutrition education in communities where food insecurity is common. She cites a study from the University of Virginia showing that the dramatic rise in childhood obesity and diabetes is most prevalent among kids of

Chillinsky was happy to see kids trying new dishes and flavors in Cheng's classes. “I would like them to say their favorite food isn't Hot Cheetos, but tacos they have made with their moms,” Chillinsky says. “It is more filling and nutritious.”

The program will continue this fall as part of Cheng's yearlong Albert Schweitzer Fellowship, a graduate student award designed to develop leaders who can address the health care needs of underserved communities.

She's hitting the books again for her second year of medical school, but Cheng will continue teaching a simpler version of the weekly cooking classes, enlisting other med students as volunteers. “I want to be able to impart some skills and confidence in the children so they feel less unprepared and alone when they are cooking.

“I would like them to say their favorite food isn't Hot Cheetos, but tacos they have made with their moms.”

selves and younger siblings while their parents are at work.

And, not surprisingly, kids tend to resort to easy options like chips and other junk food, her SDoH enrichment mentor, Melissa Chillinsky of Heritage Community Initiatives, informed her. Heritage is a nonprofit that provides out-of-school-time education and meals to youth.

That's why Cheng's SDoH enrichment project looked like a day in the kitchen with an older cousin. On a recent summer day, she stood in a brightly colored classroom, showing elementary and middle school kids how to mash avocado into a bowl, blend in cilantro and squirt in lime. They were making guacamole for a taco dish with pico de gallo.

“A lot of time, we say fat is bad; but avocado has healthy fat,” she told the 12 kids rotating between three stations.

Then came the moment of truth—would the kids eat what they made?

One little boy made a face when he saw the guacamole, saying, “I don't like green stuff.”

“Why don't you like green stuff?” Cheng asked him.

lower socioeconomic status, and that it can be attributed to changes in activity level and meal preparation.

Chillinsky, codirector of the Heritage Out-of-School Time (HOST) program, says, “A lot of our kiddos have to play a mature role at home, but they don't necessarily have the skills to do it. In past years, we've seen a lot of their daily intake of food is just chips or candies.”

Cheng had some exposure to food insecurity already: In her hometown of Chicago, she signed people up for SNAP benefits. When she worked for a tech company on the West Coast, she also taught cooking classes to low-income Bay Area families.

She still learned plenty from her experience working with Chillinsky and the teachers in the out-of-school program, including priceless tips for getting the kids involved.

They told Cheng: Pair reluctant kids with those who were more eager.

Also: Kids get motivated by doing little tasks, like juicing a lemon.

“I was surprised by how much they wanted to get involved in the entire process, even if they didn't enjoy the food itself,” says Cheng.

“Ultimately, it's about meeting the kids where they are. Hopefully, by doing so, we can help them make small healthy decisions that turn into life-long healthy habits.”

Williams' pamphlet would have been helpful to the Burke family. Although they had done everything they could think of to help Jack, Susan Burke's one regret is that he wasn't diagnosed in time to receive language and social skills therapy at an early age.

She pointed out concerns to her pediatrician, but her son was not diagnosed. He did graduate with his class, but the bullying that began in elementary school intensified in middle and high school, leaving him with severe anxiety. “He almost didn't graduate because of bullying.”

Randall points out that bullying can often escalate into discipline problems for the autistic child.

“The child will have an outburst, and then adults come running; and it gets louder and louder and the child has a heightened sensitivity. He may not even know what he is doing,

screaming and pushing people away. If he pushes the wrong person, he can be in a huge amount of trouble.

“If they’re not diagnosed when they are 2 or so, it becomes a cycle of discipline. They are getting timeouts in daycare. They can own that feeling: ‘I am a bad kid.’

“If you are not diagnosed correctly, people give you punishment instead of support.”

As Williams wrote the brochure, she thought about how her brother didn’t speak much as a preschooler and was easily overstimulated. But because he was diagnosed early, he saw a developmental pediatrician as well as speech and occupational therapists from a young age.

His therapists helped him work through difficult social situations and try to respond

to them rationally rather than emotionally. He can now adapt to typical life stressors and other unpredictable situations.

“I cannot imagine all of the children and families who do not receive that support, and how much harder that makes navigating social situations and life,” Williams says.

“It is harder to deal with an issue and adapt when you are not given the tools to do so.” ■

AWARDS HONOR SOUTH-PAUL

In the first year of the social determinants of health enrichment program, 2021, Pitt Med recognized two students with Jeannette South-Paul Awards, **Shruthi Venkatesh** and **Danielle Gruen**. The awards, named for revered former chair of family medicine South-Paul, recognize students who did exemplary work in their enrichment projects.



Shruthi Venkatesh

Venkatesh realized that sometimes people with multiple sclerosis had to buy expensive wheelchairs, stair lifts and other assistive devices to get around in their day-to-day lives. But not until she met with people who had the disease did she realize how daunting and frustrating the process can be.

For her summer project, she talked to members of the Pittsburgh MS Empowerment Support Group and Pennsylvania Keystone Chapter of the National MS Society. “Each insurance company is different in terms of approved assistive devices. Many do not offer financial assistance for purchases at all.” Getting grants from national nonprofit organizations also can be difficult, they told her. “It was eye-opening.”

Her summer research project has made Venkatesh even more interested in researching neurodegenerative diseases such as MS and Alzheimer’s. When she becomes a doctor, she says, she will be more sensitive to the day-to-day struggles of those living with chronic illnesses.

For her project, Gruen, who came to Pitt Med with a PhD in biogeochemistry, examined the history of the Freedom House Ambulance Service and its role in the foundation of emergency medical services (EMS) in Pittsburgh. The service, which became a national model, started in 1967 serving Pittsburgh’s predominantly Black Hill District community and staffed by mostly Black medics.

Gruen conducted interviews with community advisors, founders of the Freedom House Ambulance Service, including Philip Hallen, and organizations aimed at increasing diversity in EMS.

“It’s really important to amplify” voices from the community, says Gruen, who is interested in practicing emergency medicine.



Danielle Gruen



Jeannette South-Paul

This year’s South-Paul Awards went to Taylor Williams and Caitlin O’Brien.

The Ford plant in Pittsburgh assembled up to 40 Model T's a day through the early 1930s. Ford's Highland Park, Michigan, plant (shown here) was of the same design.

(Photo courtesy The Henry Ford)



THE ASSEMBLY

A FORMER MODEL T FACTORY
BUILDS THE NEXT GENERATION
OF CANCER TREATMENTS

BY MARK ROTH

A century ago, an imposing multi-story building in Pittsburgh's East End became one of the nation's first Model T Ford assembly plants, lifting materials from rail tracks below to fabricate cars from the top floor down.

Today, that same building has been transformed through a \$330 million investment by the University of Pittsburgh for a new kind of construction—creating tailor-made treatments to combat cancer and other diseases.



The Assembly is filled with images reflecting its automotive history, like this wall art (above right), which shows the rail tracks that abutted the original structure. The building includes many areas where scientists will be able to share ideas and inspiration.

Appropriately named The Assembly, the eight-story building at Baum Boulevard and Morewood Avenue will house scores of researchers largely devoted to cancer.

The building, which later housed a clothing factory and a stationery store, sits just a block away from the flagship UPMC Hillman Cancer Center building, and expands the center's research space by 50%, says Robert Ferris, Hillman Professor of Oncology and Hillman director.

"It's very fortuitous to find a place right nearby in such a crowded neighborhood," he says.

"Both Bob and I are extremely excited about the ability to move into this new space," adds

Dario Vignali, Distinguished Professor of Immunology and interim chair of Pitt's Department of Immunology, whose scientists will have a major footprint at The Assembly.

The building is filled with references to its automotive history, from vintage photos in the elevators to a 4 1/2-story atrium known as the crane shed, which occupies the space where cranes used to lift raw materials off train cars and deposit them on platforms that fed into the different floors.

Those loading platforms have been repurposed into balcony meeting spaces that look down on the crane shed, which overlooks the

East Busway.

The Assembly's architects created spaces where researchers from different disciplines can meet to share results, ideas, food—the master plan is to foster serendipity.

All told, the existing five floors of labs can accommodate more than 600 scientists.

"At the end of the day, the reason why this building is going to be successful is what always makes science successful: people," says Greg Delgoffe, associate professor of immunology and director of the Tumor Microenvironment Center, whose labs have moved to The Assembly. "The whole point of

The Assembly (top), in Pittsburgh's Bloomfield neighborhood, with Baum Boulevard on the left and Morewood Avenue in the foreground. Below is the Ford assembly plant in the 1920s at the intersection, an anchor for what was then known as Automobile Row.



MEYERD SCIENCE AND TECHNOLOGY, UNIVERSITY OF PITTSBURGH

this beautiful, historic place is that it brings together a number of really important sets of researchers.”

Computational biology groups at The Assembly (check out the “Seeing Patterns” sidebar) will help power discovery. Among other feats, those scientists are able to compare and contrast patient genomes. “The question we’re often trying to answer is, ‘Why does one person clear the tumor when another person is unresponsive?’” says Vignali.

The Assembly will also pull in cancer researchers from Magee-Womens Research Institute, including Adrian Lee, the Pittsburgh Foundation Professor of Precision Medicine, and Steffi Oesterreich, Shear Family Professor of Breast Cancer Research and codirector of the Women’s Cancer Research Center. The two are making important advances in the genetic study of breast cancers and their treatments. (See “What does the patient really need?” also in this issue.)

And while there are no spinoff companies located in the building now, such tenants could move in as commercialization opportunities emerge from the research under way,



THE HENRY FORD



Greg Delgoffe's immunology lab has moved to the facility. The Assembly's sleek labs feature built-in gas supplies, rolling cabinets and desks on the perimeter for postdocs and other researchers.

(Portrait by Tom Altany/ University of Pittsburgh)

BETTER, STRONGER T CELLS

The newest approaches to treating cancer rely on the body's immune system rather than the blunter instruments of chemotherapy and radiation.

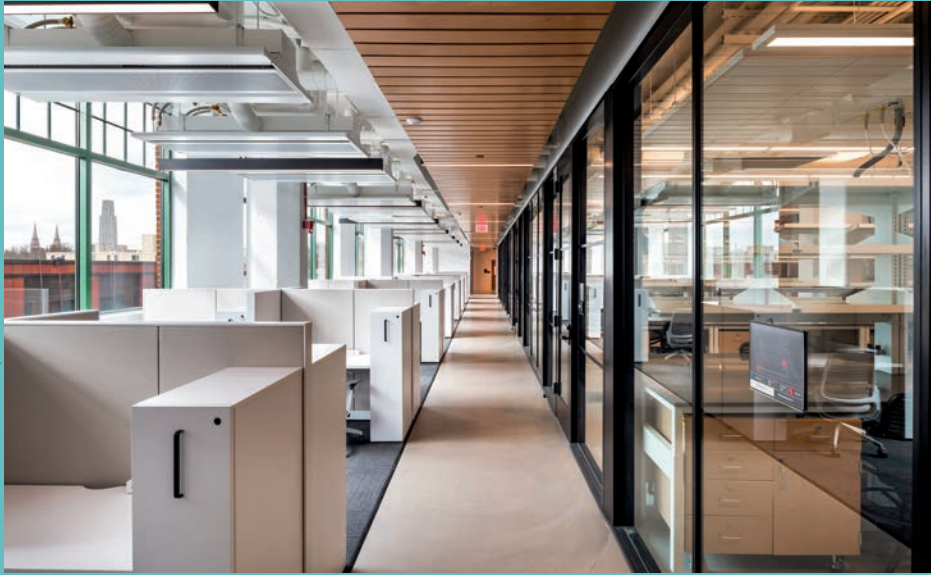
An impressive example from recent years has been CAR T cell therapy—in which a patient's immune system T cells are engineered in the lab to seek out cancer in the body. The approach has worked well against blood cancers like leukemia but hasn't had much success in solid malignancies like liver and colorectal cancer.

That's a challenge Greg Delgoffe's lab is tackling. One reason T cells don't function very well in solid cancers, he says, is that the microenvironment inside those tumors has very little oxygen or few nutrients. Those substances are consumed quickly by the proliferating cancer cells.

That impoverished landscape hinders the activity of the T cells, Delgoffe says, and they can become exhausted and lose their potency.

His lab is exploring ways to restore vitality to T cells so they can work just as well inside those tumors as they do in the bloodstream.

"With CAR T cell therapy," he says, "you genetically engineer the T cell to see the cancer. Our take is while we're redirecting T cells in that way, why not 'load them up' to be able to produce more energy? In other words, can we build a better CAR T cell that is designed to weather the storm and persist in that toxic tumor environment?" —MR



WEXFORD SCIENCE AND TECHNOLOGY, UNIVERSITY OF PITTSBURGH

The 4 1/2-story crane shed occupies the space where cranes used to lift raw materials for Model T's from the railroad tracks to the platforms above. The loading platforms have been transformed into glass-enclosed meeting spaces.



THE HENRY FORD



Ferris and Vignali say. That would add to the roster of cancer startup firms these groups have already generated, such as BlueSphere Bio, cofounded by former immunology chair Mark Shlomchik; BlueSphere is creating individualized T cell therapies. Another startup, Novasenta, founded by Delgoffe, Ferris and Vignali, develops detailed analyses of human tumor samples to seek new therapeutic targets.

When Delgoffe reflects on the history of the building, he notes that the point of the Ford plant was to end up with a car that someone could drive out of the first-floor showroom.

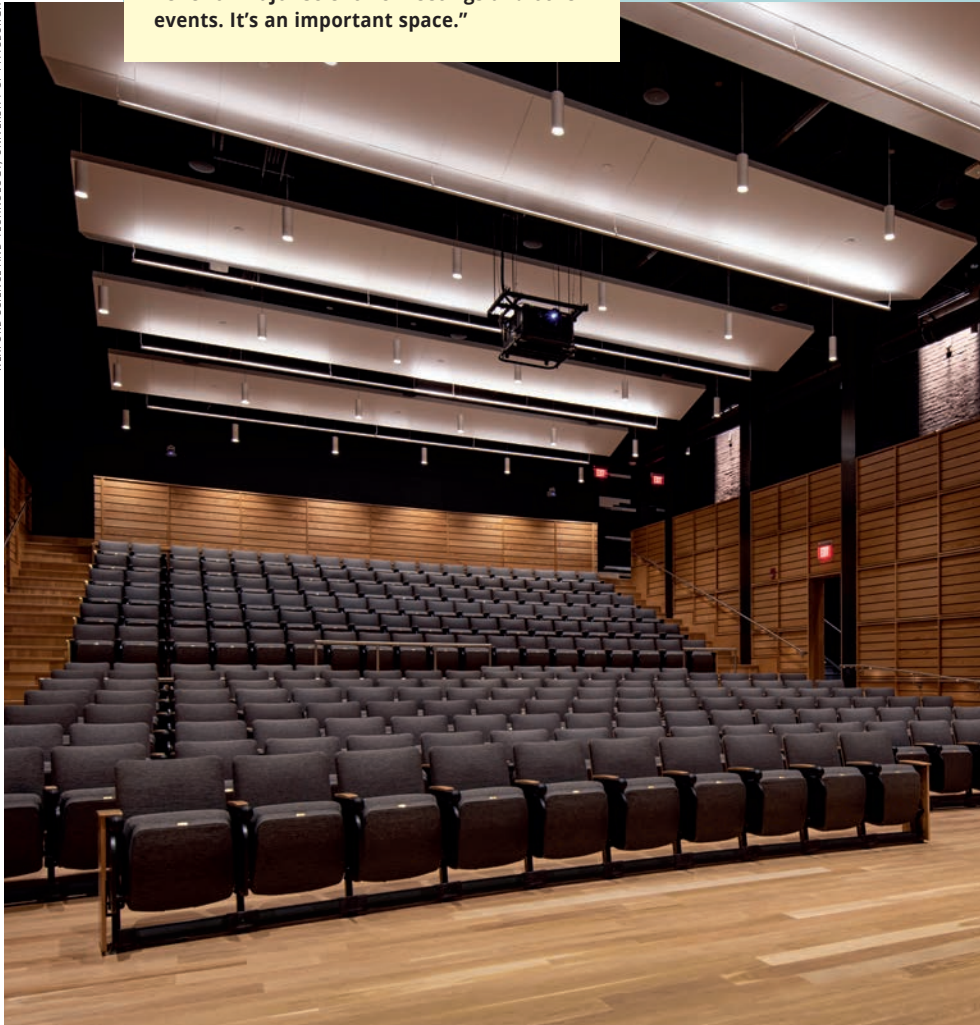
“What was the problem the Ford assembly building had to tackle? You needed to be able to concentrate your efforts and create something that could roll off the floor and be used.” In the same way, The Assembly will look at the raw materials of cancer with the goal of developing treatments that can be driven off the lot.

Some of the in-house researchers study the basic mechanisms of how bodies react to cancer; others test new approaches in animal models and conduct clinical trials.

“So it’s really soup to nuts,” Delgoffe says, “thinking about basic understanding of cancer coupled with folks who are trying to translate that into the clinic.” ■

THE RICHARDS AUDITORIUM

In October, The Assembly's auditorium was named in honor of the late Thomas Richards, chair of the University Board of Trustees at the time of his death in 2021. "This will be a place to disseminate new knowledge and generate collaborative approaches to high-risk, high-reward research questions," noted Dean Anantha Shekhar. "It is where we will convene for major scientific meetings and other events. It's an important space."



WEXFORD SCIENCE AND TECHNOLOGY, UNIVERSITY OF PITTSBURGH



SEEING PATTERNS

With tens of thousands of molecular factors at play just in the human genome, how can scientists make sense of the genetic landscape of cancer and the immune system?

Harinder Singh, whose experimental and computational biology group will be housed in The Assembly, says researchers are increasingly using machine learning approaches to find molecular patterns underlying certain cancers or autoimmune diseases—patterns that are too complex for any human to see. But the computational tools can't reveal disease mechanisms or how to target them. That's where the creative work comes in.

The professor of immunology and director of the Center for Systems Immunology says, "Machine learning is very good at predicting features" of biological processes, but it "is not able to interpret those features."

"For that, we still need human intelligence to come up with these causal explanations, which we can then experimentally test." —MR

Immunologist Harinder Singh in
the entryway.

(Portrait by Aimee Obidzinski/
University of Pittsburgh)



Listening to and partnering with patients can yield great rewards.





WHAT DOES THE PATIENT REALLY NEED?

MULTIPRONGED APPROACHES MAY KEEP PATIENTS
FROM SLIPPING THROUGH THE CRACKS

BY CARA MASSET

ILLUSTRATIONS | CAROLINA MOSCOSO

PATIENT AND DOULA NAMES HAVE BEEN CHANGED
TO PRESERVE PRIVACY.



Y

ou know, that blood pressure cuff never did come,” Gisele Bale told Janelle Jones in May. Before they became acquainted, Bale was supposed to get a cuff through her insurance. Somehow the request got lost in the vagaries of paperwork. But Bale’s cardiologist said she needs a digital cuff for daily blood pressure checks to see whether her medication is keeping her numbers down—especially now that Bale is on chemo for early stage breast cancer.

“I’ll see what I can do,” Jones, her doula, said.

Doctors found a pea-sized tumor in Bale’s breast when she went for her mammogram in the spring. The news shook her. She’s in her 50s with no family history of breast cancer.

“I cried all day,” she says. “Then I calmed myself down. I talked to myself: ‘We’re going to get through this. God doesn’t put nothing in front of you that you can’t handle.’”

Bale’s clinical team helped her enroll in a doula program for Black women with breast cancer. Bale had only heard of doulas caring for pregnant women. She feels blessed to have Jones as a guiding doula for the journey of cancer treatment.

Bale is usually the person taking care of everybody else as the oldest sibling in her family and as a grandma and neighbor who sits on the porch and keeps the kids on the block in line. She says it’s comforting to have a doula for emotional support and help with practical matters. Jones brought Bale a wig book to prepare for hair loss. Jones also offered to be a backup driver for Bale, who doesn’t have her own car, in case Bale can’t catch a ride to the clinic with her daughter or neighbors. When Bale was hospitalized for an infection following her first round of chemo, Jones helped her keep her faith. And, in June, Jones delivered that much-needed blood pressure cuff.

Black women tend to have more severe reactions to chemotherapy, says Margaret Rosenzweig, University of Pittsburgh Distinguished Service Professor of Nursing,

who founded the doula program last year. One might think all breast cancer patients have similar success rates because treatments are targeted to the tumor markers and stages of tumors. Yet Black women with the same genetic tumor types and treatment plans as white women are still more likely to struggle, she says. Nationally, Black women have the lowest five-year survival rate of any group.

“We found, through talking to patients and through looking at our own patient outcomes, that Black women were just not receiving the same, for instance, doses of chemotherapy that white women were,” says Rosenzweig, who is also a nurse practitioner at UPMC Magee-Womens Hospital. “They were recommended appropriate chemotherapy according to their tumor. And they were coming to treatment, but often they were not able to complete the recommended doses due to toxicity.”

These are motivated patients who are actively taking part in the extraordinary offerings of modern medicine, she says; yet its promise is still unfulfilled for them.

Breast cancer research is a poster child for the power of precision medicine (i.e., examining genetics to tailor treatments for individuals and patient subgroups) and the power of

translational research (i.e., generating research questions during patient care and devising new treatments). The field touts the first biomarkers, first targeted therapies and first multigene tests for interrogating the biology of tumors. While survival and quality of life for all patients have improved dramatically over the decades (today the five-year survival rate is roughly 90%), there’s still no known cure for breast cancer once it spreads, and inequities persist among patient groups.

Struggling with toxicity from chemotherapy is only one example of a larger problem faced by patients across the health care spectrum. Life expectancy is declining in the United States (not just because of COVID-19), and positive health outcomes are lower than those of comparable nations—particularly among underrepresented populations. Here’s a shameful for instance: In Pittsburgh, about 13 of every 1,000 Black babies die before they turn 1, compared to fewer than 2 of every 1,000 for white babies, according to a 2019 report by Pitt researchers.

The U.S. health care system incentivizes high-tech interventions like chemotherapy and surgery—yet it underestimates the value of providing wraparound support to guide patients physically and emotionally as they

A doula program gives breast cancer patients physical and emotional support.



prepare for interventions and procedures or deal with side effects and complications. Caretaking solutions like having a doula deliver a blood pressure cuff tend to be overlooked.

Rosenzweig and others have found that listening to and partnering with patients can yield great rewards.

Her team is evaluating ways to incorporate both low-tech and high-tech solutions for patients, balancing crucial bench-to bedside research and clinical care with extending equally crucial care on front porches and in community centers. It's a multipronged approach to get Black women with breast cancer the help they need: now and in future generations.

SUPPORT AND LOVE

In July, Bale was recovering from a round of “red devil” chemo treatment—as her Facebook breast cancer support group calls it—when she learned her longtime pharmacy unexpectedly closed for good. She urgently needed a refill of her daily blood pressure medication. Jones was out of town, but she offered encouragement to remain calm. After a number of calls, Bale got her medication.

Bale has at least 12 more weeks of treatments. She's looking forward to feeling well enough to bring out her cotton candy machine and video projector for a neighborhood family movie night. Plus, she has plans to coordinate a children's etiquette course at her local community center. Most of all, she'd like to keep up with her grandkids.

For now, she's focusing on taking slow but restorative walks around the neighborhood and forcing herself to eat her chicken or oatmeal even when she isn't hungry (because of the chemotherapy). In her meetings with Jones, they role-play what Bale will tell her doctors about her symptoms and concerns. Jones checks in on Bale's daughter when they all meet at the clinic for Bale's treatments, and they pass time chatting about common acquaintances.

Bale hopes the doula program can expand to more people, with all kinds of diseases, because everybody could use a doula to help them get better health care and live longer, productive lives, she says.

“I'd love for it to be a worldwide thing. Everybody needs support and love.”

Rosenzweig hopes the program will generate enough powerful data to convince Medicaid and insurance companies to reimburse their members for breast cancer doulas in the same way they do for pregnancy doulas.

She founded the pilot doula program in 2021 with an African American cancer support group and other community partners after noticing the weekly patient-support program she leads for people with metastatic breast cancer wasn't fully meeting many Black patients' needs.

Women would talk about the pressure to be strong, yet said they didn't always get the emotional support they needed. And they worried about what would happen to their families if they died from the disease.

About 50 Black women in Pittsburgh are diagnosed with advanced-stage breast cancer every year, and 80% live in low-income

Women would talk about the pressure to be strong, yet said they didn't always get the emotional support they needed. And they worried about what would happen to their families if they died from the disease.

neighborhoods. The doula program, which won seed funding from Pitt's Clinical and Translational Science Institute innovation program (known as PInCH), trains non-medical doulas to provide companionship outside the hospital. The doulas meet regularly with Rosenzweig's team to brainstorm solutions for patient needs. (That's how Jones was able to get Bale's digital blood pressure cuff.) And they

assist families if patients don't survive.

Rosenzweig's team is still assessing the effectiveness of the doula program for this population. Yet another program with a similar combination of high-touch and high-tech approaches has been saving lives of surgery patients referred for a range of procedures to UPMC—see sidebar, “Marathon ready.”

And a nurse navigator program supporting patients with blood cancers has been successful at UPMC Hillman Cancer Center in improving patient satisfaction and reducing hospitalizations and costs.

WE ARE STARDUST

Rosenzweig is investigating multiple avenues to figure out why there are disparities in how Black patients experience toxicity from chemo. She leads an NIH-funded study tracking, throughout their chemotherapy regimen, patients' stress-related symptoms or symptoms from underlying conditions. Initial results show Black women report higher numbers of symptoms than white women before even starting chemo sessions.

Rosenzweig's team also audiotapes clinical visits (with consent, of course) to gather data on how clinicians respond to symptoms reported by patients.

And the team collects genomic specimens for collaborators to evaluate how patients metabolize the chemo drugs causing the most toxicity. Rosenzweig is applying for grants to fund research linking her symptom data with genetic data to investigate inflammatory pathways, telomeres or immunological responses that can influence either cancer progression or the ability to withstand treatment.

Her foray into genomics came about in the early '10s after Rosenzweig met a European couple new to Pitt—breast cancer research partners and spouses Adrian Lee and Steffi Oesterreich, both professors of pharmacology and chemical biology. Lee and Oesterreich were accustomed to collaborating with cancer surgeons to get tissue samples, yet they'd never met a PhD nurse like Rosenzweig with a federally funded research portfolio—not in their native Great Britain or Germany, or at other U.S. institutions for that matter.



The U.S. health care system incentivizes high-tech interventions—often ignoring simple needs like a blood-pressure cuff.

As Lee tells it, he phoned Rosenzweig one day to ask: “What do nurses do for research?” Together, they figured out how they could use routine blood draws to build a bank of liquid biopsies, enabling the scientists to sequence tumors from bits of tumor DNA floating around in the blood rather than using tissue taken through invasive biopsy procedures.

Lee, the Pittsburgh Foundation Professor of Precision Medicine who directs the Pitt/

UPMC Institute for Precision Medicine, and Oesterreich, Shear Family Foundation Professor of Breast Cancer Research, came to Pitt in 2010, drawn by the Pitt Biospecimen Core, which contains 800,000 biological samples and counting. (It’s so big that the NIH’s Cancer Genome Atlas Project, a landmark project sequencing 33 cancer types, was greatly supported by samples from Pitt’s biobank, Lee says.)

The biobank includes more than 10,000 breast cancer samples, and Lee says when Pitt scientists and physicians started it more than 20 years ago, they had the foresight not only to collect tumor tissue samples, as was the standard at other centers, but blood samples and normal tissue samples for comparison, as well.

Lee and Oesterreich were also attracted to Pitt’s partnership with UPMC and its wealth of patient data. One of their very

recent papers answers the question of whether oncologists should prescribe certain aggressive therapies for breast cancer patients older than 70. After examining the electronic health records of more than 50,000 breast cancer patients treated at UPMC over the past 20 years, they concluded that patients older than 70 received little benefit from the aggressive therapies. “It’s an interesting case of precision medicine where you are kind of trying to ramp down how much we do,” says Lee. “We’re not giving less, we’re just trying to be more precise in what we give.”

Not long after coming to Pitt, Lee and Oesterreich realized the biobank included a few post-mortem samples from a handful of metastatic breast cancer patients who’d asked to donate their tissue after they died from the disease. Lee and Oesterreich compared tissue from when patients were in the early stages of the disease through the final stage. Their findings led to a landmark paper in the field.

“There was this morphing of the estrogen receptors over time, making endocrine therapy more—or less—effective,” says Rosenzweig. “That was the inspiration to say, ‘We really

need a formal program. This is going to yield so much information.’”

Lee, Oesterreich, Rosenzweig and colleagues established Hope for OTHERS (Our Tissue Helping Enhance Research & Science). Participants donate tissue throughout the progression of the disease and eventually, if they die from it, through a rapid autopsy when living cells are gathered within four to six hours after death. A program liaison attends Lee’s lab meetings as well as Rosenzweig’s weekly patient meetings.

The team has learned that patients find value in helping meet the needs of women who will come after them.

Participants—of all ethnicities—enrolled in the Hope for OTHERS tissue donation program say it’s gratifying to know they will be helping to cure breast cancer even after they’ve died.

Patient Stella Martinez (not her real name) notes that even though medicine has come a long way in understanding breast cancer, what’s still unknown is staggering. It makes her think about research on deep space: The universe is vast and mysterious, then along comes an advancement like the Webb telescope that leads to new clarity. Our new view of the universe is raising more questions and generating more excitement about discovery.

Martinez sees her part in the tissue donation program as leaving “her particular jar full of stardust.”

Literature suggests that Black patients are less willing to participate in research, but Rosenzweig’s own experience and her surveys about patient willingness show the opposite. She acknowledges the ugly history of unethical trials and present-day racism, but in the context of trying to better understand disparities and helping all people to achieve better health, many patients find participation meaningful and uplifting. When Rosenzweig asks, “Would you be willing to be in studies that look at your genetic profile in relation to symptoms?” the answer is usually yes. ■

MARATHON READY HIGH-TOUCH AND HIGH-TECH APPROACH HELPS SURGERY PATIENTS

In the United States, up to 20% of patients have major complications after a procedure, says Aman Mahajan, an MD, PhD, MBA who chairs the Department of Anesthesiology and Perioperative Medicine. In fact, mortality after surgery is one of the leading causes of death worldwide.

“Surgery can be incredibly difficult on a patient’s body. In some cases, it can have the same toll as running a marathon,” says Mahajan, the Peter and Eva Safar Professor at Pitt.

A wrap-around program out of the department does a risk assessment (mining UPMC’s huge patient database) for each patient case, and through shared decision-making between the patient and their doctors and surgeons, develops a pathway for optimizing patient health before surgery, reducing post-operative complications.

If the team deems surgery is the best course, the program assigns surgical coaches to help the patient be at their best health before and after the procedure. That might look like incorporating a 30-minute walk into their days, or, say, changing their diet to bring down blood sugar. The coaches check in remotely to mentor patients through their fitness challenges and surgical journey.

“So, on one hand, you can imagine we have this AI machine-learning program; but on the other end of the spectrum, we actually have this very humanistic approach to managing these patients,” says Mahajan.

And it works.

A 2018 cohort of 24 high-risk orthopaedic patients referred to UPMC’s Center for Perioperative Care (CPC) lost 32 pounds on average and had better outcomes.

Following about 10,000 patients enrolled in optimal care pathways for surgery across four UPMC hospitals throughout two years, Stephen A. Esper (MD ’07, MBA ’09) and Jennifer Holder-Murray, an MD, reported a 30% increase in survival after several types of procedures (Annals of Surgery, November 2020). Esper, an assistant professor of anesthesiology and perioperative medicine, is the director of the CPC. Holder-Murray is an associate professor of surgery and surgical director of the CPC.

UPMC Health Plan now requires patients referred for certain operations to participate in the department’s optimization programs, and a venture studio out of New York is digitizing and commercializing Pitt’s approach. Other elite medical centers are looking to the platform and coaching program, called Pip Care, to meet this critical need, says Mahajan.

—Erica Lloyd



Circus Man

His name was Daniel and he had
no one but knife-throwing eyes
pachyderm skin and tobacco tar hands
to speak for him.

His legs were thin as wires having
outrun lions pinned in the end
by tumors trampling
his heaving chest his airway
closing like a fist.

He could not raise
his voice had never
learned to write could only
nod

I understand,
If you take the tube out—

or No
I have no family
or No
I do not want a priest
and Yes, goddamn
I understand
I understand
I understand

We took it out—

And he never revealed how a man
swallows flame, how to sleep
among cats, how to fall
from a train

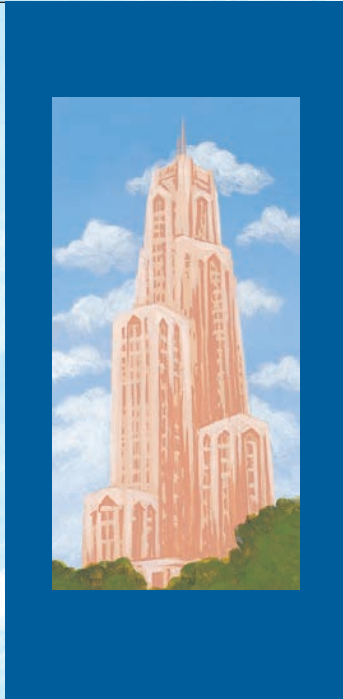
He just shuttered his eyes leaving
only his name, which
was Daniel.

By Gaetan Sgro

Illustration by Taylor Hollingsworth

Reprinted from *The Healing Muse*
(Vol. 13, No. 1)

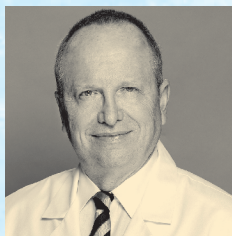
Gaetan Sgro, an MD (Res '13), was the Class of 2022's invited faculty speaker on Diploma Day. He is a clinical assistant professor of medicine, an academic hospitalist at the VA Pittsburgh Healthcare System, a storyteller and a poet. He's a recipient of the Leonard Tow Humanism in Medicine Award, the Golden Apple Award and the Carl R. Fuhrman Clinical Educator Award. He serves as the site director of the My Life, My Story Program as well as associate program director for the UPMC internal medicine residency. Sgro also codirects Pitt Med's Area of Concentration in Medical Humanities and Ethics.



CLASS NOTES '00s

'80s

When we last connected with **Eric David Peterson** (MD '88) in 2017, he was overseeing the Duke Clinical Research Institute—one of this country's largest—as its executive director. Five years later, Peterson and his vast clinical research knowledge have headed west. He's currently serving as the inaugural vice provost and senior associate dean for clinical research for UT Southwestern; he also holds UTSW's Adelyn and Edmund M. Hoffman Distinguished Chair in Medical Science. He ranks among the top 1% of published researchers in clinical medicine.



Hornicek

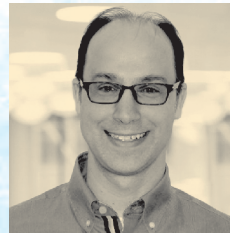
paedics chair at the University of Miami and director of orthopaedic oncology at Sylvester Comprehensive Cancer Center—was named an Orthopaedic Research Society fellow. "I look forward to continuing to advance national and international sarcoma research as an ORS fellow," says Hornicek.

'90s

Among his honors, **Francis J. Hornicek Jr.** (MD '91) became in 2007 the first orthopaedic surgeon to win Massachusetts General Hospital's Brian McGovern Award for Clinical Excellence—an award he especially treasured because winners are chosen by their faculty colleagues at Harvard. More recently, in March 2022, Hornicek—now the ortho-

'00s

Ronald Bernardi (PhD '02, MD '04) happily reports that he joined Genentech in February 2019. (The San Francisco biotechnology company was cofounded by Herbert Boyer, also a Pitt alum.) Bernardi has been lead medical director for Innovative Pediatric Oncology Drug Development (iPODD) since September 2021. He's also a member of the Product Development Oncology and Hematology team at Genentech, which is a subsidiary of Roche. The iPODD team is responsible for the global clinical development of the Genentech/Roche oncology pipeline in pediatrics. The best part of his days, he says, is "the possibility to improve the standard of care for children with cancer."



Bernardi

Elad Levy (Res '04), chair of the Department of Neurosurgery at the University of Buffalo, has just been named president-elect of the Congress of Neurological Surgeons (CNS). Levy—whose research focuses on carotid artery revascularization and stents as well as stroke causes and prevention—will oversee CNS's mission to advance neurosurgical research and support trainees, researchers and clinicians in the field. Levy is also the founder of the Program for Understanding Childhood Concussion and Stroke, a nonprofit organization which helps to support concussion research and outreach in Western New York.



Levy

As the mom of three daughters, **Angela Sanfilippo Casey** (Res '07) is conscientious about teaching them a routine for healthy skin; but she says that dermatologists have never developed a skin care line just for young girls. So she created Bright Girl: the first dermatologist-developed line created specifically for girls as young as 8. "Helping others to develop smart skin care habits is my passion," she says. Casey serves on the faculty with the OhioHealth Dermatology Department and practices at the Center for Surgical Dermatology and Dermatology Associates in Westerville, Ohio, where she regularly works with skin cancer patients—another motivation for the founding of Bright Girl.



Casey

'10s

During **Kelly Quesnelle's** (PhD '12) training in molecular pharmacology at Pitt Med, she was chosen to be a Lindau scholar, a coveted opportunity where young scientists rub shoulders with dozens of Nobel laureates. She is now chair of biomedical sciences at the University of South

Carolina School of Medicine Greenville. She says she's been working with the department's educators to "refresh our preclerkship curriculum to keep it vibrant and engaging for our learners in Greenville for many years to come." This summer, Quesnelle revisited her scientific roots: She met virtually with Pitt Med Biomedical Graduate Student Association members as part of their How to Get Your First Job panel; she'll also be speaking with students in March 2023 as part of Pitt's PhD Pathways programming.



Quesnelle

"I was fortunate," **Deborah DiNardo** (MS '15, Res '11, '13) says, to rotate at the Pittsburgh VA during her internal medicine residency. From this first assignment, her commitment to women veterans has only grown: Today, she serves as women's health medical director for the VA Pittsburgh Healthcare System and clinical assistant professor of medicine at Pitt's School of Medicine. For her outstanding service and care, DiNardo in 2020 received the Rising Star-David M. Worthen Award for Excellence in Health Professions Education, the most prestigious education award presented by the Department of Veterans Affairs.



DiNardo

—Rachel Mennies

HEARTFELT SUCCESS

It was a crazy, hectic day. Just like all the others. People living. People dying. And there was much to do. There was blood to be drawn, labs to check, internal jugular lines to sink deep within a vein.

So begins the introduction to **Kathy Magliato**'s memoir, "Heart Matters: A Memoir of a Female Heart Surgeon" (Penguin Random House, 2011).

While crazy, hectic days are nothing unusual within the medical profession, what Magliato (Fel '98) has accomplished throughout her days is inspiring.

The cardiothoracic surgeon, based in Santa Monica, California, and affiliated with multiple hospitals, is in an exclusive group of surgeons trained to perform heart transplants. She also holds an MBA and is working on a patented medical device that could help provide early detection of heart problems, which, she stresses, could save lives. "Heart disease is the number one killer for men and women in the world," says Magliato. "Yet, it is 80% preventable."

The novel device is like a blood pressure cuff that performs as a noninvasive, nonimaging tool for measuring and tracking blood vessel health. By revealing early warning signs of heart disease, Magliato believes "this technology potentially opens a window into your vascular health at a time where we can intervene."

Her memoir—which sheds light on how heart disease kills more women on average than all types of cancer combined—was a New York Times bestseller, both in print and as an ebook. More than 10 years since it was first published, she says she still receives near-daily letters and email reactions, her story having "a far greater impact than I could ever imagine," she says. It became the inspiration for the 2016 NBC medical drama "Heartbeat."

She says the book, like her specialty, was a labor of love; and Magliato, married to Nicholas Nissen (Fel '98), dedicated it to her two sons—"whose hugs and kisses at the end of each challenging day heal my heart," she writes. —*Kari Villanueva*



Magliato

GOING HIS OWN WAY

Ask **Ray Funahashi** (MD '20) about his medical career, and he'll point out: "I'm as nontraditional as they come."

Instead of starting a residency after medical school, he learned to code. And, before beginning his postdoc, he became a drug discovery manager at Pitt's Office of Innovation and Entrepreneurship partner, sciVelo.

He recently served as a postdoctoral associate at Pitt's School of Medicine and also mentored students on entrepreneurial opportunities—a sort of "innovation fellowship," as he calls it.

The mentoring was much needed, says Funahashi, because many students "have all of these ideas. [They] see and understand the problem space—but to execute some sort of solution is prohibitively difficult" because they can't find people with complementary skills in tech or business.

Seeing the potential of tech innovation to advance medicine compelled him to reevaluate his own career path.

His reevaluation took him to Gesund.ai—a Boston-based startup, where he's heading clinical affairs. For companies or academics developing medical algorithms, Gesund helps ensure their artificial intelligence is safe and effective. In February 2022, the new company received \$2 million in seed funding led by the venture capital firm 500 Global.

Funahashi says his interest in medical research was shaped in part by his family history. Helping care for his grandmother, who suffered a brain injury when he was younger, made him curious about stem cells, which led him to research positions at the National Institutes of Health and Columbia University before medical school. Funahashi says he doesn't reflect on (traditional) paths not taken.

"For health sciences students who are thinking about trying to make a difference that's outside of a traditional clinical path—there are many ways to do it." —*Rachel Mennies*



Funahashi

MICHAEL CHERINGTON

NOV. 24, 1934–JUNE 25, 2022

Although the Flash is probably the first character you'd think of if someone said "superhero" and "lightning bolt," these words also describe **Michael Cherington** (MD '60), who was known as the "Lightning Doctor" and completed 25 marathons.

He was born in Pittsburgh to Jewish parents who emigrated from Russia. Although his childhood was, at times, adverse, it was imbued with community, Shakespeare, Gilbert and Sullivan, George Gershwin and chess. (At the age of 10, Cherington played national chess champion Arnold Denker; as the story goes, the match resulted in a draw.)

His mother died when he was 14; after that, Cherington was raised by his grandparents. Through a series of summer jobs and scholarships, he put himself through undergraduate and medical school at the University of Pittsburgh. He later opened a private practice in neurology in Denver. During these early years, he was married for the first time and had three children.

In 1990, as he was winding down his practice, Cherington published a case study on a patient who'd sustained injuries after being struck by lightning. The article was the spark for his subsequent

career in keraunomedicine, the study of lightning casualties.

Cherington founded the Lightning Data Center (LDC) at St. Anthony Hospital in 1992, and following the inaugural meeting, the LDC has continued to meet once a month to gather and share information. Cherington served as the center's chair until 2007. The LDC continues to bring together an interdisciplinary group of lightning experts who share an interest in the prevention and treatment of lightning injury. The members built an injury dataset and collaborated on a paper that first proposed the 1:10 ratio of lightning deaths to injuries, a reference point still cited today. During his career, Cherington published dozens of peer-reviewed articles, many of which significantly advanced the field of keraunomedicine.

Since his death, his wife, Nancy Cherington, who met him in 1989, keeps learning more about his accomplishments: "He never ever talked about them. I found all this information that I didn't even know about him, and it just made me love him more." —*Rachel Bittner*



Cherington

IN MEMORIAM

'40s

BERNARD COBETTO, MD '47
SEPT. 9, 2022

'50s

FRANCIS ESPOSITO, MD '59
JUNE 20, 2022

JOHN FULTON, MD '55, RES '59
JULY 5, 2022

EARL SHIREY, MD '52
JULY 17, 2022

'60s

MICHAEL CHERINGTON, MD '60
JUNE 25, 2022

CARL KONVOLINKA JR., MD '60
JULY 26, 2022

MICHAEL MCCARTHY, MD '65
SEPT. 22, 2022

JAMES MRAZ, MD '62
SEPT. 20, 2022

JOHN PAAR, MD '60
SEPT. 2, 2022

'70s

CURTIS FISHER, MD '76
JUNE 3, 2022

GLENN IBEN, MD '76
AUG. 10, 2022

MICHAEL JOHNSTON, MD '71
JULY 30, 2022

JOHN KARDUCK, MD '75
JULY 1, 2022

JOHN MIKITA, RES '72
AUG. 26, 2022

BARRY WINGARD, MD '78
OCT. 1, 2022

'80s

**MARDJOHAN
HARDJASUDARMA, RES '80**
JUNE 15, 2022

KIRK MAURO, MD '88
JUNE 13, 2022

DAVID RAVELLA JR., RES '82
AUG. 1, 2022

'90s

ANTHONY KOROSI, MD '94
SEPT. 19, 2022

TODD SHUSTER, RES '92
JUNE 3, 2022

'00s

DOUGLAS ROCKACY, RES '03
JULY 16, 2022

'10s

VINAY SUNDARAM, FEL '10
JULY 14, 2022

EMILY ZHAO, MD '15, RES '20
AUG. 17, 2022

TALK ABOUT TIMING CREAGER TAKES THE HELM OF LEADING MOLECULAR DIAGNOSTICS COMPANY

BY RACHEL MENNIES



Southern California-based Creager is helping current Pitt graduate students think about their careers. (Photo: Courtesy Creager. Photo illustration: Brandon Copp-Millward)

In February 2020, Richard Creager (PhD '81) received a phone call. It was from a friend at the National Institutes of Health (NIH) who knew that Creager was taking on projects as a consultant, helping companies enter or improve their position in the global medical diagnostic market.

Would Creager be interested in working on developing mechanisms for testing infectious diseases?

Creager was especially well-suited for the NIH stint because, before becoming a consultant, he worked for nearly two decades at Beckman Coulter, a diagnostics company that develops, manufactures and markets biomedical technologies. Among his roles there: chief science officer from 2011-2016. Over the course of his career at Beckman Coulter and other companies, he led the development and commercialization of more than 160 IVD (in vitro diagnostic) products.

Creager told his friend, sure, he'd take on the NIH assignment. That was supposed to be for 3 or 4 hours a week. Then came March 2020, and the assignment turned into a 30-40 hour a week gig.

Talk about timing, says Creager.

He says, "It's still going on."

What's still going on is RADx, the NIH's Rapid Acceleration of Diagnostics initiative, which works with scientists and companies to steward speedy innovation for novel COVID-19 testing approaches from the lab bench to the public. As part of a consortium, Creager helped assess funding proposals for RADx by asking: "Do you have a novel technology? Do you have any technology that is developed and ready to go to market?" He says the team of

50 eventually winnowed applicants down and began working with the selected companies and organizations to develop testing.

At that time, the supply chain was wearing thin, and hospitals struggled to maintain their equipment supplies. RADx was forced to get creative. "I was designing experiments for them to do, but nobody could get clinical samples. We were reaching out to our networks of hospitals around the country—and," he says, "we couldn't get swabs. Nobody could get swabs. So, we were using the U.S. government, the Army to try and get us swabs." Despite those challenges and several more to come—like a scramble around Christmas 2021 to develop tests that detected the Omicron variant—Creager says he embraced the opportunity.

His efforts didn't go unnoticed by Seegene Technologies, South Korea's leading molecular diagnostics company and an international COVID-19 test pioneer, whose annual sales surged to \$1.2 billion, 10 times its pre-pandemic revenue. Seegene, headquartered in Seoul with subsidiaries around the globe, is planning to expand beyond COVID testing to establish a broader market for laboratory tests that can quickly and cheaply unveil the cause of many seasonal ailments.

To help it do so, the company recruited Creager to become CEO of its southern-California-based U.S. subsidiary, a position he

assumed in March 2022.

Creager says he was ready for the role, in large part, because of his time at Pitt.

"I really learned science there," he recalls, "how to do solid science.

"I've applied those principles throughout my career—from the bench to management to executive management."

He credits his mentor, the famed Pitt Med virologist Julius Youngner, with his strong basic science foundation—as well as other skills that've proved vital in his career.

"The most important thing that Juli taught me was how to write," he says, "and how to put a team together—how to motivate people without knocking them down."

Creager is still connecting with Pitt Med PhDs, too: He recently returned to Pittsburgh and served on a panel as a representative from industry for biomedical graduate students to explore job opportunities.

At Seegene, Creager is tasked with growing the company's American presence.

Seegene offers an array of tests for SARS CoV-2 and its ever-changing variants; and Creager notes that they were one of the first to do so. "We test all types of infectious diseases," he adds, "and we're one of the first companies to have a monkeypox test out" for high-complexity laboratory testing.

Once again it's about timing, notes Creager. ■

Reader, beware—you're in for a delightful scare: Fear has a good side.



GETTY IMAGES

FOR REAL! TWEEN SCIENCE



Phobophobia, as the name suggests, is the fear of phobias, or the fear of fear. People with phobophobia tend to avoid anything that might be scary, like horror movies, roller coasters or school presentations. For them, fear itself becomes the monster lurking in the shadows.

But fear doesn't have to be a bad thing. In fact, being willing to be scared now and then—in relatively safe situations—can make wonderful opportunities for personal and social growth.

What scares me may, or may not, scare you. And fear responses are different for all of us and throughout our lives. Think back to when you were little. Does what scared you then scare you now? If not, why? Well, you probably overcame that fear by confronting it.

For instance, were you afraid of the dark as a tyke? Maybe you still are. After all, darkness can up the spookiness of any situation—that is, until you turn on the lights only to find a pile of unfolded laundry instead of the oogie-boogie man. As we age, we learn to reason through our fears, which, in this case, allows us to eventually ditch the night-light.

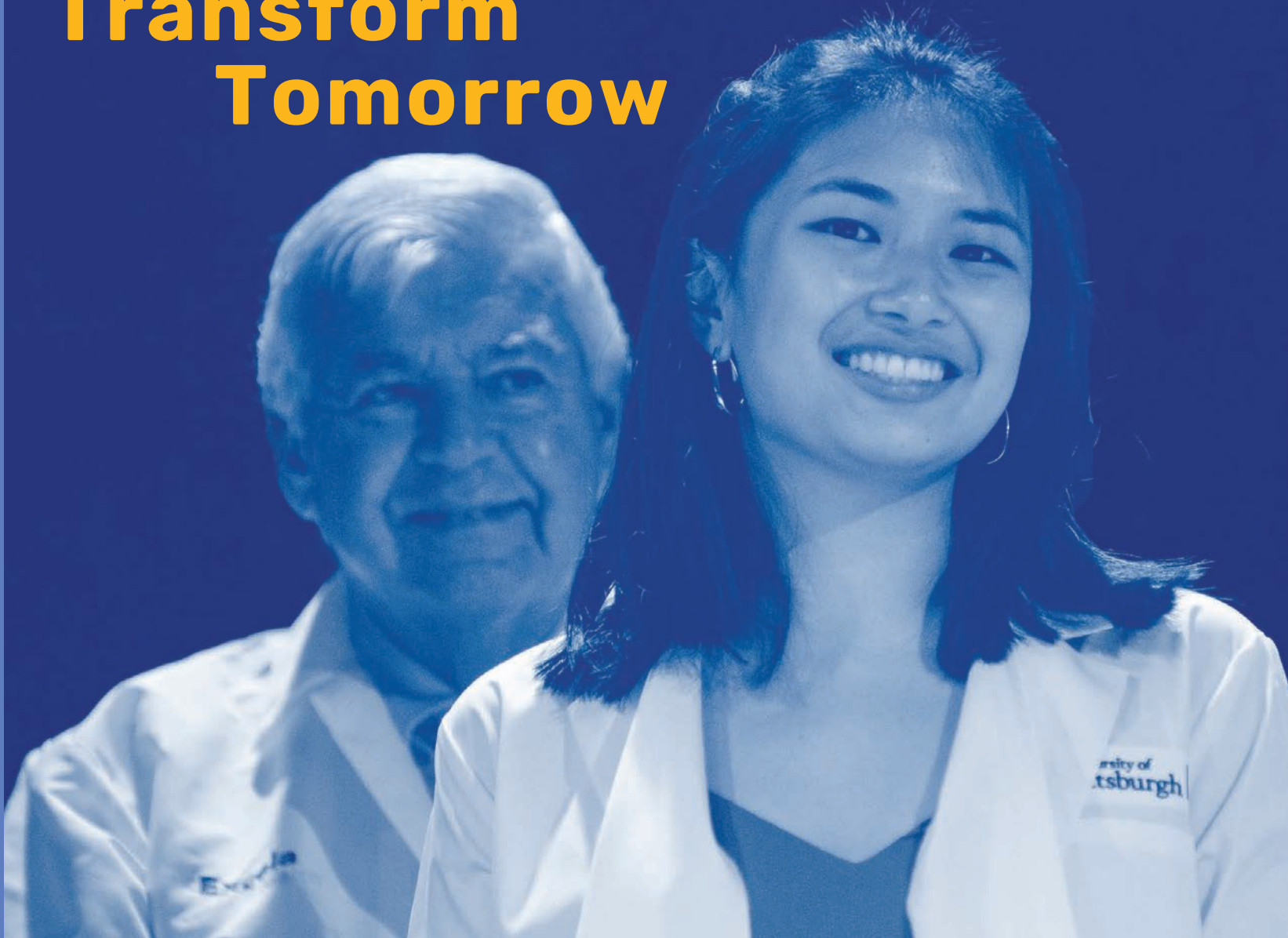
Coming into contact with something we fear can allow us to deal with the scary, on our terms, and when we're ready. By doing so, we can learn to understand our fears. Next time you feel scared, stop and ask: Why? What is it? What's happening right now? And, is my fear working for or against me in this moment?

Pushing ourselves in healthy ways like this can allow us to, ultimately, better connect with and understand different kinds of people and ideas.

Nonetheless, while approaching our fears can be a good thing, it's equally important for us to respect our fear responses. There's still power and growth in learning that you don't like something and that you don't want to deal with it. Some of us may never like insects, and that is OK. —Rachel Bittner

Thanks to Margee Kerr, a PhD sociologist and lecturer at the University of Pittsburgh, for helping us confront fear. Kerr has written books exploring fear and pain; and, believe it or not, she is a nationally recognized expert on haunted houses.

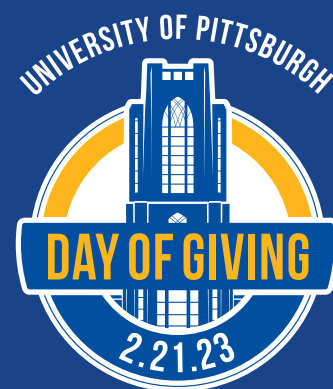
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Legends. Legacies.

Surgical giants
Mark Ravitch,
Thomas Starzl and
Henry Bahnson with
a colleague in China,
c. 1983.

After graduating from Pitt Med and finishing a surgical residency, Clyde “Ted” McAuley (MD ’79, Res ’85) served as a trauma surgeon and critical care physician in Texas at Wilford Hall, the Air Force medical center.

“I treated fighter pilots and had some challenging cases,” McAuley says. “I often only had a minute or two to solve the issue. I’d just ask myself what my teachers would do in that moment. My mentor had shown me that surgery wasn’t just a technical game; you have to be extremely knowledgeable in terms of pathophysiology to make the right decisions.”

McAuley’s mentor at Pitt was legendary surgeon Mark Ravitch. McAuley also admired and learned from Henry T. Bahnson, heart transplant pioneer and then chair of surgery; Thomas Starzl, liver transplant pioneer; and Bernard Fisher, who revolutionized breast cancer surgery and treatment.

After McAuley’s 15 years of service (both in the reserves and active duty), he and his wife, Trudi, were drawn back to Pittsburgh, a place they’d fallen in love with after both growing up in peripatetic military families. They bought a 137-acre farm outside of the city called Rich Hollow, where they cultivated an award-winning garden and raised Shetland sheep and Scottish Highland cattle. McAuley describes Trudi, who died soon after retirement, as “one of the most brilliant people you’d ever meet.”

He led various trauma and critical care units before retiring from Allegheny General Hospital. The McAuleys decided to honor Pitt by making unrestricted gifts to the School of Medicine, among other Pitt programs. “It’s a privilege to be fortunate enough to give back,” says McAuley.

“Pitt School of Medicine was excellent when I went there, but now it’s just superb.”

McAuley is proud to be part of Pitt’s surgical legacy—from being a trainee to a chief resident and trainer himself to supporting today’s surgical faculty, notably through the Andrew B. Peitzman Chair, now held by Jason Sperry. McAuley remembers Peitzman, who now holds Pitt’s Mark M. Ravitch Chair, as a resident and describes him as “absolutely outstanding—we all knew he was super sharp and would be going places.”

“I always told my residents that if they didn’t leave the program at a higher caliber than when they started, they weren’t doing their jobs,” McAuley says. “You have to always want to get better, and I think that desire is what sets Pitt apart.”



Trudi and Clyde McAuley

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