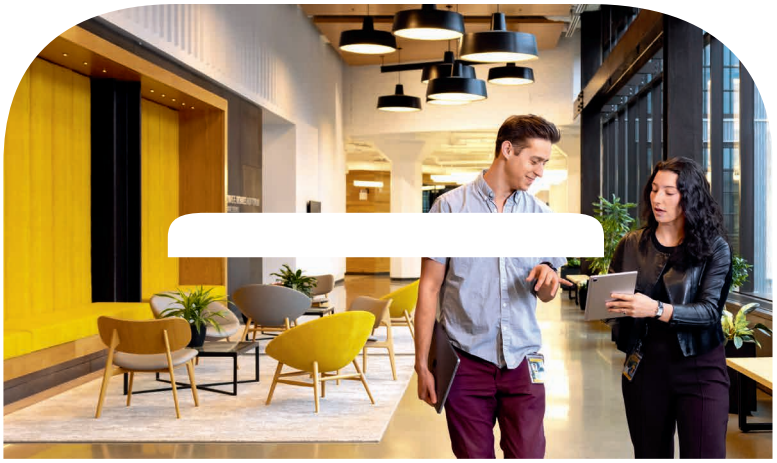
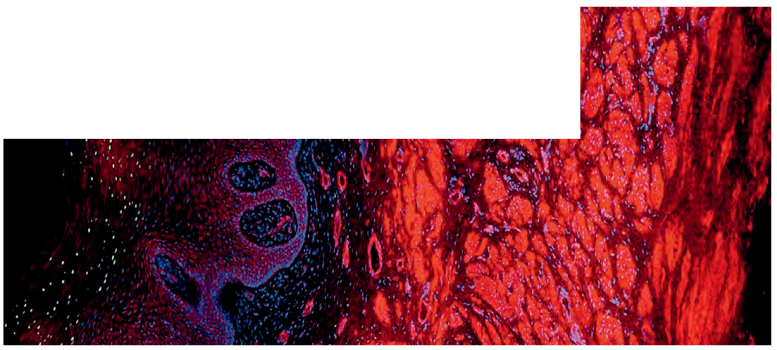




THE UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE
ANNUAL REPORT
2022

NEW CONSTRUCTION

These new Pitt and UPMC facilities promise to further enhance and catalyze the learning, research and patient care environment for our med school and larger health sciences community—and they are key to helping us build the academic medical center of the future.

West Wing of Alan Magee Scaife Hall

Location: Oakland / Opens: 2023

A stunning 101,000-square-foot addition will propel the School of Medicine into the future. Along with a new anatomy lab and 600-seat auditorium, the wing features plenty of places for students to learn, study, collaborate and decompress.

UPMC Mercy Pavilion

Location: Uptown / Opens: 2023

Designed with input from one of the world's few blind architects, Mercy's new vision and physical rehabilitation facility will house patient-centered care and innovation under one roof. A quarter of its 410,000 square feet is dedicated to research.

The Assembly

Location: Bloomfield / Opened: 2022

Once a Model T factory, this eight-story, 355,000-square-foot structure is now a hub for researchers crafting new treatments for cancer and other diseases. Although many of the treatments developed will be personalized for individual patients, the assembly-line spirit lives on—scientists here have their sights on moving bench breakthroughs to new therapies for patients.

UPMC Presbyterian Tower

Location: Oakland / Opens: 2026

Encompassing 900,000 square feet across 17 stories, the glass-encased tower rising above Fifth Avenue will incorporate 636 private patient rooms and 11 more operating rooms for UPMC's flagship hospital, translating to more opportunities for med students right in Oakland. A number of "acuity adaptable" rooms will make it easier to keep patients in place, rather than moving them to another unit as their conditions change.

BUILD

Throughout this city — on the hill where the School of Medicine sits and in neighborhoods to our east and west — the biomedical landscape is transforming.

A new wing for the medical school, enviable biomedical research and manufacturing hubs, modern patient-centered hospitals — projects years in the making are now taking shape. They are key to a larger effort that's more meaningful than brick and mortar or shining towers of glass. This is our time to build something extraordinary.

The structures rising across our campus and city will be integrated into, and integral to, a medical school that is becoming all the more interprofessional, proactive, entrepreneurial and in tune with what matters most. A school whose faculty, staff and students learn from the people and communities they serve as much as they do from benchwork or clinical rounds. And who know that they may need to step outside of convention and their own comfort zones to solve what seem to be intractable problems.

There are plenty of such problems in American health care: "inequitable," "out of reach," "unaffordable"… these are the modifiers commonly used for the ills we are tackling together. As I read about recent accomplishments of Pitt Med people in these pages, other words come to mind. Words like "ingenious," "indomitable" and "inspiring." I'm very proud of what Pitt Med people are accomplishing.

Yes, here in Pittsburgh, we are building buildings; at the same time, we're building understanding, relationships, solutions, momentum, the future. And, of course, we aren't doing this alone—but only through the generosity and support of people and organizations that share our vision. I hope you'll join us as we build an even more promising tomorrow.

Anantha Shekhar, MD, PhD

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

BUILD: UNDERSTANDING

LESSONS FROM COMMUNITY MEMBERS.

STUDENTS LEARN FROM THE COMMUNITY

Where and how we live, work, grow and age matters.

Med student **Shruthi Venkatesh** (Class of '28) knew 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 it wasn't until she talked to people in support groups that she realized how daunting and frustrating the process can be.

In 2021, as part of a new program where med students can elect to spend the summer after their first year learning from people in the community about a specific aspect of their health, Venkatesh got an earful. She spoke with members of the Pittsburgh MS Empowerment Support Group and the local chapter of the National MS Society. "Each insurance company is different in terms of approved assistive devices, and many do not offer coverage at all." Grants from national nonprofit organizations also can be difficult to access, they told her.

Venkatesh was one of two winners of the Jeannette South-Paul Award for Social Determinants of Health Enrichment in 2021.

The community interviews paired nicely with Venkatesh's Dean's Summer Research Project. For that, she studied the "exposome" in MS — that is, how the totality of environmental and other exposures over a lifetime can influence the health of someone with MS.

One woman from the support group told Venkatesh that she was able to purchase an expensive joystick-operated wheelchair and home modifications. But because her disability forced her to quit her job, she was worried she wouldn't be able to afford future out-of-pocket costs as her condition deteriorated. "It was an eye-opening experience," says Venkatesh, who is getting a dual MD/PhD degree in neuroscience.

Venkatesh also saw racial disparities. Many Black members of the support group told her they were denied workplace accommodations that employers often granted white workers.

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.

Danielle Gruen (Class of '24) also won a 2021 Jeannette South-Paul Award.

Gruen, who has a PhD in biogeochemistry from MIT and Woods Hole Oceanographic Institution, came to Pitt for her MD. She also came to explore how different people recover from trauma and prehospital care. "What determines who gets better?" she and her mentors wonder.

Her Social Determinants of Health Enrichment project examined the history of the Freedom House Ambulance Service. Started in 1967 and staffed by mostly Black medics, the service initially served Pittsburgh's predominantly Black Hill District community and went on to help shape modern EMS.

Gruen conducted interviews with community advisors, with founders of the Freedom House Ambulance Service and with leaders of organizations aimed at increasing diversity and representation in emergency medicine. John Moon, one of Freedom House's first medics, who with his colleagues would set a new standard for prehospital care, told her about prejudice he faced from hospital workers. The city shut down the service in 1975, initially replacing it with an all-white crew of paramedics.

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

Gruen also looked to the future, researching Freedom House 2.0, an initiative of UPMC that recruits, trains and hires first responders from economically disadvantaged communities.

Jeannette South-Paul Award winners

Shruthi Venkatesh

SDoH and Community Mentors:
Members of the Empowerment Support Group and Pennsylvania Keystone Chapter of the National MS Society

Dean's Summer Research Project Mentor:
Zongqi Xia, MD, PhD

WHEN SHE BECOMES A DOCTOR, VENKATESH SAYS, SHE WILL BE MORE SENSITIVE TO THE DAY-TO-DAY STRUGGLES OF THOSE LIVING WITH CHRONIC ILLNESSES.

Danielle Gruen

SDoH Mentor and Community Advisor:
Noble A-W Maseru, PhD, MPH and Philip Hallen, MA

Dean's Summer Research Project Mentors:
Jason Sperry, MD, MPH and Francis Guyette, MD, MPH

"IT'S REALLY IMPORTANT TO AMPLIFY" VOICES FROM THE COMMUNITY, SAYS GRUEN, WHO IS INTERESTED IN PRACTICING EMERGENCY MEDICINE.

ATLAS OF AGING CELLS

Molecular cartography

Most cells in the human body can divide and multiply to replace old cells and repair damaged tissue, but in response to certain stresses, cells can lose their ability to proliferate.

The rare cells that lose this ability are called senescent. They accumulate with age and probably contribute to cancer and age-related disorders, such as chronic lung disease, cardiovascular disease and dementia by pumping out signals that damage neighboring tissues.

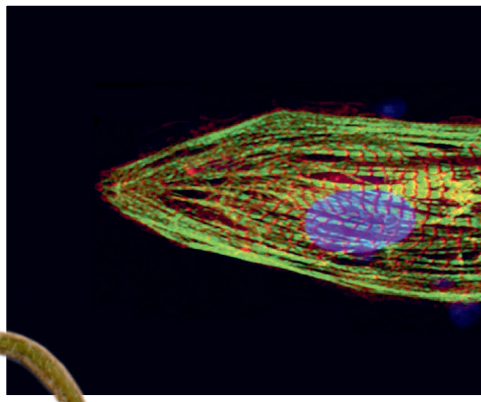
The molecular landscape of senescence has remained relatively uncharted. To address this knowledge gap, the National Institutes of Health established the Cellular Senescence Network (SenNet). The program will award $125 million to 16 teams to form the new SenNet Consortium — two of the projects are led by Pitt researchers, who will receive a combined $31 million throughout five years.

Just as Google Maps provides detailed information about every locale it stores, SenNet will provide data and analysis about the process of senescence for cells, tissues and organs down to the molecular scale. The information will be available for any scientist to access.

Toren Finkel, an MD, PhD, Distinguished Professor of Cardiology and director of the Aging Institute at Pitt and UPMC, is leading the TriState SenNet Tissue Mapping Center, one of the two projects led by Pitt. It will contribute to the atlas by developing maps of senescence in heart and lung cells.

The researchers will map gene expression and protein composition in senescent cells from human tissue slices and lab-grown mini organs and then characterize biomarkers of senescence. Finkel will collaborate with **Melanie Königshoff**, an MD, PhD, and **Oliver Eickelberg**, an MD, professors of medicine at Pitt.

"We don't know if cellular senescence is one thing or many things," says Finkel. "An analogy is cancer: Lung cancer, pancreatic cancer and lymphomas are all very different, even though we call them all cancer."

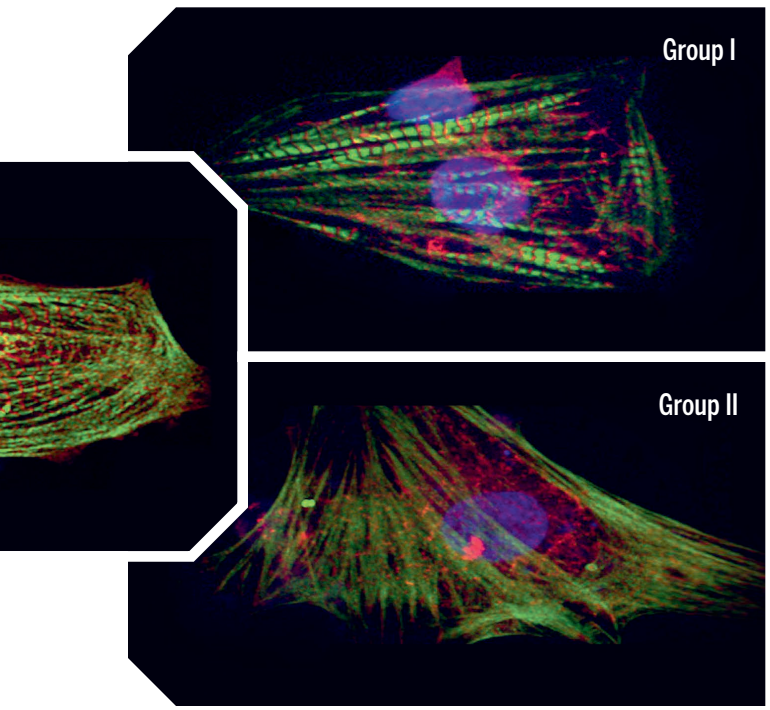


By modeling congenital heart failure in a petri dish, Cecilia Lo's group discovered how the left ventricle can become damaged. Here (groups I and II), we see how patient stem cells generate muscle with poor filament structure (green), which is worse in those with heart failure (group II). Doctors are hopeful the finding will improve the prospects and quality of life for children with the disease.

Senescence is readily apparent in plants. The accumulation of senescent cells in humans leads to age-related disorders and cancer.

Pathway found

In another discovery that advances scientists' knowledge about aging cells, the Aging Institute's **Toren Finkel** and **Jay Xiaojun Tan**, a PhD assistant professor of cell biology, identified the sequence of steps that cells take to fix leaks in their lysosomes. They call it the PITT Pathway.



PROBLEMATIC PUMPS

New hope for a dangerous childhood heart condition

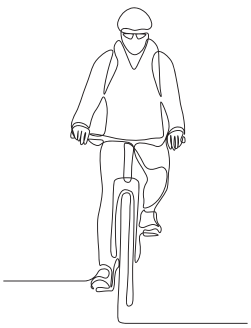
For the roughly 1,000 babies born in the United States each year with hypoplastic left heart syndrome (HLHS), the outlook is sobering: about a third don't survive to see their first birthdays. Born without a working left ventricle — the heart chamber responsible for pumping oxygenated blood to the rest of the body — many of these children struggle even after surgery that allows the right ventricle to take over the function.

And yet, others with the condition grow up to lead relatively normal lives. New research from the lab of **Cecilia Lo**, the F. Sargent Cheever Professor who chairs developmental biology, points to a culprit behind the drastically different outcomes: an energy shortage in cells.

Just as the heart pumps blood, healthy heart cells pulsate vigorously. But extensive damage to mitochondria — which provide energy to the cell — leads to languid pumping that could be fatal to a baby. Lo, a PhD, and her team found defective mitochondria in the cells of patients with both mild and severe HLHS, but the damage was more significant in the latter group.

For doctors at UPMC Children's Hospital of Pittsburgh, which already has some of the best HLHS outcomes in the country, the findings will help identify the highest-risk patients and move them to the top of heart transplant waiting lists. What's more, the researchers identified two drugs already on the market as potential treatments.

Jacqueline Kreutzer, an MD, who is the Peter and Ada Rossin Professor in Pediatric Cardiology at Pitt and codirector of the UPMC Children's Heart Institute, says, "Dr. Lo's groundbreaking research is critical to improve [HLHS patients'] quality of life and shift traditional care approaches to a new level."



PLACEBOS FOR PARKINSON'S

Tracking small miracles

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

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

Strick is Pitt's chair of neurobiology and scientific director of the Brain Institute. He and his collaborators believe they may know why paradoxical kinesia happens.

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

That circuit, left intact in Parkinson's, may be turned on when a person experiences strong emotions, like the joy of riding a bike, or stress, creating a sort of placebo for movement difficulties. "For some patients, placebos can be surprisingly effective in treating the movement disorders associated with the disease," says Strick, a PhD.

An inter-institutional team led by Strick is funded over three years by a $12 million Aligning Science Across Parkinson's (ASAP) initiative. ASAP's implementation partner, the Michael J. Fox Foundation for Parkinson's Research, issued the grant.

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

BUILD: RELATIONSHIPS

PARTNERS FOR BETTER HEALTH.

HIDDEN IN PLAIN SIGHT

Clinicians and researchers are learning from Western Pennsylvania Amish and Mennonites, and saving lives.

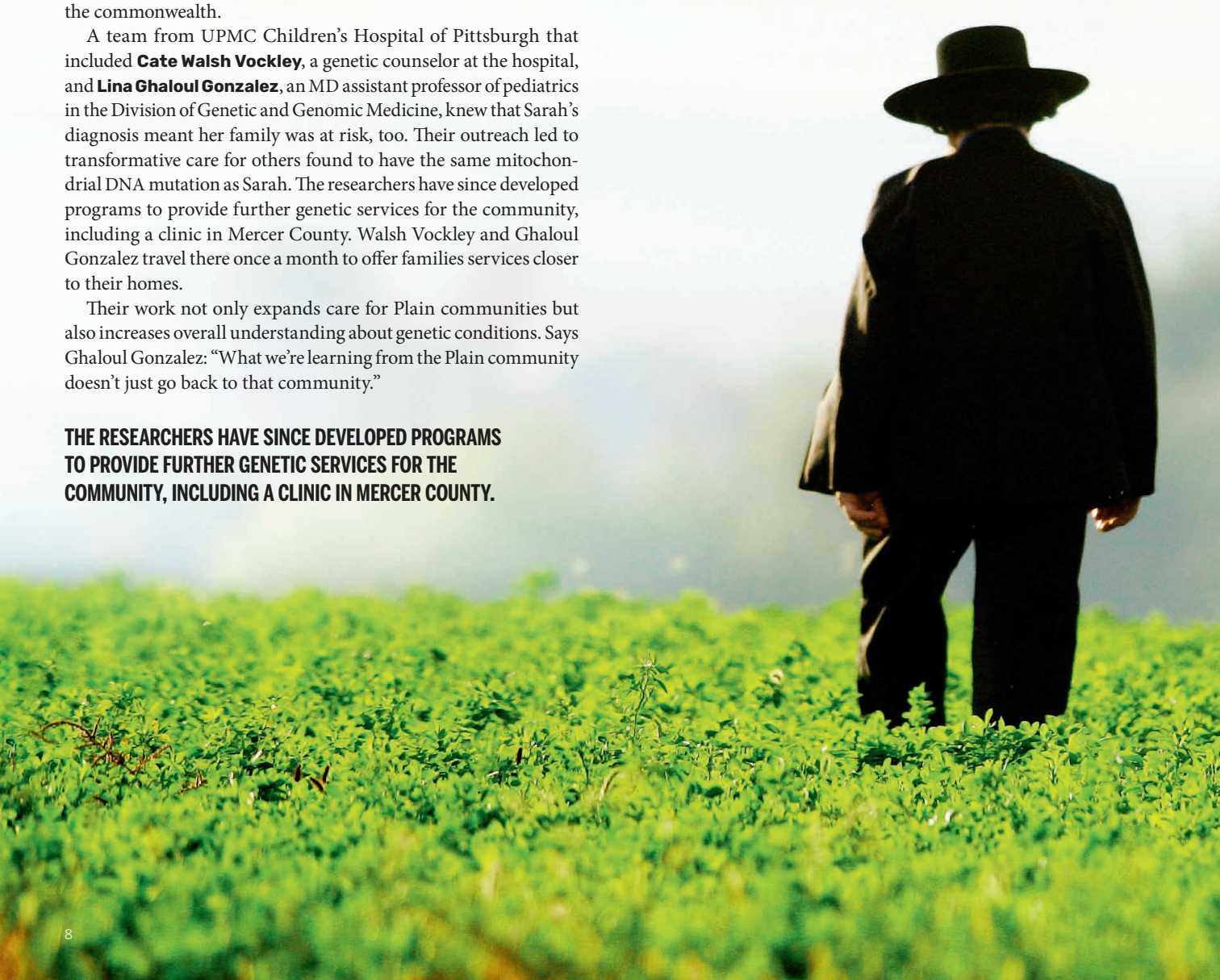
When doctors learned that 15-year-old Sarah (not her real name) had a mitochondrial genetic disorder, the diagnosis was more than a first step in alleviating her seizures, strokes and vision trouble. For Pitt researchers, it was also a chance to reach a community that's usually isolated from the medical world.

Sarah is Amish — one of Northwestern Pennsylvania's roughly 13,000 Plain people (the collective term for Amish and Mennonite communities), who eschew modern technology and largely avoid conventional health care. Centuries of living apart from the larger population has limited their genetic diversity, and the medical consequences have long remained understudied in this corner of the commonwealth.

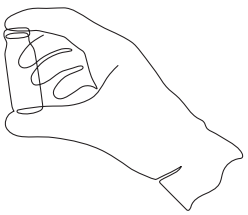
A team from UPMC Children's Hospital of Pittsburgh that included **Cate Walsh Vockley**, a genetic counselor at the hospital, and **Lina Ghaloul Gonzalez**, an MD assistant professor of pediatrics in the Division of Genetic and Genomic Medicine, knew that Sarah's diagnosis meant her family was at risk, too. Their outreach led to transformative care for others found to have the same mitochondrial DNA mutation as Sarah. The researchers have since developed programs to provide further genetic services for the community, including a clinic in Mercer County. Walsh Vockley and Ghaloul Gonzalez travel there once a month to offer families services closer to their homes.

Their work not only expands care for Plain communities but also increases overall understanding about genetic conditions. Says Ghaloul Gonzalez: "What we're learning from the Plain community doesn't just go back to that community."

THE RESEARCHERS HAVE SINCE DEVELOPED PROGRAMS TO PROVIDE FURTHER GENETIC SERVICES FOR THE COMMUNITY, INCLUDING A CLINIC IN MERCER COUNTY.



"THIS PROGRAM IS PROVIDING BIDWELL TRAINEES WITH A NEW CAREER PATH THAT CAN CHANGE THEIR PROFESSIONAL LIVES."
—STEVEN REIS



A FRESH START

This alliance launches careers and moves research forward.

In the midst of the recent labor shortage, organizers of clinical research have struggled to hire research assistants—positions critical to keeping important studies running. Pitt is bridging that gap by supporting a free workforce development program that is jumpstarting meaningful careers in the process.

The STricklAnd Research Training (START) program—part of the Bidwell Training Center's medical assistant training program—provides students the experience and education necessary to support clinical research at the University of Pittsburgh and across the country. It will also diversify Pitt's research workforce.

"The whole world is short-staffed right now," says **Laurel Yasko**, an MPPM, RN and operations executive director of Pitt's Clinical and Translational Science Institute (CTSI). "That includes the research staff we need to complete scientific discoveries."

CTSI director **Steven Reis**, an MD, and Yasko formed START in 2020 with **Bill Strickland**, former CEO of Manchester Bidwell Corporation and member of Pitt's Board of Trustees (who won a MacArthur Fellowship, aka a "genius" award, in 1996). The program's students—who are often seeking their second or third careers—are also invited to participate in a four-week externship, where they shadow researchers in a clinical setting. By fast-tracking the schooling and experience needed to become a clinical research assistant, START removes barriers that often prevent people from landing these positions.

"Partnering with Pitt's CTSI," says Strickland, "means that people who come our way to find meaningful careers now have a wider horizon of possibilities before them." Adds Reis: "It will also enhance science at Pitt by bringing diverse perspectives and lived experiences to our work."

BUILD: SYNERGY

IDEA TO IMPACT.

PLANS TO FURTHER BUILD OUT PITT'S COMMERCIALIZATION LANDSCAPE INCLUDE A VIBRANT BIOTECH ECOSYSTEM.

"THIS IS A REALLY UNIQUE OPPORTUNITY TO BE HERE IN PITTSBURGH AT THIS MOMENT, RIGHT WHILE BIOTECH IS JUST TAKING OFF."
—LEAH BYRNE

PARTNERSHIPS CRUCIAL TO CURES

Fertile ground for life sciences start-ups

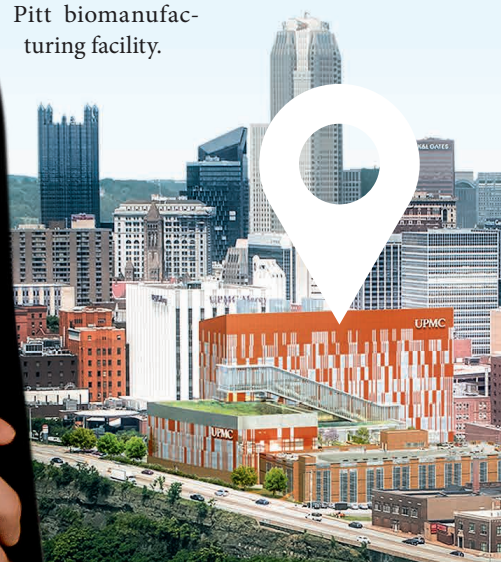
Pitt ophthalmology chair **José-Alain Sahel**, an MD and Distinguished Professor, receives emails every day from people around the world who ask if he has treatments that will restore their vision. In most cases, the answer is: Not yet. But in some cases, he's able to respond with a satisfying: Yes. Sahel's team is creating interventions for a wide range of diseases that cause vision impairment and blindness. He's launched a dozen companies to commercialize those therapies.

"I never thought I would form a company in my life," Sahel says. "But it just happens that if you want to deliver therapies to patients, it's the only way to make things happen."

Recently, along with **Leah Byrne**, a PhD assistant professor of ophthalmology, and **Paul Sieving** from the University of California, Davis (former director of the National Eye Institute), Sahel cofounded Avista Therapeutics. Byrne engineers vehicles—called AAVs (adeno-associated virus vectors)—to deliver genetic materials into eye cells for restoring vision. Avista is commercializing her invention of single-cell AAV engineering, nicknamed scAAVengr.

The scAAVengr method, which is still in preclinical development, investigates the performance of multiple AAVs in thousands of cells by tagging every AAV with a barcode and then evaluating whether each cell receives the needed genetic material from the AAV and expresses it. Byrne uses scAAVengr for vision research, but it can be adapted for broader use. "The platform could be applied to any tissue type, including the brain, heart, liver, kidney," she says.

The Avista team intends to collaborate on AAV manufacturing with a proposed Pitt biomanufacturing facility.



At this stage, Avista is funded primarily by UPMC Enterprises—this innovation arm of the health system plans to invest $1 billion in life sciences start-ups by 2024.

Pitt and UPMC's collaborative commercialization efforts extend back to the 1990s, says surgeon **Timothy Billiar**, associate senior vice chancellor for clinical academics at Pitt and executive vice president of UPMC who has chaired Pitt's Department of Surgery for 24 years. In the early days, the focus was on digital products. About five years ago, Pitt and UPMC created a more formal structure for also commercializing biological technologies. Several of the resulting companies have already made significant progress and have partnerships with, or been acquired by, pharmaceutical companies.

Avista is now partnering with Roche, notes **Rob Lin**, a PhD who is CEO of Avista, as well as a VP at UPMC Enterprises.

Moving breakthroughs and developments into the clinic so they can benefit patients is a top priority for Dean **Anantha Shekhar**, an MD, PhD, whose own discoveries for psychiatric disorders have been spun off into start-ups. He recently brought **Evan Facher**, a PhD and MBA who's Pitt's vice chancellor for innovation and entrepreneurship, onto his leadership team as associate dean for commercial translation in the School of Medicine. Among other responsibilities, Facher will help discern which med school innovations are truly ripe for commercialization. (In fiscal year 2022 alone, Pitt Med researchers filed 251 patent applications and launched 10 start-ups.)

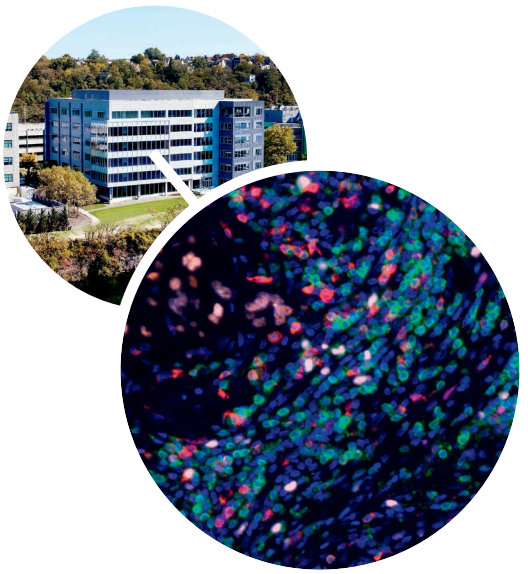
Facher's team welcomes new companies like Avista into a dynamic business environment through LifeX, an organization founded by Pitt that helps early stage life sciences companies in the region secure funding.

Shekhar's plans to further build out Pitt's commercialization landscape include a vibrant biotech ecosystem. He envisions Pittsburgh becoming a laboratory for disrupting existing biomanufacturing processes, which tend to be painfully slow and inefficient.

Pittsburgh's progress and ambition is exciting for clinicians like Sahel who are eager to respond with "yes" when patients ask: Do you have any treatments to help me?

Toward clarity

The new **UPMC Mercy Pavilion** will be a center for collaborative discovery and patient care. In addition to delivering the latest therapies, it will house a range of research specialists devoted to restoring vision and enhancing mobility.



BIGGER, BETTER

Space for innovation

Cancer researchers have been clamoring for resources to help them translate lab discoveries into clinical treatments at a faster pace. The new and improved Immunologic Monitoring and Cellular Products Laboratory (IMCPL) has gotten bigger—more space, equipment and manpower—to meet that need.

Its expansion from the UPMC Hillman Cancer Center campus in Shadyside to the Riviera building at the Pittsburgh Technology Center in South Oakland has created four times more manufacturing capacity for cell-based drugs for clinical trials. The facility, now at about 20,000 square feet, including 12 clean rooms, also offers more research and development space. And with IMCPL support, researchers and clinicians can track the success of their newly built therapies by monitoring immune function in treated patients. IMCPL also houses a Tissue Procurement Facility that banks blood and tissue for patients in clinical protocols.

For the past 30 years, faculty and staff from Pitt and UPMC Hillman Cancer Center have worked to make sure that the best operational structure and needed accreditations are in place for IMCPL to look and function like a commercial clinical lab. According to **Yen-Michael Hsu**, a physician scientist who joined Pitt as the IMCPL director in 2021, Hillman's expansion of the facility has been "visionary."

"We're actually one of the largest manufacturing cell therapy facilities within the walls of academia in the United States."

The tremendously upgraded IMCPL expects to one day partner with the proposed Pitt BioForge, a large biomanufacturing hub slated for Hazelwood.

MADE-TO-ORDER CARE

First Model Ts, now next-generation treatments

A century ago, Pittsburgh's East End became the site of 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, situated between Baum Boulevard, Morewood Avenue and Centre Avenue, has been transformed and expanded by the University of Pittsburgh for another kind of construction — creating what are often patient-specific treatments to combat cancer and other diseases.

Appropriately named The Assembly, the eight-story, $330 million structure is filling with researchers focused on four primary disciplines: immunology, cancer biology, women's cancers and computational biology.

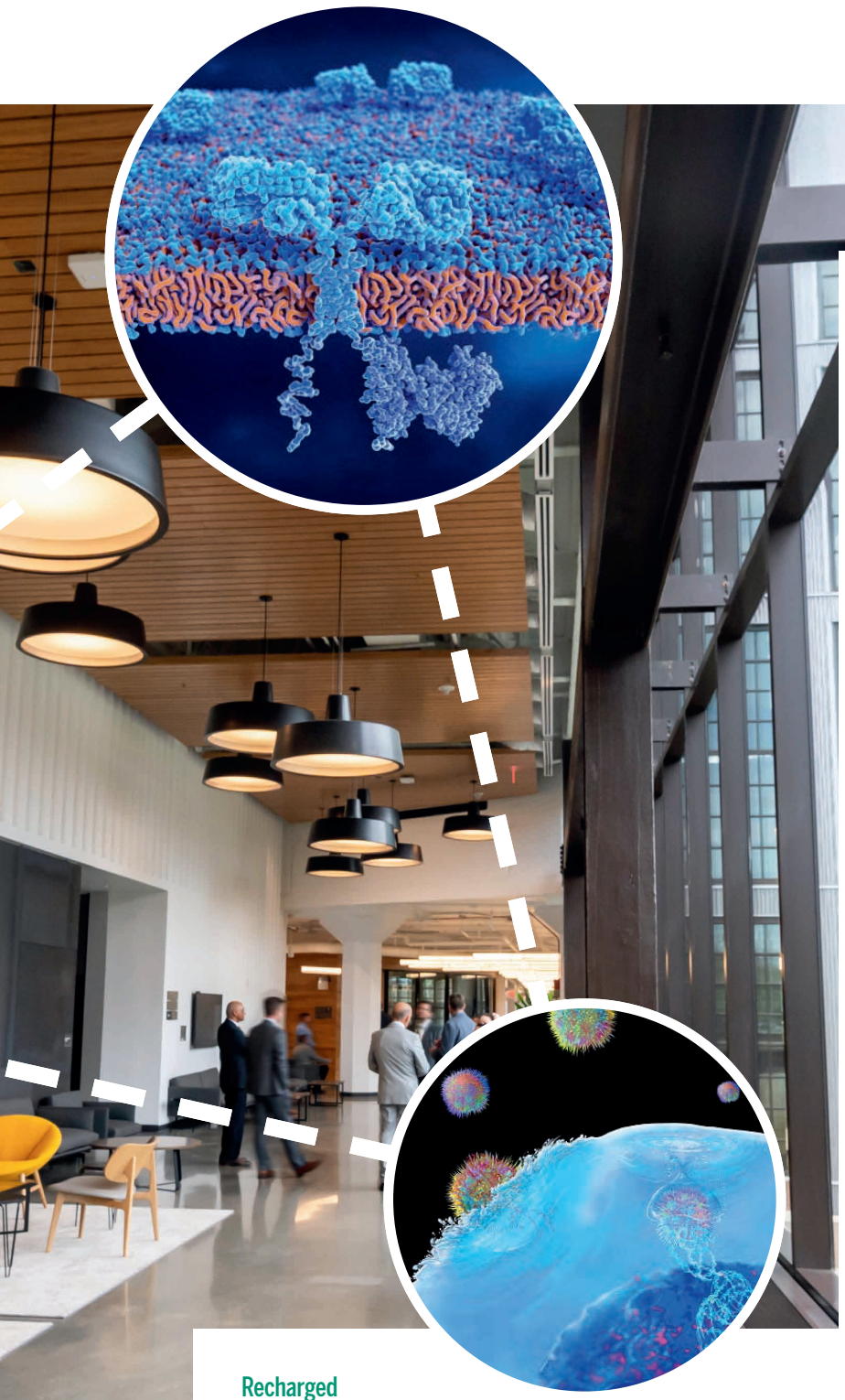
The former automobile and clothing factory sits just a block away from the flagship UPMC Hillman Cancer Center and expands the center's research space by 50%, says Robert Ferris, an MD, PhD, and Hillman director as well as the Hillman Professor of Oncology. "It's very fortuitous to find a place right nearby in such a crowded neighborhood," he says.

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, occupying the space where cranes used to lift raw materials off train cars and deposit them on platforms that fed into the different floors.

As impressive as the building is, the real magic of The Assembly is its plan to foster serendipity by creating spaces where researchers from different disciplines can meet to share coffee, food and ideas.

"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, PhD director of the Tumor Microenvironment Center, whose labs have moved to The Assembly. "The whole point of this beautiful, historic place is that it brings together a number of really important sets of researchers."

"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, Delgoffe says, The Assembly will probe the raw materials of cancer to develop treatments that can be driven off the lot.



THE ASSEMBLY, IN PITTSBURGH'S BLOOMFIELD NEIGHBORHOOD, WILL HOUSE MORE THAN 600 SCIENTISTS WORKING ON CANCER IMMUNOLOGY, COMPUTATIONAL BIOLOGY AND WOMEN'S CANCERS.

Next generation treatments

A Pitt/Hillman offshoot called **Novasenta** has finished a $40 million Series A financing round with the help of UPMC Enterprises, the health system's commercial and innovation arm. Novasenta comprehensively maps the tumor microenvironment with proprietary computational platforms to uncover new druggable targets for a range of cancers.

Tumor Microenvironment Center director **Greg Delgoffe**, Hillman director **Robert Ferris** and interim immunology chair **Dario Vignali** cofounded the firm in 2018. Novasenta is one of several startups focused on cancer care to come out of Pitt. And now, as Assembly labs get into gear, expect to see more such promising ventures.

Complex 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 is 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 "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."

Recharged

Many of the newest cancer treatments rely on the immune system rather than the blunter instruments of chemotherapy and radiation. One impressive example in recent years has been CAR T cell therapy, which has worked well against blood cancers like leukemia. But the therapy hasn't had much success in solid malignancies like liver and colorectal cancer. The microenvironment inside those tumors has very little oxygen and few nutrients, because those substances are consumed so quickly by the proliferating cancer cells. That impoverished landscape hinders the activity of the T cells, **Greg Delgoffe**, associate professor of immunology, 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.

BUILD:
NEW APPROACHES

TRANSFORMING CARE.

BETTER THAN EVER

A patient pathway to recovery through shared decision-making

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 patients and their doctors and surgeons, develops a pathway for optimizing patient health before surgery, reducing post-operative complications.

If the team deems surgery to be 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**, an MD and MBA, 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, directs 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 this new platform and coaching program, called Pip Care, to meet this critical need, says Mahajan.

"SURGERY CAN BE INCREDIBLY DIFFICULT ON A PATIENT'S BODY. IN SOME CASES, IT CAN HAVE THE SAME TOLL AS RUNNING A MARATHON."

—AMAN MAHAJAN

HOW DOES A TEAM CARE FOR THE PATIENT IN FRONT OF THEM?

The Pitt-developed PaLM app enables providers to search millions of national electronic health records for real-time guidance on diagnoses and treatments.

"In the literature, you will see things like 'Race didn't have any impact,'" says **Margaret Rosenzweig**, Pitt Distinguished Service Professor of Nursing who, with School of Medicine collaborators, studies disparities in breast cancer outcomes. "You look back at the inclusion criteria, and they are taking patients who don't have a lot of comorbidities, who are pretty healthy. And, is that the general population? Is that what you're trying to extrapolate? Probably not. There's always a tension between the rigor of needing to do the science correctly versus doing the science in a way that is meaningful and accessible."

John Maier, assistant professor of family medicine, concurs: "You often have a guideline that's built around a great study that was done at one or more institutions that was well-controlled. For a study like that, they only let in people with this and didn't let in people with that. So, in this specific group, we know that if you give them this medicine, the outcomes will be good. And that's great. But the odds—that the patient who is sitting in front of me is exactly like those patients—are really low."

Clinical trial participants often don't reflect the wide population that will be using the treatments, and it's hard to know which treatments will help each unique patient. In Pitt's Department of Family Medicine, a project is under way to take on this challenge.

With support from the American Board of Family Medicine Foundation and in collaboration with Pitt's Clinical and Translational Science Institute (CTSI), the department will sponsor a pilot study of the Pitt-developed Patients Like Mine (PaLM) app, which enables providers to search millions of national electronic health records for real-time guidance on diagnoses and treatments. They're able to tap quickly into information about people with similar overlapping health issues and backgrounds as the patient who just walked into the exam room.

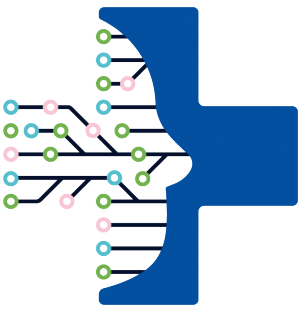
THE LONGER-TERM GOAL: REQUIRE ALL STUDENTS TO LEARN ABOUT ARTIFICIAL INTELLIGENCE TOOLS.

AI: IT'S FOR EVERY DOC

Just as they learn the intricacies of the Krebs cycle, new generations of Pitt Med docs will learn about AI and machine learning.

In response to a call from Dean **Anantha Shekhar** and in collaboration with **Shyam Visweswaran**, MD, PhD associate professor of biomedical Informatics, **John Maier**, an MD, PhD assistant professor of family medicine, introduced the entire Class of 2025 to these topics. The school's longer-term goal: Require all students to learn about these tools in enough depth to responsibly use them as they 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.



BUILD: MOMENTUM

TOP TALENT.

Honors for physician-scientists

Zachary Freyberg, an MD, PhD, and **Jason Sperry**, an MD, MPH, are among 95 newly inducted members of the American Society for Clinical Investigation (ASCI). ASCI, founded in 1908, is one of the most esteemed honor societies of physician-scientists. Membership recognizes a researcher's significant contributions, at a relatively young age, to the understanding of human disease.

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

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

AAAS fellows

Three Pitt faculty members with appointments in the School of Medicine have been named to the most recent class of American Association for the Advancement of Science (AAAS) fellows, a distinctive honor within the scientific community—and a historic one as well, dating to 1874. (Kay Brummond, PhD professor of chemistry, was also honored with a fellow designation.)

When **Sarah Gaffen**, a PhD, first opened her laboratory in 1999, the number of peer-reviewed research papers about IL-17—a family of pro-inflammatory substances secreted by our immune cells—could be counted on one hand. Now academic publications involving IL-17 number in the tens of thousands, and the AAAS has recognized Gaffen for her lab's 20-plus years of work on IL-17 in fungal immunity and autoimmunity.

Gaffen is the Gerald P. Rodnan Professor in the Department of Medicine.

Steven R. Little, a PhD, is internationally recognized for his research in pharmaceutics and biomimetic drug delivery systems. As a Distinguished Professor, the William Kepler Whiteford Professor and chair of chemical and petroleum engineering in the Swanson School of Engineering, as well as a faculty member in the bioengineering, immunology, ophthalmology and pharmaceutical sciences departments, he has developed numerous new drug formulations, including a controlled drug release that mimics the body's own mechanisms of healing and resolving inflammation. Little's research shows potential for treating glaucoma and gum disease and for avoiding organ rejection after transplantation.

Jerry Vockley, an MD, PhD, came to UPMC Children's Hospital of Pittsburgh in 2004 to lead the Division of Medical Genetics, now the Division of Genetics and Genomic Medicine. He is a professor of pediatrics and the Cleveland Family Professor in Pediatric Research at the School of Medicine and a professor of human genetics at the School of Public Health. Vockley directs an active research program on inherited disorders of energy and protein metabolism, focused on both understanding the genetic causes of these disorders and developing new treatments for them. His research has earned National Institutes of Health support continuously since the early 1990s. The diseases Vockley treats are all related to defective enzymes.

A quick look at our flourishing community of scholars.

STUDENTS 2021/2022 ACADEMIC YEAR

610

registered MD students

(including 334 women and 276 men; 231 are from Pennsylvania)

371

registered PhD students

(including those in the Medical Scientist Training Program)

and 148 MS students

2021/22 GRADUATES

87 MS, 52 PhD, 10 MD/PhD (MSTP) and 156 MD students

2022 Chancellor's Awardees

DISTINGUISHED RESEARCH AWARDS

David Brent, MD Distinguished Professor of Psychiatry

Anne-Ruxandra Carvunis, PhD associate professor of computational and systems biology

DISTINGUISHED TEACHING AWARDS

Peter Drain, PhD associate professor of cell biology

SPECIAL CHANCELLOR'S DISTINGUISHED SERVICE AWARD

The COVID-19 Medical Response Office

A new addition to the slate, this award was created to recognize the extraordinary service performed by the CMRO. At the time of the award, the office was led by John Williams, then-CMRO director and Henry L. Hillman Professor of Pediatric Immunology, and Elise Martin, associate director and assistant professor of medicine. The CMRO kept Pitt campuses informed and promoted a sense of community through exceptionally challenging times.

FACULTY

2,442 regular faculty members (as of November 2021)

1,778 volunteer faculty members

79 current members of the Academy of Master Educators

The Class of 2022 was the 16th med student class to complete the four-year longitudinal research project experience.

346 manuscripts published (81 submitted, 86 in preparation)

56 national or state research awards

397 presentations (at national or international conferences, 200 at regional or local meetings)

146 local research awards

BIG PRESENCE

31 departments

10 PhD programs

Nearly 70% of the University's overall research budget of $908 million is for research in the School of Medicine

HIGH MARKS

The School of Medicine again rates highly according to U.S. News & World Report.*

Best medical schools

PRIMARY CARE **10th**

RESEARCH **14th**

Best specialty programs

PSYCHIATRY **7th**

SURGERY **10th**

*Rankings released in spring 2022.

TRAINEES

620 postdoctoral associates and scholars (as of September 2021)

1,497 residents and 453 fellows (on the house staff of our clinical partner, UPMC, as of August 2021)

2022 PITT MED MEDICAL COHORT

Applications received: 8,393
Applicants interviewed: 931
Incoming class: 154 students

Trailblazers take on big challenges

Five University of Pittsburgh School of Medicine faculty members were singled out as doing "exceptionally novel and creative work" by the National Institutes of Health former director Francis S. Collins. They received prestigious NIH awards designed to support work that might struggle to be funded under traditional mechanisms but is recognized as being potentially transformative.

Christopher Donnelly, assistant professor of neurobiology, received a $9 million NIH Director's Transformative Research Award for a five-year multicenter effort to identify the molecular and genetic mechanisms that cause amyotrophic lateral sclerosis and a related disorder called frontotemporal lobar degeneration.

Jishnu Das, assistant professor of immunology, was given a $2.4 million New Innovator Award by the National Institute of Allergy and Infectious Diseases to create three-dimensional maps of protein interactions to study how genetic variation affects the mechanism by which infectious pathogens interact with their hosts.

Yi-Nan Gong, **Dwi Utami Kemaladewi** and **Guang Li** each received $2.4 million NIH Director's New Innovator Awards: Gong, assistant professor of immunology, wants to understand how some cells can begin to undergo a cell death process called necrosis, but eventually survive. Kemaladewi, assistant professor of pediatrics, is focusing on incorporating the element of genetic variation into the study of muscular dystrophy disease mechanisms and therapeutic development.

And Li, assistant professor of developmental biology, will develop heart "organoids" that mimic anatomical features to model and treat congenital heart defects, which occur in 1–2% of all live births.

Head-to-head comparison

The accumulation of tau protein—tangles of jumbled protein fibers clogging the brain's nerve cells—is an important marker of disease severity. But scientists wrestle with the technical limitations of detecting small amounts of tau proteins: Some tools that help identify tau tangles are more sensitive than others and can flag early Alzheimer's disease while another tool might erroneously show that the patient is free of early signs of the disease.

To suss this out, Pitt researchers led by **Tharick Pascoal**, assistant professor of psychiatry, were awarded more than $40 million from the National Institutes of Health.

To measure the amount of tau protein and detect its location in the brain, researchers use slightly radioactive compounds called tau tracers, which bind to tau in the brain and make it visible on a PET scanner. By comparing two frequently used tracers, the researchers hope to get a clear picture of the differences and similarities between the two and describe which is more appropriate for patients with subclinical Alzheimer's disease and which for patients with symptomatic Alzheimer's.

BY THE NUMBERS

The School of Medicine remains a top recipient of federal research funds. Total National Institutes of Health funding to the School of Medicine in fiscal year 2021 was **more than $476 million**.*

*This number does not include $44 million of NIH WARP Speed funding subawarded to the University of Pittsburgh as the Administrative Coordinating Center for ACTIV Integration of Host-targeting Therapies for COVID-19.

2021 NIH Funding Rankings for Pitt Med Departments:

PHYSICAL MEDICINE 1st	DERMATOLOGY 7th
PSYCHIATRY 1st	NEUROSCIENCES 7th
OTOLARYNGOLOGY 3rd	INTERNAL MEDICINE 8th
ANATOMY/CELL BIOLOGY 4th	PHARMACOLOGY 8th
SURGERY 5th	PATHOLOGY 10th

INVENTIVE

Getting promising discoveries into the clinic and into the homes of patients requires commercialization. In fiscal year 2022, research at the School of Medicine resulted in:

- 214 INVENTION DISCLOSURES
- 67 U.S. PATENTS ISSUED
- 251 U.S. PATENT APPLICATIONS FILED
- 58 PATENT COOPERATION TREATY APPLICATIONS FILED
- 149 DEALS (licenses, options, other agreements)
- 10 START-UPS

READ ALL OVER

Reporters rely on Pitt for expertise in health and medicine. In fiscal year 2021/22, Pitt health sciences faculty were featured at least **670 times** in two dozen media outlets considered top tier for science coverage, including the Associated Press, CNN, Nature, National Geographic, Newsweek, NPR, PBS NewsHour, Reuters, Science, Scientific American, The Atlantic, New York Times, Wall Street Journal, TIME, among others.

Toward vaccine confidence

Can we inspire vaccine confidence in high-risk rural communities?

Katherine Williams, an MD, MPH, is working with an interdisciplinary team across Pitt and UPMC Horizon/Shenango Valley and the Mercer County Health Equity team to address low rural vaccination rates in Pennsylvania.

Williams, research instructor in family medicine, was one of five inaugural Social Justice Fellows announced in February 2022. "I am honored to have the opportunity to add to the diligent work and strong foundation laid by the multidisciplinary Mercer County Health Equity team over the past year," says Williams.

As part of the fellowship, she worked to enhance vaccine messaging and motivation using principles developed by the Department of Family Medicine as well as human-centered design techniques.

The team is devoted to understanding the personal experiences of community members and health workers in the Mercer County area as they develop messaging and motivation strategies. Together, they are addressing the disparities of COVID-19 vaccination rates that are generally lower, and COVID-19 death rates that are consequently higher, in rural areas by empowering residents to advocate for COVID-19 vaccine administration.

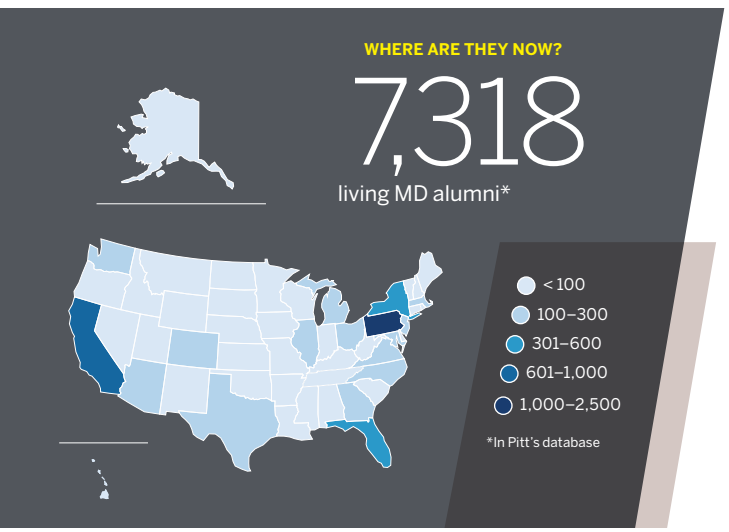
The Social Justice Fellowship spans all six health sciences schools.

Antibiotics v. ear tubes

Alejandro Hoberman, an MD, executive vice chair of pediatrics, received the 2022 Top 10 Clinical Research Achievement Award from the Clinical Research Forum, a nonprofit association of clinical research experts and thought leaders from the nation's leading academic health centers. **Hoberman, the Jack L. Paradise Professor of Pediatric Research, is the first person to receive this award from the Forum on two separate occasions.** Most recently, the award recognizes Hoberman and his research team for a May 2021 paper in the New England Journal of Medicine; their paper reported that, compared to the use of episodic oral antibiotics, they found no advantage to surgically placing ear tubes in a young child's ears to reduce the rate of recurrent ear infections over a two-year study period.

NCI continuing support for specialized programs at Hillman

The UPMC Hillman Cancer Center is the host institution for several Specialized Programs of Research Excellence (SPOREs) that have received additional rounds of funding from the National Cancer Institute. Among them, the Skin Cancer SPORE received a five-year grant in 2021 for nearly $11 million, and the Head and Neck Cancer SPORE received a five-year, roughly $11 million grant, says **Robert Ferris**, an MD, PhD, who serves as the Hillman Cancer Center director and Pitt's associate vice chancellor for cancer research.



HIGHLY CITED

The UK's Clarivate Institute for Scientific Information has determined that **20 researchers** with appointments in the School of Medicine are among the most highly cited researchers in the world.

Top educators

NEW DISTINGUISHED PROFESSORS

Toren Finkel, MD, PhD
Distinguished Professor of Medicine

Robert Friedlander, MD, MA
Distinguished Professor of Neurological Surgery

Alejandro Hoberman, MD
Distinguished Service Professor of Pediatrics

John Kellum, MD
Distinguished Professor of Critical Care Medicine

Thomas Kleyman, MD
Distinguished Professor of Medicine

Arthur S. Levine, MD
Distinguished University Professor of Health Sciences

Ann Thompson, MD, MCCM
Distinguished Service Professor of Critical Care Medicine

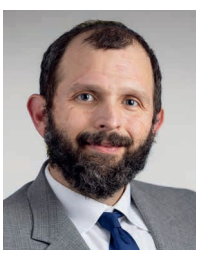
Dario Vignali, PhD
Distinguished Professor of Immunology

Donald Yealy, MD
Distinguished Professor of Emergency Medicine

New chairs named

MaCalus V. Hogan is now the David Silver Professor and chair of the Department of Orthopaedic Surgery at Pitt. At Pitt and 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 throughout the world. He is a prominent foot and ankle expert and consultant to a number of collegiate teams, as well as the Pittsburgh Ballet Theatre.

An MD and an MBA, he most recently served as professor of orthopaedic surgery at Pitt, with secondary appointments in bioengineering, clinical and translational science, and business, and as 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.



Heath D. Skinner, an MD, PhD, is professor and chair, Department of Radiation Oncology.

Skinner is working to advance UPMC Hillman Cancer Center's radiation oncology services nationally and enhancing access to care. In service to these goals, he is fully committed to a department that represents the community it serves by increasing diversity at all levels.

Board-certified in radiation oncology, Skinner completed a combined MD/PhD program at West Virginia University and a combined internship and residency in radiation oncology at the University of Texas MD Anderson Cancer Center. He has most recently served as an associate professor of radiation oncology at Pitt and as an investigator at UPMC Hillman Cancer Center. Skinner specializes in the study and treatment of head, neck and lung cancers. As a physician-scientist, he maintains an active translational research laboratory focused on identifying novel, clinically targetable biomarkers of resistance to radiation.

José P. Zevallos, an MD, MPH, has been appointed the Eugene N. Myers Professor and chair, Department of Otolaryngology.

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

At the School of Medicine and UPMC, Zevallos focuses on further elevating the Department of Otolaryngology's status as one of the premier research and clinical otolaryngology programs in the country by making continued investments in clinical and translational research, defining new paradigms of clinical care and enhancing the department's already excellent educational and training programs.

BUILD: TEAMS

INVESTING IN OUR PEOPLE.

Welcoming new talent

In 2020, the University of Pittsburgh established a cluster hire and retention initiative to build on its expertise regarding issues of equity and inclusion. The initiative called for the hire of 50 faculty members throughout four years, with the schools of the health sciences responsible for half of that total. **By November 2022, the University had recruited 44 new faculty as part of this effort, with 36 in the health sciences.**

These scholars are conducting research, educating students and engaging in service designed to eliminate health disparities and improve well-being in the Pittsburgh region, nationally and around the world. And across a range of fields, they are sparking inspiration as role models and as individuals who offer new perspectives to our teams

"WHERE YOUR MIND GOES, THE BODY USUALLY FOLLOWS—BUT NOT THE OTHER WAY AROUND."
—YETSA TUAKLI-WOSORNU

LEAPS FORWARD

Yetsa Tuakli-Wosornu's holistic approach to injury and life

As a long jumper for the Ghana National Team and 2016 Olympic hopeful, **Yetsa A. Tuakli-Wosornu** knows about high-level competition. As a physician with an MD from Harvard and an MPH from Johns Hopkins, she knows musculoskeletal medicine and wellness. Adding her athletic and wellness expertise to a sports-focused city like Pittsburgh was a perfect match.

Tuakli-Wosornu's recruitment from Yale School of Public Health to Pitt was supported by the University's Race and Social Determinants of Equity, Health and Well-Being Cluster Hire Initiative. The Pitt associate professor of physical medicine and rehabilitation specializes in interventional spine and sports medicine treatments, incorporating "holistic mind-body development" and therapies. Her practice at UPMC serves a wide range of clients.

In Pittsburgh, she's found other opportunities to channel her uncommon skill set. Here, she quickly connected with **Ryan Shazier**, the retired Steelers linebacker who started the Ryan Shazier Fund for Spinal Rehabilitation after his own experience recovering from a spinal injury, and **Yardon Brantley**, fitness entrepreneur and former member of the Philadelphia Eagles. The three partnered to create Pitt-affiliated 3D Sports Rx PGH so they could offer inclusive, sports-based rehabilitation for people with spinal injuries. Even in Pittsburgh's established adaptive-sports community, 3D Sports Rx PGH is a program unlike any other.

"After meeting and talking with Ryan, what stood out to me was the critical importance of his family, immediate and extended, every step of the way through his spinal-injury recovery period," says Tuakli-Wosornu. "Spinal injuries are family-unit injuries. Everybody has to adjust to a new reality, so it's important to address with a community intervention. We wanted to scale Ryan's recovery model—the two pillars of sports and family—for other spinally injured patients."

In Brantley, Tuakli-Wosornu found another essential part of 3D Sports Rx PGH: He is president of SHAPE Training, a fitness facility focused on coach-led programming. Now, with the support of family, people recovering from spinal injuries through 3D Sports will benefit from SHAPE's expertise. 3D Sports Rx PGH is in its pilot phase and has begun enrolling participants.

From their own experiences in competition, Tuakli-Wosornu, Shazier and Brantley understand that dead lifts and shuttle sprints only get you so far. That's why mental training is the vital third component of 3D Sports Rx PGH. "Where your mind goes, the body usually follows — but not the other way around," says Tuakli-Wosornu. "When working with my patients, I'm always bringing them to mental balance and wellness, not only in those moments: I'm also challenging them in their day-to-day life to train their mental skills so that they can better respond to some of the stressors from their injury or just regular life."

Tuakli-Wosornu is also the founding director of Sports Equity Lab, an independent research lab with the dual goals of eliminating inequities in sports while also using sports to eliminate inequities in society. It's yet another way Tuakli-Wosornu believes people can break down barriers and accomplish the unexpected.

Ascending stars

Pitt health sciences has recognized especially notable work of junior faculty for several years with its Senior Vice Chancellor's Research Seminars. Now, to honor highly productive and creative mid-career faculty, the health sciences has created the Ascending Stars program. The inaugural awards went to four associate professors, each of whom received $25,000 in research support and delivered a lecture highlighting their work.

The winners were **Susanne Ahmari**, MD, PhD associate professor of psychiatry; **Greg Delgoffe**, PhD director of the Tumor Microenvironment Center; and **Matthew Neal**, an MD and the Roberta G. Simmons Associate Professor of Surgery—all in the School of Medicine. **Ying Ding**, PhD associate professor of biostatistics, in the School of Public Health was also recognized.

"This award is just one small but tangible way in which we can recognize the excellence of faculty members whose career trajectories continue to offer great promise and to encourage them to continue that upward momentum, while also serving as role models and mentors to their junior colleagues," says Dean **Anantha Shekhar**.

From top: Ahmari, Delgoffe, Neal, Ding

"MID-CAREER FACULTY OFTEN HAVE LITTLE TIME TO FOCUS ON THEIR OWN CAREER GROWTH."
—ESA DAVIS

TRANSFORM will fill a void felt across the nation.

A LEADERSHIP PATH

Faculty from underrepresented minorities (URM) make up a very small percentage of the senior academic faculty in biomedical sciences in the United States, but a new Pitt-led program aims to change that. Mid-career URM faculty members will have an opportunity to refocus their career development with the help of a new program called TRANSFORM. Created specifically for faculty at the associate professor level, the program is designed to help promote these faculty into leadership positions at a pivotal time in their careers—and when attrition of URM faculty is most likely.

"The idea is to fill a void," says **Esa Davis**, an MD, MPH, who is the program director of the National Institute of General Medical Sciences–funded TRANSFORM. "There are a lot of programs for early stage investigators and for senior faculty, but there's not much in between."

Mid-career faculty often have little time to focus on their own career growth, says Davis, who's also an associate professor of medicine. They're mentoring, teaching, serving on different committees and pursuing their own work, and their own career development gets stuck as a result.

Davis' coprincipal investigator is Pitt's **Audrey Murrell**, a PhD professor of business administration, psychology and public and international affairs. Pitt is one of the TRANSFORM program's five sponsoring sites.

BUILD: SOLUTIONS

DIGGING DEEPER TO FIND ANSWERS.

VAGINAL WELLNESS VALUED

Pitt people are behind significant initiatives in women's health.

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

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

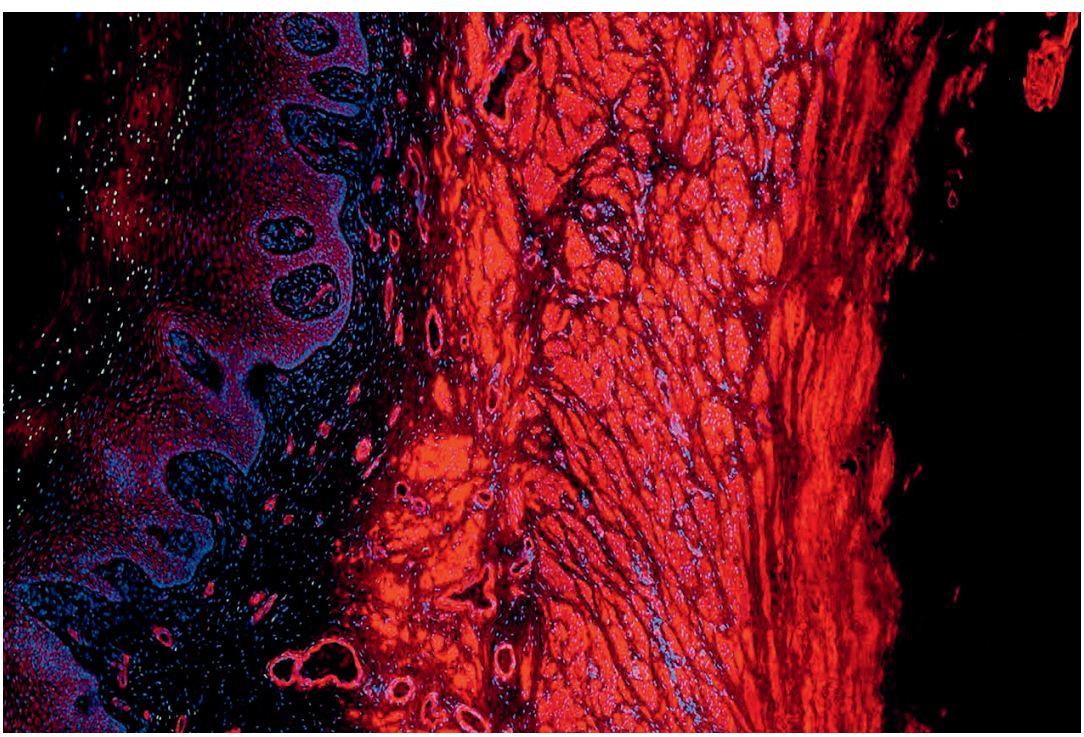
Orwig, a PhD, and Moalli, an MD, PhD, are both members of the Magee-Womens Research Institute. Caroline Gargett, a PhD from Monash University in Australia, has joined them in their studies of vaginal stem cell populations as a possible basis for regenerative medicine solutions. **Krystyna Rytel**, an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

> **"THE VAGINA HAS TREMENDOUS REGENERATIVE POTENTIAL. IF WE CAN BIOFABRICATE KIDNEYS AND LIVERS, WE MOST CERTAINLY CAN MAKE VAGINAS."**
> —PAMELA MOALLI

The group will use the prize funds to develop new biomaterials for repairing tissue loss in women with compromised vaginal structure and function. They are hopeful that developing a better understanding of vaginal stem cells and their "niches" will be key. If successful, the work could have sizeable therapeutic potential, helping women and girls with congenital defects, repairing damage from cancer treatment, restoring loss of function from aging and perhaps contributing to gender-affirming procedures.

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

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



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

"AS DIFFICULT AS THEY WERE TO ACCEPT, THE VOICE RESULTS COMPLETELY CHANGED OUR APPROACH. THEY COMPELLED US TO DO THINGS DIFFERENTLY AND UNDERSTAND THE COMMUNITIES WE WERE WORKING WITH MUCH BETTER."
—SHARON HILLIER

HIV PREVENTION: ASK THE EXPERTS—THE PATIENTS

Protection from HIV, and a reckoning

The Microbicide Trials Network (MTN), which conducted 43 HIV prevention studies involving more than 18,000 participants on four continents, wrapped up in 2021 after 15 years of funding from the National Institute of Allergy and Infectious Diseases (NIAID). Microbicides are vaginal and rectal products designed to help prevent the sexual transmission of HIV.

This huge effort, led by **Sharon Hillier**, a PhD and vice chair of obstetrics, gynecology and reproductive sciences at Pitt, contributed to regulatory approval of the first biomedical HIV prevention method developed specifically for women — a slow-release dapivirine vaginal ring that the user inserts monthly.

The ring, which reduces the risk of acquiring HIV by about half, was recommended by WHO in 2021 and is now approved for use in several African countries, based in part on data from eight MTN studies.

The ring is a crowning achievement for the MTN. Its legacy also includes the international network's first flagship trial, called VOICE — for very different reasons.

VOICE had a noble goal: Offer women methods for HIV prevention — a daily pill or a daily gel — that they could control, unlike, say, a condom. But when the results of VOICE came out in 2013, researchers were stunned. None of the products the study tested were found to be effective. Most of VOICE's participants had not used the products every day as directed, despite indicating otherwise throughout the four-year study. As it turned out, they weren't interested in products they had to fuss with every day. Why didn't they speak up sooner? They didn't want to disappoint the researchers.

The VOICE results made it clear that daily methods were not going to work for women like those who took part in the study, which was conducted in three African countries.

Other options were needed; so researchers set their sights on the promise of a vaginal ring to be inserted monthly that MTN's second flagship study, ASPIRE, had already begun evaluating.

In ASPIRE and other studies moving forward, researchers began monitoring product use during the study so that any problems could be addressed in real time; they also looked to better understand the lives and social contexts of study participants and the factors that might be influencing decisions about whether or not to use a product.

VOICE was also a wake-up call for the entire field, notes Diane Rausch, a PhD and director of the Office on AIDS at the National Institute of Mental Health (NIMH). After VOICE, data that came from MTN about acceptability, usability, attitudes and behaviors related to products for HIV prevention made a huge difference in the field, she notes. NIMH and NIAID cofunded the MTN, as did the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

"As difficult as they were to accept, the VOICE results completely changed our approach," says Hillier. "They compelled us to do things differently and understand the communities we were working with much better."

Hillier now leads MATRIX, a five-year $125 million cooperative agreement funded in 2021 by the U.S. Agency for International Development focused on early research and development of HIV prevention products for women.

"The study organizers willl consider what women want in an HIV prevention product before the first clinical trial is even conducted and integrate end-user feedback all along the way," says Hillier.

Pitt key to vetting COVID-19 therapies

A New England Journal of Medicine paper from August 2021 describes how therapy with the anticoagulant heparin in moderately, but not in critically, ill COVID-19 patients increased the likelihood of survival to discharge without organ support compared to usual care. (Usual care was thromboprophylaxis, which involves medication as well as mechanical methods for improving blood flow in the legs.)

"The paper was practice changing and resulted in updated clinical guidelines from the NIH" and professional societies, notes **Matthew Neal**, an MD and Roberta G. Simmons Associate Professor of Surgery, who cochaired the inpatient study of what's known as the ACTIV-4 Antithrombotics trial.

Like other international trial networks in which Pitt plays a major role (including one called REMAP-CAP, which also contributed findings to the study), the ACTIV trials are adaptive trial networks, meaning they learn and hone recommendations as they progress.

As part of Operation Warp Speed, the NIH Foundation funded a series of ACTIV-4 Antithrombotics trials to quickly assess the use of blood thinners in treating COVID-19. In addition to Neal, other Pitt people have taken major roles in these trials, notably **Frank Sciurba**, a professor of medicine and education (outpatient study), **Alison Morris**, UPMC Professor of Translational Pulmonary and Critical Care Medicine (post-discharge study), and **Maria Mori Brooks**, professor of epidemiology and biostatistics, who codirects Pitt's Epidemiology Data Center. Epidemiologist **Steve Wisniewski** led coordination of the entire ACTIV-4 Antithrombotics trial series.

For the wider Warp Speed effort, Pitt served as the Administrative Coordinating Center for ACTIV. That came with $99 million in federal support in 2020 and $44 million in 2021.

REGENERATING THE LIVER, REDUCING TRANSPLANTS

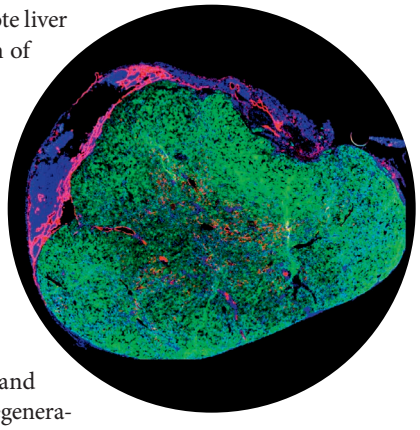
What if a drug could help the liver regenerate and eliminate the need for many transplants?

Paul Monga, professor of pathology and medicine and Pittsburgh Liver Research Center director, has found a new drug that has shown success, in mice, in regenerating and repairing the liver after severe injury or partial surgical removal.

Working with proteins known to play an important role in liver function and regeneration, Monga and his team were able to identify which ones control regeneration, where they are found in the liver and which are responsible for the divide-and-conquer strategy liver cells have that determines the functions they perform in the liver's three sections or "zones."

The drug, an antibody called FL6.13, shares similar functions with the proteins Monga and his team focused on, including activating liver regeneration. The antibody also was tested on mice with liver damage from toxic overdoses of Tylenol. The result? Enhanced repair of liver tissue.

"My team and I believe that improving the liver's ability to repair itself could help circumvent the need for transplantation," Monga said in an article he wrote for The Conversation. "Further study of drugs that promote liver regeneration may help curb the burden of liver disease worldwide."



Extra liver

You might say that **Eric Lagasse** is in the body-building business; he helps bodies build miniature livers. For more than a decade, Lagasse has been researching the regeneration of organ tissue.

The associate professor of pathology and member of the McGowan Institute for Regenerative Medicine explores cell-based therapies. Through this research with his team, he discovered that liver cells, when introduced into the lymph node, will grow miniature livers and restore the original organ's functions. In effect, the lymph nodes become bioreactors. "This novel approach opens the possibility of extending the lives of people suffering from end-stage organ failure, bridging them to a potential transplant or even eliminating their need for an organ transplant," he says. Now Lagasse is off and running with his startup, LyGenesis. The firm has raised more than $18 million and received FDA clearance to begin a phase 2a trial of its bioreactor therapy for patients with end-stage liver disease.

BUILD: LEGACIES

GIFTS THAT EMPOWER US TO REACH HIGHER.

LEGACIES

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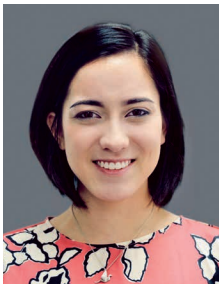
SPOTLIGHT

AN ALLY AND ADVOCATE


Dena Hofkosh


Elyse Mark

Since Dena Hofkosh came out in her 40s, a lot has changed for LGBTQ+ people in medical fields — and she couldn't be happier about it.

"There seems to be more space for those who are far braver than I was — those whose identities cannot or will not be hidden, those who choose to stand up, speak and be seen for who they are," Hofkosh, an MD, MEd and longtime professor of pediatrics, said at a recent benefit for a fund named in her honor. Created by Pitt's Medical Student Pride Alliance (MSPA) and the School of Medicine, the fund supports LGBTQ+ medical students at Pitt.

Although it took her decades to share her true self with colleagues, Hofkosh more than made up for lost time. She championed queer communities through many leadership positions, most recently as vice chair for faculty development in the Department of Pediatrics. Working with colleagues, she created a support network that became Pitt and UPMC's PRIDE Health, an affinity group for LGBTQ+ faculty, staff, students, residents, fellows and providers.

"I have found that acknowledging my sexuality and using my authentic voice in allyship and advocacy have brought me such a sense of meaning, joy and peace," she said at the fundraiser. Hofkosh retired in 2021 after nearly 40 years as a faculty member.

There's still work to be done, and the new fund supports those who are taking on the challenge. The awards will be based on students' financial need and their service to diverse communities at the School of Medicine. The first recipient, Elyse Mark (Class of '24), was a student coordinator of the MSPA. She intends to specialize in psychiatry, with hopes of improving the quality of care for LGBTQ+ patients.

"I plan to take a research year before finishing medical school so I can learn more about clinical practice at Pitt. This award will help support some of my financial needs during that time, allowing me to focus more on learning," Mark says.

The fund now totals more than $135,000, every dollar of which will directly benefit students.

"I'm very happy to have my name associated with this fund, because it's really all about supporting the students," Hofkosh says. "I feel very honored."

SPOTLIGHT

CRITICAL INTERVENTIONS

Ann Thompson

From her adolescence during the civil rights movement to her current role as vice dean of the School of Medicine, Ann Thompson has noticed an uncomfortable truth: Very little of her education in social justice came from formal schooling.

"The more stories I hear and the more I read, the more that I realize what I didn't learn in high school, college, medical school," Thompson says, "and the more I feel it needs to be incorporated into everyone's learning."

Thompson, an MD, MCCM professor of critical care medicine and pediatrics, has been highly influential her field. In the 1980s, she was involved in early uses of extracorporeal life support in pediatrics. As chief of pediatric critical care at UPMC Children's Hospital of Pittsburgh from 1981 to 2009, she presided over growing clinical and fellowship programs and helped to define the entire field along the way.

Later in her career, Thompson has focused more and more on addressing barriers to success for underrepresented communities in academic medicine. Her appointment as vice dean of Pitt Med in 2014 gave her a new platform to do something about it.

Thompson helped establish Toast to Diversity, an annual celebration that brings together women and underrepresented communities at the school; the event has spurred new connections and research collaborations. She also has continually advocated for the school's curriculum to include more about health disparities and social determinants of health; she herself is a certified unconscious bias educator.

Confronting such issues, she says, is integral to the health of the country — which she compares to a patient on life support: "I've come to see racism and social injustice as the chronic critical illness of America."

Thompson has announced she will step down from her vice dean role in fall 2023; her social justice legacy will endure. She recently endowed a new professorship for social justice in medicine.

The holder of what eventually will be known as the Ann E. Thompson, MD Professorship for Social Justice in Medicine will through research and teaching explore what it takes to equitably serve those whom the medical system has left behind. But the recipient will also be expected to put findings into action, collaborating with community members to establish — and maintain — new services in underserved areas. Earning their trust will be key.

Thompson would like to see more opportunities for her colleagues to identify "not just the challenges but the best ways of working with communities — and establish services that people in the communities want.

"If we could have more people focused on this work and bring them together," she says, "we would get farther faster."

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SPOTLIGHT

ON THEIR FEET

Emerson and Mary Farley

Mary and William Markle

Emerson Farley and William Markle have a lot in common. Both their wives, named Mary, were Pitt-trained nurses who helped put their husbands through medical school. Both families recently established major gifts supporting experiences for Pitt Med students abroad.

When the retired internist "missed being a doctor" in the early 2000s, Farley, who graduated from Pitt Med in '64, traveled to Kenya to help fund the initial development of an intensive care unit at a hospital there. His daughter Marcie, an ICU nurse, also stepped in to help. "The next year we went back, and they had set up some outpatient clinics," Farley says. "It was amazing to watch" the growth over the years.

"We thought, 'We ought to start something at Pitt to fund more training trips for students like this.'"

And they did. The Emerson D. Farley Jr., MD, and Mary S. Farley Medical Student International Travel Fund will allow fourth-year med students to train in resource-poor locations abroad. For the next 10 years, the fund will support students taking part in a month-long intensive learning experience.

"I think [med school curricula] should expose students to health care delivery systems outside of North America," Farley says. "It's a great challenge to think on your feet."

There are other mediating challenges, however.

Funding their own experiences abroad is a tall order for most med students. William Markle, an MD, and Mary Markle helped rectify this when they started a fund supporting international study opportunities for Pitt Med students. The Markles were inspired in part by the Farleys' generosity and in part by their own experiences volunteering in India, Honduras, Indonesia, Haiti and elsewhere. "It's a calling," he says.

During his time on the family medicine faculty from 2004–2019, Markle noticed "interest in international experiences grew. Some students felt they couldn't do it because of financials. I always said, 'The money will turn up somewhere.'" He started a global health journal club and an international health elective track.

Like Farley, Markle devoted his career to serving the underserved, abroad and locally. For many years Markle was in solo practice in a rural Virginia county of about 8,000 people. He helped start the 9th Street Free Clinic in McKeesport.

Another Farley fund supports Pitt Med students with a preference for those from West Virginia, like the Farleys themselves.

"We want to give early exposure to providers in training to be clinicians, not technicians," says Farley. "We want to train students to look at the whole environment, the whole community, to help people, without asking for anything in return."

SPOTLIGHT

RESETTING THE CLOCK

Stephen Chan and Colleen McClung

It's going to be a long flight that involves a couple of connections. But if you are prone to jet lag, your problems go beyond working your way through crowded airports and trying to find space for your carry-on.

Jet lag is troublesome enough that it has its own medical name: desynchronosis. People who experience it can struggle with extreme fatigue and have trouble concentrating, which is especially unwelcome for the businessperson stepping off a plane and into a meeting. And those with certain underlying conditions may be putting themselves at risk.

Circadian rhythms influence a lot more than how awake we are throughout the day. They are key to health. Disturbing the circadian cycle can disturb any number of regulating processes — blood pressure, appetite, heart rate and more; and it can contribute to a host of diseases.

Pitt research on the circadian clock will be supported by two generous grants from WoodNext Foundation, the philanthropy of tech innovator and Roku CEO/founder Anthony Wood and his wife, Susan. A grant of more than $2.8 million will help researchers explore the genetic reason why people get jet lag and use that knowledge to attempt to create a medication or other intervention that can help. A related project, funded with a $3.4 million grant from WoodNext, will investigate cardiovascular, pulmonary, psychiatric and other diseases related to the body's master clock.

Stephen Chan, professor of vascular medicine, says treatments for circadian problems should begin by understanding what happens at the molecular level that makes a person a jet lag victim — or even an early bird or night owl.

"We don't know why, but there are certain hotspots in our DNA that do that," he says. "What we want to do is look at why hotspots in the DNA may actually harbor activity that underlies that association."

Colleen McClung, professor of psychiatry and clinical and translational science, has done extensive research on circadian rhythms. She directs Pitt's Center for Adolescent Reward, Rhythms and Sleep.

"People who have a mood or substance-abuse disorder have very disrupted circadian clocks," she says, noting that Parkinson's and other conditions can be influenced by circadian rhythms, as well.

McClung and Chan aim to prevent disease and, as needed, alter the sleep-wake cycle through pharmacological intervention and perhaps the simulation of what are known as the suprachiasmatic nuclei. These brain structures sense daylight and darkness — in addition to many other things — and work with genes in every cell to keep the human clock in check.

Attacking circadian problems from various angles and from a cross-disciplinary perspective should be of great benefit, Chan says. Ultimately, the goal is to usher in a new era of precision medicine where health and well-being can be improved by a more stable circadian clock.

"Enhancing our understanding of the circadian clock has the potential to improve the lives of millions affected by circadian disturbances," says Wood. "Perhaps one day Drs. Chan and McClung's work will even lead to a cure for jet lag."

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