UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | WINTER 2020/21

PITTMED

MOVING MOUNTAINS

ALUM ALA STANFORD TAKES COVID-19 TESTING TO THE PEOPLE

MASKED DISEASE

I am so pleased that the University of Pittsburgh gave voice to a major vicissitude of Black Americans. I received my MD from Pitt in 1989. I am a Black American female. There were many "unspeakable" incidents that are part of my Pitt experience, but I am appreciative for receiving the opportunity to acquire medical training that has withstood the test of time and prejudicial attitudes.

Thank you, Elaine Vitone, for a very well written expose on the "unmasking" of America's long-standing disease (racism) that disproportionately disables "people of color." Those of us who experience health disparities institutionalized in the United States are so aware of the inequities, whereas "the comfortable" seldom venture to become aware of travesties/negative treatments.

Jasmine Green, I love your depiction/picture on the Pitt Med cover. The masked brown woman represents the silencing of the affected population, as well as showing the masking requirement to protect from aerosolizing/transmission of SARS-CoV-2.

Since my graduation in 1989, this is the first Pitt publication that moved me to reach out and say "thank you" for the cover story article.

Velva Boles, MD, PhD
Class of 1989

Excerpt of Dean Shekhar's response:

Thank you very much for writing.

I'm saddened, though not surprised, to hear of the types of challenges you experienced in pursuing your MD. It's heartening, however, to know you persevered in making the most of your medical training. My colleagues and I intend to better support current and future physicians and scientists, to explicitly address racism and ensure trainees do not face such challenges alone. While it is gratifying that our nation is becoming more cognizant of racism and the disparities its legacy creates, we clearly have significant work ahead of us in the pursuit of equity, within and outside the realm of medicine.

Once again, thank you for your feedback. I hope that you find future issues of Pitt Med to be similarly engaging. If you visit Pitt after the medical school renovations are complete, you'll see Ms. Green's paintings gracing the walls of Alan Magee Scaife Hall.

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

RECENT MAGAZINE HONORS

2020 Press Club of Western Pennsylvania Golden Quill Awards
- **Best in Show: Ray Sprigle Memorial Award—Magazines**
- **Excellence in Written Journalism, Magazines—Medical/Health (G. Jenkins, "Oct. 27, 2018: Pittsburgh's Darkest Day and the Mass Casualty Response")**

2020 Press Club of Western Pennsylvania Golden Quill Award
- **Excellence in Corporate, Marketing and Promotional Communications—Written, Medical/Health (G. Jenkins, "Surviving Survival")**

2020 Press Club of Western Pennsylvania Golden Quill Award
- **Excellence in Corporate, Marketing and Promotional Communications—Audio, Medical/Health (E. Vitone, J. Faust, M. Palko and E. Lloyd, Pitt Medcast: "Polio Pioneers")**

CORRESPONDENCE

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

Email: medmag@pitt.edu
Phone: 412-624-4354

For address corrections:

ATTN: Aimee Bernard
Email: ALB472@pitt.edu
Phone: 412-648-9741

Value-Added

We're working to make selected Pitt Med articles eligible for CME credits in our future issues. Stay tuned.

CONTRIBUTORS

JEREMY BERG ["Primer: Making Sense of Various COVID-19 Vaccine Technologies"] is associate senior vice chancellor for science strategy and planning, as well as professor of computational and systems biology. Before coming to Pitt, he was the director of the National Institute of General Medical Sciences. Until 2019, he was editor in chief of the Science family of journals. Berg wanted to write about the COVID-19 vaccines because while working on a new edition of Biochemistry—one of his four books—he discussed the topic at length with his coauthors. "I wanted to share the insights I have gained with Pitt Med readers," he says. Berg adds that he has always found writing satisfying because it's like teaching but with a larger classroom. He also believes it's a great way to learn: "There is nothing like trying to explain something to someone else to force you to question how well you really understand it."

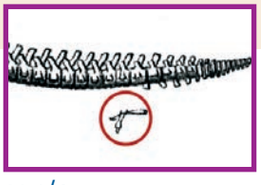
After graduating from Smith College, SAMANTHA PAIGE ROSEN ["More Time for Stroke Victims," "Critical (Student) Care"] landed a job as a researcher for HBO's "Real Time with Bill Maher." Among other tasks, she read books authored by the show's guests and wrote summaries for Maher and producers. Lauded for her ability to make complex books on an array of topics accessible to her bosses, she became interested in science writing after summarizing "Missing Microbes" by Martin J. Blaser for the show. Today, Rosen lives in her native suburban Philadelphia, where she freelances as a writer, editor and writing tutor. She has written for The Washington Post, The Week and Ms. Magazine, and she earned an MFA in creative nonfiction writing from Sarah Lawrence College.

PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, WINTER 2020/21
VOL. 23, ISSUE 1

5

9



40 1/2

18

FEATURES

COVER

When Black Philadelphians had trouble getting tested for COVID-19, pediatric surgeon and Pitt Med alum Ala Stanford stepped up. (Cover: AP Photo/Matt Rourke © 2021.)

PITTMED

PUBLISHER
Anantha Shekhar, MD, PhD

EDITOR IN CHIEF
Erica Lloyd

ART DIRECTOR
Elena Gialamas Cerri

SENIOR EDITOR
Elaine Vitone

ASSOCIATE EDITOR
Gavin Jenkins

CONTRIBUTING EDITOR
Cara Masset

PRODUCTION MANAGER
Chris Markle

CIRCULATION MANAGER
Aimee Bernard

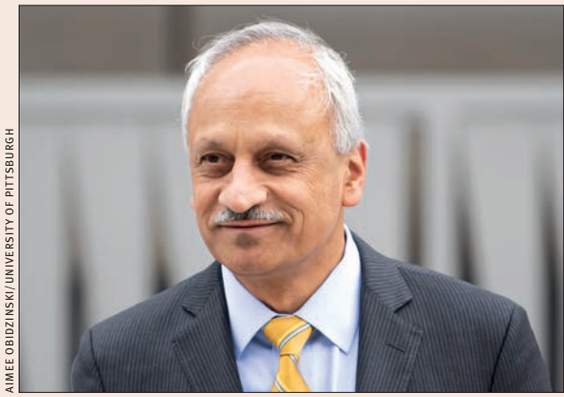
INTERN
Nithya Kasibhatla

University of Pittsburgh

Pitt Med is published by the Office of the Dean and Senior Vice Chancellor for the Health Sciences in cooperation with the Office of University Communications. It is produced quarterly for alumni, students, staff, faculty and friends of the School of Medicine. PR 6753

My ambition was to bring to bear on medicine a chemical approach. I did that by chemical manipulation of viruses and chemical ways of thinking in biomedical research.

—Jonas Salk



AIMEE OBIDZINSKI/UNIVERSITY OF PITTSBURGH

Dear Pitt Med Reader,

Consider some of the challenges the world confronted during the polio pandemic more than 60 years ago.

An infected person could spread the virus without even knowing they carried it. Disease symptoms varied from none at all to lethal.

Scientists were called on to develop effective vaccines. Then, the world dealt with intellectual property barriers, production cost issues and the logistics of vaccine distribution. Famously, Dr. Salk did not patent the Pitt team's vaccine. ("Could you patent the sun?" he asked.) That, by the way, would not be such a simple decision to make today.

After all that, public health officials had to address vaccine hesitancy in many segments of our population.

This all sounds familiar, doesn't it? History is repeating itself.

Yet we can also take pride in how the situation has evolved: In Jonas Salk's time, our nation pulled together; even children funded the effort by donating their dimes. Today, scientists throughout the globe are sharing information and collaborating, making COVID-19 breakthroughs at a rapid pace. Chinese researchers sequenced the novel coronavirus genome and made it public in January 2020. By the end of the same year, we were inoculating frontline care providers and residents of long-term care homes in the United States.

Though researchers apply some basic principles to manipulate viruses in vaccine development—as Dr. Salk alludes to in the quote above—science has also learned a lot from past outbreaks. The fields of virology and vaccinology have made impressive progress since the 1950s.

Just like our nation did during the polio pandemic, I gain inspiration from the work of Pitt people. In this issue, we feature surgeon Dr. Ala Stanford, who trained here. She set up pop-up COVID-19 testing centers last year to make sure that disproportionately affected Black communities in Philadelphia had access to testing. And patients from throughout the world benefit from the legacy of our own Dr. Eugene Myers, a giant in otolaryngology, whom you can also read about in this issue.

There's not enough room in this 40-page magazine to share all the noteworthy work coming out of our medical school. There never is; yet the scientific efforts this pandemic has galvanized are stunning. For instance, Pitt scientists co-led the efforts to show that steroids are effective in the recovery of severely ill COVID-19 patients. I write this letter just after the U.K. authorized repurposing of approved arthritis medications tocilizumab and sarilumab for emergency use in COVID-19 patients receiving organ support. It turns out these drugs block the effects of the damaging immune molecule IL-6 to improve outcomes in these critically ill patients. REMAP-CAP, the international clinical trial network that learns and adapts as it progresses, was instrumental in demonstrating the potential of these lifesaving treatments. Pitt physicians, notably critical care medicine chair Dr. Derek Angus, led this network with colleagues at universities in Australia, the U.K., Canada and Europe.

Finally, you may have heard that medical schools in this country have received substantially more applications this year than is typical. Applications to Pitt Med are up 20%. Some people attribute this rise to the so-called Fauci Effect. Other factors may be at play, but this much is clear: Young people want to be part of the solution. They want to help us heal. These are our future leaders; we can take solace in that.

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

Special COVID-19 Report

Insight on Inflammation

Why do some people with COVID-19 develop severe inflammation? A collaboration between the University of Pittsburgh and Cedars-Sinai has produced a likely answer.

The study, published this fall in the Proceedings of the National Academy of Sciences, uses computational modeling to zero in on a part of the SARS-CoV-2 spike protein that may act as a "superantigen," kicking the immune system into overdrive as happens in toxic shock syndrome.

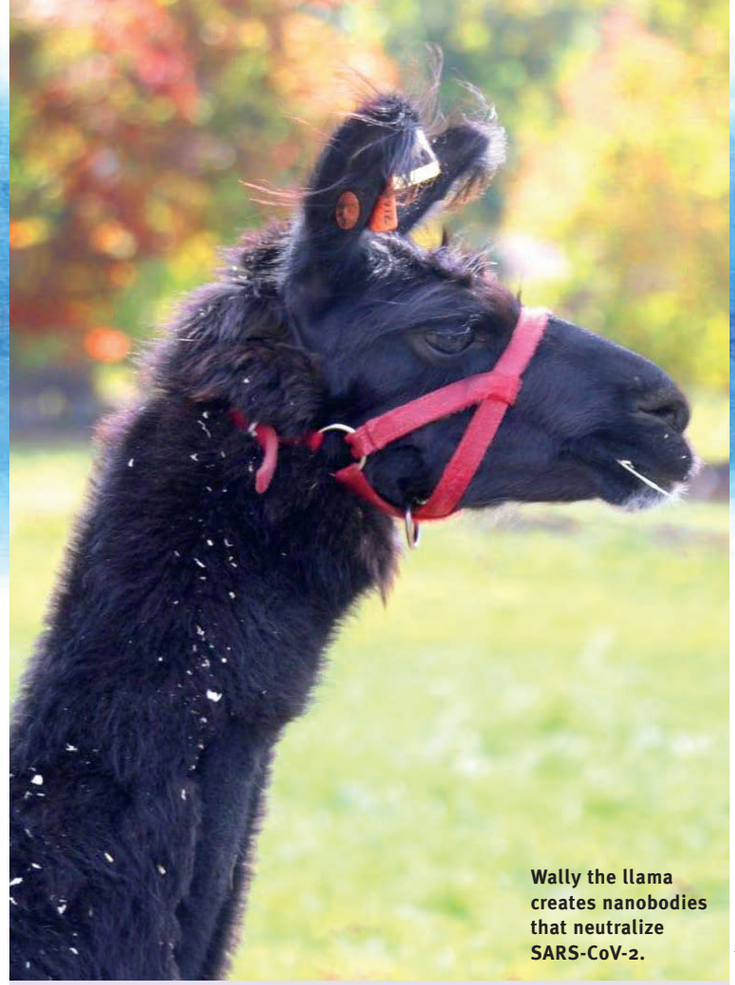
Symptoms of a condition in pediatric COVID-19 patients known as multisystem inflammatory syndrome in children (MIS-C) include persistent fever and severe inflammation. While rare, the syndrome can be serious or even fatal.

The first reports of this condition coming out of Europe caught the attention of study cosenior author Moshe Arditi of Cedars-Sinai, who is an expert on another pediatric inflammatory disease—Kawasaki disease.

Arditi contacted longtime collaborator Ivet Bahar, Distinguished Professor and John K. Vries Professor of Computational and Systems Biology at Pitt, and the two started searching for features of SARS-CoV-2 that might be responsible for MIS-C. Bahar and her team created a computer model of the interaction between the SARS-CoV-2 viral spike protein and the receptors on the foot soldiers of the immune system—T cells. When T cells are activated in abnormally large quantities, as is the case with superantigens, they set off what's known as a cytokine storm, leading to inflammation.

Using the model, the team was able to see that a region on the spike protein with superantigenic features interacts with T cells. They compared this region to a bacterial protein that causes toxic shock syndrome and found striking similarities in both sequence and structure. "Everything came one after another, each time a huge surprise," says Bahar.

"Our research raises the possibility that therapeutic options for toxic shock syndrome . . . may be effective for managing and treating MIS-C in children and hyperinflammation in adult coronavirus patients," says Arditi. Since the PNAS publication, the Bahar lab has found an antibody specific to the superantigen, which in tests conducted in vitro also interferes with viral entry. *—Erin Hare*



Wally the llama creates nanobodies that neutralize SARS-CoV-2.

SONYA PASKE AT CAPRALOGICS, LTD.

That's a Good Llama!

Animals that thrive in environments we think of as extreme have immune systems worth noticing. Think Greenland sharks, quite happy at 7,000 feet below sea level—they live to probably more than 400 years. Think camels who trek for days in the desert. Or their camelid cousins, llamas, guarding livestock and carrying packs in the Andean highlands.

It turns out that llamas create special antibodies, called nanobodies, which are much smaller than human antibodies and—here's the really good part—many times more effective at neutralizing the SARS-CoV-2 virus. They're also much more stable.

"Nature is our best inventor," says Yi Shi, assistant professor of cell biology at the University of Pittsburgh.

With others here at Pitt and at Hebrew University of Jerusalem, Shi has created a new method to extract tiny but extremely powerful SARS-CoV-2 antibody fragments from llamas, which could be fashioned into inhalable therapeutics with the potential to prevent and treat COVID-19. The breakthrough was reported in the journal Science on Dec 18.

"The technology we developed surveys SARS-CoV-2 neutralizing nanobodies at an unprecedented scale, which allowed us to quickly discover thousands of nanobodies with unrivaled affinity and specificity," says Shi, senior author.

To generate these nanobodies, Shi and his colleague Yufei Xiang, a research scientist in the Shi lab, turned to a black llama named Wally—who resembles Shi's black Lab of the same name.

The researchers immunized the llama with a piece of the SARS-

Sources for this special section include Pitt and UPMC reports.

CoV-2 spike protein and, after about two months, the animal's immune system produced mature nanobodies against the virus.

Using a mass spectrometry-based technique that Shi has been perfecting for three years, lead author Xiang identified the nanobodies in Wally's blood that bind to SARS-CoV-2 most strongly.

Then, with the help of Pitt's Center for Vaccine Research, the scientists exposed their nanobodies to live SARS-CoV-2 virus and found that just a fraction of a nanogram could neutralize enough virus to spare a million human cells from being infected.

These nanobodies represent some of the most effective therapeutic antibody candidates for SARS-CoV-2, hundreds to thousands of times more effective than other llama nanobodies researchers have studied for years.

Shi's nanobodies can sit at room temperature for six weeks and tolerate being fashioned into an inhalable mist to deliver antiviral therapy directly into the lungs, where they're most needed. Since SARS-CoV-2 is a respiratory virus, the nanobodies could find and latch onto it in the respiratory system, before the virus has a chance to do damage.

In contrast, traditional SARS-CoV-2 antibodies require an IV, which dilutes the product throughout the body, necessitating a much larger dose and costing patients and insurers around $100,000 per treatment course. "Nanobodies could potentially cost much less," said Shi. "They're ideal for addressing the urgency and magnitude of the current crisis." *—Erin Hare and Erica Lloyd*

AIMEE OBIDZINSKI/UNIVERSITY OF PITTSBURGH

A Good Day

Rachel Marini holds up a COVID-19 vaccine vial on Dec. 16, 2020, during the first week of vaccinations in Pittsburgh. Marini is a UPMC clinical infectious disease pharmacist who is on the faculty of the Department of Medicine. She prepared doses of the vaccine so that students from Pitt's School of Pharmacy could inoculate providers who were slated to vaccinate UPMC employees in the area in the weeks to come. Marini, 31, a native of Bethel Park, says she has been training for this moment her entire career. "This is exactly what I've been dreaming of, in all honesty," she says, tears building in her eyes. "Not to have a pandemic by any means, but to have the ability to help other people." Marini, who leads the UPMC Presbyterian/Shadyside immunization committee and the Presbyterian pharmacy emergency response team, says the mask she wore hid the smile on her face as she prepared the doses. "It's a moment that I'm going to keep with me forever," she says. *—Gavin Jenkins*

Blood Thinners Help Moderately Ill

Many patients who've died from COVID-19 formed blood clots throughout their bodies, including in their smallest blood vessels. This unusual clotting causes multiple complications, from lung and other organ damage to heart attacks, pulmonary embolisms and strokes.

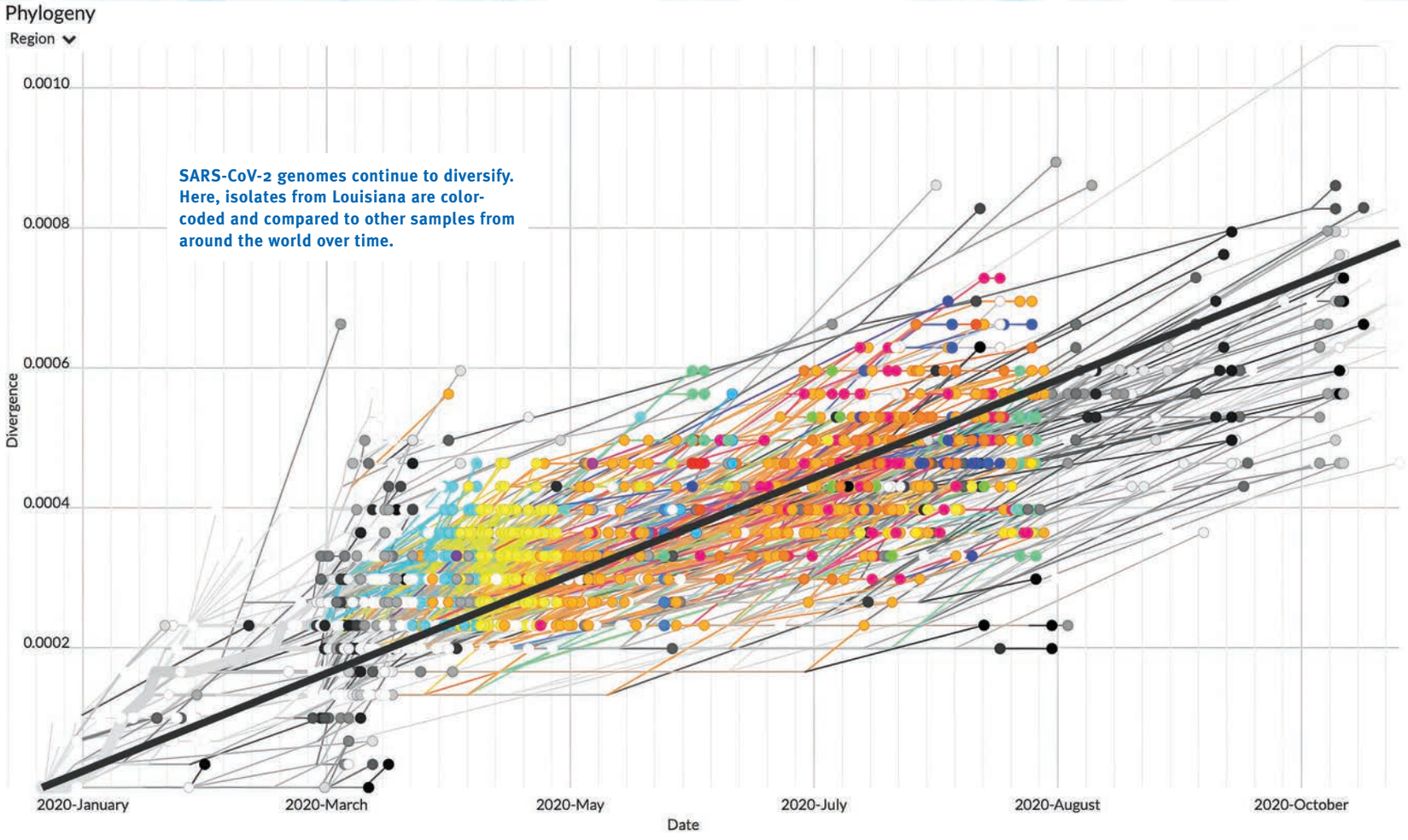
A worldwide consortium of clinical trials, coordinated in part by researchers at the University of Pittsburgh, has found that giving full dose anticoagulation treatments, or blood thinners, to moderately ill patients hospitalized for COVID-19 reduced the need for vital organ support—such as the need for mechanical ventilation. Adopting the cheap, readily available treatment could help reduce the burden on intensive care units.

Although interim analysis of data from the inpatient trial proved beneficial to moderately ill patients, organizers paused recruitment of critically ill patients in late December due to early signs of futility and a trend toward harm.

The studies are part of the ACTIV-4 partnership. ACTIV stands for Accelerating COVID-19 Therapeutic Interventions and Vaccines, and ACTIV-4 focuses on the evaluating the role of antithrombotics for treating COVID-19. Incorporated into UPMC and Pitt's self-learning trial platform, the trials examine progress of those infected with COVID-19 within three groups: outpatients, inpatients and those released from the hospital. Other universities hosting study sites are Harvard University, New York University, the University of Illinois at Chicago and the University of Michigan, among others.

"This has been an amazingly cooperative endeavor—unequivocally the most rapidly moving, complex but also highly collaborative experience of my life," Matthew Neal, the Roberta G. Simmons Associate Professor of Surgery, says of the worldwide effort.

Neal is a lead investigator for the inpatient platform. Frank Sciurba, a professor of medicine and education, is a lead on the outpatient platform. Stephen Wisniewski, vice provost for budget and analytics, leads the coordination of the entire ACTIV-4 effort. Maria Mori Brooks, professor of epidemiology and biostatistics, who codirects the Graduate School of Public Health's Epidemiology Data Center along with Wisniewski, leads the study design and analysis of the inpatient and outpatient trials. *—Staff Reports*



SARS-CoV-2 genomes continue to diversify. Here, isolates from Louisiana are color-coded and compared to other samples from around the world over time.

LSU HEALTH SHREVEPORT EMERGING VIRAL THREAT LABORATORY AND GISAID. BUILT BY FREITAS ET AL WITH AUSPICE AND AUGUR. DATA MADE AVAILABLE THROUGH GISAID EPICOV.

What Bug's in You?

Say an elementary school has an outbreak of COVID-19, with three confirmed cases in one week. While quarantining and contact tracing are the best tools we have for ending lines of transmission, those tools can't always tell you where each of those kids got the virus in the first place.

And for the school, weighing its options on what to do next, the million-dollar question is: Did these families get the bug on campus or someplace else? There's a good way to answer that, says Vaughn Cooper, Pitt professor of microbiology and molecular genetics. His lab is taking positive COVID-19 tests and sequencing the entire genome of each virus found therein—all 29,000 nucleotides. And, using techniques his team developed, they're turning it all around in 72 hours or less.

Viruses propagate by copying themselves, a less-than-perfect process. In SARS-CoV-2, there's a new mistake, or mutation, in a given viral lineage about once every two weeks. Because of this, the genomes of the viruses found in cases around the globe have enormous variety—many thousands of distinct flavors.

When the team sequences a virus, they can compare it "with literally every other sequence ever decoded on the planet," Cooper said recently on Washington Post Live.

Take our hypothetical elementary school: If the three virus genomes are identical, "then that's likely a spreading event, and that might be support for a closure"—to deep clean and test folks en masse. If the genomes are all different, though, that's more in line with random infections coming from elsewhere in the community.

"You would just isolate those cases and their families, and you could probably keep the facility open," he says.

Cooper has partnered with the Louisiana Department of Health and Louisiana State University to help quash SARS-CoV-2 outbreaks in that state's nursing homes, jails and agricultural sites. And here at home, he's been using these sequencing techniques for years to sleuth out bacterial pathogens within UPMC hospitals. "We were kind of primed to do this when COVID hit," he says.

Cooper's thoughts on B.1.1.7, the new variant that turned up in December? The reason we know about it, he says, is because the U.K. had the foresight to invest in sequencing. "This shows how important it is that our country rebuild and reinvest in infrastructure like this."

He adds: "All of the primary ways of controlling this virus still matter. And we think that the vaccine is going to work just fine against [the variant]." *—Elaine Vitone*

Vaughn Cooper talks about predicting evolution and tracking the novel coronavirus in our Pitt Medcast, "Evolving Situation"at **pi.tt/pittmedcast**.

Primer: Making Sense of Various COVID-19 Vaccine Technologies

By Jeremy Berg

Graphics created with Biorender.com

This winter, with the delivery of the first batches of SARS-CoV-2 vaccines, providers and laypeople alike have questions about the technologies behind them. We thought a primer would be helpful.

Using Tamed Viruses

Three-quarters of a century ago, Jonas Salk and collaborators in Pittsburgh developed a much-needed vaccine for polio using strains of the poliovirus that had been inactivated by treatment with formalin. In parallel, Albert Sabin developed a vaccine based on weakened ("attenuated") strains of poliovirus. The attenuated virus is capable of infecting some cells but does not cause disease (except in very rare cases); it can be given orally, in contrast to the Salk team's vaccine, which requires injection.

Employing Just Pieces of Virus

Two threads came together to set the stage for the next phase of vaccine development. First, genetic engineering methods allowed scientists to modify cells and viruses with great precision. Second, knowledge of immunology expanded. Scientists discovered which parts of viruses elicited the best immune responses. For example, our bodies can produce antibodies that bind to proteins on viral surfaces and, in some cases, short-circuit viral infection. So it seemed that vaccines might be made based on these viral surface proteins alone, without the need for the entire virus—eliminating fears that the vaccine itself could cause infection.

Scientists have used this approach successfully. By producing large quantities of genetically engineered viral proteins in the lab, they've created effective vaccines against human papilloma virus (HPV), a virus that can cause cervical and other cancers.

Harnessing Alternative Viruses

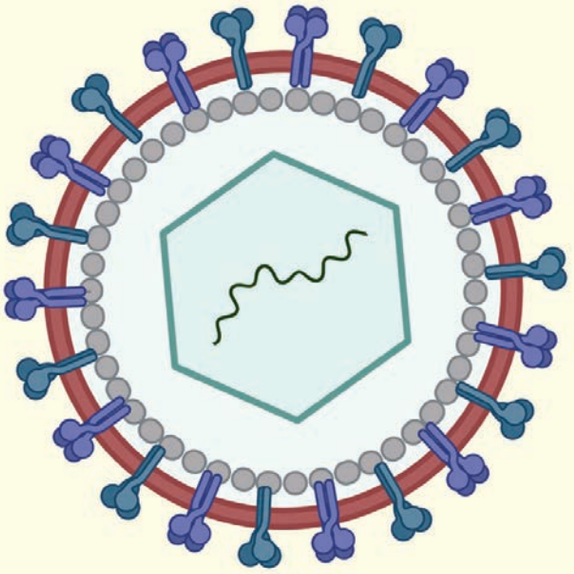
Some vaccine developers use completely different viruses, engineered so as not to cause disease, to produce the surface proteins from the dangerous virus. This method generated the first approved vaccine against Ebola virus. Hundreds of groups are using similar methods for generating candidate vaccines against COVID-19, based on the so-called "spike" protein present on the SARS-CoV-2 surface. Some of these candidate vaccines, including one from the University of Oxford and AstraZeneca, employ modified adenoviruses as a carrier virus. At the Center for Vaccine Research at the University of Pittsburgh, Paul Duprex, professor of microbiology and molecular genetics, and his collaborators are developing a modified measles virus as a vaccine. Several of these vaccines will likely be approved for use in the United States once development and testing are completed.

Injecting Instructions for Building Pieces of Virus

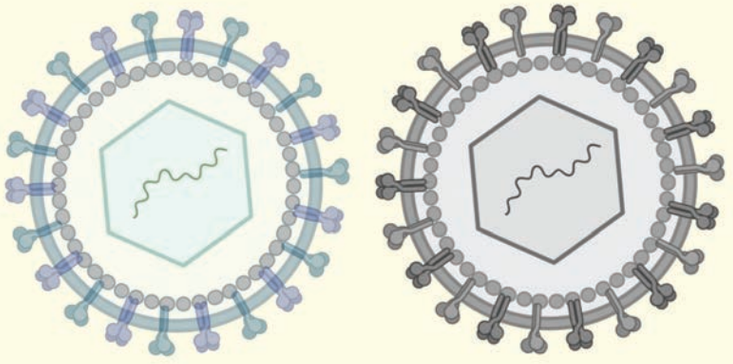
An even more streamlined approach has produced the first approved SARS-CoV-2 vaccines. When proteins, including viral proteins, are produced by cells, information in the genome for the protein is transcribed into messenger RNA (mRNA). The mRNA then moves to the protein factories in cells, where it is translated into the proteins themselves (hence the name "messenger"). These mRNA molecules are used to engineer the viruses previously discussed. So, researchers wondered, could mRNA be produced in the laboratory and injected directly?

There were obvious obstacles. The mRNA molecules need to enter the cells to produce protein. Furthermore, RNA molecules break down notoriously easily. Fortunately, scientists learned that packaging the mRNA in tiny balls of

STARTING POINTS

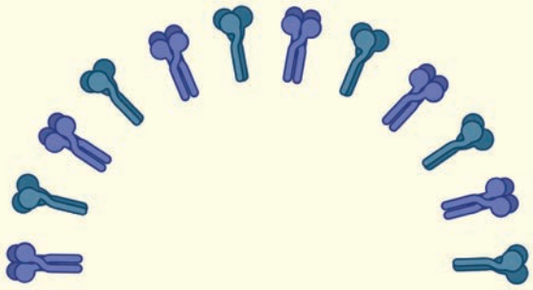


SARS-CoV-2: The virus that causes COVID-19, diagrammed, showing an outer ring of proteins (spikes) with messenger RNA, or mRNA (squiggle in the middle).

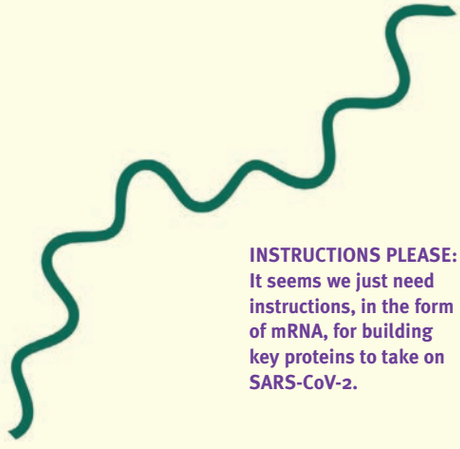


TAMED: For several decades, scientists have used weakened or killed viruses to create an immune response. Those approaches are still common today in vaccine development.

STREAMLINED

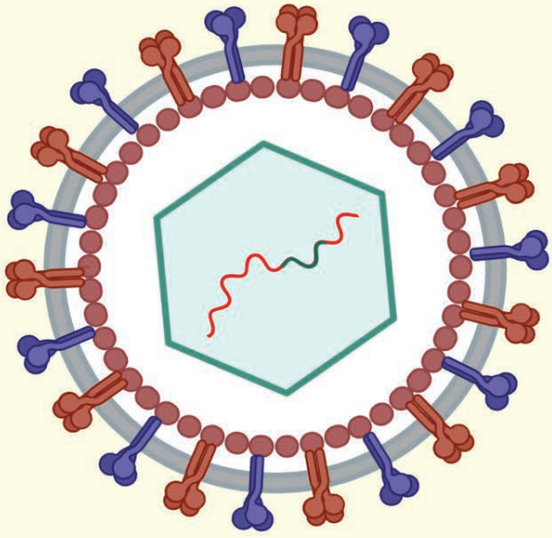


VIRUS PIECES: Researchers later learned that they didn't need the entire virus; they started including just proteins in vaccines. Of course, it would have to be the right protein to elicit an immune response.



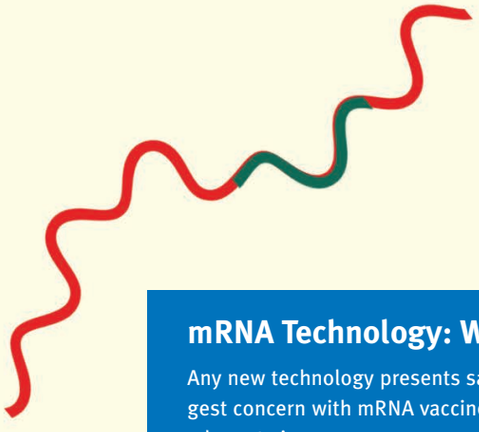
INSTRUCTIONS PLEASE: It seems we just need instructions, in the form of mRNA, for building key proteins to take on SARS-CoV-2.

ALTERNATIVE CARRIERS



Some groups take a different virus entirely, make it benign, and use it to generate the proteins that are key to an effective immune response against the virus of interest.

That's how a Pitt team built a candidate vaccine to fight the novel coronavirus. TOP LEFT: The weakened measles virus used in a measles vaccine. BOTTOM LEFT: Measles vaccine mRNA merged with mRNA from the SARS-CoV-2 spike protein. The result is a vaccine for measles and for the novel coronavirus. This is one of a few Pitt vaccines undergoing testing.



fat-like molecules (called "liposomes"), along with making some additional modifications, both enabled mRNA entry into cells and helped protect these messages. But, would this unproven approach work?

The SARS-CoV-2 vaccines created by Pfizer and Moderna use SARS-CoV-2 "spike" protein mRNA, and clinical trials have demonstrated that these vaccines protect inoculated study volunteers from getting COVID-19 with impressive efficiency! The relative simplicity of producing RNA compared to protein or viruses allows these vaccines to be manufactured in large quantities.

The Salk team's triumph allowed people to move past a world of iron lungs, crutches and fear. And now, thanks to these vaccine breakthroughs—with plenty of other candidates in the pipeline—we can also envision a return to a more normal world. We will still have to wear masks, wash our hands and keep our distance for a bit longer though.

This watercolor of an mRNA vaccine shows mRNA (pink) enclosed in material that protects the message from the immune system until it can be read.

mRNA Technology: What are the issues?

Any new technology presents safety and other concerns and challenges. The biggest concern with mRNA vaccines, however, was that they would not produce an adequate immune response—yet, as we can see from the clinical trial results, that is not an issue.

Likewise, the trials show that the mRNA vaccines are safe. There should be no concerns with using mRNA directly. The mRNA just helps produce the spike protein and then is naturally degraded. It is not incorporated into cells in any other way and cannot mutate. (By the way, the sore arm and mild fatigue you are likely to get with many inoculations are signs that the immune system has been called into action.)

One major challenge with mRNA vaccines is that they are relatively unstable; this is why they must be stored at low temperatures—to prevent mRNA breakdown. The Pfizer vaccine, which requires transport and storage at -70 degrees Celsius or lower, is especially vulnerable, adding to the huge logistical challenges of vaccinating a substantial percentage of the world population.

Jeremy Berg is a Pitt professor of computational and systems biology and associate senior vice chancellor for science strategy and planning, health sciences. From 2016 to 2019, he served as editor in chief of the Science family of journals.

Watercolor illustration by David S. Goodsell, RCSB Protein Data Bank; doi: 10.2210/rcsb_pdb/goodsell-gallery-027

The new individual biocontainment unit (tested here in a simulation) draws away and traps contaminated air so as not to spread virus.

JACK CARLSON/UPMC

In the Hood

In settings where personal protective equipment (PPE) is in short supply, inserting a breathing tube down a patient's throat poses a major risk of SARS-CoV-2 exposure for providers as viral particles are released from the airway.

University of Pittsburgh and U.S. Army researchers have created an individual biocontainment unit, or IBU, to keep frontline health care workers safe while they provide care. The device is described in a study published Sept. 3 in the Annals of Emergency Medicine. Earlier attempts to minimize exposure to health care workers involved placing a plexiglass intubation box over a patient's head and shoulders. With that setup, clinicians place their hands through two large holes in the box to intubate the patient inside. Although such a device may contain the worst of the splatter, it can't keep aerosols from leaking out. Because of concerns about the potential of airborne viruses to leak from the plexiglass boxes, the Food and Drug Administration has revoked its emergency use authorization for these enclosures.

"Having a form of protection that doesn't work is more dangerous than not having anything, because it could create a false sense of security," says David Turer (Res '20), a plastic surgeon who recently completed his residency at UPMC. Turer was a colead author on the September study.

The Pitt/Army solution, the IBU, is designed to suck contaminated air out of the box with a vacuum and trap infectious particles in a filter before they seep into the room.

In a simulation, the IBU trapped more than 99.99% of virus-sized aerosols and prevented them from escaping into the environment.

Several months ago, Turer and colleagues submitted an emergency use authorization application for the IBU; they are preparing to manufacture the devices for distribution as they await approval.

"It intentionally incorporates parts from outside the medical world," says Turer of the IBU. "So, unlike other forms of PPE, demand is unlikely to outstrip supply during COVID-19 surge periods." In addition to protecting providers during intubation, the IBU can also provide negative pressure isolation for COVID-19 patients, supplying an alternative to scarce negative pressure hospital isolation rooms, as well as helping to isolate patients on military vessels.

"The ability to isolate COVID-19 patients at the bedside is key to stopping viral spread in medical facilities and on board military ships and aircraft," said study colead author Cameron Good, a research scientist with the U.S. Army Combat Capabilities Development Command Army Research Laboratory. Devices similar to IBUs were first used by military personnel in the Javits Center field hospital in New York City when New York hospitals were overrun with COVID-19 patients during the first wave of the pandemic. *—EH*

Testing the Tests

There are two main types of tests for SARS-CoV-2, the virus that causes COVID-19: those that tell whether someone has the virus and those that tell whether someone had it.

A recent study by Pitt pathologists sheds new light on the latter type—known as an antibody assay—by comparing the performance of various commercially available tests at different times after illness. COVID-19 antibody assays are mostly used to find out how many people in a given population already had the virus and to determine who can donate convalescent plasma. They also may be important in assessing the effectiveness of vaccines.

"We were surprised to see such large differences in antibody detection both at early and later timepoints," says senior author Sarah Wheeler, Pitt assistant professor of pathology and associate medical director of clinical immunopathology at UPMC. The study results appeared in the American Journal of Clinical Pathology.

Antibodies are produced by the immune system in response to foreign pathogens. When antibodies against a virus are found in someone's blood, it's a telltale sign that person previously encountered the virus.

Wheeler and her colleagues compared six commercial SARS-CoV-2 antibody assays for how well they correctly identify people who are positive or negative for antibodies (otherwise known as a test's sensitivity and specificity) and the reliability of the test depending on when it was administered after infection.

"We found that some assays detected 20% to 30% fewer convalescent cases than other assays," says Wheeler. She noted that this could significantly affect studies that seek to determine what proportion of people in a given community have already had the virus.

The team did not specify one test as better than the others, but rather noted that different tests work better in different situations. For example, one test detects antibodies quickly after infection, but does not reliably detect antibodies about a month out, meaning it would be better for determining recent infection compared to infection from an earlier outbreak.

—Allison Hydzik

Devoted to noteworthy happenings

at the medical school

PAULA BURCH

Lichtveld

LICHTVELD IS NEW DEAN OF PUBLIC HEALTH

For 18 years, **Maureen Lichtveld** worked for the Centers for Disease Control and Prevention and the U.S. Department of Health and Human Services Agency for Toxic Substances and Disease Registry. She designed public health research tools and protocols—adopted by each state—to guide national environmental health studies in communities living near hazardous waste sites.

This January, Lichtveld joined the University of Pittsburgh's Graduate School of Public Health as dean. She has nearly 40 years of experience in environmental public health. Before joining Pitt, she served as the director of the Center for Gulf Coast Environmental Health Research, Leadership and Strategic Initiatives within Tulane University's School of Public Health and Tropical Medicine.

Her research focuses on environmentally induced disease, health disparities, environmental health policy, disaster preparedness, public health systems and community resilience.

Lichtveld says she is honored to oversee Pitt Public Health: "Together, we will make science work for our communities—especially those most vulnerable, locally, nationally and globally."

Anantha Shekhar, senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of Pitt's School of Medicine, says that he and the search committee sought a talented scholar and bold collaborator who could elevate the school's record of academic and research excellence.

"We wanted a seasoned leader who could advance our commitment to helping communities—and the people within them—grow stronger and healthier," Shekhar says. "Dr. Lichtveld checked all these boxes and more."

A respected researcher and scholar, Lichtveld holds a Master of Public Health from Johns Hopkins University and a Doctor of Medicine from Anton de Kom University of Suriname and the Leiden University in the Netherlands.

Lichtveld succeeds Interim Dean Everette James, who took the helm of Pitt Public Health following Donald Burke's 13-year tenure in the role.

—Ellie Graves

Shared Vision

As the world population of older adults continues to grow, the number of people with visual impairment is expected to triple by the year 2050.

Pitt is formally collaborating with the U.S. Food and Drug Administration to address the needs of the visually impaired. Under the agreement, Pitt and the FDA will work together for the next five years on scientific, educational and outreach initiatives designed to address the epidemic of vision loss.

"It's really exciting. This will put Pitt in a position where we can work with the FDA on the validation of new technological approaches by developing programs and protocols," says José-Alain Sahel, Pitt's Eye and Ear Foundation Professor, chair of ophthalmology and one of the world's top experts in retinal diseases and vision restoration research. "Patients' voices will nurture our projects and define the successes we all want to deliver."

"We appreciate this phenomenal opportunity to partner with the University of Pittsburgh. Developing new methods to assess visual impairment and the impact on daily activities is important to helping the FDA better characterize the consequences of vision loss and also helping the FDA to reliably assess the benefit of novel therapies and rehabilitation technologies," says Malvina Eydelman, director of the Office of Ophthalmic, Anesthesia, Respiratory, ENT and Dental Devices in the FDA's Center for Devices and Radiological Health.

—Amerigo Allegretto

LEFT: Bezak
RIGHT: Schenker

TOM ALTANY/UNIVERSITY OF PITTSBURGH

Overheard

Palliative Care in the Time of COVID

Working with a patient's care team, palliative care specialists base their treatment on the person, not a prognosis. Their focus is to provide relief from symptoms and the stress of an illness, while also comforting the families. Relatives often play a role in the treatment plan, but COVID-19 safety protocols have prevented many family members from even entering hospitals. This fall, we spoke with Yael Schenker, director of Pitt Med's Palliative Research Center, and Karl Bezak, clinical assistant professor of medicine and medical director for palliative care at UPMC Presbyterian, to learn more about how their teams offered support despite the challenges of the pandemic.

How did you adjust to the COVID-19 safety measures last spring?

Karl Bezak: Initially, we would try to describe a patient's condition to their family over the phone. It wasn't until we were able to do video conferencing that the family could really see just how sick their relatives were. People who had been saying they wanted everything done [to keep the patient alive] really saw how this was not an acceptable quality of life. It was challenging, but helpful, in terms of painting a picture for those who were making decisions on behalf of the patient.

Aside from family not being there in person, what was the biggest challenge you have faced because of the pandemic?

Yael Schenker: The degree of uncertainty—that was particularly acute back in the early spring when we really didn't know what we were dealing with. That in itself caused a lot of suffering and fear. What we're trained to do in palliative care is really walk with people who are suffering and sit with that uncertainty. Being sick in the hospital is scary in usual times, but even more so now. I think a really important role for us was being that glue to bring people together who weren't able to be together in the physical space.

Was there a particular situation that stood out for you?

Karl Bezak: We had a patient who had chosen to stop receiving treatment for pneumonia. Her best friend was able to be at her bedside via iPad as she died. It was really a magical moment. The flexibility and willingness of patients and families to work around the restrictions and policies, to be there as much as possible, especially in a person's last moment, was just absolutely heartening. *—Christina Frank*

Faculty Snapshots

When someone sustains severe muscle damage—as a result of a combat injury, for example—the tissue often can't regenerate. Instead, the damaged muscle is replaced with scar tissue, which can lead to a significant loss of limb function.

Stephen Badylak, deputy director of Pitt's McGowan Institute for Regenerative Medicine, leads a team of researchers from eight institutions who are developing an implantable device that would regrow functional muscle tissue, even after a drastic loss from something as severe as a motorcycle accident. The team was awarded a $22 million grant from the Defense Advanced Research Projects Agency (DARPA) to pursue the project.

The implantable patch contains microelectrodes, hydrogels (polymer chains that create a moist healing environment) and cell factories. It will monitor key molecular signals at each stage of healing, from shortly after the injury occurs to the days and weeks that follow. An artificial intelligence component will direct the delivery of specific molecules at specific times.

Badylak

"The hydrogels we contribute will serve as the covering for the wounds and the physical support for the electrodes," says Badylak, a professor of surgery at Pitt. "I think of it a little bit like a mini Manhattan Project, and it's fun."

Wagner

Amy Wagner and Toren Finkel joined 29 current and former Pitt Med professors this fall when they were elected to the National Academy of Medicine.

A professor of physical medicine and rehabilitation and neuroscience at Pitt, Wagner uses biomarkers and statistical modeling to predict how well patients will recover from brain injury. The data she collects guide clinical decisions along the way—a strategy she calls "personalized rehabilitation medicine." Her clinical work, in turn, informs her research studies of in vivo preclinical models aimed at identifying intervention strategies that promote neurorecovery.

Finkel

Finkel, a professor of cardiology and director of the Aging Institute, researches how oxidative stress and the function of mitochondria alter the rate of aging. His long-term goal is to uncover the molecular basis of aging and age-related diseases through the study of a variety of different cellular pathways.

Election to the Academy is considered one of the highest honors in the fields of health and medicine. *—CF*

Get Cooking

GETTY IMAGES

No more instant ramen for first-years! The culinary medicine interest group created Pitt Med cookbooks and gave them to the incoming class in the fall. The group was founded this spring when the Culinary Medicine course—a mini-elective that started in 2019—couldn't meet in person because of the pandemic. The cookbook includes contributions from fellow Pitt Med students, faculty, alumni and staff.

"Cooking can be a wonderful way for students to take a break and get to know other members of the Pitt Med community through recipes, recommendations on cooking and wellness and tips for grocery stores in the area," says Eva Roy, a third-year student and founder of the culinary medicine interest group.

Roy especially recommends associate dean Donald DeFranco's chicken scallopine recipe or the gazpacho recipe from Jack Schumann, recently retired anatomy course director.

—Gavin Jenkins

More Time for Stroke Victims

As a volunteer EMT in high school, Anthony Schulien was fascinated by stroke and brain injury. In the case of ischemic stroke—where blood clots form, leading to cell death—he wondered if the death of cells could be stopped before clots are even removed. This led him to study neuroscience as an undergraduate at Pitt. He's now in his final year of Pitt's Physician Scientist Training Program. With a team led by his mentor, Elias Aizenman, professor of neurobiology, Schulien has helped develop a drug that could protect the brain during and after a stroke.

The drug targets neurons in a brain region (called the ischemic penumbra) that are at risk of dying as a stroke evolves. It aims to halt the progression of cell death pathways in this tissue and slow the progression of the stroke. The authors of the study, which was published in Science Advances with Schulien as lead author, suggest that the drug may reduce brain-tissue loss following stroke and allow patients more time to reach the hospital to have the clot removed. Mice that received the drug in the study showed a smaller region of infarcted brain tissue and better long-term neurological function.

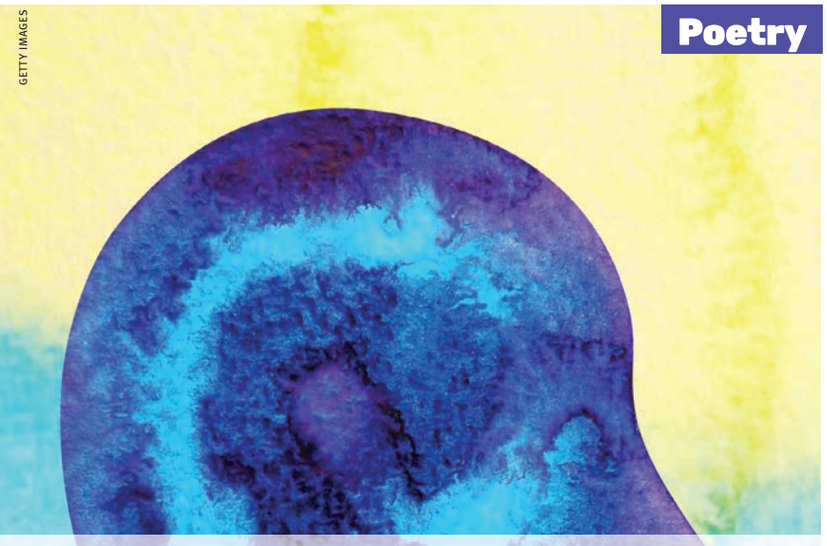
Schulien credits Aizenman, and the more than 20 years of foundational work his mentor has logged researching neuronal cell death, with the breakthrough. Schulien says Aizenman has taught him to stay focused on the big picture as they conduct further studies. "Those are the steps that are needed to take this to real people," he says. *—Samantha Paige Rosen*

DOLLAR BANK

FLASHBACK

We stand corrected—John Paul Golden (MD 1888) is the first known African American to graduate from the Western Pennsylvania Medical College, which became the University of Pittsburgh School of Medicine. In 2011, we reported it was Allen Gilbert Gantt (MD 1901). After graduating, Golden built a successful practice, with offices located on what is now Pittsburgh's North Side (known then as Allegheny City) and in South Carolina, where he and his wife moved in 1897, returning in 1913. Golden's father, Samuel, was a porter for more than 50 years at the Monongahela House—there, he met Abraham Lincoln, P.T. Barnum and other celebrities. Golden's great grandnephew, Samuel W. Golden IV (MD '80), graduated from Pitt Med and researched and treated AIDS/HIV until his death in 2004.

GETTY IMAGES



Poetry

Anatomy Practical

I am searching for the phrenic nerve
when I remember the bad feeling I have about you.

Formalin pricking my nose, an attentive hush
pressing all around me.
This test is timed, but
I look into the body, and I'm lost.

The word itself makes me anxious,
sounds frantic, frenetic.
Lightning strike climbing up beside the heart.

Now my eyes won't focus, and I remember
sleeping, head on your chest on the airport floor,
how my dreams
were full of rhythms:
a locked door and someone knocking
with a strange kind of urgency—
steady but ceaseless.

At the same time I notice the fingernails on the
bloodless hands, yet undissected,
are painted pink.

And the timer sounds.

—Amelie Meltzer (Class of '22)
This poem first appeared in the
Winter 2019/20 issue of Ploughshares.

Innovating in a Pinch

Erick Forno never imagined his asthma research would be used during a pandemic. But, when COVID-19 arrived in the United States, he and his team at Acoustic Waveform Respiratory Evaluation (AWARE) realized they could make a contribution.

AWARE is a smartphone-based app for monitoring at-home lung function; it was developed for people with disorders like asthma, COPD and cystic fibrosis. Forno, an assistant professor of pediatrics at Pitt, and his team recognized it might also be helpful for monitoring the lung health of patients exposed to the novel coronavirus. So they paused their research operation and instituted precautions allowing them to shift their focus.

Their adaptability paid off this fall, when AWARE earned one of three grand prizes of $100,000 at the 2020 Pitt Innovation Challenge (PInCh). AWARE also won a $25,000 bonus for addressing aspects of the pandemic.

With the prize money, the team will gather data from healthy volunteers to advance the app and then examine patients with respiratory illnesses. The AWARE team includes Wei Chen, associate professor of pediatrics and biostatistics, and Wei Gao, associate professor of electrical and computer engineering at the Swanson School of Engineering.

PInCh awarded two other grand prizes for 2020. Liliana Camison, a plastic surgery resident, and Jesse Goldstein, associate professor of plastic surgery, developed a custom-made cartilage ear implant that decreases the complexity and operative time of facial surgeries; to build it, they employed a high-precision cartilage milling process. Their product is called REPLICA. The other grand-prize winner, LungTarget—created by Maliha Zahid, an assistant professor of developmental biology at Pitt— is a novel set of lung-targeting peptides that can deliver molecules able to disrupt protein coding (small interfering RNAs) to treat cystic fibrosis. *—AA*

Synthetic Biologist Awarded Dickson Prize

Bioengineer **James J. Collins** has been awarded the 2020 Dickson Prize in Medicine, the School of Medicine's highest honor.

Collins

In 2000, Collins described how his team built a stable synthetic gene circuit in E. coli bacteria. That paper has been cited more than 4,000 times and marked the arrival of an important new discipline in biomedicine—synthetic biology.

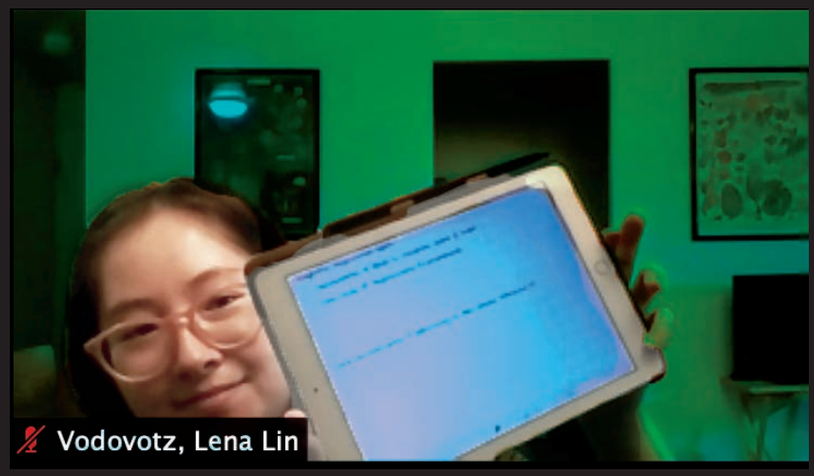
More recently, Collins created engineered microbes and whole-cell biosensors to serve as diagnostics and therapeutics. One platform that he and colleagues developed embeds freeze-dried, cell-free synthetic gene networks onto paper and other materials; it has a wide range of potential clinical and research applications.

"Dr. Collins is defining what's possible in the disciplines of synthetic and systems biology. His highly creative work applying engineering design principles to molecular biology has generated numerous new diagnostics and therapeutics," says Anantha Shekhar, Pitt's senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of Medicine.

Collins is the Termeer Professor of Medical Engineering and Science at Massachusetts Institute of Technology and is affiliated faculty with the Broad Institute of MIT and Harvard University as well as the Wyss Institute at Harvard. He has received a MacArthur Foundation "Genius" grant, NIH Director's Pioneer Award and Sanofi-Institut Pasteur Award. "I am thrilled and honored to receive the Dickson Prize in Medicine," he says.

Pitt's prize is given annually to an American biomedical researcher who has made significant, progressive contributions to medicine. It includes a $50,000 honorarium and invitation to speak at the University's annual campuswide showcase of research. Both the showcase and Dickson Lecture have been postponed until a date to be determined.

—Michele Baum



When in comes to studying, many students say they do better together.

SOCIAL STUDIES

The group study session—it's a fixture of medical school: people around a table, open books, laptops, cups of coffee, scribbles on a nearby whiteboard, young minds being honed together. Before COVID-19, students might have taken these sessions for granted. Jason Rosenstock, associate dean for medical education and professor of psychiatry, believes that being part of a study group not only facilitates learning, but also fosters community, reducing isolation. Some students say they appreciate the dedicated energy these groups generate, rescuing them from YouTube's unrelenting pull.

In response to the pandemic, the University implemented safety precautions for the group study rooms in Alan Magee Scaife Hall. Once accommodating 15 people, the reconfigured rooms now hold no more than a mask-clad three, sitting physically-distanced at X-marked spots. Students must sanitize surfaces after using them. Many students have, of course, incorporated video chats into their studious camaraderie, and that can be surprisingly effective. In an online practice session for Intro to Medical Interviewing, for example, first-year Baraa Nawash and others entered breakout rooms to rehearse and critique their partners. "It was great to observe my classmates' perspectives and improve my own skills," Nawash says. Students appreciate the little things, too: shared digital flashcards, pets slinking past cameras.

The virtual study sessions remind Nawash, 22, of the moment she realized Pitt was her top choice for medical school.

In spring 2020, when Nawash joined more than 40 others in her first virtual meetup for admitted students, she wasn't sure if Pitt Med was the next step in her educational journey. But multiplayer games and icebreakers turned into late-night heart-to-heart conversations. She left the video call smiling, and soon after, she was Pittsburgh-bound.

"I felt like I was already talking to lifelong friends. If not for those evenings, I wouldn't be here today," says Nawash. *—Nithya Kasibhatla*

Explorations and revelations taking place in the medical school

ABOVE: Spinal leads exit the back to connect to an external stimulator. Pitt researchers showed that spinal stimulation can be used to create tactile sensations in a prosthetic limb. Next up: designing fully implantable devices.

A NEW SENSATION

COMMON IMPLANT FOR CHRONIC PAIN SIMULATES TOUCH IN A PROSTHETIC ARM

BY ERIN HARE

Imagine tying your shoes or taking a sip of coffee or cracking an egg but without any feeling in your hand. That's life for users of even the most advanced prosthetic arms.

According to a new study from the University of Pittsburgh's Rehab Neural Engineering Labs, spinal cord stimulators commonly used to relieve chronic pain could provide a straightforward and universal method for adding sensory feedback to a prosthetic arm.

For this study, published in July in eLife, four amputees received spinal stimulators, which, when turned on, create the illusion of sensations in the missing arm. The study was funded by the U.S. Army Research Office and the Defense Advanced Research Projects Agency.

"What's unique about this work is that we're using devices that are already implanted in 50,000 people a year for pain—physicians in every major medical center across the country know how to do these surgical procedures—and we get similar results to highly specialized devices and procedures," says study senior author Lee Fisher, a PhD assistant professor of physical medicine and rehabilitation at Pitt.

The strings of implanted spinal electrodes, which Fisher describes as about the size and shape of "fat spaghetti noodles," run along the spinal cord, where they sit slightly to one side, atop the same nerve roots that would normally transmit sensations from the arm. Because it's a spinal cord implant, even a person with a shoulder-level amputation can use this device.

Fisher's team sent electrical pulses through different spots in the implanted electrodes, one at a time, while participants used a tablet to report what they were feeling and where.

All the participants experienced sensations somewhere on their missing arm or hand, and they indicated the extent of the area affected by drawing on a blank human form. Three participants reported feelings localized to a single finger or part of the palm.

"I was pretty surprised at how small the area of these sensations were that people were reporting," Fisher says. "That's important because we want to generate sensations only where the prosthetic limb is making contact."

When asked to describe not just where but how the stimulation felt, all four participants reported feeling natural sensations, such as touch and pressure, though these feelings often were mixed with decidedly artificial sensations, such as tingling, buzzing or prickling.

Although some degree of electrode migration is inevitable in the first few days after the leads are implanted, Fisher's team found that the electrodes, and the sensations they generated, mostly stayed put across the monthlong duration of the experiment. That's important for the ultimate goal of creating a prosthetic arm that provides sensory feedback to the user.

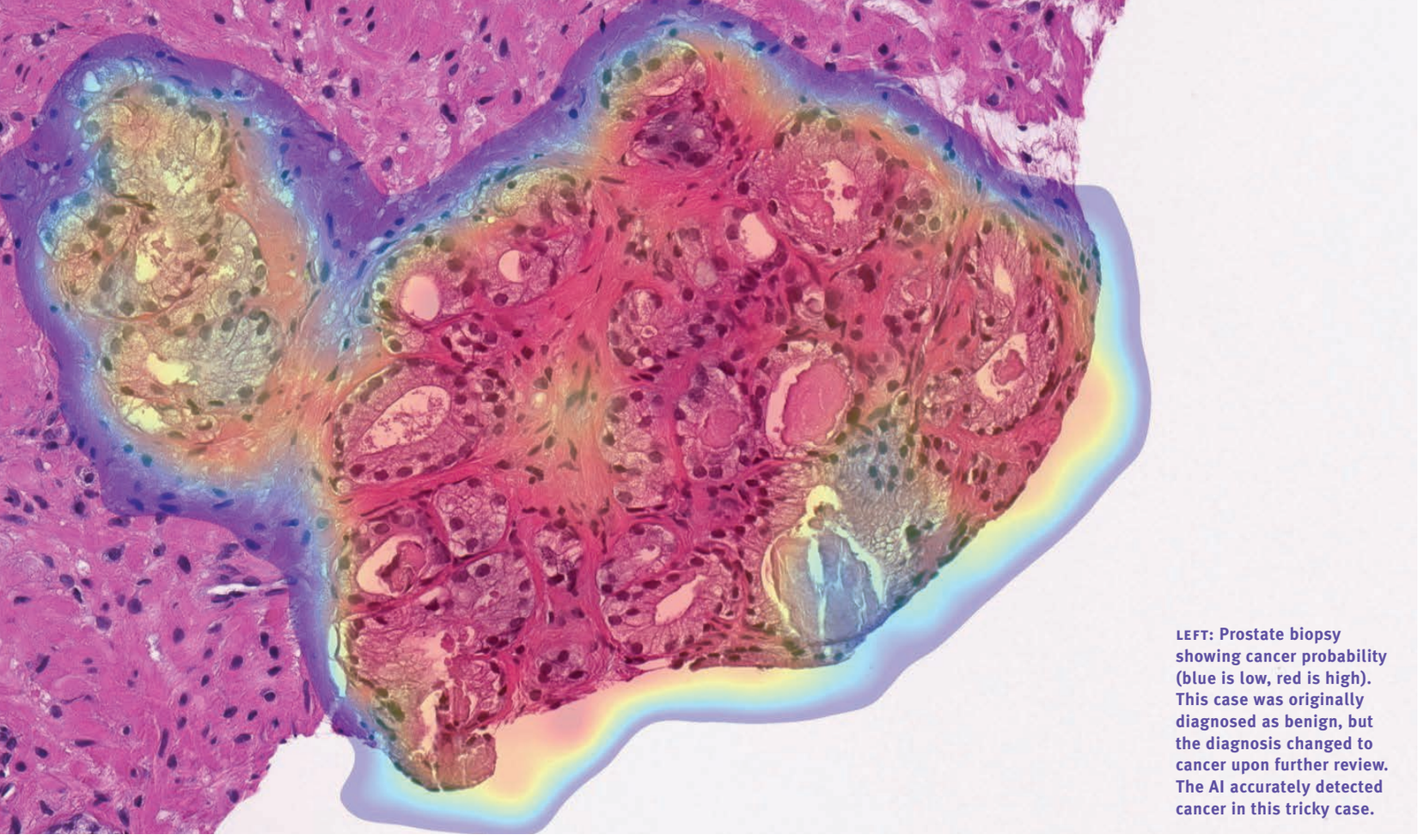
"Stability of these devices is really critical," Fisher says. "If the electrodes are moving around, that's going to change what a person feels when we stimulate."

The next big challenges are to design spinal stimulators that can be fully implanted, rather than connected to a stimulator outside the body, and to demonstrate that the sensory feedback can help to improve the control of a prosthetic hand. The researchers would like to see patients able to do everyday tasks like tie shoes or hold an egg without accidentally crushing it. Shrinking the size of the contacts—the parts of the electrode where current comes out—is another priority. That might allow users to experience even more localized sensations.

"Our goal here wasn't to develop the final device that someone would use permanently," Fisher says. "Mostly we wanted to demonstrate the possibility that something like this could work." ■

Physicians in every major medical center across the country know how to do these surgical procedures.

COURTESY UPMC



LEFT: Prostate biopsy showing cancer probability (blue is low, red is high). This case was originally diagnosed as benign, but the diagnosis changed to cancer upon further review. The AI accurately detected cancer in this tricky case.

IBEX MEDICAL ANALYTICS

PATHO-BOT

AI PARTNERS WITH DOCS

BY ERIN HARE

University of Pittsburgh researchers have demonstrated the highest accuracy to date in recognizing and characterizing prostate cancer using an artificial intelligence (AI) program. The Lancet Digital Health published their study results in August.

"Humans are good at recognizing anomalies, but they have their own biases or past experience," says senior author Rajiv Dhir, MD chief pathologist and vice chair of pathology at UPMC Shadyside and professor of biomedical informatics at Pitt. "Machines are detached from the whole story. There's definitely an element of standardizing care."

To train the AI to recognize prostate cancer, Dhir and his colleagues provided images from more than a million parts of stained-tissue slides taken from patient biopsies. Each image was labeled by expert pathologists to teach the system how to discriminate between healthy and abnormal tissue. The algorithm was then tested on a separate set of 1,600 slides taken from 100 patients seen at UPMC for suspected prostate cancer.

During testing, the AI demonstrated 98% sensitivity and 97% specificity at detecting prostate cancer—significantly higher than previously reported for algorithms working from tissue slides.

Also, this is the first algorithm to extend beyond cancer detection. It also performed well at grading and sizing tumors (assessing how likely they are to grow and spread) and determining whether they'd invaded surrounding nerves. All of these features are clinically important and required as part of the pathology report.

AI also flagged six slides that were not noted by the expert pathologists.

But Dhir, who also is affiliated with UPMC Hillman Cancer Center, explained that this doesn't necessarily mean that the machine is superior to humans. Yet for less experienced pathologists, the algorithm could act as a fail-safe to catch cases that might otherwise be missed.

"Algorithms like this are especially useful in lesions that are atypical," Dhir says. "A nonspecialized person may not be able to make the correct assessment. That's a major advantage of this kind of system."

Although these results are promising, Dhir cautions that new algorithms will have to be trained to detect different types of cancer. The pathology markers aren't universal across all tissue types. But he doesn't see why that couldn't be done to adapt this technology to work with breast cancer, for example.

What does this study mean for patients? Technology like this will help further fine-tune cancer detection and standardize diagnosis. ■

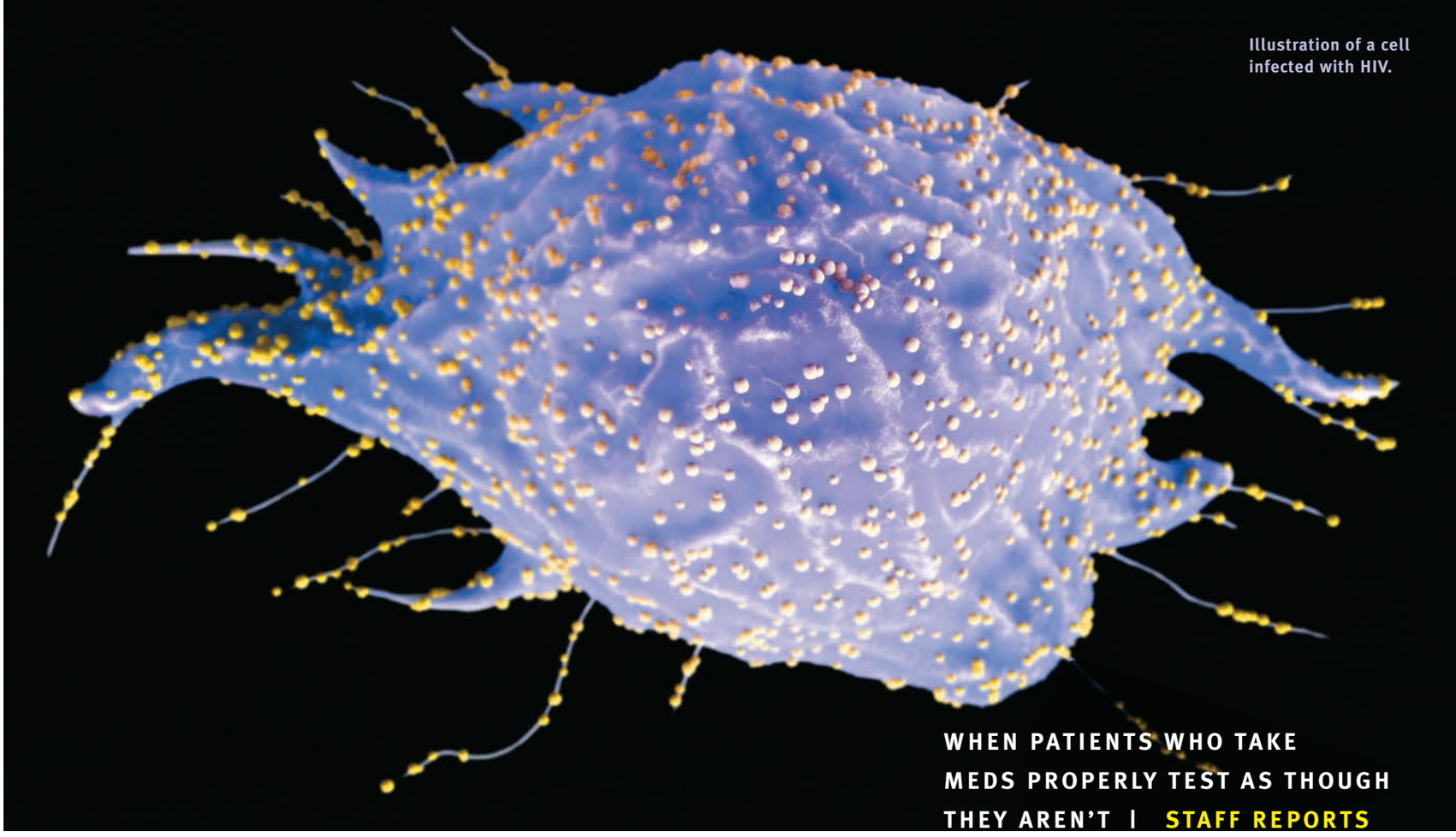


Illustration of a cell infected with HIV.

GETTY IMAGES

WHEN PATIENTS WHO TAKE MEDS PROPERLY TEST AS THOUGH THEY AREN'T | **STAFF REPORTS**

THE MYSTERY BEHIND PERSISTENCE OF HIV IN BLOOD

John Mellors kept hearing the same story from perplexed physicians: a patient with HIV insists they're taking daily medication to keep the virus in check. But testing says otherwise.

Late last year, Mellors—chief of the Division of Infectious Diseases at Pitt and UPMC who holds the Endowed Chair for Global Elimination of HIV and AIDS—and a team of researchers solved this mystery in a study published in the Journal of Clinical Investigation.

These patients, they showed, are hosting large clones of HIV-infected cells, "repliclones," that produce infectious virus particles so plentiful that it could "appear that antiretroviral therapy isn't working even when it is," says Mellors.

HIV typically replicates by taking over a cell's machinery and using it to produce more virus, which can infect other cells.

When taken daily, antiretroviral therapy prevents HIV from infecting new cells so that even though the virus can't yet be cured, it can be controlled to the point that it isn't detectable in blood tests.

Mellors and Elias Halvas, an assistant professor in Pitt's Division of Infectious Diseases, led a multidisciplinary team of HIV scientists in investigating the medical records and blood from eight patients with nonsuppressible HIV viremia—i.e., detectable virus in the blood—despite adherence to antiretroviral medications. Repeated samples of each patient's blood revealed identical viral genetic sequences that did not change over time.

Halvas says, "This indicates that, in the individual patients, the virus in their blood was coming from identical cellular factories"—repliclones.

Thanks to the antiretroviral medications these patients are taking, new cells are not becoming infected by the virus that's produced by repliclones. However, repliclone products could cause other problems, such as chronic inflammation, says Mellors, who is also Distinguished Professor of Medicine at Pitt.

"If the patient were to stop drug therapy, the virus could have a head-start on rebounding. And repliclones are a key barrier to developing a true cure for HIV," Mellors says.

What else does this mean for patients and their doctors?

Because switching treatments may not suppress viremia, says Mellors, clinicians should continue to watch for changes. Viremia might decline if repliclones shrink, which they often do—though not always.

Two remaining challenges for scientists: figuring out how repliclones escape the immune system and how they can be efficiently killed.

The team speculates that smaller repliclones may linger undetected and might even be responsible for the rapid rebound of HIV in patients who stop their therapy.

Scientists around the globe are working hard to track down repliclones and destroy them, says Halvas. ■

LIK

SOLAR SEVEN/GETTY IMAGES

E DAUGHTER, LIKE MOTHER

SHARED CELLS FROM PREGNANCY: DO THEY HELP OR HARM THE MOTHER?

BY ELAINE VITONE

From Greek mythology, the chimera was a fire-breathing two-headed monster, part lion, part goat, part snake. In medicine, it's a real-life biological mishmash: when an individual harbors DNA from someone else.

Doctors have been inducing a kind of chimerism to cure diseases like leukemia through bone marrow transplants since the 1950s. It's a daunting procedure: First, chemo and radiation. Then, an infusion of healthy blood-forming cells from a donor. If all goes well, the cells kick into gear, functioning and multiplying; and from then on, the donor's DNA is coursing through this patient's veins, right alongside their own.

As Pitt's Thomas E. Starzl noted, chimerism happens in solid organ transplants sometimes, too. For reasons scientists can't yet explain, self and nonself somehow learn to coexist, without the need for drugs that are normally used to stop the body from rejecting the donor organ. Pitt researchers are attempting to better understand how this works.

But by far the most common form of what scientists now call microchimerism occurs in nature every day.

Decades ago, scientists began finding something curious in autopsies of women—cells with male chromosomes. These were, as it turned out, their sons' cells. And though their numbers were very small, the cells were found colonizing in organs all throughout the women's bodies, even decades after they'd given birth. This was later found to be true of daughters' cells, as well. And amazingly, the mother-child transfer of cells works both ways.

Which begs the question: If a woman might harbor her children's cells throughout her life, what does that mean for her health?

In February 2020, we sat down with an expert on the topic, **R. Swati Shree** (Res '14), at Pitt Medcast's live taping at the annual meeting of the American Association for the Advancement of Science. Shree, who trained in ob/gyn and maternal fetal medicine at Magee, is assistant professor of maternal fetal medicine at the University of Washington.

ERICA LLOYD

Elaine Vitone (right) interviews alumna R. Swati Shree for Pitt Medcast at the 2020 American Association for the Advancement of Science conference in Seattle in February 2020.

What are studies telling us? Are these cells helpful or harmful?

It's very complicated, and it probably depends on a few factors, including circumstances under which the cells are transferred, gestational age and genetics.

J. Lee Nelson [of the Fred Hutchinson Cancer Research Center], one of my mentors, found that some women who have rheumatoid arthritis have more of these cells in their blood and tissues. We don't know exactly what these cells are doing—maybe causing some damage, or maybe these cells are being recruited to areas of tissue damage for repair—but we understand that they are likely very important.

Many women who have rheumatoid arthritis harbor a gene that predisposes them to it. The gene is part of our HLA system, which determines what is "self" and what is not "self." Interestingly, there's a subset of women who have rheumatoid arthritis and don't have that gene. But one study found that gene in their [microchimeric] cells.

In the breast cancer literature, there have been a few key studies by Vijayakrishna Gadi at the University of Illinois. He looked in blood and breast tissue and found that women who had breast cancer had lower levels of these cells, suggesting a possible protective benefit. Women who've had pregnancies seem to be less likely to get breast cancer later in life—maybe this is a mechanism for that.

You've studied how mode of delivery might affect this cellular crossover. What have you found?

We could detect these cells in women's blood within hours after delivery, and there appeared to be a higher number in women who'd had a C-section.

Another group found that women who'd had C-sections had increased risk for an autoimmune disease in the years following delivery. We can't put those two together as a causation, but it's certainly thought-provoking that maybe these cells play a role.

You've also studied these cells in the context of preeclampsia—spontaneous, dangerously high blood pressure in pregnant women that can kill the mother unless the baby is delivered quickly, ready or not. What are you finding?

We found more of these cells in the blood of women who had preeclampsia than in those who did not.

Decades out from their delivery, women [who have had preeclampsia] are at significantly higher risk for cardiovascular disease or heart disease. Risk factors for preeclampsia are some of those same risk factors that put them at risk for cardiovascular disease. But another really interesting study controlled for those risk factors and found that they alone [didn't explain the increased risk, suggesting] there's something about the pregnancy itself.

What questions are you focusing on now?

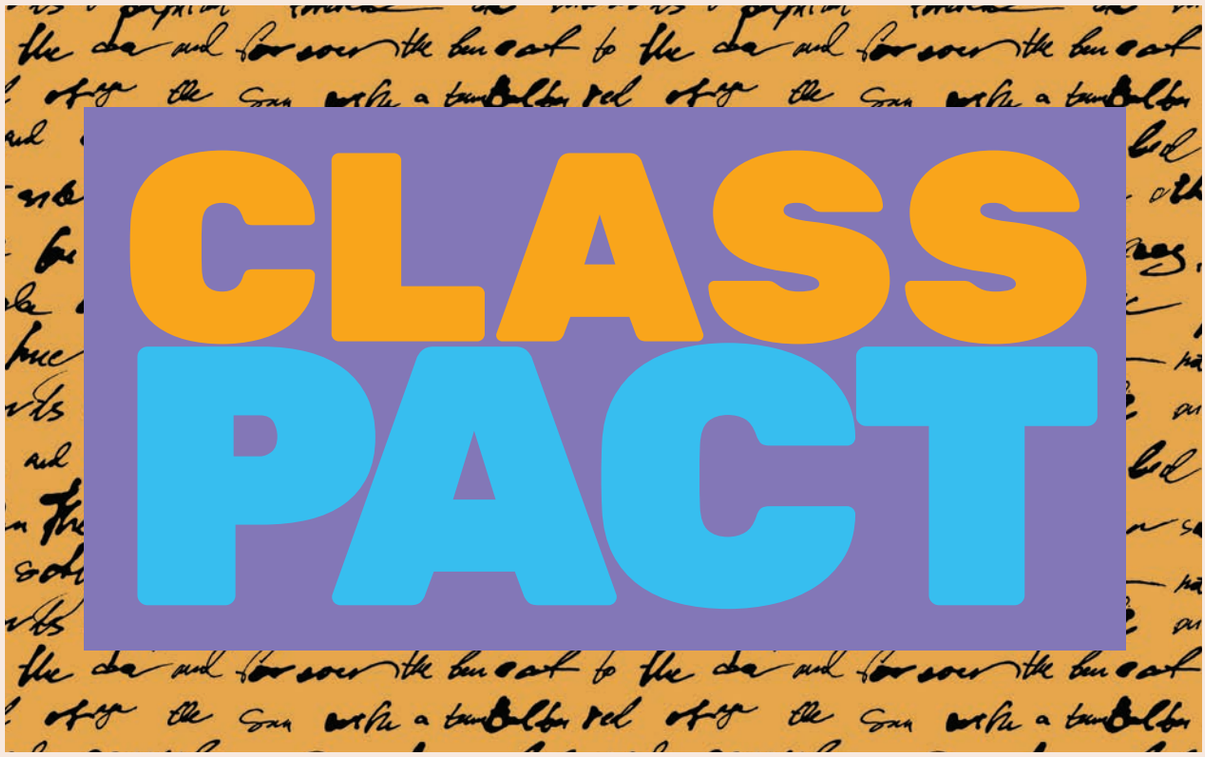
Are there more of these cells in women who had preeclampsia and later developed cardiovascular disease? If so, the next step would be to understand how those cells cause cardiovascular damage. That work will probably take decades.

Preeclampsia is a big mystery, but the thinking is that it happens because something goes wrong when the placenta first sets up shop. But it's undetectable until much later, when, suddenly, it's an emergency. Are you thinking this work could help change that?

Absolutely. We've become interested in something called cell-free DNA, which is DNA that's free-floating and continuously shed into the mother's blood [from all her organs]. We found that women with preeclampsia had much higher levels of total cell-free DNA in their blood compared to women without preeclampsia. Interestingly, the fraction deriving from the placenta was not different, suggesting that maternal sources are contributing to this higher amount of cell-free DNA. We think it's potentially related to maternal organs that are known to be injured in preeclampsia: the kidneys, liver and brain. [Shree's manuscript on these findings is currently under review.]

We believe that we should be able to potentially find markers of that [placental development] process that went wrong in the blood of these mothers. If we find markers, then we could look for them earlier in pregnancy, find out who may be at risk and tailor their care. And a pipe dream would be some sort of treatment to prevent preeclampsia from ever happening. ■

Editor's Note: Listen to the discussion at **pi.tt/pittmedcast**.



BACKGROUND IMAGE: GETTY IMAGES. TYPOGRAPHY: ELENA CERRI

THE CLASS OF 2024 WRITES ITS OWN OATH

BY KAYLA PAPAKIE

In July, incoming Pitt Med students received an email with one of their first assignments: Write a class oath.

More than 40 hours of video-chat discussions later, the students had a working draft.

Chenits Pettigrew, an EdD who is associate dean for diversity, equity and inclusion at the School of Medicine, says, "It is really important that the students begin to understand what they're taking on and what a privilege it is to be let into the intimate spaces of people's lives.

"These are students who come from all different places and backgrounds. This exercise helped them identify their similarities and differences and then apply those discussions to one very important experience that they will be sharing together."

The Class of 2024 upheld the tradition of reciting the Hippocratic Oath at their virtual White Coat Ceremony on Aug. 16, 2020; yet, says first-year Nathalie Chen, an update was in order: "Patients are no longer viewed just in terms of their symptoms and sicknesses. Physicians now seek to understand each patient's narrative and how their socioeconomic status may impact their health," she says.

All 149 incoming students helped draft the oath. (They initially met in groups of five.)

"We worked collaboratively but disagreed at times," says Tito Onyekweli, who, with Chen and others, served on the committee that finalized the oath. "We brought up topics that were triggering for some but did not push the status quo enough for others. We were diverse in the most collective sense. More than anything, this process was human."

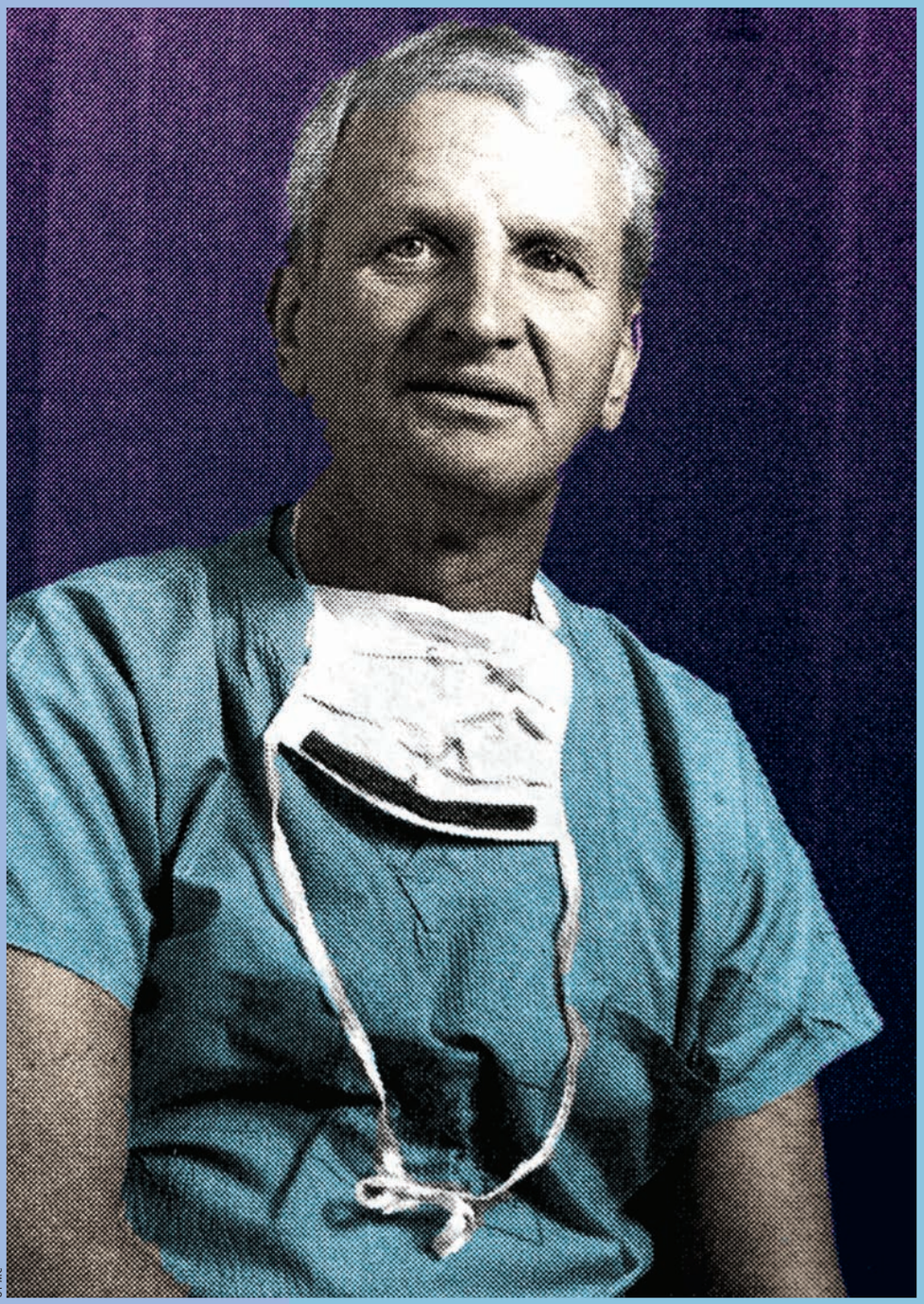
In their "Oath of Professionalism," the students pledge to work toward restoring trust in providers among disenfranchised people. They also commit to championing diversity in medicine and society and to stand as allies to those of low socioeconomic status.

"We start our medical journey amidst the COVID-19 pandemic and a national civil rights movement reinvigorated by the killings of Breonna Taylor, George Floyd and Ahmaud Arbery," the oath begins. "We honor the 700,000-plus lives lost to COVID-19, despite the sacrifices of health care workers."

At the end of their orientation week in August, students officially presented their oath to Anantha Shekhar, an MD, PhD, senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of the School of Medicine. "I am excited to watch them put this promise into practice," says Shekhar.

Moving forward, each incoming Pitt Med class will write its own oath, says Pettigrew: "This exercise solidified the class in a way I've never seen before. We will do it again."

Read the whole oath here: **pi.tt/pittoath2024**



UPMC

Eugene Myers transformed Pitt's Department of Otolaryngology, and along the way, he trained 27 future department chairs, including his son.

THE CHAIRMAKER

EUGENE MYERS NURTURED A GENERATION OF OTOLARYNGOLOGISTS

BY GAVIN JENKINS

One evening in 1938, a man enters the South Philadelphia home of his primary care physician. The doctor's young son watches as the patient offers his father a jar of homemade spaghetti sauce.

By day, the father, David Myers, trains to be an otolaryngologist, but his preceptorship at Temple University Hospital doesn't pay enough to support his wife and two children. So he moonlights by running a private practice out of his family's living room. But it's the height of the Great Depression, and most of his patients can't afford to pay him. They often bring food in lieu of money to their appointments.

On this night, the patient, an Italian immigrant, hands over the jar of red sauce and says, "When I have money, I bring you."

UPMC

Eugene Myers, seen here with a patient, is a second-generation otolaryngologist. His son, Jeffrey Myers, followed in his footsteps, and Jeffrey Myers' son, Keith Myers, will graduate from Temple University's School of Medicine in spring 2021.

Eugene Myers, Distinguished Professor Emeritus of Otolaryngology at the University of Pittsburgh and chair emeritus of the department, was the boy watching that night. He witnessed many interactions like this between his dad and his dad's patients during those hard times. When Eugene Myers tells the story, he'll add that his maternal grandfather, Samuel Nicholas, a physician with a successful private practice, gave his father money each week to help the family survive. Nicholas placed the cash in a fruit bowl, pinning it down with chocolate for his grandson and granddaughter.

Eugene Myers likes to share this story when he talks about his career. Why? Because it's an allegory for how his father—the son of Romanian immigrants who owned a tailor shop—was passionate about medicine and helping patients. And it shows that if you're a Myers, medicine is a family affair.

Jeffrey Myers (Res '96), who is the Alando J. Ballantyne Distinguished Chair of Head and Neck Surgery at the University of Texas MD Anderson Cancer Center in Houston.

Some of Eugene Myers' protégés have trained otolaryngologists who have become department chairs, as well. "I consider them my grandchildren," Myers says, then smiles.

Eugene Myers, 87, could be called the Bill Walsh of otolaryngology because, like the legendary San Francisco 49ers's head coach, many of his protégés have borrowed his business style and leadership philosophy. Johan Fagan (Fel '97), chair of the Department of Otolaryngology at the University of Cape Town, says he molded his division after Pitt's.

Myers taught Fagan to build the careers of others by being generous with coauthorships. Also, he told him, surround yourself with the best possible people, regardless of whether or not their work outshines yours.

Godfather" because of his tremendous influence. Hao is now chair of the Department of Otolaryngology at Shin Kong Wu Ho-Su Memorial Hospital and program director of otolaryngology at Fu Jen Catholic University in Taiwan.

During his fellowship, Hao spent a couple of hours each Saturday after teaching rounds with Myers in his office. At the time, Hao thought he was there to discuss the "poor" state of his manuscripts. But later, when he returned to Taiwan, he realized that Myers was mentoring him.

"He taught me everything" during those meetings, Hao says, including "professionalism, his philosophy."

The chair-tree Myers has grown almost didn't get planted. Despite looking up to a father, grandfather and three uncles who were physicians, he majored in economics at the University of Pennsylvania's Wharton School.

"That seemed like a miracle to me," Myers says of stapes mobilization. "And I wanted to be in the miracle business, not the business world."

In May 2021, when Eugene Myers' grandson, Keith Myers, graduates from Temple University's Lewis Katz School of Medicine, he will be a fifth-generation physician and the eighth doctor in his immediate family.

America has lots of families with multiple generations of doctors, but the Myers family stands out. They are royalty in the field of otolaryngology. The Myers family includes three department chairs of otolaryngology. And they ready others for that role.

It began when David Myers became chair of Temple University's Department of Otolaryngology in 1955 (he held the position until 1961). Eugene Myers followed in his footsteps; as the first full-time chair of Pitt's Department of Otolaryngology, he served for 33 years. Eugene Myers ushered the department into a modern era of head and neck surgery, and he cultivated an environment that emphasized academics.

Eugene Myers trained 27 otolaryngologists who have gone on to become department chairs around the world, including his son,

"Most importantly, he taught me to lead by example," Fagan says. "He was the hardest working person in the department when I was at Pitt."

An avid traveler who has been to 103 countries, Myers set out to improve head and neck surgery throughout the world. As chair, he recruited international fellows like Fagan, and then visited them once they returned to their home countries. Myers also built international relationships by serving on boards, attending conferences and lecturing at medical schools on nearly every continent.

Fagan shares that international approach. The University of Cape Town is the only university on the continent with an otolaryngology fellowship program, and many of Fagan's fellows have returned to practice head and neck surgery in their native sub-Saharan countries.

"He has changed the face of head and neck surgery in Africa by starting a fellowship program," Myers says proudly.

Sheng-Po Hao (Fel '93) calls Myers "the

He changed his career path after graduating when Samuel Rosen, a prominent New York otologist, visited Philadelphia to meet with his father. Rosen was there to talk about stapes mobilization, an operation that he had developed, which remobilizes the footplate of the middle-ear bone to relieve a conductive hearing impairment.

"That seemed like a miracle to me," Myers says of stapes mobilization. "And I wanted to be in the miracle business, not the business world."

Among Myers' most notable contributions to the treatment of cancer involved cases in which cancer cells infiltrated beyond the nodes in the lymph, or ECS (extracapsular spread). In 1979, the idea that ECS had a profoundly negative effect on the outcome of head and neck cancer patients was new to American otolaryngologists. Gordon Snow, professor and chair of otolaryngology at the Free University, Amsterdam, had found that using radiation therapy gave patients more control over the cancer in their neck. However,

BOTH PHOTOS: COURTESY MYERS

Eugene Myers has mentored otolaryngologists around the world, including Johan Fagan, department chair at the University of Cape Town in South Africa, and Sheng-Po Hao, director of otolaryngology at Fu Jen Catholic University in Taiwan. LEFT: Jeffrey Myers, Eugene Myers, Marion Fagan, Johan Fagan and Barbara Myers pose at a black-tie event. RIGHT: Eugene Myers talks with Sheng-Po Hao.

many patients still died from distant metastasis. Eugene Myers added chemotherapy following surgery and radiation therapy, and his team found that the survival rate increased.

"When the drugs were refined, we went to a program of concomitant chemoradiation following the surgery and found that the cure rate was enhanced and the treatment time was reduced considerably," Eugene Myers says.

As this became the standard treatment for patients with ECS, Pitt's Department of Otolaryngology became internationally recognized. Eugene Myers served as president of all five major societies in the field, including the American Board of Otolaryngology-Head and Neck Surgery. He is a diplomate of the American Board of Otolaryngology and Honorary Fellow of both the Royal College of Surgeons of Edinburgh and the Royal Society of Medicine in London.

On a cold morning, Myers sits in the small office he keeps at the Eye and Ear Institute. Framed honorary doctorates and lifetime achievement awards hang on the walls; the shelves are lined with books that his former students have written. Reflecting on how he became a chairmaker, Myers attributes his success to timing and management style.

Myers became chair of Pitt's Department of Otolaryngology in 1972, when Dean Donald Medearis had shifted the School of Medicine's focus toward the hiring of academic-minded faculty members. Before Myers, the department was staffed with private practitioners who worked with residents on a part-time basis.

"When I took over, the residents we attracted wanted to be involved in clinical otolaryngology," Myers says. "We had no reputation for anything else."

Myers hired research-minded experts to full-time appointments: academics like Charles Bluestone, a Distinguished Professor of Otolaryngology who specialized in pediatrics, and Jonas Johnson, a renowned head and neck cancer surgeon who succeeded Myers as the department's chair in 2005.

Myers followed a management by objective philosophy that he learned at Penn. He pushed faculty members to publish papers, and he led the charge, writing more than 300 articles and contributing to nearly 150 book chapters. However, he is best known for writing "Cancer of the Head and Neck," with coauthor James Suen, a Distinguished Professor of Otolaryngology at the University of Arkansas Medical School. The book is now in its fifth edition.

"That book became the Bible of the field," says Nancy Snyderman.

After her residency here, Snyderman (Res '83) was appointed to the faculty at the University of Arkansas. She thought she was on track to become chair—today, there are just five women chairs in American otolaryngology departments (including Cecelia Schmalbach, the David Myers Chair at Temple, which Myers and his wife, Barbara, endowed in his father's name). Yet a career in television got in Snyderman's way.

After doing a few spots on local news in Little Rock, Snyderman became a medical correspondent for NBC. She's arguably Myers' most well-known mentee. But when her television opportunities first began rolling in, she feared that being on television would hurt her academic career and about backlash from her colleagues in the medical profession. So, she called Myers.

"He told me to tune out the background noise and keep doing what I was doing. That's what I did and proceeded with my career," Snyderman says.

A lot of people would probably look at the Myers family legacy and assume that pressure is placed on some children to continue the doctoring tradition. But, just as Myers didn't urge Snyderman to stay in academics, family members say they didn't grow up feeling they were expected to become physicians. Though, Jeffrey Myers likes to joke otherwise, saying: "My parents said I could do whatever I want after medical school."

Instead of pressure, it's passion for medicine and caring for patients that's inspired the Myers family, according to Jeffrey Myers, who is Keith's father. And he thinks that's why Eugene Myers has trained so many future department chairs.

"My dad and grandfather worked long hours, but it was fun to them," Jeffrey Myers says. "My dad never complained . . . Rather, it was always, 'I met with this patient today, and she was really interesting. She had this fascinating condition that we helped her with.'" ■

Philadelphia residents wait in line to be tested by the Black Doctors COVID-19 Consortium.

ALUM ALA STANFORD TAKES COVID-19 TESTING TO THE PEOPLE | BY RACHEL MENNIES
PHOTOGRAPHY | BLACK DOCTORS COVID-19 CONSORTIUM

MOVING MOUNTAINS

"Hello, beautiful! How are you this morning? I see you've put my little office in the corner." I hear Ala Stanford (Res '04) say this to someone I can't see while I have her on a cell call.

Stanford

Stanford has just arrived at the Mt. Zion United Methodist Church in Darby, Pennsylvania—roughly five miles southwest of downtown Philadelphia. This morning, the staff of the Black Doctors COVID-19 Consortium has already begun to set up their mobile testing site in the church's parking lot. Stanford has fit in this remote interview with me while the team prepares for the day's first patients, some of whom are already present and waiting.

"When we show up," Stanford says, "we build a triage unit. We've got all our supplies and PPE, we've got our computers, our printers, our surge protectors, our shredder, everything… We'll go anywhere where folks ask us to come out and where there's a need."

Since March, Stanford has run pop-up COVID-19 testing sites like this one as the consortium's founder and lead physician. Stanford—probably the first Black woman graduate of UPMC's general surgery residency—established the consortium in March in response to the already disproportionate rate that Black Philadelphians had fallen ill and died from COVID-19. According to the city's public health department, Black residents are more likely to die or become infected or hospitalized for COVID-19 than any other racial group in the city. In Philadelphia in May 2020, Black patients were dying of coronavirus at a rate of 4.1 for every 10,000 people—more than 30% higher than the death rate among white patients.

After the first reports came out revealing the discrepancy, Stanford says, "I reached out to the city health department and my state senators and others… only to learn that there was no concerted effort to reduce the spread, [not] at the state, federal or city level."

Stanford—born and raised in Philadelphia—was getting call after call from local Black residents unable to receive needed testing. The kinds of reasons hospitals turned them away: "Because they didn't have a prescription," she notes. "Or because they took a bus, and they weren't in a car for drive-up testing." This served as Stanford's call to action, and the consortium was born. From March to November, consortium providers tested 14,000 people for COVID-19, more than 90% of whom are Black and most of whom are located in the Philadelphia area.

The consortium chooses testing sites that are familiar and easy for residents to access—most commonly church parking lots, but also those near public transit hubs and local schools. Stanford's team relies on social media, particularly Instagram and TikTok (dancing breaks out often), to spread the word about its testing locations. Stanford stresses the importance of meeting her patients "where they are."

By September, the health department reported that rates of infection, hospitalization and deaths had diminished dramatically for Black Philadelphians. Yet a November surge brought a rise in hospitalizations, again at disproportionate rates for Black residents.

This is Stanford's step toward countering the racist legacy that's embedded in the American health care system. She draws a straight line from "the 1800s, when surgical procedures were being performed on Black women without their consent and without anesthesia… to the 1900s, when you have Tuskegee, and you have Holmesburg Prison" to "the present-day coronavirus" and its outsized effect on Black patients.

"I think the sooner as health care professionals we acknowledge that [history] and take ownership of the fact that this is what we're dealing with, the better health care outcomes will be."

By deliberately naming her organization the Black Doctors COVID-19 Consortium, by centering the name in their logo and on shirts they often wear to testing sites, Stanford hopes to address any possible reticence to seek testing. "I wanted people," she says, "to feel some level of comfort [seeking care], just based on who was there, who was testing them and who was going to talk to them about their medical history." The consortium now numbers roughly 50 providers.

The consortium's website and Instagram account both regularly feature photos of people being tested, helping to demystify the process. Stanford's team now offers both adult and pediatric flu immunizations as well. Stanford received hers live on camera; she and Philadelphia's health commissioner, Thomas Farley, administered each other's shots.

Stanford, a pediatric surgeon, owns and operates Stanford Pediatric Surgery in Jenkintown, Pennsylvania, a Philadelphia suburb; she's also the founder of R.E.A.L. Concierge Medicine, which provides a boutique array of offerings for higher-profile patients. For now, though, Stanford is testing, testing, testing. Because of COVID-19-related elective surgery restrictions, she's on temporary hiatus from the pediatric OR. She's navigating 2020's "new normal" alongside her three sons, who've all begun the school year virtually.

"My testing times will often start at 10 a.m. during the week—and that's on purpose," Stanford says. That way, she notes, "I can make sure my kids are settled, that we've worked out any glitches with the computer system, that they've had breakfast, that they've seen me. And then I have the babysitter come in and be with them. I usually finish up [on site] around 3 or 4 p.m., and I come home, I decontaminate, and we talk about our day." In this truly unprecedented year, she says, "I try to get us as normal as I can."

"I wanted people," she says, "to feel some level of comfort [seeking care], just based on who was there, who was testing them and who was going to talk to them about their medical history."

Timothy Billiar, chair of Pitt's department of surgery, says Stanford is a "trailblazer."

Stanford credits her time at Pitt as key to her growth and success. "The resources I had to really do my best were right there," she recalls.

Still, there were difficulties breaking a path at a storied institution. "[People] were used to Black women cleaning rooms," she says, "emptying trash cans, maybe being your nurse—but not being your surgeon. And that was tough." Billiar recalls Stanford as a driven, committed resident even as she contended with these obstacles: "She taught many of us to think differently about what it means to be a surgeon."

Stanford sees a future for American medicine that addresses medical racism head on: one that must carry with it the hard lessons learned from COVID-19's unequal spread. "Folks need access," she says, "they need empathy, and they need action; and once you see something needs to be changed, you need to change it; and you have to acknowledge that we all have implicit biases. Every single one of us. Know what yours is, and then make a conscious effort, every single day, to change it—and first do no harm." ■

Stanford's team chooses sites that are easy for locals to access.

After getting their consent, the consortium takes photos of people getting tested and posts them on its website, so people know what to expect.

LEFT: Stanford's team at a church testing site. ABOVE: Consortium volunteers have tested more than 14,000 people. They've also administered flu shots.

NO RECHARGE FOR THE WEARY

STRESS IS AN INEQUITABLE ARBITER OF HEALTH

BY ELAINE VITONE

PAINTING BY JASMINE GREEN

When the University of Pittsburgh's Naudia Jonassaint goes to the doctor, she keeps it casual. She wears sweatpants. And she does not mention she's a doctor herself.

Unless, of course, she has to. And a few years ago, when she was pregnant for the third time around, she did.

Jonassaint felt off. Checking her blood pressure at home, she was alarmed to find it was 180/90. She headed for the hospital. A nurse took her vitals and history. And Jonassaint told her: "I feel more swollen than normal."

To this, a shrug. "Your blood pressure isn't that high."

In fact, Jonassaint's systolic pressure was 30 points above her usual. Granted, this was maybe not so strange. But it should have been a red flag, given what Jonassaint had just told her:

Her first pregnancy ended in a miscarriage 27 weeks in.

Her second pregnancy resulted in a beautiful baby boy—but the experience was harrowing. She delivered early, at 31 weeks, in the throes of severe preeclampsia syndrome, a life-threatening condition that sends the mother's blood pressure sky high, as well as another pregnancy complication known as HELLP.

The nurse knew all of this and didn't bat an eye.

For Black women in this country, being dismissed is all too common, says Jonassaint, medical director of clinical hepatology at UPMC Presbyterian and assistant professor of medicine at Pitt, as well as the department's first vice chair for diversity, equity and inclusion.

And from time to time she reaches a point where she has to refuse to be dismissed.

"I'm a hepatologist," she finally told the nurse, "and I know edema [swelling]. I see it day in and day out. This is unusual for me."

In an instant, the trajectory of her care changed—and likely saved her life.

In the United States, Black babies and mothers have exponentially higher mortality rates than do white babies and mothers. That disparity holds true when controlling for factors like obesity in the mother. For Black mothers, even high education or income isn't protective in the same way it is for mothers who are white. Astonishingly, it seems to put them at higher risk.

A strong correlate to preterm birth has been shown in "chronic worry"—about racial discrimination, specifically.

There is bias, says Jonassaint. And in reaction to that and more, every waking day there is stress that, as a Black woman, "you just take on" as part of living, she says.

The March of Dimes reports that acute stressors lead to pregnancy complications. And for a number of other conditions, chronic stress has emerged as an inequitable arbiter of health. It's a lived reality for millions of Americans of color.

Our bodies are designed for threats that are fleeting: a predator, a natural disaster, a one-off brush with danger. And whether a body opts to fight or to fly, it has to rise to the occasion: blood pressure climbing, breath and pulse off at a gallop, adrenal glands releasing glucose to fuel muscles, cortisol to sharpen our readiness to use those muscles and adrenaline to kickstart it all. This is how it should be.

But when crises linger as ever-present specters, the same self-made fury that steals us away from the lions can slowly devour the body from within. Arteries stiffen. Vessel linings wither. The blood sugar balance forgets itself. The immune system falters, or mutinies.

This summer, the American Medical Association (AMA) took a stand on the issue of police brutality, both physical and verbal, noting that it disproportionately affects racially marginalized communities. The AMA called such violence "a critical determinant of health" with rippling effects—and not just to those with personal connections to it.

Citing a 2018 study in Lancet, the AMA noted there is a "spillover effect" on the population. Within the highly segregated neighborhoods where police encounters cluster, stress and anxiety levels are high. These same communities experience high rates of hypertension, diabetes and asthma, and the fatal complications of all of the above. African Americans report between one and seven additional poor mental health days per year for each police killing in the person's state, and the distress takes on many forms: loss of self-regard, increased fear and vigilance, broken trust in social institutions, anger, rehashing of prior traumas, heightened perception of inequity, bereavement.

Simply living in communities where there is greater police presence, says the University of Minnesota's Rachel Hardeman in an episode of the CME podcast Clinical Problem Solvers, has a "direct" correlation with preterm birth rates, according to her latest study. The episode begins a new series on antiracism in medicine, cohosted by Pitt's Utibe Essien, assistant professor of medicine and a core investigator with the Center for Health Equity Research and Promotion in the VA Pittsburgh Healthcare System.

In "Stolen Breaths," a New England Journal of Medicine essay published this summer, Hardeman and her coauthors write that "Black people cannot breathe because we are preemptively grieving the 1 in 1,000 Black men and boys who will be killed by police." Black men are about three times more likely than white men to die in a police encounter.

Stress, broadly speaking, is when the challenges of what you're up against seem to exceed your capacity and resources to cope. And it's stressful to be threatened, period, even if the threat is just a low-lying question that nags in the background, says David Levinthal, who in both the lab and the clinic (he's a GI specialist) focuses on the effects of stress, anxiety and depression on the body, as well as the neural connections that tie it all together. Levinthal is an assistant professor of medicine at Pitt and director of UPMC's Neurogastroenterology and Motility Center.

It's long been known that emotional well-being and bodily health are linked, explains Levinthal's mentor turned research partner, Peter Strick, who is Pitt's Thomas Detre Professor, chair of neurobiology and scientific director of the Brain Institute. But the mechanisms of how that works were largely a mystery until just a few years ago. In a 2016 paper in Proceedings of the National Academy of Sciences, Strick and Levinthal traced the nerves connecting a visceral organ to the brain; no one had done that before.

"Just *thinking about* conflict drives the adrenal medulla in the same way as if it's actually occurred."

That visceral organ was the adrenal gland—specifically, a portion thereof called the adrenal medulla that is the ignition of the flight-or-fight response. And hardwired directly into it, they found, are brain regions responsible not only for fighting and flying, but also appraising stress and other meaning from the events in our lives.

"Our research," says Strick, "shows that just *thinking about* conflict drives the adrenal medulla in the same way as if it's actually occurred. And that's key. The system was designed for the actual circumstance. But if you're feeling fearful and angry in the long term, you're driving these systems."

The team uses animal models for their cel-

lular-level studies of this "stress-and-depression connectome." Further validating their results is a complementary line of work from Peter Gianaros, professor of psychology, who uses functional MRI (fMRI) imaging in humans.

In projects led by Gianaros' former PhD students Dana Jorgensen (PhD '18) and Kimberly Lockwood (PhD '19), he has also investigated race and ethnicity in cardiovascular and cerebrovascular health, and what drives those links.

The team has compared age-related brain changes to stress-related and socioeconomic factors like income, education and material resources, hunting for markers of whose cognitive health might be at risk in midlife and beyond. In a study funded by the National Institute of Diabetes and Digestive and Kidney Diseases, Gianaros and Anna Marsland, a Pitt professor of psychology, are following over time Pittsburghers living in various neighborhoods across the city. This ongoing work launched with a study published in Cerebral Cortex in 2017, which found that neighborhood-level disadvantage was indeed associated with poorer brain health. The group hypothesizes that just as the heart, kidneys, lungs and other organs decline in an onslaught of constant stress, so does the brain.

The cardiovascular system is supposed to be dynamic, marshalling oxygen and chemicals throughout our body when we need them. And conversely, when we don't, powering down is extremely important, as well. Sleep, where we spend about a third of our lives, "has a function—it's restorative," says Karen Matthews, Distinguished Professor of Psychiatry and a leader in Pitt's decades-old powerhouse in studies of stress and cardiovascular disease.

During healthy sleep, blood pressure dips by 10% to 20% as part of the body's natural recharging process. But studies indicate that in African Americans, blood pressure doesn't go down as it should. This steady state is not desirable: It probably damages endothelial cells, which line blood vessels throughout the body; and it's been shown to lead to cardiovascular disease down the road.

And sadly, Matthews has shown, Black Americans are missing out on this battery recharge as early as adolescence.

In 2013 and 2014, she published papers on a study of both Black and white healthy adolescents from middle- and lower-income families. Matthews found that African American teens were particularly likely to have elevated night/day systolic blood pressure ratios, and this was true regardless of how much money their parents made or how much education they had attained.

Compared to white counterparts in the study, Black adolescents also reported more negative emotions, like depression, anger and cynicism; fewer "positive resources," like self-esteem and optimism; and more "unpleasant interactions" plaguing their days, like conflicts and disagreements.

But among white participants who reported these same social-emotional hardships, blood pressure dipped just fine.

The medical literature has shown that throughout adulthood, Black individuals sleep less and have more fragmented sleep. This too begins in high school, Matthews found, with Black male adolescents sleeping the least and worst among their peers.

Matthews showed that among menopausal women, too, African Americans have the poorest sleep across ethnic groups. This finding came from a massive, multisite, longitudinal effort known as the Study of Women's Health Across the Nation (SWAN). Among the biggest drivers for Black menopausal women's sleep disturbances, she and her coauthors reported, was financial hardship.

Without proper recharging, from a physiological standpoint, we wake up with more to deal with and less energy to do it, says Matthews.

In time, poor sleep has powerful cumulative effects on the body, from head to toe. It's essential for our organs, our emotions and our ability to develop, learn and endure. It's known to have direct links to immunological function, to pain, to appetite and metabolism, to aging. To virtually every known aspect of our health.

Jonassaint still mourns her first baby who didn't make it. And adding to that sting are the what-ifs: She knew something was wrong, and told her doctor so when she called. This was more than just a little spotting. But he said not to worry. *No need to come in. Rest. Drink fluids.* The end.

The next morning, she started having contractions and rushed to the hospital. There was no heartbeat. And there was no comfort, either. Instead of extending condolences, the first thing her doctor thought to do was defend yesterday's advice.

"It was not like, *Sorry your baby is deceased*," Jonassaint recalls—just defensiveness. On top of her grief, to be written off like that was devastating.

And then, in quick succession, it kept happening.

Jonassaint went to the florist, distressed, newly not-pregnant, and told the clerk she was looking for some flowers. The clerk snapped, "Well, what type of flowers? It's a flower shop."

"Baby's funeral," she said.

And the clerk was horrified.

A few weeks later, the clinic's receptionist lectured her for missing her 30-week visit.

"Well, ma'am," Jonassaint said, "I'm no longer pregnant. I lost my baby."

And the receptionist was horrified.

To this day Jonassaint is convinced she would've been treated differently in that grief-stricken blur had she been white, though she acknowledges that of course it's impossible to know for sure.

And there's the rub. What-ifs are always running in the background, draining the battery. On those days scarred by loss, she says, "I felt as though my intersectionality at that point took my humanity away."

Throughout her career, Pitt's Sarah Pedersen, associate professor of psychiatry and psychology as well as codirector of the psychiatry department's Youth and Family Research Program, has studied how discrimination, both in the moment and as a chronic presence, can lead to difficult life circumstances. Her current study, now in its third year, is funded by the National Institute on Alcohol Abuse and Alcoholism.

As part of the study, Pittsburghers record incidences of discrimination. And among white participants, about 20% have such an experience at some point within the length of the entire protocol, which is 17 days.

For Black participants, it's 87%. And on average, Black young adult males report expe-

riencing discrimination on the basis of their racial identity *at least* daily.

And yes, this is current data, Pedersen stresses. "This is real time. This is where we live. It's devastating."

What do those stress-inducing experiences look like? Pedersen says that, unfortunately, they come in many varieties:

Being treated with less respect than others. Seeing people around them cower and act afraid. Hearing people assume they don't have money or can't possibly be smart.

"A lot of our participants really do report being pulled over by police, being treated poorly by police," Pedersen says, as well as days filled with a hyperawareness of their bodies moving through space: how they look, what they wear, where they are.

Microaggressions—brief, everyday indignities, slights and insults, both intentional and unintentional—are commonplace for people of color. They are a form of discrimination, which is widely considered a "salient psychosocial stressor," according to a 2017 American Psychological Association report on health inequities, which was coauthored by Pitt's Peter Gianaros.

Sometimes, people say hurtful things fully believing they're anything but. Backhanded compliments like the infamous "You're so articulate." And the phrase "I don't see color," is innocuous to white participants who hear it, Pedersen says; but Black participants in her study find it insulting across the board, albeit to widely varying degrees. They find it dismissive of another's lifetime of discrimination, stress and disadvantage, Pedersen says.

In the American Psychological Association report, the authors note that with stigma and disenfranchisement come vulnerability to social harm. At the same time, would-be protections from it, like social, personal, educational and material resources, are harder to come by.

Cultural, institutional and interpersonal racism can lead to internalized forms of these poisons. All of the above have been shown to fuel toxic stress, which is recognized by the World Health Organization as one of the top 10 determinants of disparities in health.

Pedersen, who has a longstanding research interest in problematic alcohol use, notes that people who identify as African American are less likely than white people to drink at all. But among those who do, they're more likely to develop alcohol problems at the same level of use. Which is puzzling.

"Usually, if you drink more, you have more problems," says Pedersen.

She has been investigating this discrepancy. Pedersen is finding that the stress-dampening effects of alcohol are more strongly related to alcohol use for Black drinkers compared to white drinkers.

"The effect of alcohol is potentially more reinforcing because of having to manage chronic and acute life stressors and discrimination," she says.

Microaggressions, too, can have macro implications.

During healthy sleep, blood pressure dips by 10% to 20% as part of the body's natural recharging process. In many African Americans, blood pressure doesn't go down as it should.

At 3 p.m. on a recent Friday, Jonassaint answers a video chat on the go. "Hello," she says into her smartphone, eyes smiling above a surgical mask. Her third grader, also masked, waves and bounds along beside her as they head for the car after his well-child visit.

It's a day of doctor appointments and errands. The kind most moms would dress down for. But as she unmasks and puts the phone on the dashboard, it's not sweats, but a sharp peacoat and collared shirt that come into view.

We start our interview, about racial inequities in health, specifically in her area of expertise, liver disease, as she drives home.

"Transplantation is boutique medicine," she says.

"I mean, you can't get anything more fancy than that."

And unfortunately, in order to get that boutique donor organ, a person has to have the sort of job that allows for three months' worth of leave time to recover—and a loved one with the same who can take care of them around the clock.

"As my cardiologist friend says, 'Wealth buys health,'" she says.

The sad fact is that, with all our interventions—open-heart surgeries, statins, stents, lasers, robotics—Black men are still 1.6 times more likely to die at any age than white men, and that number has hardly changed in 70 years. "That should tell us that innovation is not everything," she says. "We have to apply those innovations in a way that's fair and equitable in order to get the outcome that we want.

"If we want it."

Chatting as she drives, we cover vast terrain: From her MD thesis—about how health disparities arise from disparities in education—to the ways that stress, imposter syndrome and internalized stereotyping fuel that fire. And how living outside of the social majority can shroud everything in uncertainty, from the moment you wake up and get dressed.

The reason why she decided against sweatpants this morning, she says, is because her day of errand-running started at the bank. "I didn't want them to question my deposit."

The car pulls up to the family home, and her son walks in, passing his dad and preschool-age sister playing on the porch. Jonassaint hangs back in the car parked outside and tells me the story of another little boy who should've been there. And the things she does to protect herself and her family from a world that won't always give them the benefit of the doubt.

"It's hard for me to talk about one thing in isolation," she says.

"Because I think this is all one big issue. One big continuum." ■

People and programs that keep the school healthy and vibrant

UNIVERSITY OF PITTSBURGH

Student champion Joan Harvey (in burgundy) retired in 2020; she's shown here surrounded by students and colleagues on Match Day 2018.

CRITICAL (STUDENT) CARE

EMERGENCY FUND HONORS JOAN HARVEY

BY SAMANTHA PAIGE ROSEN

In August, when Chloe Heintz, Pitt Med major gifts officer, asked Joan Harvey what kind of support students could really use from alumni, she answered without hesitation: an emergency fund.

Harvey, who retired as associate dean of student affairs and associate professor of medicine in September, saw personal emergencies create substantial roadblocks for students even before the pandemic hit. "Med students have bumps in the road just like everybody else, but they're also going through this very challenging curriculum," she says.

A summer 2020 survey conducted by Pitt Med's admissions and financial aid office revealed the extent of this need. Fifty-seven percent of respondents said the COVID-19 pandemic worsened their finances and a third reported job loss in their immediate family. Faculty and administrators mobilized.

Named in honor of the recent retiree, the Joan Harvey, MD, School of Medicine Student Emergency Fund provides temporary assistance to students facing unanticipated financial hardships. Students in any School of Medicine program are eligible to receive funding. They can apply once per term and are awarded a maximum of $500 per term. The fund helps addresses acute needs like groceries and rent, unforeseen medical expenses, travel associated with a personal or family emergency and technology for remote schooling.

"We want it to be as easy as possible to apply and get it into students' hands," says Chenits Pettigrew Jr., associate dean for diversity, equity and inclusion and assistant dean for student affairs.

As of November 2020, faculty, staff and alumni had made $160,000 in donations and pledges to the fund. Ann Thompson, vice dean, Beth Piraino, associate dean of admissions and financial aid, and alumnus Edward Puccio (MD '90) were the first to donate. Shortly after, they were joined by Anantha Shekhar, senior vice chancellor for the health sciences and John and Gertrude Petersen Dean.

"Faculty members have told me that 'we were all students once' and that it was especially important to them to help students through this stressful time," says Heintz.

Harvey, who says she is humbled to be honored with the fund's name, expressed relief that Pitt Med students would receive resources as they develop "skills of resiliency."

Pitt Med community members rave about the longtime dean's dedication to students. "Dr. Harvey has supported students through dramatic changes in our society, our medical school curriculum and the evolving expectations our country has for doctors," says Thompson.

Harvey started at Pitt 30 years ago. Her career took her from New York to Massachusetts to rural Minnesota, where she served with the National Health Service Corps, to Bethesda, Maryland. Before moving to Pittsburgh, she served as an associate professor of clinical medicine and a lieutenant commander of the U.S. Navy Reserve at the Uniformed Services University of the Health Sciences, as well as an attending staff physician in rheumatology at Walter Reed Army Medical Center. In 1991, she assumed her position at Pitt Med.

Harvey has championed an advisory dean house system and programs that foster a supportive environment for medical students, including Faculty and Students Together and the Student Health Advocacy Resource Program. These initiatives connect students with faculty, students with students, and students with mental health professionals.

"At the end of my second year of medical school," C. Nic Moga (MD '01) recalls, "I ran myself into complete exhaustion and had what laypeople refer to as a 'nervous breakdown.' I didn't really know what was wrong aside from the fact that I had to take some time off to readjust my life.

"I'll never forget walking into Dr. Harvey's office and trying to explain this to her." He was met with warmth, compassion and understanding, he says. "The support I had from her and everyone in the administration at Pitt was responsible for not only helping me graduate from medical school but also for making me a better person." ■

CLASS NOTES

'60s

These days, **Constance Keefer** (MD '69) is "to a great extent retired—but I can't seem to give up the work!" This semi-retirement includes working as assistant professor of pediatrics at Harvard Medical School and as a child development specialist at Boston Children's Hospital. As an expert in newborn behavior and infant mental health, she's also teaching for the medical staff at the Brigham and Women's Hospital nursery. Before semi-retiring, Keefer traveled the world as a developmental teaching pediatrician; that work included yearly trips to Iran.

Keefer

'70s

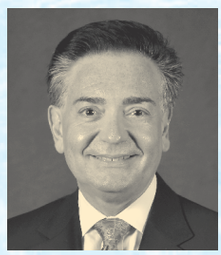
Vicki Rubin Kelley (PhD '77), professor of medicine at Harvard University, researches destructive inflammation—"the common denominator of almost every disease," she notes. Her recent work focuses on potential therapeutic targets for lupus nephritis, an inflammation of the kidneys that is common in patients with lupus. Kelley advises her students to follow their gut, saying she wouldn't have achieved success if she hadn't strayed from convention. She credits her unconventional efforts to seek out grants in person as a Pitt Med PhD candidate with ultimately landing her a position in Harvard's renal division.

Kelley

'80s

Paul McDermott (PhD '84) is on the faculty of the Medical University of South Carolina's cardiology division in its department of medicine. McDermott is associate dean for faculty affairs and faculty development as well as professor of medicine. He oversees the preclinical medical curriculum and is also the director of the university's Academy of Medical Educators. McDermott's daughter Anne McDermott is in her second year at Pitt Med.

McDermott



Troianos

Christopher Troianos (MD '85) is chair of the Cleveland Clinic's Anesthesiology Institute. He oversees anesthesia-related care at the clinic's 10 hospitals and seven surgery centers in Ohio and provides administrative support to their hospitals in Florida, Abu Dhabi and London. Troianos also serves as professor of anesthesiology at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University and practices as a cardiac anesthesiologist at Cleveland Clinic. He says the value of anesthesiologists has certainly come to light with COVID-19. "We're on the front lines in caring for these patients, from intubating their airways to managing their ventilation to caring for them in the ICUs."

'90s

Timothy Klatt (MD '92) serves as professor and head of the Medical College of Wisconsin's Division of General Obstetrics and Gynecology and as the medical director of patient safety at Froedtert Hospital in Milwaukee. "I am truly a generalist," he says of his clinical ob/gyn practice. In June, Klatt was honored with Froedtert's Thomas L. Smallwood Award for Clinical Excellence, the highest honor bestowed by the hospital. The best part of the recognition, according to Klatt? His colleagues: "the people who nominated me—the fantastic people with whom I work every day."

Klatt

Elisa Konieczko (PhD '92) is professor of biology at Gannon University in Erie, Pennsylvania, where she primarily teaches anatomy, cell biology and other courses. She recently completed a 20-year collaboration with researchers and physicians at UPMC Hamot investigating the hormones relaxin and estrogen in joint injuries and diseases. Responding to the sixfold increase of anterior cruciate ligament (ACL) injuries in women compared to men, the team confirmed the hormones' partial roles in the disparity. She is especially proud of the 40 undergraduate biology and pre-professional students from Gannon who participated in the collaboration.

Konieczko

While pursuing her doctorate at Pitt Med, **Kathleen Yee** (PhD '93) delved into neuronal pathfinding of visual sensory systems. During her career, she has broadened her attention to include auditory systems. Yee, assistant professor of neurobiology and anatomical sciences at the University of Mississippi Medical Center, began investigating the Zika virus's impact on the inner ear after reports surfaced of patients experiencing hearing impairment. She published a study in September's Hearing Research that is "the first to show the molecular and morphological damage to the inner ear" caused by Zika infections and "suggests multiple mechanisms" that contribute to that hearing loss.

Yee

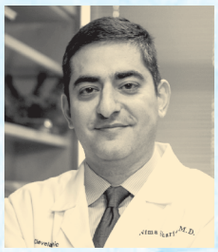
Hackney

'00s

David Hackney (MD '00, Maternal Fetal Medicine Fellow '08) is associate professor of reproductive biology at Case Western Reserve University and division director of maternal fetal medicine at University Hospitals Cleveland Medical Center. As vice chair for the Ohio section of the American College of Obstetricians and Gynecologists, Hackney meets with legislators to advocate for women's health. Hackney and his wife, **Lisa Hackney** (MD '02, Pediatric Hematology/Oncology Fellow '08), a pediatric oncologist, both trained with Pitt doctors—and their Pitt connection spans a generation. "Our first son, Abe," says Hackney, "was born at Magee while we were fellows."

McNeil

Brian Keith McNeil (MD '01) recently added associate dean for clinical affairs at SUNY Downstate Health Sciences University to his titles, an extensive list that includes vice chair of Downstate's urology department. In our 2018 write-up on McNeil, we noted his longstanding efforts to address health care inequities. Now as associate dean, McNeil is overseeing the medical school's senior class curriculum, and he's revamping student rotations with Brooklyn-area hospitals as part of a broader effort to better prepare students to care for underserved populations. Last year, as part of the Downstate Coronavirus Preparedness Task Force, McNeil worked closely with his colleagues to organize redeployment of residents and faculty to meet critical patient needs.



Sharifi

Nima Sharifi (MD '01) studies sex steroids that control the progression of prostate cancer. In light of the COVID-19 pandemic, he's following a new thread: whether these steroids play a role in the disproportionate number of men who've become seriously ill or died from COVID-19 compared to women. There may be clues from his study published last year in Proceedings of the National Academy of Sciences; he discovered a genetic anomaly related to prostate cancer that's common in patients with poor outcomes from asthma treatment. Sharifi is the Kendrick Family Endowed Chair for Prostate Cancer Research at the Cleveland Clinic.

—Nithya Kasibhatla and Rachel Mennies

SPOTLIGHT

JENNIFER COPE: WASH AND GO

COURTESY COPE

Cope has been deployed by the CDC.

In February 2020, while most Americans were still living normally in the growing shadow of the COVID-19 pandemic, CDC medical officer Jennifer Cope (MD '04) was deployed to the Los Angeles International Airport (LAX) to screen travelers arriving from China for SARS-CoV-2. Two passengers who had been stuck in Wuhan for months were ordered to quarantine at a U.S. naval base. "They were both so gracious," Cope recalls. "I don't know how many people would have been. [Imagine] flying halfway across the world, you're tired, you haven't seen your family in maybe months."

During her LAX deployment, Cope also experienced the stress of quarantining after being exposed to a confirmed-positive individual. In addition to being concerned about getting sick, she had to work from her hotel room (in February, before remote work was the norm) and delay going home. Cope says it was "the longest that I'd been away from my kids since they were born. It was tough."

Yet she was driven to contribute more. She was home in Atlanta for only a few weeks before deploying to North Dakota to expand testing capacity there—most memorably by testing workers at a manufacturing plant during an April snowfall. (Her head-to-toe PPE kept her warm.) In the summer, Cope returned to Atlanta to pitch in at the CDC's emergency response center.

Cope is the CDC's subject-matter expert for free-living amoeba infections, which spread to humans through water. She's still busy confirming amoeba-infection cases, but as the team leader of the Domestic Water Sanitation and Hygiene (WASH) Epidemiology Team at the CDC, she's now using her expertise in waterborne disease surveillance to help implement a new system for monitoring the spread of SARS-CoV-2.

The WASH team is working with the wastewater sector and local public health officials nationwide to build a national wastewater surveillance system for SARS-CoV-2, which is shed in stool. Testing the sludge at a wastewater treatment plant can offer an early warning of a COVID-19 outbreak.

"This tells you, 'This is probably a place where we need to ramp up clinical testing,'" she notes. *—Rachel Mennies*

BERTRAM LUBIN

JULY 21, 1939–JUNE 27, 2020

Lubin

As a teenager in Pittsburgh, Bertram Lubin (MD '64)—then a budding jazz drummer—experienced a once-in-a-lifetime breakthrough: The drummer for jazz legend Thelonious Monk had fallen ill before the show that Lubin had snuck out of the house to attend. Lubin, excited, offered to pinch-hit on the drums—and performed with Monk onstage.

Lubin, a hematologist and pediatrician and the former president and CEO of UCSF Benioff Children's Hospital Oakland, died in June. He's remembered by friends and family for his twinned lifetime dedications to music and medicine—both shaped by the city of Pittsburgh.

"My father loved science, medicine and jazz," reflects his son Alex Lubin. "These were passions he developed in Pittsburgh and at Pitt Med. He dedicated his life to helping others, to creating meaningful change in health outcomes and access, and to seeing the best in everyone he encountered."

Commitment to underserved communities characterized Lubin's medical career, including breakthroughs in sickle-cell research that led to the founding of the Children's Hospital Oakland Research Institute (CHORI). His standard-setting push to screen newborns for sickle-cell disease became law in California; that policy was adopted in all 50 states. At CHORI, Lubin also created an umbilical cord blood storage program for the siblings of children in need of a stem cell transplant; it was the first program of its kind in the world.

Pittsburgh was always in his heart, Alex notes. He says his father always kept a copy of Pitt Med magazine on his coffee table. In 2007, Pitt Med awarded Lubin its Hench Distinguished Alumni Award.

—Rachel Mennies

MARTHA D. NELSON

OCT 15, 1931–AUG 6, 2020

Nelson

As a Pitt Med student, Martha D. Nelson (MD '56) frequented Jonas Salk's lab. "We would spend lunchtimes watching the monkeys—the ones that [Salk] used to come up with the polio vaccine," recalls classmate Herbert Croft (MD '56).

Studying at Pitt during that time inspired Nelson to become a champion of public health. She found her calling in Ohio's Summit County Health Department. She was hired in 1961 as director of medical services and soon became the youngest health commissioner in the state.

Croft witnessed Nelson's impact, having also moved to Summit County. During his first year of medical practice, he spent Sundays administering the Salk team's polio vaccine at schools under Nelson's department's purview.

Nelson served as health commissioner for 38 years. Besides organizing immunization campaigns, school health programs and access to quality health care, she was a founding member of Planned Parenthood of Akron and served on its medical advisory board.

When Nelson retired in 1996, the Akron Beacon Journal noted that she had garnered respect for her ability to accomplish any project. As her daughter, Jane Nelson, CEO and executive director of the Oklahoma Nurses Association, puts it: "My mother was out there doing it and not talking it." The Summit County Board of Health named the Martha D. Nelson Public Health Clinic in her honor.

Nelson's husband, Roger Nelson, says she loved her position because "she felt that she was impacting more lives through public health practices than she would have in private practice." Indeed, Jane Nelson says her mother "saw the community itself as her practice."

—Nithya Kasibhatla

LINTON TRAUB

FEB 6, 1962–OCT 19, 2020

Traub

Linton Traub was finishing his PhD at the Weizmann Institute when he and wife, Jill, bought their first original lithograph—a rooftop cityscape evocative of the view from their Israeli apartment. The acquisition launched a local arts patronage that spanned three decades as the pair moved first to St. Louis for Linton's postdoctoral fellowship at Washington University and then to Pittsburgh, where he spent 20 years on the faculty of Pitt's Department of Cell Biology. "We're running out of space on the walls," says daughter Simone.

And yet when Traub died, his family decided to hang one more original—a series of Coomassie blue–stained protein gels from the London-born scientist's lab notebooks. "His gels were perfect," says Texas Tech University's Peter Keyel (PhD '06), who trained with Traub. "He wanted data of a quality that was incontrovertible."

Traub investigated how the protein clathrin affects the passage of macromolecules from the eukaryotic cell surface to the inside of the cell. The process influences cellular uptake of iron and other critical substances. "His work was fundamental to our current understanding of how clathrin-coated structures are assembled, how cargo is recruited into these structures and the physiological role of this process," says Pitt cell biology department chair Alexander Sorkin.

Traub's final paper was a single-author report on molecular tools he'd developed, illustrated with his characteristically impeccable gels, to elucidate the earliest steps in clathrin coat formation. Says Sorkin: "Linton's hunger for research, resilience, rigorousness and boundless knowledge of scientific literature were second to none."

—Sharon Tregaskis

NELSON PHOTO: © AKRON BEACON JOURNAL. 1993. USA TODAY NETWORK

'50s

RAYMOND N. KILLEEN, MD '52
SEPT 11, 2020

GEORGE F. MACDONALD, MD '52
OCT 22, 2020

RUSSELL L. ANDERSON JR., MD '54, RES '57, FEL '58, RES '60
OCT 14, 2020

LOREN M. ROSENBACH, MD '54
NOV 9, 2020

JOHN FRANCIS ZEEDICK, MD '54
AUG 18, 2020

NORBERT L. DUGAN JR., MD '56
MAY 16, 2019

JOSEPH G. RITTER, MD '56
NOV 7, 2020

DAYNE F. WAHL, MD '58
SEPT 12, 2020

JOHN J. GEORGE, MD '59
OCT 29, 2020

AWARD-WINNING IS AN UNDERSTATEMENT: CARL FUHRMAN

BY ADAM REGER

NIKHIL B. AMESUR/PHOTO ILLUSTRATION: ELENA CERRI

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

"Don't even think about using the word 'prominent.' Foreheads are prominent. If you're going to tell me about what you've seen, you need to tell me about the structure's size, its shape, its contour, its position. No 'prominent.'"

That's the sort of guidance radiologist Carl Fuhrman (MD '79) was famous for giving. A celebrated teacher, Fuhrman challenged students to be precise in their language and observations.

Born in Erie, Pennsylvania, Fuhrman attended Pitt for his undergraduate and medical studies. He became a full professor in the Department of Radiology in 1994 and served as chief of thoracic radiology for the next 27 years. He died unexpectedly in June, while reading X-rays.

Speaking at a memorial celebration in July, Christopher Faber characterized Fuhrman's teaching as "the Socratic method, but with a Carl Fuhrman twist." By asking binary questions such as "Which lung is larger?" Fuhrman guided students' observations. "At the end, you would believe you had come up with the correct diagnosis," Faber, associate professor of medicine, said.

"Everybody was brighter when they were around Carl."

"His passion was teaching," said Melissa McNeil (MD '80), professor of medicine and a friend for more than 40 years. "He loved our students, and they loved him." At the memorial, McNeil read excerpts from Fuhrman's teaching evaluations, which she said contained more exclamation points than she had ever seen. "Dr. Fuhrman!!!" read one evaluation. "Everyone has got to listen to his lectures."

Fuhrman was a nine-time winner of the Golden Apple Award, given annually by medical students to the top-rated professor. His peers in the national Association of University Radiologists voted him top teacher in 2013. And Pitt awarded him the Chancellor's Distinguished Teaching Award. Fuhrman won his department's teaching award 15 times—so often that in 2016 it was renamed in his honor.

For those who worked with and learned from Fuhrman, his skill as a teacher was inseparable from his excellence as a clinician. "You can't be a gifted teacher unless you know your field backwards and forwards," says Jules Sumkin, chair of radiology. "Carl just had all the pieces."

Marion Hughes (MD '00), who trained with Fuhrman and later became his colleague as associate professor of radiology, says: "To be excellent as a radiologist there's a lot of inferring, and he was very good at that. He was extremely accurate and very fast, a rare combination."

Fuhrman also possessed a legendary memory. At Fuhrman's memorial, Jacob Sechrist, assistant professor of radiology, said, "Not only did he remember their medical history but he could tell you when they got divorced and how much their spouse got in the settlement."

As a researcher, Fuhrman distinguished himself with more than 100 publications, contributing to the understanding of lung cancer, interstitial lung disease and chronic obstructive pulmonary disease. Early in the COVID-19 pandemic, Fuhrman created a tutorial to aid radiologists across the UPMC system and beyond in correctly identifying the virus on a chest X-ray.

He was often reading chest X-rays by 5 or 6 a.m., Hughes says, so he could be finished in time to hear student presentations. Each Friday, from 7 to 8 a.m., he held a conference that was wildly popular.

"I learned something from Carl in every interaction," said Faber. "Regrettably my education lasted only 33 years. In that time I learned perhaps 1% of what he knew. I was hoping to get to 2%."

"It's an incomparable loss," says Hughes. "When you [are] not only great yourself but train hundreds of other people to be great, that's your legacy." ■

IN MEMORIAM

'60s

ROBERT N. LIGO, MD '61
SEPT 13, 2020

CHARLES GOODSTEIN, RES '62
APRIL 30, 2020

JOHN A. HERMAN, RES '63
JAN 14, 2019

JOHN S. NAJARIAN, FEL '63
AUG 31, 2020

WILLIAM H. MARCHL, MD '64
NOV 15, 2020

EDWARD J. MCCLAIN JR., RES '64
OCT 20, 2020

ROBERT EMMETT KEEFE, MD '65
AUG 10, 2020

JOHN F. LANCASTER, RES '65
SEPT 21, 2019

CLOVIS M. SNYDER, RES '65, FEL '65
OCT 1, 2020

HANS R. WILHELMSEN, RES '65
OCT 9, 2020

VICTOR S. ANDERSON, RES '66
JAN 20, 2020

CHARLES A. STRINGFELLOW, RES '66
MAR 5, 2019

JUAN T. MUNOZ, RES '67
NOV 11, 2019

CHARLES HALL ASHFORD, RES '68
MAY 15, 2020

RAYMOND SESTI BONIFACE, RES '68
MAR 1, 2020

EDGAR O. HORGER III, FEL '68
DEC 25, 2019

MICHAEL DAVIDSON, MD '69
NOV 8, 2020

'70s

SWAMIKKAN A. NALLATHAMBI, RES '70, FEL '72
DEC 29, 2019

NARAYAN T. NAYAK, RES '72, '77
AUG 11, 2019

WILLIAM H. THIES, PHD '72
AUG 16, 2020

RONALD J. NORTH, RES '76
NOV 7, 2020

'80s

BENEDICT J. SEMMES, FEL '83
JUNE 18, 2020

'90s

RAYMOND H. THORNTON, MD '98
OCT 1, 2020

KATHY A. EDWARDS, RES '99
DEC 7, 2019

'00s

JAMES W. HUNDERUP, RES '02
DEC 18, 2019

FACULTY

ROBERT E. LEE, MD '56
OCT 29, 2020

MARITA D. KENNA, RES '64
NOV 13, 2019

PAUL C. FIEHLER, MD '76
OCT 6, 2020

LYDIA BUKOWY DANIELS, PHD '83
SEPT 14, 2020

"Alright . . . Mr. Death. See now . . . I'm gonna tell you what I'm gonna do. I'm gonna take and build me a fence around this yard. See? I'm gonna build me a fence around what belongs to me. And then I want you to stay on the other side. See?"
—Troy Maxson character in "Fences," by August Wilson

In October, the University of Pittsburgh Library System announced it had acquired the August Wilson archives. Wilson, one of America's most important playwrights, set nine plays of his 10-play magnum opus, the American Century Cycle, in the Hill District, which neighbors this academic medical center.

"He left Pittsburgh in 1978, but he took the Hill, the three rivers, the streets, the steel mills, the fish sandwich shops and the cadence of the language he heard in cigar stores and barbershops with him," Constanza Romero, Wilson's widow, says. His work was an intimate look at the African American struggle for cultural, economic and self- preservation. As the late Wilson himself once put it:

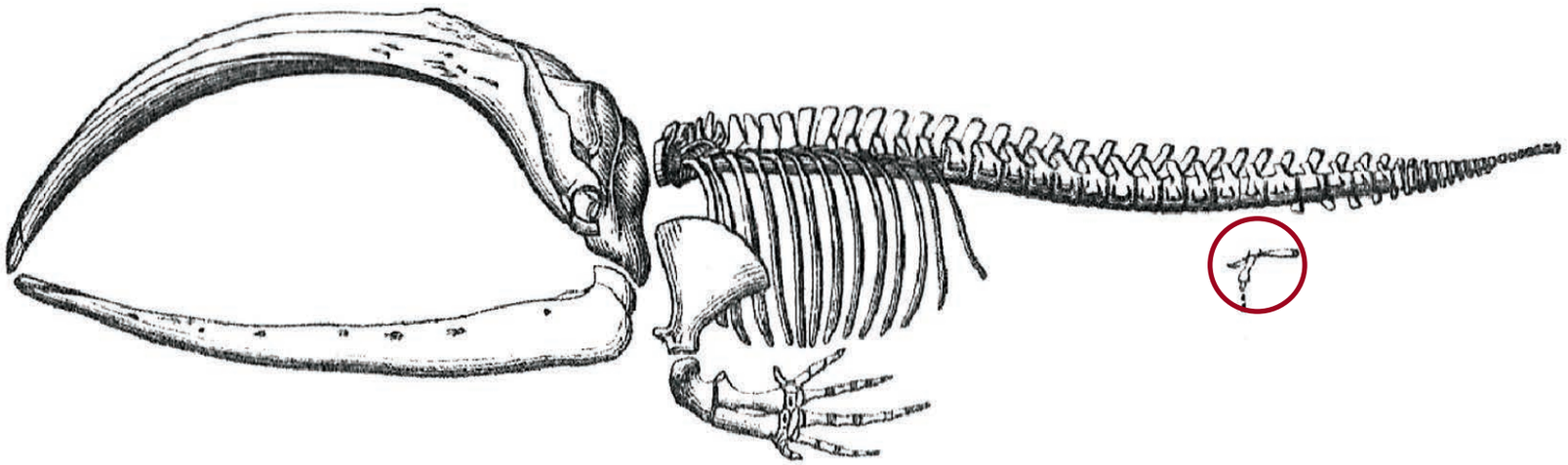
"I once wrote a short story called 'The Best Blues Singer in the World,' and it went like this: 'The streets that Balboa walked were his own private ocean, and Balboa was drowning.'

"End of story. That says it all. Nothing else to say. I've been rewriting that same story over and over again. All my plays are rewriting that same story." *—Erica Lloyd*

—Photography: Archives & Special Collections, University of Pittsburgh Library System

Logan Street in the Hill District, September 1938.

Let's hear it for retro body parts. Did you know that some whales have useless hind limbs, left over from eons ago, when their ancestors walked around?



WIKIMEDIA COMMONS

FOR REAL! TWEEN SCIENCE

Magic isn't the only thing that can make objects disappear. Evolution, over millions of years, can do away with parts that become harmful or no longer serve a purpose.

Imagine an animal born with a harmful trait—like a strange tendency to trust tigers. Such animals would be more likely to die before having babies, so that trait is less likely to be passed down to other generations. Eventually, the trait becomes less common and might eventually, as generations go on—poof!—disappear.

Sometimes, however, if a trait does not make the organism much worse off, that trait might stick around. Even if it no longer has a purpose.

For instance, you once had a tail.

Yup, we're talking to you, human.

When you were a four-week-old mass of cells in your mom's belly, you began to build a tail. But then, before you were born, those cells that made up you edited out most of the tail, leaving your tailbone—a small attachment site for muscles and tendons. That human "tail" you used to have is considered a "vestigial structure." Like the computer modem (look it up) from the '90s that your grandpa still has in the closet, it's retro and probably useless.

Sometimes these vestigial structures develop, but serve no clear reason for being. The flightless kiwi has wings, and some whales have tiny back legs.

Lots of people point to the human appendix as a vestigial structure. At one point, scientists believe, the appendix helped our vegetarian ancestors digest food and maintain normal gut bacteria. But the food of modern humans is more easily digestible, so the function of our appendix has been less clear. In fact, the organ can occasionally pose a threat. Appendicitis, an infection of the organ, arises in about 8% of Americans.

But don't write off the appendix just yet. Growing evidence suggests that the organ actually helps us fight other diseases. As researchers further clarify this role, then, poof!—so much for the idea that the appendix is just another useless structure.

—John Hansen and Erica Lloyd

Thanks to Pitt Med's Jack Schumann, recently retired favorite anatomy instructor, for helping us sort out form from function.

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

COURTESY WELLS FAMILY

Robert Wells with his mentor, the late Klaus Hofmann, son, Kevin, and Frances Finn Reichl, Hofmann's widow, circa 1981.

Inspired. Invested.

Before he joined H.G. Khorana's team at the University of Wisconsin that did Nobel-Prize-winning work by cracking the genetic code, before he became the biochemist behind paradigm-shifting work on unorthodox DNA structures, Robert Wells (PhD '64) was a coal-town kid.

"I grew up in a poor home, and that has had an impact on my life," says the Uniontown, Pennsylvania, native.

"Bob would come over in his little car to see me," recalls his wife, Dotty Wells, of their courtship in high school. Wells was doing odd jobs at the time, tarring roofs in the summer and other scut work for Dotty's neighbor, a brute of a man who had a moving business that sometimes hauled meat. In between, Wells had to clean the truck. Says Dotty Wells, "That man would come to the corner to see if Bob's car was at my parents' house, and if it was, he would call my parents [to enlist Bob]. I mean, he was a devil."

"I came to the realization that a way out of all this was education," Wells says.

As a PhD student, he came under the tutelage of Pitt's Klaus Hofmann, a Swiss-German known worldwide for his work synthesizing and revealing the molecular structure of hormones; Hofmann also ran the biochemistry department with an iron fist.

But Hofmann was no devil. "I was accustomed to working hard and working with difficult individuals," Wells says. "And that was a great experience." From this formative mentorship, he learned focus, diligence, an appreciation for excellence—"and that hard work pays off."

Robert and Dotty Wells

Wells went on to make formative contributions to our understanding of DNA structure, molecular biology and genetics in many human diseases. He founded the Center for Genome Research at Texas A&M, led the Federation of American Societies for Experimental Biology and served as an advisor to the Senate and the White House. In 2014, Pitt named him a Legacy Laureate, the highest honor the University bestows on an alumnus.

Moved by their gratitude for the institution that launched their success, Robert and Dotty Wells have bequeathed a major gift in Hofmann's honor to support PhD students at Pitt Med. The gift is a nod, too—to the notion that before any great scientist's star rises, the uphill climb is steep, and often strained by the demands of raising a family. (For the Wellses, that strain meant going home to their parents some weekends to stock up on food.)

"Pitt is an extraordinary school," Wells says. "It has transformed itself over the years into an even stronger and more forward-thinking institution. We appreciate very much my education at the University of Pittsburgh."

To make a gift, contact Jen Gabler: 412-802-8317, jag188@pitt.edu, Giveto.pitt.edu