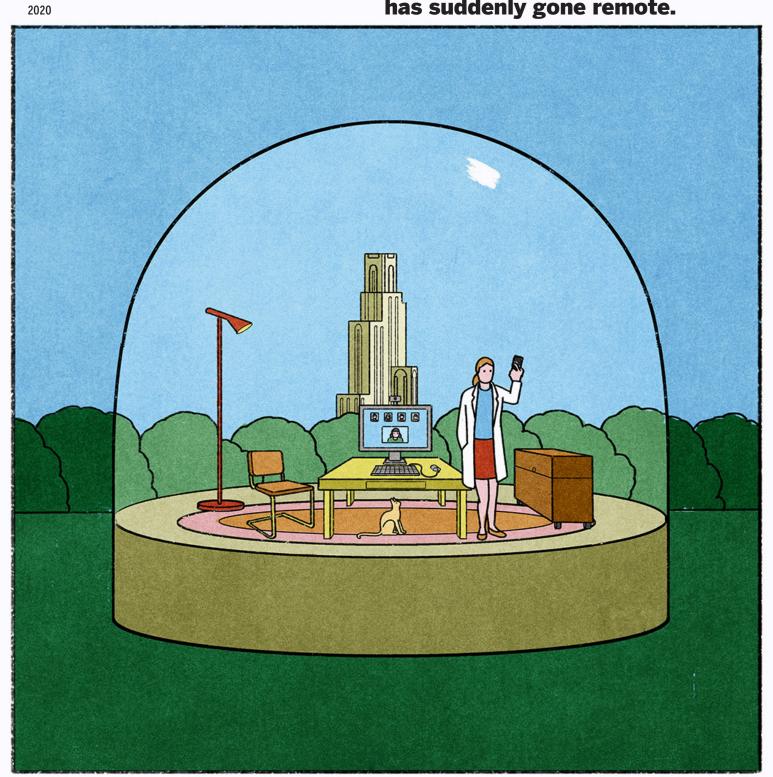
Pitt Med adapts to a world that has suddenly gone remote.



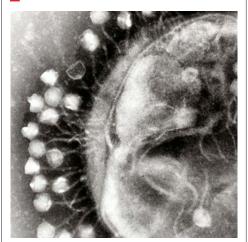
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On January 7, 2020, Anantha Shekhar, MD, PhD, a nationally recognized educator, researcher, and entrepreneur with major contributions in medicine and life sciences, was named senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of the School of Medicine. Learn more about his background, his experiences, and what Pitt Med can expect.

UNIVERSITY
OF PITTSBURGH
SCHOOL OF
MEDICINE

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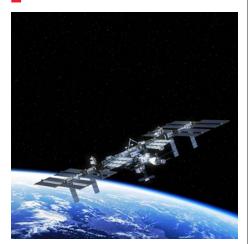
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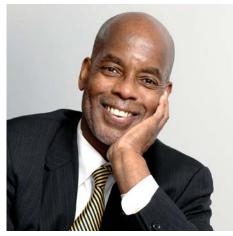
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On the cover

The pandemic may have isolated us physically, but the School of Medicine community has adapted by staying connected with the world virtually and by unflinchingly moving forward with research, learning, achievements, and benevolence.

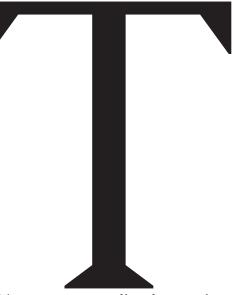
Artist: Klaus Kremmerz

"Anantha's capacity to envision solutions. galvanize partnerships, and produce results is second to none, and his record of propelling both people and institutions to success is unparalleled."

Chancellor Patrick Gallagher

MEET: ANANTHA SHEKHAR, MD, PHD

First Impression



he doctor, on his first shift as a psychiatric resident, walks into the room of a patient, who is a white, middle-aged, Midwestern woman. The patient, understandably, has no way of knowing the credentials of the doctor.

The journey to walking into that room for Anantha Shekhar included scoring among the top 1% of high school seniors on ASSET, a test taken by all of India's high school students to help determine college placement. Two years later, he again scored among the very best in another placement test to gain admittance to St. John's Medical College, the sole Catholic medical school in Asia, which admits only about 60 students from tens of thousands of applicants. Six years later, he received a coveted NIH-funded psychiatry fellowship and boarded an airplane for the first time to further his medical career at Indiana University.

The patient, unaware of how fortunate she is to be in Shekhar's care, hears him say hello. She then looks him straight in the eye and replies:

"Pardon my French, but I don't want any f*cking [N-word] examining me."

Her response was uttered in the early 1980s but has never been forgotten by Shekhar:

"I was stunned and had no idea what to do because I never really encountered racism until then. My attending didn't do anything; he just kind of asked me to leave because the patient didn't want me in the room. That's when I realized that there is a subset of our society that has strong prejudices toward skin color and Blacks in particular.

"And that's why, to this day, I feel so passionate that to have a just society we have to do things differently."

In his leadership role at Pitt, he says he's more than ready to leave his mark on all of the traditional benchmarks; and, he emphatically adds, he's eager to remove—for both faculty and patients—any undercurrent of being an "other." ●



Who is Dr. Shekhar?

The lifelong journey of Anantha Shekhar, MD, PhD, began years ago in one of India's tiniest villages. His childhood education in a two-room schoolhouse morphed into a career in medicine that, by June 2020, brought him to Pittsburgh as the new senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of the School of Medicine at the University of Pittsburgh, succeeding Arthur S. Levine, MD.

Dr. Shekhar's journey has encompassed scientific excellence, clinical prowess, successful entrepreneurship, and outstanding leadership—all accomplished without losing sight of inclusivity and compassion.

"Anantha's capacity to envision solutions, galvanize partnerships, and produce results is second to none, and his record of propelling both people and institutions to success is unparalleled," says Chancellor Patrick Gallagher.

Jeffrey Romoff, president and CEO of UPMC, concurs: "Dr. Shekhar's bold vision and collaborative spirit will further the successful partnership between UPMC and Pitt, enabling us to continue pushing the boundaries of academic medicine to the benefit of patients around the world."

Shekhar's credentials speak for themselves.

After completing a psychiatry residency in 1989 and a PhD in neuroscience in 1992, both at Indiana University, he remained on Indiana's faculty for nearly three decades before coming to Pitt. Highlights of his multiple leadership roles at Indiana include growing NIH funding 73% while overseeing Indiana's research during the past five years; cofounding several successful biotech companies; forming two commercial incubators; directing a highly productive laboratory; leading curriculum reform at Indiana's School of Medicine; and forming the Indiana **Clinical and Translational** Sciences Institute, the only statewide institution of its kind, which is a collaboration among Indiana, Purdue, and Notre Dame Universities to improve the region's health care.

Although arriving at Pitt during a pandemic, he's unfazed. "I'm optimistic that the world will be a better place in 2021, definitely by 2022," he says, "and I'm confident that Pittsburgh will be, just as it has always been, a prominent contributor."

Why Pittsburgh?

In-person at Alan Magee Scaife Hall: Dr. Shekhar, sitting in his School of Medicine office—and keeping a social distance—discussed off the cuff the past, present, and future.

Do you sometimes think back and wonder how a young boy growing up in a tiny village in India is now responsible for 6,000 faculty and staff and 5.000 students?

AS: [chuckles] I sometimes wonder how is it possible that this has all happened. Life takes you on all sorts of journeys. Many professional people, my teachers, colleagues were all wonderful to me along the way.

So how did the journey begin?

AS: It started with my parents, who were very committed to me being educated. Fortunately, I enjoyed school—liked reading, liked learning, was always very curious.

You certainly excelled in school, which enabled you to pursue your interest in a medical career. Why psychiatry in particular?

AS: My closest friend, we grew up together from primary school, and I were both interested in health and medicine. When we were first-year students at college, I found him one evening as dusk was settling in, bumping into pillars in our dorm. I was taken aback and had him get medical attention the next day. It turns out he had a massive brain tumor that had begun to compress his optic nerve. He passed away about four months after that [pause]. What happened to him made me want to better understand the brain. The more I learned about the brain in medical school, the more it really fascinated me. I wanted to get more training and education, which is why I pursued a psychiatry residency and a PhD in neuroscience at Indiana University.

You had quite an impressive run in your nearly 40 years as a post-graduate trainee and longtime faculty member at Indiana before coming to Pitt. What are some of the things that stand out to you during your time there?

AS: Well, it's where I first met my wife [Gina Laite, MD] while we were both part of the IU residency [smiles; they now have two grown children]. I'm also proud of helping lead the Precision Health Initiative, where we brought together researchers from Indiana, Purdue, and Notre Dame to improve treatments and find cures for some of the state's and nation's most dreaded diseases. The initiative had an estimated statewide economic impact of nearly \$200 million in just four years, and

we hired more than 100 scientists and created four companies and recruitment of another one to Indiana.

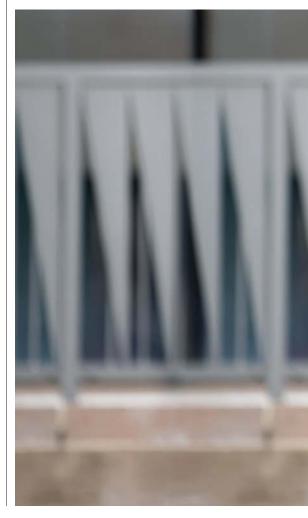
Very impressive. With all of your success there, why come to Pitt?

AS: What I could do in Indiana, like with the Precision Health Initiative, I can do three times faster and three times bigger with Pitt. There's tremendous skill here. Pitt has its own engineering school, plus we have Carnegie Mellon University next door. Creating an ecosystem of collaborations here will increase the number of patents issued. Then we will increase the number of commercial entities using a patent to build a product and, ultimately, improve health care.

Another attraction of Pitt is having UPMC as a partner, not only as a health care provider but as an insurerhalf of its business is actually insurance. So it makes fiscal sense to train our physicians of the future on the importance and impact of addressing social determinants. Take a chronic diabetic for example. The care is focused on clinics and hospitals. We aren't paying attention to all the prevention and management measures. We have no coverage for their nutritional status. Exercise. Personal care. Social aspects of their disease. Instead, we are constantly prescribing expensive medications for them. Bringing them in for expensive tests. And then, once necessary, they have expensive surgery. It's a medical model and a disease and a treatment model, not a lifestyle and prevention model. By focusing more on health care excellence, the savings that occur for UPMC's insurance plan can then be put to good use for medical advancements while we're also keeping our patients healthier.

Sounds like a meaningful goal. Have you had a chance to formulate other goals for the health sciences at Pitt and the School of Medicine in particular?

AS: Yes, I have several goals that I think are attainable by 2025. Educational, research, clinical, and translational excellence go without saying. I expect us to be considered among the top 10 in the nation in each of those areas. I also want us to be a national leader in commercialization and product development. I want to make precision medicine part of routine clinical care. To do so, we need to have large data sets from patients, which includes various genetic as well as health utilization data, so we can better understand patterns in order to predict outcomes—it can all be tailored to individual patients and their genetics and their disease. We'll need, of course, lots of data and sophisticated computing and data analysis capabilities. Pitt and UPMC probably make Pittsburgh the best place where this can happen because of the size, the complexity of the health system, the talent here at Pitt, as well as the AI and computational talent at Carnegie Mellon University. Pittsburgh could very well be the place to make precision medicine the norm and routine within the next five years or so.



"There's tremendous skill here. ... Creating an ecosystem of collaborations here will increase the number of patents issued. Then we will increase the number of commercial entities using a patent to build a product and, ultimately, improve health care."

Anantha Shekhar, MD, PhD

What concerns do you have?

AS: Health disparity is a major concern and not just for Pittsburgh. In many of our country's urban areas there are zip codes where health outcomes are worse than Bangladesh while there are other zip codes that are better than Sweden. In Indianapolis, there is a train track that goes from Louisville to Chicago and cuts right through the city. Along those tracks, within a 12-mile radius the lifespan of the population drops by 14 years—65 years in the inner city, 81 years in the suburbs. That can't go on.

It's difficult to comprehend why such a health disparity hasn't been addressed.

AS: Part of the challenge is that the underserved don't trust the system because the health care professionals don't look like them. The disparity is never going to end unless we start training more doctors who are persons of color; it's never going to change until we train leaders, not just in research, but in social impact—leaders who are going to disrupt health care and create a new model, doctors who are going to look at social determinants of health. Ultimately, to change our society's health, we

need to focus not only on the biology, because that's only 20% of the diseases; 80% of the outcomes of any disease—other than some infections and certain types of cancer—are a patient's behavior, a patient's environment, a patient's lifestyle, so we have to focus more on the entire picture.

When you talk about increasing diversity among medical students, some might argue that could lead to a lessening of standards in order to have a diverse class.

AS: I completely reject the argument that we'll need to compromise our standards or our mission by increasing diversity. We get 7,000 applicants for 140 seats, so it's not like we don't have a choice. The cream of the crop apply. Take the top MCAT scores. There are, on an average, 100 Black students who ace the MCAT. Why don't they come to Pitt? Well, we don't have enough scholarships, and we don't have enough diversity. We need to work on creating an environment where they want to come here. Increase diversity. Make medical school more affordable. Perhaps make the fourth year of medical school a paid hybrid year in which the student is a trainee. That could reduce a student's debt by as much as \$75,000.

It seems like you're talking about a true paradigm shift in training doctors.

AS: Don't get me wrong; we're incredibly successful in research—and we're not going to diminish the importance of research—but now it's time to increase our expertise in other dimensions as well. Think of it this way. In the past, doctors couldn't carry a medical library with them and check a reference in their office just as they were about to see a patient. But today there's more information in an iPhone than there was in my medical school library.

Times have changed!

AS: What hasn't changed is that we need to learn from the patient and think through the problems and create solutions, which has been our University's wonderful history.

From the chancellor on down, people at Pitt have mentioned how pleased they are to have you here. Do you think—given the somewhat perilous state of the world—it's still possible for a youngster living today in a tiny village in India to follow in your footsteps?

AS: I think so; I would hope so.

With that optimistic reply, Dr. Shekhar smiled and concluded the session. ●



NEWS



As of winter 2020, COVID-19 remains a worldwide crisis. Pitt is among notable institutions leading the way in pursuing treatments and vaccines. Learn more, starting on page 8, about the School of Medicine's efforts.

Notable Faculty Achievements

The year 2020 will be memorable for many reasons, including these bright spots for Pitt faculty:

Stephen Badylak, DVM, PhD, MD, professor of surgery and deputy director of the McGowan Institute for Regenerative Medicine, was presented with a Lifetime Achievement Award by the Tissue Engineering and Regenerative Medicine International Society for his work to advance extracellular matrix-driven tissue regeneration.

Jan Beumer, PharmD, PhD, professor of pharmaceutical sciences, School of Pharmacy, was named editor-in-chief of the Cancer Chemotherapy and Pharmacology journal. Beumer has a secondary appointment as professor of medicine and is director of the UPMC Hillman Cancer Center Cancer Pharmacokinetics and Pharmacodynamics Facility.

Peter Strick, PhD, Distinguished Professor and chair of neurobiology, Thomas Detre Professor of Neuroscience, and founding scientific director of the University of Pittsburgh Brain Institute, received the Krieg Cortical Kudos Discoverer Award from the Cajal Club Neuroscience Society in recognition of his contributions to the understanding of the cortical circuits involved in motor control.

John Williams, MD, Henry L. Hillman Professor of Pediatric Immunology, is the 2020 recipient of the Norman J. Siegel Outstanding Science Award from the American Pediatric Society in recognition of his significant contributions to the field of pediatrics. He is an international leader in the field of respiratory virus biology, particularly human metapneumovirus. ●





(I-R) Birmaher Girard

Congratulations!

he School of Medicine congratulates **Boris Birmaher, MD**, Distinguished Professor of Psychiatry, who was elected to membership in the Association of American Physicians, and **Timothy Girard, MD**, associate professor of critical care medicine, who was elected to membership in the American Society for Clinical Investigation. Election to these societies recognizes significant achievement in scholarship and research. •

Prestigious Recognition

he National Academy of Medicine—which has more than 2,000 members chosen by their peers in recognition of outstanding achievement in their fields, as well as their willingness to engage in advisory activities—has elected two Pitt physician-scientists this past year:

Toren Finkel, MD, PhD, G. Nicholas III and Dorothy B. Beckwith Professor of Translational Medicine and director of the Pitt Aging Institute, and **Amy Wagner, MD**, Physical Medicine and Rehabilitation Professor of Translational Research, School of Medicine, and professor of neuroscience, Dietrich School of Arts and Sciences.

Finkel's work centers on how oxidative stress and the function of mitochondria alter the rate of aging. Recently, his focus has been on autophagy—the body's natural way of clearing out old and damaged parts of cells—as a target for anti-aging therapeutics.

Wagner uses biomarkers and statistical modeling to predict how well patients will recover from brain injury and to guide clinical decisions along the way—a strategy she calls "personalized rehabilitation medicine." Her experimental research focuses on how dopamine systems, hormones, inflammation, and rehabilitation-relevant therapeutic agents affect plasticity and functional recovery. She also treats patients with neurological conditions during their acute care hospitalization and inpatient rehabilitation.

Including Finkel and Wagner, 20 Pitt School of Medicine faculty are among the academy's elite membership. ●

Humanism Honors

The School of Medicine congratulates those who have recently been inducted into the Charles G. Watson Chapter of the Arnold P. Gold **Humanism Honor** Society. The society honors medical students, residents, fellows, and others selected by a vote of their peers who demonstrate high standards of humanistic clinical care, leadership, compassion, and dedication to service.

New members from the Class of 2021:

Ololade Adebiyi Lauren Auster Patricia Campos Bryce Churilla Catherine Corey Camille Davis Mikaela Fenn Valerie Gobao Alexandria Harris Rafa Ifthikhar Evan Keller Song Kim Kathleen Koesarie Anna Leone John Leech Kara McClain Arthi Narayanan Cristine Oh Katherine Orr Vivianne Ovefusi Rahilla Tarfa

Leadership News

Among the newest appointments to leadership roles in the health sciences and School of Medicine are these:

Derek C. Angus, MD, MPH, Distinguished Professor, Mitchell P. Fink Professor, and chair of critical care medicine, is the health sciences schools' inaugural associate vice chancellor for health care innovation. This role complements his appointment as UPMC's chief health care innovation officer and fosters more strategic linkages between Pitt and UPMC to improve learning of health systems and clinical care delivery.

Stephen Chan, MD, PhD, professor of medicine, is director of the Vascular Medicine Institute. He also continues to direct the Center for Pulmonary Vascular Biology and Medicine and work with the cardiology fellowship research program.

Paula Davis, MA, is associate vice chancellor for diversity, equity, and inclusion, health sciences, a new position. She is responsible for coordinating the recruitment and retention of diverse faculty, students, and staff in the health sciences schools; developing cultural competence education; and working to create a more inclusive environment.

Mark W. Geraci, MD, professor of medicine, is associate vice chancellor for interdisciplinary research, health sciences. In this newly reconfigured role, Geraci will advance research efforts across all six health sciences schools to support the University's expanding biomedical research activities. Prior to joining Pitt, Geraci served as John B. Hickman Professor and chair of the Department of Medicine at Indiana University.

Alda Maria Gonzaga, MD, MS, associate professor of medicine, is associate dean for student affairs. Gonzaga is known for her leadership in efforts on diversity, equity, and inclusion. She succeeds Joan Harvey, MD, who retired after 30 years at Pitt.

Evelyn C. Reis, MD, professor of pediatrics, is associate dean for the learning environment. Reis is an educational leader in communication skills and the doctor-patient relationship. She was the founding medical director of the University's Clinical and Translational Science Institute pediatric practice-based research network, Pediatric PittNet.

Jason Rosenstock, MD, professor of psychiatry, is associate dean for medical education. Rosenstock has won multiple teaching excellence awards, helped to found the medical school's neuroscience area of concentration, and has served as chair of the curriculum committee since 2015. ■

Distinguished Faculty

he School of Medicine now boasts 13 additional faculty members who have been awarded the title of Distinguished Professor, the highest honor the University can accord to its faculty.

They are **Boris Birmaher**, **MD**, and **David Brent**, **MD**, Distinguished Professor of Psychiatry; **Gregory Cooper**, **MD**, PhD, Distinguished Professor of Biomedical Informatics; **Terence Dermody**, **MD**, Distinguished Professor of Pediatrics; **John Kirkwood**, **MD**, Distinguished Professor of Microbiology and Molecular Genetics; **John Kirkwood**, **MD**, Distinguished Service Professor of Medicine; **Patrick Kochanek**, **MD**, Distinguished Professor of Critical Care Medicine; **Fadi Lakkis**, **MD**, Distinguished Professor of Surgery; **John Mellors**, **MD**, Distinguished Professor of Ophthalmology; **Mark Shlomchik**, **MD**, PhD, Distinguished Professor of Immunology; **William Wagner**, **PhD**, Distinguished Professor of Surgery; and **Adriana Zeevi**, **PhD**, Distinguished Service Professor of Pathology. ●

COVID-19 INFECTS THE WORLD PITT MED RESPONDS

PITT IS A LEADER IN COVID-19 FIGHT

cientists and clinicians across
Pitt's six health sciences schools,
along with colleagues from other
academic departments, have taken
a prominent role in responding to
the pandemic. In all, Pitt is home
to more than 400 ongoing studies
related to COVID-19 and SARS-CoV-2.

Perhaps foremost among these are studies in the University's Center for Vaccine Research (CVR), which integrates efforts in virology, immunology, and other disciplines to develop diagnostics, therapeutics, and vaccines against known and emerging infectious diseases. CVR houses one of the few labs nationwide qualified to handle pathogens like SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2), which causes COVID-19. CVR director **W. Paul Duprex, PhD**, received permission from the U.S. Centers for Disease Control and Prevention (CDC) to bring the virus to Pittsburgh in mid-February 2020.

A POTENTIAL VACCINE IN THE PRECLINICAL PHASE—PITTCOVACC— IS ADMINISTERED USING A FINGER-TIP-SIZED PATCH OF 400 TINY NEEDLES THAT DELIVERS LAB-MADE CORONAVIRUS SPIKE PROTEIN PIECES INTO THE SKIN. ... THE DELIVERY METHOD HAS ADVANTAGES FOR GLOBAL DISTRIBUTION AND POTENTIAL APPLICATIONS OUTSIDE OF THE PANDEMIC.

A team led by Duprex is working on a COVID-19 vaccine candidate that harnesses a measles vaccine engineered to express SARS-CoV-2 proteins on its surface to generate immunity to the virus. CVR is partnering with the Serum Institute of India to bring the vaccine to phase I clinical trials.

Also in CVR, **William Klimstra, PhD**, associate professor of immunology, is investigating a polyclonal antibody therapy (SAB-185) that could be used to both treat and prevent COVID-19. Clinical staff began injecting SAB-185 into healthy volunteers for a phase I trial in August 2020.

Two pharmaceutical companies, Moderna and AstraZeneca, partnered early with Pitt and UPMC on vaccine trials. The phase III trials were led by **Judith Martin, MD**, director of the Pittsburgh Vaccine Trials Unit and CVR member, and **Sharon Riddler, MD**, director of clinical research in Pitt's Division of Infectious Diseases. (See page 10)

Another potential vaccine, called Pitt-CoVacc, was developed by a team led by Louis Falo, MD, PhD, professor and chair of dermatology, and Andrea Gambotto, MD, associate professor of surgery. PittCoVacc is administered using a fingertip-sized patch of 400 tiny needles that delivers lab-made coronavirus spike protein pieces into the skin, where the immune reaction is strongest. The patch goes on like a Band-Aid, and then the needles simply dissolve. When tested in mice, the vaccine produced antibodies specific to SARS-CoV-2 at quantities thought to be sufficient for neutralizing the virus.

Although PittCoVacc, unlike some other vaccine candidates, is still in the preclinical phase, Falo believes that if PittCoVacc is approved, its delivery method has global distribution advantages and potential applications outside of the pandemic. •

STEROIDS IMPROVE COVID-19 PATIENTS' SURVIVAL

n the race to find treatments for COVID-19 patients, an international team led by Pitt and UPMC clinician-scientists found that administering widely available, inexpensive steroids boosts critically ill COVID-19 patients' survival odds. The study's results even prompted the World Health Organization (WHO) to update its COVID-19 treatment guidance.

"It is relatively rare in medicine that you find drugs where the evidence of their effectiveness in saving lives is so consistent," says lead author **Derek Angus, MD, MPH**, Distinguished Professor, Mitchell P. Fink Professor, and chair of critical care medicine. "This is, in many respects, the single clearest answer we've had so far on how to manage terribly ill COVID-19 patients," adds Angus, who is also associate vice chancellor for health care innovation in the Schools of the Health Sciences.

The findings, which were published across four JAMA articles, stem from the "Randomized Embedded Multifactorial Adaptive Platform-Community Acquired Pneumonia (REMAP-CAP)" trial, a large-scale international initiative to evaluate treatments at numerous hospitals. Because REMAP-CAP can simultaneously test multiple combinations of potential therapies—as opposed to





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Derek Angus, MD, MPH

Former Pitt Fellow Leads Wuhan's Pandemic Response



Today, Zhiyong Peng, MD, PhD, is professor and chair of critical care medicine at Zhongnan Hospital of Wuhan University in China, a region considered Ground Zero for the COVID-19 pandemic. But his crisis management skill derives, in part, from lessons Peng learned in Pittsburgh.

As a fellow and later researcher

associated with Pitt Med's Department of Critical Care Medicine from 2006 to 2014, Peng focused on studying complications from acute kidney injury and severe infections like sepsis.

"He really ran the sepsis laboratory; it was my lab, but we worked closely together, and I trusted him to run it," says **John Kellum, MD**, Professor of Critical Care Medicine Research.

"My time at Pitt was very valuable," says Peng. "I learned a lot, including how to manage teams and be a leader."

Peng has been at the forefront of his hospital's COVID-19 response and has presented and published important clinical care insights on the first COVID-19 cases in Wuhan.

the traditional, slower clinical trial process that tests one therapy at a time—the initiative is well-suited for rapidly identifying effective treatments during the COVID-19 pandemic.

Between March and June 2020, the REMAP-CAP corticosteroid trial randomized 403 adult COVID-19 patients admitted to an intensive care unit to receive the steroid hydrocortisone or no steroids at all. (Steroids can reduce inflammation and modulate the immune system.) The trial found a 93% probability that giving patients a seven-day intravenous course of hydrocortisone would result in better outcomes than not giving the steroid. The results, which involved compiling data from 121 hospitals in eight countries, were consistent across age, race, and sex.

REMAP-CAP was one of several international trials testing steroids. After REMAP-CAP investigators coordinated with the other trials' researchers and WHO to pool and analyze data, the teams observed that the results were consistent across all trials—a major finding and collaborative effort, Angus notes, because, amid urgency to uncover breakthrough COVID treatments, such clear results are rare. The trials' findings were published alongside a simultaneous meta-analysis of the work.

During the study, steroids were given only to hospitalized COVID-19 patients needing respiratory support, since applying them unnecessarily can dampen the immune system and cause serious side effects. The REMAP-CAP corticosteroid trial was conducted primarily in resource-rich countries across Europe, North America, and Australasia, so the findings may not translate to low- and middle-income countries.

"REMAP-CAP and our findings on corticosteroids are possible because of a global community of clinicians and scientists coordinating and sharing data across different languages and countries," says coauthor Christopher Seymour, MD, MSc, associate professor of critical care medicine and Translational and Clinical Science Program director at Pitt's Clinical Research, Investigation, and Systems Modeling of Acute Illness (CRISMA) Center. "This is how we get definitive answers as fast as possible on how to best treat patients. Outcomes in Amsterdam are helping patients at UPMC Altoona."

ACTIV-4 CLINICAL TRIALS RELYING ON PITT

he National Institutes of Health (NIH) selected the University of Pittsburgh to lead a trio of phase III clinical trials involving COVID-19 patients. Collectively known as ACTIV-4 Antithrombotics, these trials will explore the use of blood thinners in saving lives and improving care, particularly among adult COVID-19 patients who are at risk of developing life-threatening blood clots.

As the coordinating center for these trials, Pitt is occupying a leading role in NIH's Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) initiative, funded through Operation Warp Speed. Six other universities—Harvard University, New York University, the University of Illinois at Chicago, the University of Michigan, the University of North Carolina at Chapel Hill, and the University of Vermont—are also participating in the initiative, which will continue to add qualifying institutions.

"This is a massive undertaking supported by NIH—one that is leveraging a global network to help improve patient outcomes for COVID-19," says **Anantha Shekhar, MD, PhD**, Pitt's senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of Medicine. "It is also a challenge that the University of Pittsburgh, a longtime leader in health care innovation, is perfectly positioned to tackle."

THIS IS A MASSIVE **UNDERTAKING** SUPPORTED **BY NIH-ONE THAT IS LEVERAG-ING A GLOBAL NETWORK TO HELP IMPROVE PATIENT OUTCOMES** FOR COVID-19. IT IS ALSO A **CHALLENGE THAT** THE UNIVERSITY OF PITTSBURGH. **A LONGTIME LEADER IN HEALTH CARE INNOVATION, IS PERFECTLY POSITIONED** TO TACKLE."

Anantha Shekhar, MD. PhD Researchers and clinicians have noted that many patients who have died from COVID-19 formed blood clots throughout their bodies, including in their smallest blood vessels. This unusual clotting—one of many life-threatening effects of the disease—causes multiple health complications, from lung and other organ damage to heart attacks, pulmonary embolisms, and strokes.

Antithrombotics, also known as blood thinners or anticoagulants, keep blood protein and platelets from turning into clumps or sticking to each other. Doctors are determining whether COVID-19 blood thinners are effective in treating patients with this condition and, if so, at what point they should be applied.

Stephen Wisniewski, PhD, Pitt's vice provost for budget and analytics, and two physician-scientists from Pitt—**Matthew D. Neal, MD**, Roberta G. Simmons Associate Professor of Surgery, and **Frank Sciurba, MD**, professor of medicine, who directs the Pulmonary Function Exercise Physiology Laboratory—are leading this effort.

"Understanding how to treat coagulation risk in COVID-19 patients is critical to lessening the impact of this pandemic," says Wisniewski. "Pitt's ability to innovate and collaborate enables us to help ensure that these trials will be completed with the rigor and speed necessary to make an impact at this critical moment. In collaboration with NIH and our peer institutions, we will use the combined tools of biology and statistics to advance the treatments of this deadly virus."

"This has been an amazingly cooperative endeavor—unequivocally the most rapidly moving, complex but also highly collaborative experience of my life," says Neal.

"While the greatest focus on blood clotting complications has been in the inpatient setting, earlier attention in more stable patients prior to hospitalization may have an important impact on progression to the more

serious consequences of COVID-19," says

Sciurba.

PITT PLAYS KEY ROLE IN COVID-19 VACCINE CLINICAL TRIALS

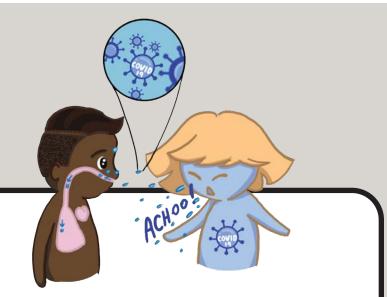
IH's COVID-19 Prevention Network and Operation Warp Speed vaccine program are counting on the University of Pittsburgh to play a key role in COVID vaccine clinical trials—and it's no wonder. Vaccines and Pittsburgh go way back, most notably to the 1950s, when Pitt researchers led by Jonas Salk, MD, developed the first safe, effective vaccine against polio—the most feared disease of the era.

Beyond developing vaccines, conducting vaccine clinical trials is a crucial process, one with which Pitt has considerable experience. The Pittsburgh COVID vaccine clinical trials site is enlisting 750 participants, and several hundred volunteers have received the COVID vaccine as part of nationwide phase III clinical trials, says **Judith Martin, MD**, professor of pediatrics and director of the Pittsburgh site for the Moderna vaccine research study. The registry of Pittsburgh volunteers numbers almost 5,000 individuals, including many members of the Black and Latinx communities, which have been disproportionately affected by COVID-19.

Inaddition to the Moderna COVID vaccine, a second Pittsburgh site for the Astra Zeneca vaccine is being directed by **Sharon Riddler, MD**, professor and clinical research director in the Department of Medicine's Division of Infectious Diseases. The studies, which focus on vaccine efficacy and duration of immunity, have enrolled hundreds of patients from the region and contributed to the early vaccines' success.

Martin is also working with Janssen, the vaccine arm of Johnson & Johnson, and further notes that a Moderna pediatric vaccine study may be the next step for Pitt researchers.

"Pittsburgh has done vaccines for a long time," says Martin, who also directs the Pittsburgh Vaccine Trials Unit at UPMC University Center. "I think what's so wonderful about this environment is that we have the resources and we have such a collaborative nature," which, she says, has been key to enrolling diverse participants and rapidly obtaining the necessary infrastructure and personnel to conduct the trials.



COVID-19 in Other Words and Pictures

Before the COVID-19 pandemic, School of Medicine student Carly O'Connor-Terry was conducting research with the Pittsburgh Center for Autistic Advocacy. When the virus hit Pittsburgh, she formed a volunteer effort with her med school peers and contacted the center to see if there was anything they could do to help.

Opal M. said they were thankful O'Connor-Terry contacted them because an entire community was in need.

"When Carly emailed us, I had just tested positive for COVID-19," said M., the center's assistant director and an autistic, disabled, queer/nonbinary parent of children who are autistic and disabled. "I looked and looked—even asked several of my physician contacts—and couldn't find any materials whatsoever written in plain language to help better understand the virus."

M. said it can be difficult for autistic people and people with intellectual disabilities to recognize cues in their own bodies, like hunger or thirst, or when they are sick or tired.

For O'Connor-Terry, a Pittsburgh native, she can personally relate to these concerns. O'Connor-Terry has an autistic brother with whom she does not communicate orally. She said this is part of the reason it was so important to help.

The same day she connected with M., O'Connor-Terry quickly got to work on the guide, recruiting help through a Slack group of med students across the country.

Using the CDC guidelines for reference, the team produced a plain language guide describing what COVID-19 is and what to do if a person experiences symptoms.



"We classified the symptoms into groups. The 'emergency group' is the most important, which includes shortness of breath. The 'ask for help group' includes fever and cough, and the 'stay home group' includes more general symptoms, like sore throat, runny nose, and muscle pain. We have a picture for each symptom, and we describe how the symptom could feel," said O'Connor-Terry, who is also a Clinical Scientist Training Program research scholar.

O'Connor-Terry and the team had their guide vetted by two infectious disease doctors at Pitt, along with other clinicians with relevant experience, including Peter J. Veldkamp, MD, MS, professor of medicine and director of education and of travel health in the Department of Medicine's Division of Infectious Diseases.

M. is so thankful for the guide and thinks it will be of great assistance. "People look for things that are illustrated to show how things feel in their bodies—and describe those feelings—so they can better understand what's happening," said M. ●

IMMEDIATE COVID-19 RESEARCH RESPONSE

hen the COVID-19 pandemic began, Pitt's Clinical and Translational Science Institute (CTSI) wasted no time coordinating funding for the vital research and work needed to combat the outbreak across all fronts. In April 2020, CTSI's COVID-19 Pilot Grant Program awarded \$900,000 to 17 Pitt research projects addressing various aspects of the pandemic.

"We are optimistic that the impact of research will provide insight and results," said CTSI director Steven Reis, MD. "We are proud to be part of this thriving research community that has shown how Pittsburgh really steps up when called upon."

Awardees were selected after an accelerated, extensive peer-review process. The recipients' projects covered everything from clinical and community serosurveillance, pneumonia severity biomarkers, neurologic manifestations, maternal infections and newborns, modeling strategies, therapeutic nanobodies, and much more. Pitt's CTSI, Office of the Provost, Office of the Senior Vice Chancellor for Research, and the DSF Charitable Foundation funded the program.

Reis, who is also Distinguished Service Professor of Medicine and associate senior vice chancellor for clinical and translational research, health sciences, said the grant program was created to support research initiatives aimed at immediate progress toward reducing the harm to individuals, groups, and society from COVID-19. "We need to look at all options to deal with the COVID-19 pandemic, and the response to the call for proposals was overwhelming," said Reis, alluding to the program receiving more than 150 proposals from 590 investigators across 14 schools. "As encouraged as we were with the number, we were even more impressed with the thinking that went into the proposals from so many different parts of the University," he added. •

WE ARE PROUD TO BE PART OF THIS THRIVING RESEARCH COMMUNITY THAT HAS SHOWN HOW PITTSBURGH REALLY STEPS UP WHEN CALLED UPON."

Steven Reis, MD



ANTIBODY MAY POTENTIALLY TREAT AND PREVENT COVID

drug developed by Pitt researchers could be highly effective at preventing and treating COVID-19. Neutralizing the SARS-CoV-2 virus is not strictly a job for vaccines and their resulting antibodies. Pitt researchers and their collaborators have developed an antibody domain called Ab8 aimed at preventing and treating SARS-CoV-2 infection. Ab8 binds to the SARS-CoV-2 spike protein, preventing its attachment to healthy cells. Their findings were published in Cell.

"Ab8 not only has potential as therapy for COVID-19, but it also could be used to keep people from getting SARS-CoV-2 infections," says study coauthor John Mellors, MD, Distinguished Professor of Medicine. Professor for Global Elimination of HIV and AIDS, and chief of the Department of Medicine's Division of Infectious Diseases, "Antibodies of larger size have worked against other infectious diseases and have been well tolerated, giving us hope that it could be an effective treatment for patients with COVID-19 and for protection of those who have never had the infection and are not immune," Mellors says.

Using antibodies to treat COVID-19 patients takes a similar approach to convalescent plasma therapy, which harnesses antibodies from people who already had COVID-19 to treat those battling infection. Yet this therapy is still being tested in clinical trials, and there may not be enough plasma to benefit all in need.

collaboration with other U.S. and international universities—is 10 times smaller than a fullsized antibody, meaning it can better penetrate tissues to neutralize the virus and could possibly be administered through inhalation or intradermal injection, as opposed to more standard intravenous antibody administration. The antibody does not bind to human cells, so it is unlikely to cause side effects in humans. After the researchers infected mice with a modified version of SARS-CoV-2, those treated with even low doses of Ab8 contained 10-times less infectious virus than untreated

The Ab8 antibody—which was tested in

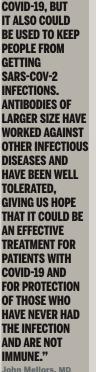
prevented SARS-CoV-2 infection in hamsters. The researchers sifted through a pool of more than 100 billion antibody components, using the SARS-CoV-2 spike protein as bait to determine which antibodies would latch on and become potential therapeutics. Senior author **Dimiter Dimitrov**, **PhD**, **ScD**, professor of medicine in the Division of Infectious Diseases and director of Pitt's Center for Antibody Therapeutics, was among the discoverers of neutralizing antibodies for the original SARS coronavirus in 2003. He and his team discovered other infectious disease

mice. The drug also effectively treated and

Abound Bio, a newly formed, Pittsburghbased company, has licensed Ab8 for worldwide development, and the researchers hope to begin clinical trials in early 2021. •

antibodies in ensuing years, hastening the

search for effective SARS-CoV-2 antibodies.



AB8 NOT ONLY

HAS POTENTIAL

AS THERAPY FOR





Equitable Skin Care

n the Department of Dermatology, the Skin Health Equity (SHE) program has enhanced underserved communities' access to dermatologic care since 2017.

The program is vital, in part, because academic literature in dermatology contains a disproportionate amount of white skin compared to Black skin; and skin color influences how certain diseases look, according to **Alaina James, MD, PhD**, assistant professor of dermatology.

For example, people of color face increased melanoma morbidity because melanoma is often diagnosed at a more advanced stage in people of color, James says. "Through SHE, we are trying to improve all those aspects: education about skin of color, access for patients with skin of color, and education of patients with skin of color so that they can advocate for themselves."

SHE, after partnering with Pittsburgh community health centers and determining a community's dermatologic needs, deploys teams of dermatologists, residents, medical students, and undergraduates through MobileDerm, SHE's outreach program, to provide care in-person or via tele-consultation. James is director of SHE and MobileDerm.

Now, SHE is expanding. In 2020, the MobileDerm program was awarded a pilot grant from Pitt's Clinical and Translational Science Institute to expand outreach to rural regional communities, some of which are dermatology deserts, James says, with large populations lacking any dermatologists in the community.

James can't stress enough the importance of skin awareness: "[Skin] is in tune with the rest of the body and reflects a lot of what's going on with the overall health of the patient. We can commonly diagnose patients with internal medical conditions based on changes that are present on their skin." ●

New Center Tackles Pelvic Pain

Ithough endometriosis and pelvic pain affect as many as one in 10 women of reproductive age, a proper diagnosis can take years. A new center established at UPMC Magee-Womens Hospital aims to improve early diagnosis and treatment of endometriosis and other pelvic pain disorders and to advance research through tissue sample collection and coordination of resources.

Endometriosis occurs when the uterine lining—called endometrial tissue—grows elsewhere in the abdominal cavity. Like normal endometrial tissue, these displaced lesions react to monthly hormonal cues, causing inflammation.

Symptoms include pain during a period and intercourse, generalized pelvic pain outside of the menstrual cycle, and unexplained infertility. Because it can't be detected with imaging equipment, the only way to definitively diagnose endometriosis is through exploratory surgery.

"Chronic pelvic pain can be so difficult to diagnose," says **Nicole Donnellan, MD**, associate professor of obstetrics, gynecology, and reproductive sciences and director of the Chronic Pelvic Pain and Endometriosis Center. "There are many different conditions that can cause pelvic pain, including bladder or muscle spasms, uterine issues, and even gastrointestinal problems."

The new clinic embraces a unified team approach to patient care, providing patients with the opportunity to meet with gynecologic surgeons, behavioral health therapists, and physical therapists during the same appointment, helping to begin treatment sooner.

"Many women come to the clinic in frustration after being told their pain is psychological," notes **Suketu Mansuria, MD**, associate professor of obstetrics, gynecology, and reproductive sciences.

"Someday, we'd like to have a blood test to detect endometriosis, but we need to understand the pathology of the disease first," says Donnellan, who, along with researchers at Magee-Womens Research Institute, is on the case. ●

Pitt Innovation by the Numbers **Invention Disclosures** +124% +27% 1,402 37 2011-15 2016-20 2011-15 2016-20 **Transactions** 658 277 2011-15 2016-20 2011-15 2016-20 FISCAL 2020: **INNOVATION INSTITUTE FOR** COMMERCIALIZATION ENTREPRENEURIAL EXCELLENCE Invention disclosures: 394 1,900+ businesses received 1:1 consulting Patents: 88 \$25,600,000+ **Transactions: 132** in capital formation UPMC agreements: 16 8,500+ hours of consulting Startups: 15 10,000+ jobs supported Revenue: \$12,375,660 and/or created 52 startups launched

i4Kids Initiative

"We're finding collaborative ways to fight debilitating infectious and immune-mediated diseases that affect children's lives, like pneumonia, bronchitis, diabetes, and asthma."

John Williams, MD



orldwide, the leading cause of death for children under age 5 is infection. In the United States, more children are hospitalized for infectious and inflammatory diseases than for any other cause.

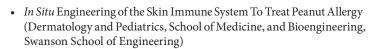
The Institute for Infection, Inflammation, and Immunity in Children, i4Kids, is a joint initiative launched in 2020 by the University of Pittsburgh and UPMC Children's Hospital of Pittsburgh to become a center of research, discovery, prevention, and treatment of these diseases in children as the

foundation of improving the health of future generations.

"We're finding collaborative ways to fight debilitating infectious and immune-mediated diseases that affect children's lives, like pneumonia, bronchitis, diabetes, and asthma," says **John Williams, MD**, Henry L. Hillman Professor of Pediatric Immunology and the institute's director.

"We have great strengths in infection biology and immunology research here in Pittsburgh, and i4Kids will build on those strengths," adds **Terence Dermody, MD**, Distinguished Professor, Vira I. Heinz Professor, and chair of the Department of Pediatrics, who conceived the idea of such an institute more than 30 years ago. "We are also united in our goals for improved childhood health, which allows us to recruit for additional strength."

Currently, 39 faculty members from across the University's research enterprise are affiliated with i4Kids. Multidisciplinary team pilot projects funded for 2020 include:



- Acoustic Waveform Respiratory Examination for Pediatric Inflammatory Airway Diseases (Pediatrics, School of Medicine, and Electrical and Computer Engineering, Swanson School of Engineering)
- CRISPRi Repression of Group B *Streptococcus*-Externalized Proteins To Identify Key Mediators of Macrophage Responses During Neonatal Infection (Pediatrics and Medicine, School of Medicine)
- Role of Protists in Virus-Mediated Loss of Oral Tolerance and Celiac Disease (Pediatrics and Immunology, School of Medicine)

At the same time, the institute's Pittsburgh Phage Project is bringing together several dozen faculty from medicine, public health, and the Dietrich School of Arts and Sciences to investigate new uses for bacterio-phages—viruses that infect and destroy bacteria.

In September 2020, the R.K. Mellon Foundation announced a \$1.5 million grant to support development of a candidate vaccine or therapeutic treatment against acute flaccid myelitis, an infection linked to neurological complications and paralysis in children.

All of this is very good news to **Anna Wang-Erickson**, **PhD**, assistant professor of pediatrics and the institute's associate director, who states, "We are very excited about the development of new collaborations." ●



Surgical Engagement

he COVID-19 pandemic, the calls for social justice, and other tumultuous events of 2020 have demanded new means of taking action on equity and outreach and that includes the School of Medicine.

In the Department of Surgery, **Timothy Billiar**, **MD**, Distinguished Professor, George V. Foster Professor, and chair of surgery, recently formed the Division of Community Engagement, which builds and fosters health equity, trust, and commitment among Pittsburgh's communities through educational and engagement initiatives. The division shares information and discussions on COVID safety, nutrition, trauma treatment, and many more topics of concern, while also working to inspire interest in science and medicine among young community members. Billiar appointed **Steven Evans, MD**, clinical professor of surgery, as community engagement division director.

"Our mission has to be to serve the needs of our surrounding communities, and that includes those who are underserved, underinsured, and underrepresented minorities, in a culturally sensitive way," says Evans. "I feel it's really incumbent on us as educators to focus on the root causes of these disparities and outcomes that we see."

While the pandemic restricts gatherings, the division's messaging has been shared across Pitt and UPMC channels and via social media, videos, and virtual town hall meetings, often in partnership with organizations attuned to education, social justice, and combatting disparities. Two of those partners include the Gateway Medical Society, an organization associated with the National Medical Association working to eradicate disparities in health care, and 1Hood Media, a collective of socially conscious artists and activists.

The division's outreach also emphasizes cancer screenings, which have taken a hit during the pandemic. "We're looking now at a potential uptick in cancer diagnoses," Evans says, "because of people no longer screening due to the pandemic." Breast cancer and colon cancer are leading killers among Black women and men, Evans says. The division reinforces the COVID safety measures taken by places like UPMC Hillman Cancer Center to keep patients and the community safe while continuing screenings. "We want to educate on prevention and treatment, as opposed to having conversations that accuse the community of not being responsible themselves," Evans says. •

"OUR MISSION HAS TO BE TO SERVE THE
NEEDS OF OUR SURROUNDING COMMUNITIES, AND
THAT INCLUDES THOSE WHO ARE UNDERSERVED,
UNDERINSURED, AND UNDERREPRESENTED MINORITIES,
IN A CULTURALLY SENSITIVE WAY."

Steven Evans, MD

"Stories are just so powerful. They are an incredible way to communicate; they can cross cultures, and they're a way to convey very technical information without using very technical language."

Kathleen M. McTigue, MD, MPH, MS

Storytellers Could Improve Health Outcomes

S

tory Booth is a research project that collects people's stories about their health experiences and shares them with researchers. The project's roots are in PaTH, one of 33 networks that comprise the Patient-Centered Outcomes Research Institute's National Patient-Centered Clinical Research Network.

"The mission of Story Booth is to promote patient-centered research," says Kathleen M. McTigue, MD, MPH, MS, associate professor of medicine. "We wanted to make it easier to foster the development of research that addresses questions patients feel are important. Stories are just so powerful. They are an incredible way to communicate;

they can cross cultures, and they're a way to convey very technical information without using very technical language."

People who volunteer to share their stories with Story Booth often record them over the telephone and agree to allow researchers to listen to the stories. The idea is that if researchers know what topics people think are important, researchers will design studies around those topics. Then, those studies can, hopefully, generate findings that may better people's health.

McTigue, also associate professor of epidemiology at Pitt's Graduate School of Public Health, explains that 72% of storytellers have expressed an interest in getting involved in health research as partners who help guide the research process. Story Booth researchers support team-building by introducing storytellers and researchers with shared health interests.

She says, "We knew that many researchers are intrigued by patient-centered research but don't really know how to make it happen and often feel uncomfortable. Likewise, we know many patients are interested in the concept but are sometimes intimidated because they don't know how to find or connect with researchers, and they may use different vocabularies than researchers. Story Booth is a way to bring those two different groups of people together."

In 2019, Story Booth was affiliated with a Pitt Year of Creativity award that funded a project with University of Pittsburgh at Bradford undergraduates and faculty artists. Each picked a story that inspired them and created artwork based on the story.

"It's another way we're trying to amplify the storytellers' voices," says McTigue. •



hen [the COVID-19 pandemic] hit and we were told to shelter in place, it hadn't hit me yet. I was still going to the store without a mask or gloves, but then I started to see the shelves emptied of hand sanitizer, hand soap, toilet paper, etc. I hadn't really felt the impact of it. I was in shock. Then, I started wearing gloves, a hat, a double mask, and I was really scared—really petrified of people and of being in public spaces. But I had to go out and get necessities. I also have an 80-year-old mother who lives on the other side of town. She definitely couldn't be going out shopping, so I had to be the one to do it. One time, I had just come from dropping off groceries to my mom and had to drive back across town to get home and unload my groceries. At the time, they didn't know whether the virus could last on packaging, so I put my groceries on the floor and used bleach mixed with water to wipe everything down before I put it away. I just broke down. It was a lot. I had to remember everything I touched

before I got into the house and then everything I had touched once I got inside the house and clean it all. It was overwhelming. I think I had a panic attack or something. Then, I would go to the grocery store and have to tell my mom that they had run out of a lot of things, and we were just going to have to take what we could get. It took about until the middle of May before I felt like I had a groove. But then I started seeing people without masks because they thought [the pandemic] was over. People stopped social distancing. I think we opened up way too early. I just need to do whatever I have to in order to keep myself and my mother safe. It still scares me when people get too close or they're not wearing masks or wearing them inappropriately. I wonder when I'm going to snap out."

— adapted from a Story Booth recording of a woman's experience living through the COVID-19 pandemic as someone who is HIV positive and caring for her aging mother

EDUCATION



(Above) On Match Day, med school students shared their future residencies (and excitement!) online. (Top R) "The Lyme King," this past year's Scope and Scalpel production, took place virtually and can still be viewed on YouTube.



A Virtual Year

ith the cancellation of most in-person events during the COVID-19 pandemic, the School of Medicine has reinvented how it celebrates its traditional milestone events and builds community. Strict physical distancing meant meeting virtually for most of 2020.

MATCH DAY

Match Day 2020 at Pitt Med was a virtual celebration of the hard work and accomplishments of the graduating medical students. Students fundraised for four years to make their Match Day a celebration to remember. When the arrival of COVID-19 forced their festivities online, the students opted to donate their party funds to local organizations supporting the community during the COVID-19 crisis. That's a celebration that will leave an indelible memory.

SCOPE AND SCALPEL

By late March, it seemed like Scope and Scalpel—the annual production put on by graduating medical students—would end its 65-year streak of roasting all things Pitt Med. But students were able to film individual parts of "The Lyme King" and screen it as a whole via Zoom in May. Proceeds from this year's show went to the Greater Pittsburgh Arts Council's Emergency Fund for Artists.

DIPLOMA DAY

Students in the School of Medicine virtually celebrated Diploma Day on May 18, 2020. It was streamed on YouTube, had all of the traditional pomp and ceremony, and has been viewed more than 7,000 times. David Fajgenbaum, MD, MBA, MSc, assistant professor of medicine at the University of Pennsylvania and a survivor and researcher of Castleman disease, delivered the commencement address. He wrote the acclaimed memoir "Chasing My Cure: A Doctor's Race to Turn Hope into Action," reflecting on his journey as a patient and physician-scientist.



















WHITE COAT CEREMONY

The White Coat Ceremony is a symbolic event marking the entry of first-year students into the medical profession. School of Medicine administrators and faculty members virtually welcomed students of the Class of 2024; and Vaughn S. Clagette, MD, MBA, physician, Southeast Permanente Medical Group, and member, Pitt Board of Trustees and UPMC Board of Directors, gave the keynote address: "Your journey is about to begin," he told the medical students. "At Pitt, with continued work, you can become any and everything

you want to be in life." As for the students, they declared their commitment to integrity, ethical behavior, and honor by reciting the Hippocratic Oath. This year, in addition to the traditional Hippocratic Oath, Chenits Pettigrew Jr., EdD, associate dean for diversity, equity, and inclusion and director of diversity programs, challenged students to write their own class oath for the first time in the school's 134 years. The new oath was more explicitly inclusive of all people, including those historically overlooked by the medical community. •

"We believe that our oath acknowledges the context of U.S. history and medicine and uses it to explain our current state. We used the past and present to clarify our future goals as physicians."

Tito Onyekweli '24



DO NO HARM

Hippocratic Evolution

n addition to reciting the traditional Hippocratic Oath during the White Coat Ceremony in August, members of the University of Pittsburgh School of Medicine's Class of 2024 started a new tradition by writing their own class oath to acknowledge their ever-evolving responsibilities as physicians.

At orientation, Chenits Pettigrew Jr., EdD, associate dean for diversity, equity, and inclusion, challenged med students to update the oath. After circulating a draft to the entire medical school class for feedback, students officially presented the new oath to Anantha Shekhar, MD, PhD, senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of the School of Medicine.

"At Pitt, we challenge our students to change the world—and the future of medicine—for the better. This class didn't wait," said Shekhar. "Their class oath, the first of its kind in our program's 134-year history, speaks to the power and importance of clinical

care and research in creating a more inclusive and just society, and I am excited to watch them put this promise into practice."

The oath, which highlights issues like COVID-19, health care disparities, and racial injustice, is not merely about current events, said first-year medical student Tito Onyekweli, one of 12 students on the oath writing committee.

"We believe that our oath acknowledges the context of United States history and medicine and uses it to explain our current state," Onyekweli said. "We used the past and present to clarify our future goals as physicians."

The students acknowledged that they are beginning their careers in medicine at an unforgettable moment in history. The oath addresses championing diversity in medicine and society, being an ally to those of low socioeconomic status, and restoring trust in the health care community.

"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+ lives lost to COVID-19, despite the sacrifices of health care workers."

In the future, each incoming School of Medicine class will be invited to write its own unique oath during orientation week to help them establish their professional identities as physicians. •

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE CLASS OF 2024 OATH

As the entering class of 2020, 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. We honor the 700,000+ lives lost to COVID-19, despite the sacrifices of health care workers.

We recognize the fundamental failings of our health care and political systems in serving vulnerable communities. This oath is the first step in our enduring commitment to repairing the injustices against those historically ignored and abused in medicine: Black patients, Indigenous patients, Patients of Color, and all marginalized populations who have received substandard care as a result of their identity and limited resources.

Acknowledging the privilege and responsibility that come with being a physician, I take this oath as a call to action to fulfill my duty to patients, to the medical profession, and to society.

THEREBY, I PLEDGE AS A PHYSICIAN AND LIFELONG STUDENT OF MEDICINE:

I will support and collaborate with my colleagues across disciplines and professions, while respecting the patient's vital role on the health care team.

Iwill honor my physical, mental, and emotional health so as to not lessen the quality of care I provide.

Iwill carry on the legacy of my predecessors by mentoring the next generation of diverse physicians.

I will recognize the pivotal role of ethical research in the advancement of medicine and commit myself to endless scholarship with the ultimate goal of improving patient care.

I will care for my patients' holistic well-being, not solely their pathology. With empathy, compassion, and humility, I will prioritize understanding each patient's narrative, background, and experiences, while protecting privacy and autonomy.

Iwill champion diversity in both medicine and society and promote an inclusive environment by respecting the perspectives of others and relentlessly seeking to identify and eliminate my personal biases.

I will be an ally to those of low socioeconomic status, the BIPOC community, the LGBTQIA+ community, womxn/women, differently-abled individuals, and other underserved groups in order to dismantle the systemic racism and prejudice that medical professionals and society have perpetuated.

I will educate myself on social determinants of health in order to use my voice as a physician to advocate for a more equitable health care system from the local to the global level.

Iwill restore trust between the health care community and the population in which I serve by holding myself and others accountable and by combating misinformation in order to improve health literacy.

In making this oath, I embrace the ever-changing responsibilities of being a physician and pledge to uphold the integrity of the profession in the clinic and beyond.

"Our students, with the support and leadership of Dean Shekhar, have been leaders in this change, pushing us to make our curriculum more antiracist, more attentive to social medicine themes."

Jason Rosenstock, MD

Medical School Curriculum Undergoes Major Advances

he time is now for "disruptive change" (the good kind) in the curriculum for Pitt medical students. That assessment comes from School of Medicine educators, based on rapid changes in biomedical science, medical practice, pedagogical shifts, and student feedback.

"We continually upgrade the curriculum, but for larger changes you need a broader revival effort," says Jason Rosenstock, MD, associate dean for medical education and professor of psychiatry, who spearheads the curriculum reform. "We also wanted to address some specific themes."

One of the themes is interprofessional education. In a working environment, physicians interact with pharmacists, nurses, physical therapists, and other health professionals to provide the best care for patients. Interprofessional education blends students and learning from different health care fields. Rosenstock and others believe the current new construction to increase space and flexibility in Alan Magee Scaife Hall—the medical school's home—is essential to the new styles of learning. In fact, Anantha Shekhar, MD, PhD, senior vice chancellor for the health sciences and Petersen Dean of Medicine, made changes to the layout plans soon after arriving in Pittsburgh in June 2020 to ensure suitability for interprofessional learning.

The change in space puts the medical school at the forefront of curriculum reform because it gives students ready access to different technologies, like point-of-care ultrasound, and also reinforces the school's emphasis on smaller, more active learning groups.

Another focus is social medicine — social determinants in medicine, race and ethnicity in medicine, and

LGBTQ-specific needs in medicine—a theme that has been growing in the curriculum but came to the forefront during this past year's social justice movement.

"Our students, with the support and leadership of Dean Shekhar, have been leaders in this change, pushing us to make our curriculum more antiracist, more attentive to social medicine themes," points out Rosenstock.

Instead of waiting for the curriculum reform to be launched in fall 2023, Pitt Med has already refreshed elements of the curriculum, including a class in winter 2021 to address bias and racism in medicine. An already existing social medicine focus will be strengthened throughout the curriculum, and another suggested plan is to include students' projects examining health care disparities in Pittsburgh and working on solutions that involve collaboration with local agencies and other professionals.

Medical students have also asked educators to reexamine the first two years of the curriculum. Rosenstock says the committee is looking at condensing or making more efficient the basic science curriculum and at how assessment and feedback are given to students for them to be better prepared for exams and clerkship experiences.

The school is giving the curriculum update the time and effort it deserves, with more than 70 people on five subcommittees representing voices at every level, including basic science faculty, physician-educators, students, education and education technology experts, and student affairs, faculty affairs, and admissions personnel.

"Everything is affected by curriculum reform," says Rosenstock. "Changes can affect the educators we need and the students we admit. It's really the lifeblood of our institution." ●

BY THE NUMBERS SAFETY PROTOCOLS

Who We Are

2020-21 Academic Year

599
MD students

327 (55%) women and 272 (45%) men; 211 (35%) Pennsylvania residents; with 18% underrepresented minority students

368 registrants in PhD programs

152 students in MS programs

34 students in certificate programs

For 2020,

7,177 applications for admission

734 prospective students interviewed for a first-year class of 149 students

2,424 regular and 2,190 volunteer faculty members; 81 are members of the Academy of Master Educators





On-Campus COVID-19 Testing

n effort to keep the University community healthy, Pitt, through the School of Medicine's leadership, is working to monitor and contain the spread of COVID-19 on and off campus by using surveillance testing of asymptomatic students.

The strategy is designed to detect substantial shifts in trends of positive tests and helps give a sense of the prevalence of the virus in the larger community. Students are randomly selected—based on the work of statisticians and epidemiologists in the Graduate School of Public Health—to be tested for the virus.

Students receive an email from Pitt's COVID-19 Medical Response Office—directed by infectious disease specialist **John Williams, MD**—notifying them that they have been selected to get tested. The percentage of the student population tested has aligned with recommendations from both the Centers for Disease Control and Prevention (CDC) and the American College Health Association. (Mass testing of asymptomatic students didn't take place because it places undue stress on testing capacity, and lag time for results diminishes their medical relevance.)

For the fall semester, two cohorts of 280 randomly selected students on the Pittsburgh campus, who weren't experiencing symptoms of COVID-19, were tested each week at the on-campus outdoor testing site. Testing takes only about 15 minutes, using a simple nasal swab. The students and their test results remain confidential.

If students test positive, they are isolated at a University-designated facility or at home. Contact tracing is also conducted to identify people who may have been exposed to the virus through close contact. During on-campus isolation, food is delivered to the students, and they are monitored daily by a health care professional who determines the most appropriate care.

For the semester, 7,766 students underwent surveillance testing: there were 33 positive tests, for an overall rate of 0.42% among asymptomatic students. Overall, there were approximately 700 students who tested positive, which included symptomatic students, many of whom were tested through student health services.

MusiCare Show Goes On

or seven years, School of Medicine students have been singing, playing, and performing music for hospital patients through the school's MusiCare program. Small bands of students take up their guitars, keyboards, cellos—everything—and head to area hospitals to share the comforting, healing qualities of music with patients. They play pop covers, classical music, and much more for patients on dialysis, in palliative care, and in other settings. They perform Disney songs at UPMC Children's Hospital of Pittsburgh.

But then came the COVID pandemic, which threatened to silence the music.

"We all put our heads together in the spring when everything was shut down," says Julia Knight, a second-year medical student and MusiCare coordinator who also sings and plays ukulele for patients. "We knew that, especially during that time, it was even more important to provide this music to patients. Notably, they were separated from their families and visitors weren't really allowed in the hospital."

So, the students launched the MusiCare Connections YouTube channel to share their performances virtually. To get the word out, students took to social media and partnered with other students and hospital staff to distribute business cards with QR codes and info on MusiCare to patients and their families.

Even though recordings can't capture the same connectivity as live performances, going virtual has let alumni and even students at other medical schools partake in the music making, Knight says. But she looks forward to performing for patients in-person again when safe to do so. "Within a few minutes of playing and singing, [patients] kind of light up. And I think that's such a rewarding experience to be able to provide that for them and for their families."







(L-R), Davis, Humphrey

Snacks for STEM

F

or Camille Davis, the moment came during a rotation in pediatrics. A young patient, who looked familiar, was talking with her about how she wanted to be a physician or scientist when she grew up because she likes math and science. The patient described a program at her elementary school where medical students came in to discuss careers in medicine and STEM-related fields. Davis happened to be one of those

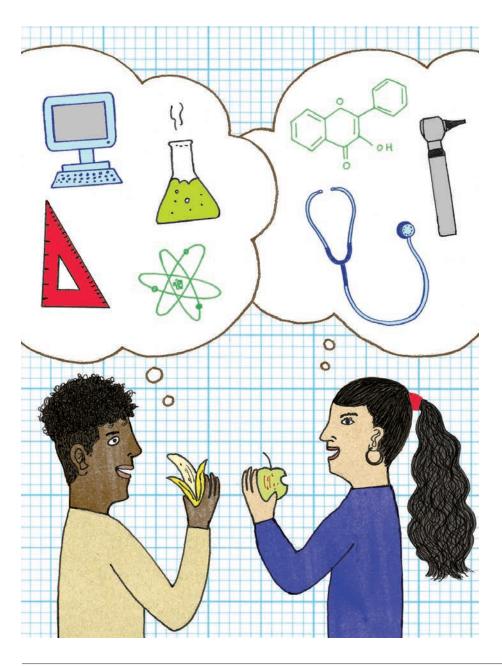
visiting med students through the program, Snacks for STEM, which she co-created with fellow student Victoria Humphrey. The program is meant to provide children from underserved communities more exposure to STEM careers, while also helping to combat food insecurity.

A couple of years ago, after a Student National Medical Association meeting, Davis and Humphrey decided to act on their mutual passions for education, equality, and service. They created Snacks for STEM, a community service organization that gives healthy treats and information about STEM-related careers to children at Pittsburgh Fulton PreK-5, a city school with a percentage of its student body coming from underserved communities. In addition to being funded through allocations from campus organizations for community outreach, Snacks for STEM received a 2020 Martin Luther King Jr. Day of Service grant.

"We bring some physician tools and talk to the children about what we do and what the career possibilities are in fields like science, technology, or engineering to just open up their minds to different possibilities," says Humphrey.

"Sometimes all it takes is a 30-second conversation for them to realize that they could be doctors, scientists, or engineers, too."

Camille Davis



Davis and Humphrey, both now fourth-year med students, bring snacks to school because they know many families struggle with food insecurity, and they talk about professions in STEM because they know that representation matters. Both women had similar experiences in elementary school, where they saw someone who looked like them who worked in a STEM field.

"It's so important that Black, Latinx, and historically marginalized populations have that exposure to positive representation, especially from someone who looks like them," says Humphrey. "It reaffirms that if they can't see you, they can't be you."

"Sometimes all it takes is a 30-second conversation for them to realize that they could be doctors, scientists, or engineers, too," says Davis. "That's how it worked for me when I was in their shoes in elementary school."

While they cannot be in Pittsburgh Fulton PreK-5 right now because of the COVID-19 pandemic, Davis and Humphrey are figuring out new ways to help the community, including possibly putting the Snacks for STEM grant toward sponsoring some teachers' educational wish list items.

Both Davis and Humphrey want to continue programs similar to Snacks for STEM in their residencies next year; and, wherever they end up, they also want to continue working toward representation and equality.

"I'm currently applying to pediatrics residency programs that focus on underserved populations," says Davis. "I'll be involved in increasing minority representation in medicine and helping Black and Brown children make it into STEM fields in general."

Humphrey agrees and says, "I'm also passionate about increasing representation within my intended field of dermatology and working with underserved and minority communities through clinical practice and community outreach." ●



Jenny Jiao, a visiting research scholar from Tsinghua University School of Medicine, at work in the lab.

Pitt Mentorship Program Coveted by International Students

n a University of Pittsburgh School of Medicine lab, a team of scientists is using zebrafish and a technology they developed — chemoptogenetic ablation of neuronal mitochondria — to understand the mechanisms underlying cell death in Parkinson's disease. Simply put, they are studying how nerve cells die in neurodegenerative diseases. The development and use of this new technology encompasses the doctoral work of one team member, Binxuan Jiao (who uses the name "Jenny").

"Jenny is extremely smart, works very hard, and is a great colleague," says her mentor, Edward A. Burton, MD, DPhil, Professor of Movement Disorders in Neurology and associate professor of neurology.

For the past two years, Jiao has been working in Burton's lab as a visiting research scholar, part of Pitt Med's collaboration with Tsinghua University School of Medicine, one of China's premier universities, through which the Pitt School of Medicine provides two years of mentored research training to qualifying students in Tsinghua's eight-year MD program. The visiting scholars must complete a master's-level thesis based on their research at Pitt as a requirement to receive their Tsinghua MD. In 2019, Tsinghua added an MD/PhD

track to its medical school degree offerings for a selected, very small group of students to spend an additional year engaged in mentored research at Pitt, the results of which would qualify them for the PhD portion of their MD/PhD.

Of her years at Pitt, Jenny says, "Pitt has such a great environment for research. My mentor, Dr. Burton, is my career role model. He's very helpful and supportive and has taught me a lot about how to do research and think like a scientist. My project is very exciting because it has just reached the point where I can dig deeply into the mechanisms underlying cell death in Parkinson's disease."

Jiao feels fortunate to have the opportunity to continue her studies at Pitt, especially in the midst of the COVID-19 pandemic.

"Tough things will pass eventually, while my experience here will stay with me for a lifetime," she says. •

"Jenny is extremely smart, works very hard, and is a great colleague."

Edward A. Burton, MD, DPhil

Nurturing Underrepresented Undergrads in Biomedical Sciences

he college student-to-scientist career pipeline is not always constructed the same for all students, especially students who are underrepresented minorities. Some students know they like science but haven't had the exposure or formative experiences that help them solidify a decision to pursue it as a career. To capture these students, faculty members and graduate students in the School of Medicine's Program in Microbiology and Immunology (PMI) developed and fast-tracked the Microbiology and

Immunology Diversity (MID) Scholars Program.

With financial support and enthusiasm from Anantha Shekhar, MD, PhD, senior vice chancellor for the health sciences and Petersen Dean of Medicine, and the Departments of Immunology and of Microbiology and Molecular Genetics, the program moved from concept to four funded scholars in just a few months (four additional scholars will be selected to begin the program in the 2021 spring semester). Similar programs exist at the University, but engaging students as undergraduates makes the MID program unique.

"We created this program at the undergraduate level because it's during this time when students who have an interest in biomedical sciences get lost because they don't get resources or support," says Partha Biswas, PhD, associate professor of medicine (Division of Rheumatology and Clinical Immunology) and of immunology and program director. "We want to pick them up early on, put them in a research lab, introduce them to biomedical science, and see how their interest grows. This support at the initial level is important because, by the time their undergraduate years are finished, their interest in science may not have been supported, and they've already moved away from science as a career."

Students from underrepresented minority groups accepted into the MID program are funded for two years

in order to complete long-term basic, clinical, and/or translational research projects within the graduate program in microbiology and immunology under the mentorship of experienced researchers and principal investigators. Scholars also receive peer-based mentoring and career advice from PMI graduate students, are encouraged to attend career and professional training sessions, and receive travel awards to present their projects at local and national conferences.

"The idea for the MID program came from PMI graduate students and was also borne out of the social justice movement in the past few months," says Biswas. "We want to nurture and mentor these scholars and their interests. There has been a tremendous enthusiasm for the program so far, and now we're looking at long-term sustainability and how to reach more students." ●

"The idea for the MID program came from PMI graduate students and was also borne out of the social justice movement in the past few months."

Partha Biswas, PhD



RESEARCH



A new alliance—between Pitt and the International Space Station (ISS) U.S. National Laboratory—aims to advance regenerative medicine by enabling research to take place onboard the ISS. (Above, a flight engineer at work in space.) See page 34.

De-liver-ing

sing skin cells from human volunteers, School of Medicine researchers created fully functional mini livers, which they transplanted into rats. These lab-made organs survived for four days inside their animal hosts, **Alejandro Soto-Gutiérrez, MD, PhD**, associate professor of pathology, and colleagues, wrote in Cell Reports.

"Seeing that little human organ there inside the animal—brown, looking like a liver—that was pretty cool," said Soto-Gutiérrez, who is also affiliated faculty with the McGowan Institute for Regenerative Medicine and the Pittsburgh Liver Research Center.

These mini livers secrete bile acids and urea like a normal liver. Soto-Gutiérrez and colleagues reprogrammed human skin cells into stem cells, coaxed those stem cells to become various types of liver cells, and then seeded those human liver cells into a decellularized rat liver, completing what would normally be a two-year maturation process in under a month.

Four days after the lab-grown livers were transplanted into rats bred to resist organ rejection, researchers investigated how well the implants were functioning. Although blood-flow problems had developed within and around the graft, the transplanted mini livers worked, and human liver proteins were detectable in in the rats' blood.

Significant challenges, including long-term survival and safety issues, remain, the authors noted.

"The long-term goal is to create organs that can replace organ donation; but in the near future, I see this as a bridge to transplant," Soto-Gutiérrez said. "For instance, in acute liver failure, you might just need hepatic boost for a while instead of a whole new liver." ■

"The long-term goal is to create organs that can replace organ donation; but in the near future, I see this as a bridge to transplant."

Alejandro Soto-Gutiérrez, MD, PhD



"Living-donor liver transplant should be considered the first and best option for most patients with liver disease."

Abhinav Humar, MD

8,000
LIVER TRANSPLANTS
PERFORMED ANNUALLY

LESS THAN

5%

OF OPERATIONS INCLUDE LIVING DONORS

ABOUT

25%

OF PEOPLE ON THE NATIONAL WAITING LIST DIE EACH YEAR WAITING FOR A TRANSPLANT

PROFILE: ABHINAV HUMAR, MD

Prioritize Living-Donor Liver Transplants

n what is often a life-or-death option for treating liver disease, living-donor transplants can improve outcomes and survival rates and reduce costs compared to deceased-donor transplants, the more common procedure.

Nationally, of the 8,000 liver transplants performed annually, less than 5% of operations include living donors, which involves removing a portion of the donor's liver that grows back to full size and function within eight to 10 weeks.

About 25% of people on the national waiting list die each year waiting for a transplant and experience poorer health at the time of transplant because of the prolonged wait. For these more than 14,000 people, living-donor transplant could be a viable, preferable option.

"The consequences for patients on the waiting list can mean the difference between life and death because the longer they are waiting, the sicker they become," says **Abhinav Humar**, **MD**, Thomas E. Starzl Professor of Transplantation Surgery and clinical director of the Thomas E. Starzl Transplantation Institute. "Living-donor liver transplants, in tandem with deceased-donor liver transplants, represent an opportunity to significantly decrease the risk of wait-list mortality and give us the ability to transplant a person sooner."

In a retrospective review published in the Annals of Surgery, Humar and other Pitt researchers evaluated 245 adult living-donor liver transplant recipients and 592 deceased-donor recipients whose procedures were performed over the last 10 years at UPMC, which houses the country's largest living-donor liver transplant program. Here's what they found:

- Living-donor liver transplants' three-year patient survival stood at 86%, hospital stays averaged 11 days, and there was a 53% likelihood of needing intraoperative blood transfusion and a 1.6% likelihood of needing post-transplant dialysis. In comparison, for deceased-donor transplants, the recipients' three-year survival was 80%, hospital stays averaged 13 days, and there was a 78% likelihood of needing intraoperative blood transfusion and a 7.4% likelihood of needing post-transplant dialysis. In addition, hospital costs were also 29.5% lower for living-donor recipients.
- Patients and donors were followed for at least two years post-transplant.
 There were no deaths among the living donors, who had an overall complication rate of 20%.
- "Living-donor liver transplant should be considered the first and best
 option for most patients with liver disease," Humar says. "It is not
 only an option for those on the waiting list but could perhaps offset
 the fact that not everyone who may benefit from transplant qualifies
 to receive a deceased-donor transplant based on today's current rules
 of allocation." ●

Making Progress

2019 NATIONAL INSTITUTES OF HEALTH FUNDING UNIVERSITY OF PITTSBURGH

\$582 M

80% School of Medicine



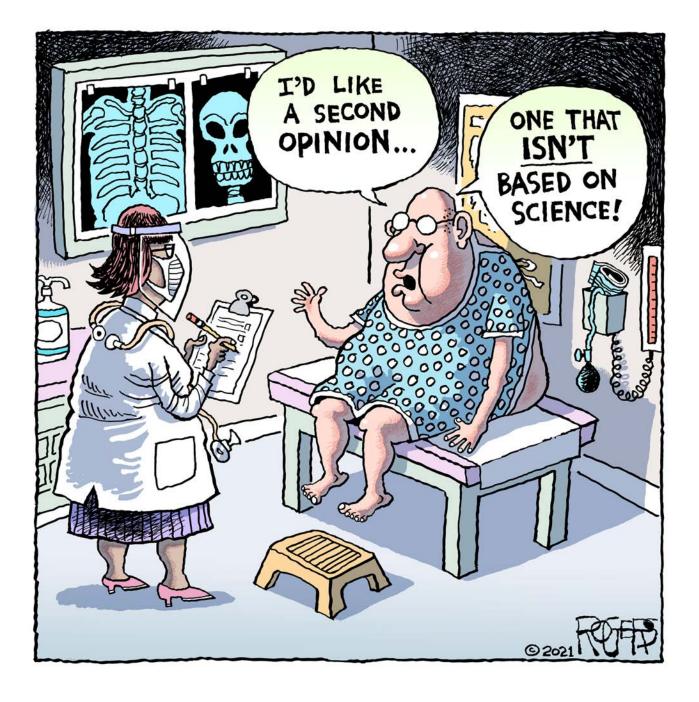
Rank 6th

2020
PITT TOTAL RESEARCH BUDGET

\$874 M

70% School of Medicine





Published Advancements 2020

JAMA

SEP 2019 | VOL 322 | ISSUE 11

PITT AUTHOR: Halina Zyczynski, MD, Professor of Obstetrics, Gynecology, and Reproductive Sciences

Effect of Vaginal Mesh Hysteropexy vs Vaginal Hysterectomy with Uterosacral Ligament Suspension on Treatment Failure in Women with Uterovaginal Prolapse

Compared to traditional vaginal hysterectomy with uterosacral ligament suspension of the vaginal apex, a uterine suspension with transvaginal mesh results in comparable three-year anatomic and symptomatic outcomes in women with pelvic organ prolapse.

JAMA SURGERY

MAR 2020 | VOL 155 | ISSUE 3

LEAD AUTHOR: Anita Courcoulas, MD, MPH,

Anthony M. Harrison Professor of Surgery

Interventions and Operations 5 Years after Bariatric Surgery in a Cohort from the U.S. National Patient-Centered Clinical Research Network Bariatric Study

According to a national, multicenter cohort study involving tens of thousands of bariatric surgery patients, in the five years following bariatric surgery, patients who underwent a gastric bypass operation were more likely to experience a readmission to the hospital or to undergo an additional abdominal operation or intervention compared to patients who underwent a gastric sleeve operation.

NATURE STRUCTURAL & MOLECULAR BIOLOGY

AUG 2019 | VOL 26 | ISSUE 8

SENIOR AUTHOR: Bennett Van Houten, PhD,

Richard M. Cyert Professor of Molecular Oncology, Professor of Pharmacology and Chemical Biology

Damage Sensor Role of UV-DDB during Base Excision Repair

Beyond detecting DNA damage caused by ultraviolet exposure, the ultraviolet-damaged DNA-binding (UV-DDB) protein can also scout for oxidative DNA damage and, in turn, help DNA repair molecules to fix damage often buried deep in chromosomes.

SCIENCE TRANSLATIONAL MEDICINE

OCT 2019 | VOL 11 | ISSUE 513

SENIOR AUTHOR: Bernhard Kühn, MD, PhD,

Associate Professor of Pediatrics

Control of Cytokinesis by β -adrenergic Receptors Indicates an Approach for Regulating Cardiomyocyte Endowment

Beta blocker drugs could stimulate cardiomyocyte cell division in infants with congenital heart defects to improve heart function.

eLIFE

SEP 2019 | ONLINE JOURNAL

SENIOR AUTHOR: Vaughn Cooper, PhD,

Professor of Microbiology and Molecular Genetics

Evolutionary Pathways to Antibiotic Resistance Are Dependent Upon Environmental Structure and Bacterial Lifestyle

Whether bacteria live as independent cells or grow into communal biofilms determines how they evolve anti-biotic resistance, which could expose vulnerabilities in drug-resistant infections.

CLINICAL EPIGENETICS

NOV 2019 | ONLINE JOURNAL

SENIOR AUTHOR: **Mellissa Mann, PhD**, Associate Professor of Obstetrics, Gynecology, and Reproductive Sciences

Perturbations in Imprinted Methylation from Assisted Reproductive Technologies but not Advanced Maternal Age in Mouse Preimplantation Embryos

Fertility treatments, not advanced maternal age, may cause the epigenetic changes associated with Beckwith-Wiedemann, Silver-Russell, and Angelman syndromes, as shown in mice.

THE LANCET

JAN 2020 | VOL 395 | ISSUE 10219

LEAD AUTHOR: Kristina Rudd, MD, MPH,

Assistant Professor of Critical Care Medicine

Global, Regional, and National Sepsis Incidence and Mortality, 1990–2017: Analysis for the Global Burden of Disease Study

2017 data reveals that sepsis—the body's potentially fatal response to infection that injures its own tissues and organs—is associated with one in five deaths worldwide, largely in low- or middle-income countries.

CELL

AUG 2019 | VOL 178 | ISSUE 4

SENIOR AUTHOR: Daniel Kaplan, MD, PhD,

Professor of Dermatology

Cutaneous TRPV1+ Neurons Trigger Protective Innate Type 17 Anticipatory Immunity

Pain-sensing nerves in skin could also detect pathogens, triggering an immune response to fight infections.

JAMA PEDIATRICS

MAR 2020 | VOL 174 | ISSUE 3

SENIOR AUTHOR: Elizabeth Miller, MD, PhD, Edmund R. McCluskey Professor of Pediatric Medical Education, Professor of Pediatrics

An Athletic Coach-Delivered Middle School Gender Violence Prevention Program

The Coaching Boys Into Men program, aimed at stopping violence and sexual assault against women and girls, successfully reduces abusive behaviors among middle school athletes, demonstrating the program's success with younger adolescents.

JAMA NEUROLOGY

APR 2020 | VOL 77 | ISSUE 4

AUTHORS: Michael W. Collins, PhD, Professor of Orthopaedic Surgery; Anthony Kontos, PhD, Professor of Orthopaedic Surgery

Association of Time since Injury to the First Clinic Visit with Recovery Following Concussion

Athletes treated within a week after experiencing a concussion recovered faster than athletes not treated until eight days to three weeks after injury, indicating the importance of seeking appropriate, specialized care early on.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

JUN 2020 | VOL 117 | ISSUE 23

AUTHORS: David Levinthal, MD, PhD, Assistant
Professor of Medicine (Division of Gastroenterology,
Hepatology, and Nutrition); Peter Strick, PhD,
Distinguished Professor and Chair of Neurobiology
and Thomas Detre Professor of Neuroscience

Multiple Areas of the Cerebral Cortex Influence the Stomach

The brain-body connection has largely focused on the gut's influence on the brain, but neural pathways connecting the brain to the stomach reveal that the brain influences stomach function and development of stomach ulcers.

eLIFE

FEB 2020 | ONLINE JOURNAL

NATURE COMMUNICATIONS

FEB 2020 | ONLINE JOURNAL

SENIOR AUTHOR: Anne-Ruxandra Carvunis, PhD, Assistant Professor of Computational and Systems Biology

Synteny-Based Analyses Indicate that Sequence Divergence Is Not the Main Source of Orphan Genes

De novo Emergence of Adaptive Membrane Proteins from Thymine-Rich Genomic Sequences

De novo genes, born from noncoding regions of the genome, may trigger more species-specific and beneficial traits in organisms than previously thought.

RESEARCH NOTEWORTHY GRANTS INNOVATIVE RESEARCH

Pioneering Grants 2020

VISION RESTORATION SUPPORTED

Restoring lost vision could lie in understanding how the eye and the brain work together and using this knowledge to advance brain-computer interfaces and novel genetic technologies. Pitt's Department of Ophthalmology is pursuing this research with the support of a **\$6 million** grant from the Richard King Mellon Foundation.

MANAGING PAIN AND OPIOID MISUSE

Key research for treating pain associated with the lower back, end-stage renal disease, osteoarthritis, and other conditions has been bolstered by **\$32 million** in NIH grants to Pitt and UPMC researchers studying opioid misuse and pain management. As part of NIH's Helping to End Addiction Long-term (HEAL) initiative, the nine grants received support research on sleep and opioid use, prescription medication misuse in young adults, *in utero* opioid exposure and neurological development, and other areas.

REGENERATIVE REHABILITATION AND TRAINING

Integrating regenerative medicine with rehabilitative medicine can better assist people with disabilities, which is a primary goal of the Alliance for Regenerative Rehabilitation and Training (AR3T). With a five-year, **\$5 million** grant, NIH has renewed support for AR3T, which comprises a multi-institutional network of laboratories at Pitt, Stanford University, the University of Texas at Austin, and the Mayo Clinic.

REGENERATING DAMAGED MUSCLE

Regrowing muscle tissue is a much sought-after ability because, when more than 20% of a muscle is damaged, as is common in combat injuries, tissue can't regenerate, and a stiff scar forms. That's why a **\$22 million** Defense Advanced Research Projects Agency (DARPA) grant is supporting a multi-institution research team, led by Pitt, to develop a device that combines artificial intelligence, bioelectronics, and regenerative medicine to regrow muscle tissue.

DIVERSITY AND PALLIATIVE CARE

The importance of palliative care is reflected in its expanded availability in hospitals across the country. However, palliative care specialists are most often not minorities. In response, a \$250,000 award from The Arthur Vining Davis Foundations is supporting an initiative for minority physicians led by the UPMC Palliative and Supportive Institute and School of Medicine faculty to foster career paths in palliative care at minority-serving medical schools. To do so, the program, in part, sends UPMC palliative care physicians to those institutions for mentoring faculty on how to better incorporate palliative care into student and resident education.

FUNDING VACCINE DEVELOPMENT

To help combat today's pandemic, an international, academia-industry partnership has generated funding for SARS-CoV-2 vaccine development. The intergovernmental organization Coalition for Epidemic Preparedness Innovations (CEPI) has committed nearly \$5 million to a consortium led by the Institut Pasteur research center in Paris, collaborating with Themis in Vienna and Pitt's Center for Vaccine Research. The funding aims to support vaccine research and phase I clinical trial rollout.

Rethinking Research (and Care)

here is a time for tradition and a time—
a now—for transformation. To meet
the challenges of deadly diseases like
COVID-19, H1N1, and sepsis, Pitt's School
of Medicine and UPMC are advancing
research and clinical practice with a new
twist on research: randomized trials
concurrent with patient care.

Centered in the newly formed Office of Health Care Innovation, the initiative is headed by **Derek Angus, MD, MPH**, Pitt's inaugural associate vice chancellor for health care innovation and UPMC's chief health care innovation officer.

"The goal must be a system that has a more integrated approach to learning while doing," Angus wrote in a May edition of the Journal of the American Medical Association, calling on clinicians and researchers to "lean in" and expand their approaches to testing and trying new therapeutics.

"We like to use the analogy of a stadium," explains pulmonologist **Christopher Seymour, MD, MSc**, one of a cadre of physician-scientists who are associated faculty in the new office. "In traditional clinical trials, you build a stadium, you play one game, and you tear it down. Our approach is to build a stadium and play lots of games."

Formally known as the Randomized Embedded Multifactorial Adaptive Platform (REMAP) (see page 8), the approach is less program and more purpose—one that percolates through day-to-day clinical decisions in patient care and includes quality-improvement activities, new treatment paradigms, and computer modeling, all connected with electronic health records.

In essence, the new office is a conduit for innovation that unites the extensive biomedical sciences, public health, and health policy research based at Pitt with UPMC's vast clinical and commercial expertise. Using pretrial simulations, various therapeutic, behavioral, or quality improvement strategies can be explored to identify trial designs that can quickly be adapted to changing conditions.

"We work closely with the Clinical and Translational Science Institute and Department of Biomedical Informatics at Pitt, as well as UPMC Enterprises and clinical analytics, to take the research that Pitt wants to test in an integrated, multicenter way to move the science forward," says Seymour, associate professor of critical care medicine

"It's exciting," he adds. "There aren't too many opportunities in the U.S. where a health care system and clinical efforts can fuse with research." ●



Bahar Reflects on Coveted NAS Honor for Scientists

Ivet Bahar, PhD, Distinguished Professor, John K. Vries Professor, and chair of computational and systems biology, discusses her 2020 election to the National Academy of Sciences (NAS), one of the highest honors a scientist can receive. Responses have been edited for length and clarity.

What was the first thing you said when you found out and to whom did you say it?

A colleague congratulated me by email. By mistake, I looked at the American Academy of Arts and Sciences online and didn't see my name. [Pitt structural biology department chair and NAS member]

Angela Gronenborn called, and I kept telling her that she was mistaken—until I saw a flood of congratulatory email messages from friends/colleagues who are NAS members. I ran to my husband and elder son and told them I couldn't think of any scientific recognition that could make me happier.

Your research in protein dynamics has many potential applications. What are you working on now and why?

A law always wanted to understand how proteins and biomolecular systems undergo structural changes during their biological activities. These changes are called conformational dynamics. We developed network models and analytical methods for predicting the structural changes that proteins can undergo while retaining their fold and stability. Establishing the link between biomolecular structure and function, through dynamics, is crucial. Understanding the dynamic capabilities of proteins encoded by their structure also opens the way to designing modulators of function that would alter the dynamics for therapeutic purposes—hence the broad applicability of our methods in drug design and discovery.

What future directions do you anticipate for your investigations?

A machine-learning algorithm we developed (Ponzoni and Bahar, PNAS 2018) is now available in a new server, called *Rhapsody*. Our plan is to further extend it to facilitate applications in precision medicine. We also think implementing fundamental theory and methods into computational tools/software is very important for enabling efficient use by the broader community. For example, our *ProDy* interface for predicting and analyzing protein dynamics has been downloaded more than 2 million times to date and has more than 130,000 users worldwide. New components to *ProDy* make it applicable to a wide range of areas from molecular mechanics to pharmacology.

In the past decade, I've focused on understanding neurobiological systems dynamics and, specifically, on neurotransmission at the molecular level—how neurotransmitters are transported by membrane proteins across cell membranes. Understanding how the deregulation of neurotransmitter transport and signaling may lead to neurodegenerative disorders (including drug addiction) is an important topic that needs significant work.

Other topics of interest are modeling protein-lipid interactions, including the molecular and cellular implications of lipid peroxidation events, understanding at the molecular level how the adaptive immune system responds to pathogens, and combining molecular- and systems-level quantitative methods for drug discovery and repurposing. For example, we recently started to understand the molecular origin of the cytokine storm observed in some severe COVID-19 patients, including children with multisystem inflammatory syndrome (Chen, et al., PNAS 2020) in collaboration with Cedars-Sinai. ●



"We've licensed five patents and have a portfolio of products."

Kacey Marra, PhD

PROFILE: KACEY MARRA, PhD

Breakthrough Nerve Repair



ince **Kacey Marra**, **PhD**, and colleagues reported successfully regenerating portions of damaged nerves using a polymer tube filled with growth-promoting protein in January 2020, the technology has inched a bit closer to clinical trials in humans thanks to growth of an entrepreneurial kind.

"We have a startup and have licensed the technology from Pitt," says Marra, a professor of plastic surgery and core

faculty member of the joint Pitt-UPMC McGowan Institute for Regenerative Medicine.

So far, tests in monkeys show that the biodegradable nerve guide can promote enough nerve growth to bridge a two-inch gap between the nerve stump and its target muscle. The guide has proven "comparable to, and in some ways better than, a nerve graft," says Marra.

While the company, Nerve Repair Technologies, seeks U.S. Food and Drug Administration approval for a clinical trial in humans, Marra pursues funding. "We've licensed five patents and have a portfolio of products." Finding angel investors is next on the agenda.

The U.S. Department of Defense has funded the Marra team for the past 12 years and has great interest in seeing their work progress. Half of wounded American soldiers return home with injuries to their arms and legs, which aren't well protected by body armor, often resulting in damaged nerves and disability. Among civilians, car crashes, machinery accidents, cancer treatment, diabetes, and even birth trauma can cause significant nerve damage, affecting more than 20 million Americans.

Options for a clinical trial include enrolling a few patients or doing a larger, multisite trial in collaboration with Walter Reed National Military Medical Center.

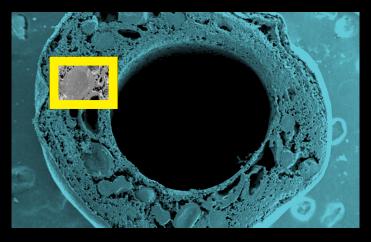
Peripheral nerves can regrow up to a third of an inch on their own; but if the damaged section is longer than that, the nerve can get knotted into a painful ball called a neuroma.

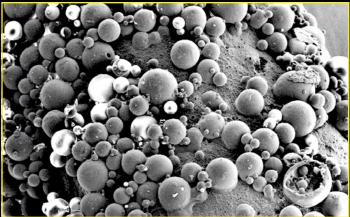
The most common treatment for longer segments of nerve damage is to remove a skinny sensory nerve at the back of the leg—which causes numbness in the leg and other complications but has the least chance of being missed—chop it into thirds, bundle the pieces together, and then sew them to the end of the damaged motor nerve, usually in the arm. But only about 40% to 60% of motor function typically returns.

"It's like you're replacing a piece of linguine with a bundle of angel hair pasta," Marra says. "It just doesn't work as well."

Marra's nerve guide, by contrast, returned about 80% of fine motor control in the thumbs of four monkeys.

"Now that we feel we've developed a successful nerve tube, we're focusing our studies on therapies for the de-enervated muscle to restore function even more," she says, adding that previous experiments in rats (published in Muscle and Nerve, May 2019) found efficacy in restoring some muscle function when rats were injected with adipose-derived stem cells after nerve injury.



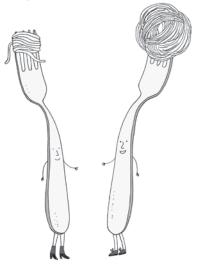




(Above) Microspheres containing a neural growth factor adhering to the nerve conduit during the manufacturing process. A cross-section image of the nerve conduit embedded in microspheres. (Left) Photo of the 5.2-cm nerve guide.

"It's like
you're
replacing
a piece of
linguine
with a
bundle of
angel hair
pasta. It
just doesn't
work as
well."

Kacey Marra, PhD



Developing Medical Technologies in Space

pace is the final frontier for explorers; and, increasingly, it is becoming a place for new commercial enterprises. For the biomedical industry, researchers are working to leverage microgravity to create products for patients on Earth.

The International Space Station (ISS) U.S. National Laboratory has teamed up with Pitt's McGowan Institute for Regenerative Medicine to map out the most promising technologies for biomedical development and manufacturing in low Earth orbit. The alliance is a key effort for the ISS National Laboratory as it works across many technological areas to increase the commercial use of space and builds on decades of experimentation performed on the space station.

The ISS National Laboratory and the McGowan Institute have enlisted a broad range of industry partners, other academic research centers, and government agencies to further expand the scope of medical technology development on board the ISS and to focus on new microgravity research to demonstrate the value of the space environment.

McGowan Institute director and Distinguished Professor of Surgery **William Wagner**, **PhD**, says that the space station offers a unique platform for regenerative medicine. The microgravity environment distinctly affects the properties of certain materials and substances, enabling processes not possible on Earth. Stem cells, for example, behave and reproduce differently in low gravity, Wagner says, and growing them in space might bolster cellular therapies for a variety of diseases and conditions like traumatic brain injury and type I diabetes.

Microgravity also permits 3D printing of complex tissue structures that would collapse or deform under full gravity. Miniaturized organ models reproduce certain diseases in microgravity, potentially permitting the study of treatments for conditions such as kidney failure and osteoporosis.

Given the cost and resources required to conduct space research, the partnership also focuses on rigorous business analysis to determine which areas of medical technology development are most likely to benefit patients on Earth. ●





"The reason the intravenous route is so effective is that the vaccine travels quickly through the bloodstream to the lungs, the lymph nodes, and the spleen, and it primes the T cells before it gets killed."

JoAnne Flynn, PhD

PROFILE: JOANNE FLYNN, PhD

Improving TB Vaccination Effectiveness

mproving the protective power of the tuberculosis vaccine could dramatically reduce TB burden and deaths. In recent years, tuberculosis has killed more people across the world than any other infectious disease, even though a vaccine is widely available. The Bacille Calmette-Guérin (BCG) tuberculosis vaccine uses a live, weakened form of TB bacteria and is typically injected under the skin. But the vaccine is not very effective and leaves some susceptible to infection.

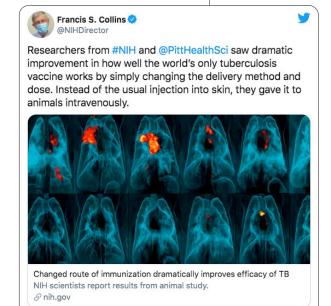
Simply changing the vaccine's route of administration might drastically boost its effectiveness, however. Describing their work in Nature, researchers from Pitt and the National Institute of Allergy and Infectious Diseases found that, in nonhuman primates, intravenous vaccination produced superior TB protection.

"The reason the intravenous route is so effective is that the vaccine travels quickly through the bloodstream to the lungs, the lymph nodes, and the spleen, and it primes the T cells before it gets killed," explains senior author **JoAnne Flynn, PhD**, Distinguished Professor of Microbiology and Molecular Genetics. "When we compared the lungs of animals given the vaccine intravenously versus the standard route, we saw a 100,000-fold reduction in bacterial burden. Nine out of 10 animals showed no inflammation in their lungs."

To test the method of administration's effects, Flynn and collaborators separated the nonhuman primates into groups: unvaccinated, standard human injection, stronger dose and standard injection, mist, injection plus mist, and stronger dose administered intravenously. Six months later, the researchers exposed the nonhuman primates to TB and monitored them for infection.

The intravenously vaccinated animals all had BCG and activated T cells in their lung tissue. The other animals had no detectable BCG in lung tissue, and their T-cell responses were only modest. Virtually no TB bacteria were found in the lungs of the intravenously vaccinated animals, and only one primate in this group developed lung inflammation or disease.

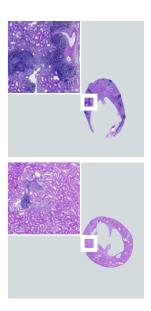
The researchers hope to eventually test intravenous TB vaccination in humans, but they're first studying whether lower doses of intravenous BCG could provide equally robust TB protection. The larger dose can cause side effects, primarily temporary lung inflammation. Before human translation can occur, however, the method must also be proven safe and practical; intravenous vaccination requires more skill to administer and can also more readily cause infection. •



Jan 2, 2020

"Knowing exactly how the innate immune system plays a role opens the door to developing very specific drugs, which allows us to move away from broadly immunosuppressive drugs that have significant side effects."

Fadi Lakkis, MD



PROFILE: FADI LAKKIS, MD

Minimizing Chronic Organ Rejection



breakthrough immune system finding could help minimize organ transplantation complications. While transplants have saved countless lives, for some patients, chronic rejection of transplanted organs can cause future complications. It's been almost six decades since immunosuppressive drugs made organ transplantation a clinical reality, yet many organ recipients will still need a second transplant in their lifetimes.

Using a genetically modified mouse model, Pitt researchers and their collaborators at

Houston Methodist Hospital recently found that the innate immune system may be able to "remember" foreign cells—an ability previously thought exclusive to the adaptive immune system. This finding, described in Science, could ultimately help prolong transplanted-tissue survival and prevent the need for second transplants.

"Knowing exactly how the innate immune system plays a role opens the door to developing very specific drugs, which allows us to move away from broadly immunosuppressive drugs that have significant side effects," says senior author **Fadi Lakkis, MD**, Distinguished Professor of Surgery, Frank and Athena Sarris Professor of Transplantation Biology, and scientific director of the Starzl Transplantation Institute.

Innate immune cells are the first to detect any foreign agents in the body; and they activate the adaptive immune system, which "remembers" various invading viruses, bacteria, and other agents in order to quickly impede them if they reemerge. This process is vital to immunity; but it also results in transplanted organs' eventual rejection, even with immunosuppressive drugs.

Innate immune cells like monocytes and macrophages haven't been thought to possess immunological memory. However, the researchers found that these cells' capacity to remember foreign tissues is as specific as that of adaptive immune cells, like T cells and B cells.

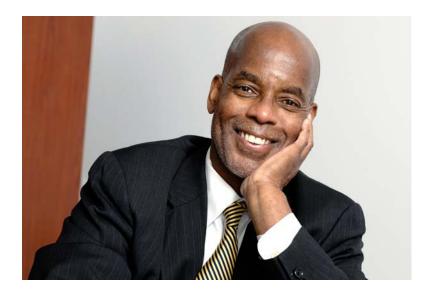
Using molecular and genetic analyses, the researchers showed that the paired Ig-like receptor-A (PIR-A) molecules were essential to the innate immune cells' memory. By blocking PIR-A molecules with a synthetic protein or genetically removing them from the host animal, the cells' memory was abolished, enabling transplanted tissues to survive for much longer. Essentially, the murine innate immune cells, after being exposed to foreign tissue, could initiate an immune response if exposed to that same foreign tissue again.

Beyond improving transplant outcomes, this finding could have implications for treating cancer, autoimmune conditions, and other diseases, says senior author **Martin Oberbarnscheidt, MD, PhD**, assistant professor of surgery. Further understanding of innate immune memory mechanisms could lead to developing targets for improving effective immune responses against tumors or restoring self-tolerance in autoimmune diseases. •



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Thank you.



PROFILE: LLEWELLYN HYACINTHE, MD, MBA

Pay It Forward



hen Llewellyn Hyacinthe, MD, MBA, was a medical student at the University of Pittsburgh, a mentor unexpectedly came into his life at a time when he most needed him. He believes that this mentor, Myrven Caines, MD, helped him stay at Pitt, get his medical degree, and enjoy a decades-long career as a physician and educator.

Now associate professor and director of operations, Department of Urology, SUNY Downstate Health Sciences University, and staff urologist, University Hospital of Brooklyn, Dr. Hyacinthe describes his first

year of medical school as a "daily struggle." He didn't grow up with a particular interest in science or medicine; he just had a desire to help people and solve problems, and his parents were keen on him being a doctor.

"Probably like many medical students, I was having trouble putting together all this data they were throwing at us every day," recalls Dr. Hyacinthe. "I really felt isolated and didn't feel as if there were any teaching faculty members I could go to to help me transform all this data into information that would help me become a physician."

In Dr. Hyacinthe's second year, Dr. Caines contacted him and other Black and Brown students in his class. He began meeting with them for an hour over lunch in his office every day, after their morning lectures and before their afternoon lab classes.

"My first-year knowledge was lacking," says Dr. Hyacinthe. "So, we'd review organ systems and disease processes, and he helped bring me up to speed. He gave me the pathway to catch up and to build up that foundation so I could move forward. Being able to pull all that information together gave me confidence that I just didn't have. More than anything, he gave us support and reassurance. I'm not sure I would've finished Pitt if not for his intervention."

At the time, Dr. Caines was an associate professor of pathology and associate director of laboratories for the Pittsburgh VA Medical Center and had his own busy schedule. Jagjit Singh, MD, assistant professor of pathology, is a former colleague of Dr. Caines and knew him in the mid-1980s when Dr. Caines was mentoring Dr. Hyacinthe.

"He was gentle, calm, had a Zen-like persona, and a warm, caring personality," remembers Dr. Singh. "He was a people person; and I sought advice from him, especially when he held his administrative role at the VA. He was a great listener and was fair and impartial in his feedback."

Dr. Singh has since heard about Dr. Caines' own experiences when he arrived in Pittsburgh from Trinidad and thinks they may have influenced Dr. Caines' desire to help other students. In an interview for Pittsburgh History in 1995, Dr. Caines describes his reception by colleagues at the School of Medicine in the late 1960s:

"I ran straight into racism full, square, and center. There were some white professors in the department who point-blank refused to teach me anything, who hid materials from me, and it was very clear that their intentions were that I should not succeed. My reaction to them was probably similar to what you would find from most immigrants, which is that we viewed these as roadblocks [that] one would have to overcome. So my philosophy was to turn every negative experience into a positive experience."

Dr. Hyacinthe benefitted from Dr. Caines' desire to turn his negative experiences into positive ones for the students he helped. To honor the commitment and dedication of Dr. Caines, who died in 2014, Dr. Hyacinthe has established the Myrven Joseph Caines, MD, Fund for Medical Diversity to support the School of Medicine's Office of Diversity, Equity, and Inclusion.

"From my position now, I realize how much of a sacrifice he made for us. I have enjoyed virtually every day of my career as a physician, as a urologist, so I'm very thankful. I can't imagine ever doing anything else," says Dr. Hyacinthe. "My main motivation is to just pay it forward; it's impossible to pay it back. I look around and African American males—we're still a rare species in medicine, unfortunately, so I'm trying to do my part to address it. Dr. Caines certainly did his part." ●

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PROFILE: JOHN TIPPINS

Family Foundation Remembers Its Patriarch

ohn Tippins comes from a family that knows well the value of hard work and innovation. His grandfather, Leon Tippins, the first of 11 children to go to college, moved to Pittsburgh to find a job in his field of electrical engineering. In 1923, he ended up starting a small family business, Tippins Machinery Co., in reconditioning used mining machinery. John's father, George, was also an electrical engineer.

When George returned to Pittsburgh from serving in World War II, he wanted to help his father build the company. His father let him take the lead in 1946, and George built a two-employee company into a nearly 300-employee strong company that became the world leader in refurbishing, designing, and building rolling mills and other equipment for the steel and metals industries. By the time he retired, he held more than a dozen patents for machines and metals processes.

George Tippins was also known for being the major investor in the acquisition of Allegheny Ludlum Steel Corporation, the nation's largest stainless steel producer at the time, from its parent, Allegheny Ludlum Industries. His investment was widely credited as saving the steel company from being sold to out-of-state financiers who planned to close it and sell it piecemeal to foreign companies. He was board chair and majority owner of Allegheny Ludlum Steel from 1980 through 1986, by which time the company was once more successful and growing into a world leader in the stainless and titanium steel markets.

Sadly, George Tippins was diagnosed with Alzheimer's disease in his later years. Even though he knew it was too late for him to benefit, he had the foresight, again, to create a family foundation before he died in 2005.

"He wanted to endow the foundation to do good things," says John (now a managing director at Stonewood Capital Management, after the family business was sold). "The three areas the foundation supports are entrepreneurialism (one of the recipients is the University of Pittsburgh's Institute for Entrepreneurial Excellence), general philanthropy, and Alzheimer's disease research."

Though the Tippins Family Foundation supports numerous Alzheimer's disease research initiatives, it is a large supporter of a research powerhouse in its own backyard, the University of Pittsburgh Alzheimer's Disease Research Center (ADRC), led by Oscar Lopez, MD, Levidow-Pittsburgh

Foundation Professor of Alzheimer's Disease and Dementia Disorders in the Department of Neurology, professor of neurology and of psychiatry, School of Medicine, and of clinical and translational science.

Pitt scientists know more than a little about hard work and innovation, too. In addition to other research advances, Pitt is the home of Pittsburgh Compound B (PiB), invented and developed by a team of researchers led by Chester Mathis, PhD, Distinguished Professor of Radiology and Professor of Radiology PET Research, and William Klunk, MD, PhD, Distinguished Professor of Psychiatry, Levidow-Pittsburgh Foundation Professor of Alzheimer's Disease and Dementia Disorders in the Department of Psychiatry, and codirector, ADRC. In addition to making possible the early diagnosis of Alzheimer's disease, PiB should help clinicians monitor the disease's progression. PiB works by binding to telltale beta-amyloid plaque deposits found in the brains of patients with Alzheimer's. These plaques are thought to kill brain cells, and their presence differentiates Alzheimer's disease from other dementias. PiB can be injected into the bloodstream of patients, and specialists can then use PET imaging to locate the plaques associated with Alzheimer's. Before Pittsburgh Compound B, it was possible to confirm Alzheimer's disease only after a patient's death at autopsy.

The Tippins Family Foundation supports numerous areas of research at Pitt, including cancer and urology, but ADRC has become an unofficial focus. And, like George Tippins, John and his family support the research being done in Western Pennsylvania.

"We really want to try to help solve the real problem for humanity, if we can," says John Tippins. "It's wonderful that we have an organization like Pitt right here that is truly outstanding." •

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Kurt Weiss, MD, cancer survivor and researcher, friend of the Hardesty and Garcia families, and grateful recipient of their support for his sarcoma research

PROFILE: JOHN GARCIA & JOHN HARDESTY

An Inspiring, Grateful Reunion

hen John Garcia was a student at West Virginia University, he decided to look for a summer job. John Hardesty hired him to work over the summers, and it was the beginning of a decades-long friendship. Over the years, Mr. Garcia would eat meals, go on vacations, and spend holidays with the Hardestys, who welcomed him as a member of the family. Mr. Garcia got to know Mr. Hardesty's son, Johnny, very well.

In 1998, Johnny was a student at the University of Georgia when Mr. Hardesty received a call from the

university's clinic with a message to pick up Johnny right away. What Johnny suspected was only a sore leg from playing touch football was actually something more serious. A quick visit to a physician in Morgantown confirmed a grim diagnosis.

"Johnny was diagnosed with osteogenic sarcoma, a cancer that begins in the bones," said Mr. Hardesty. "The doctor told me my son was probably not going to live. That's when I said, 'Well, that's bullshit."

Mr. Hardesty sought recommendations to get the best care for Johnny and ended up taking him to Shadyside Hospital (now UPMC Shadyside). During Johnny's time in the hospital, the Hardestys were befriended by the Weisses, another family whose son, Kurt, also had osteogenic sarcoma as a teenager. Kurt and Johnny endured similar chemotherapy, operations, and leg amputations, and their parents bonded over their sons' diagnoses and treatments.

"Mary Anne, my wife, and Mrs. Weiss went through many of the same sufferings together," says Mr. Hardesty.

Kurt eventually received treatment in a clinical trial that put his cancer into remission. After numerous attempts at treatment, Johnny went home to Morgantown. One of the last times he left his bed was to go downstairs and visit with Mr. Garcia and his family. About two and a half years after his diagnosis, Johnny died.

"To watch that young man and what he went through in those years—he never lost faith, never lost his sense of humor," says Mr. Garcia. "His strength was just incredible."

So, years later, when Mr. Garcia was on a fishing trip and heard of an orthopaedic cancer physician at the University of Pittsburgh with a story just like Johnny's, he told Mr. Hardesty, who realized the physician was Kurt Weiss, and a reunion was set in motion through mutual acquaintances. Kurt Weiss, MD, associate professor of orthopaedic surgery, welcomed the Hardestys and the Garcias to his Pitt lab to reconnect with his parents and to show them his transformation from bone cancer survivor to surgeon and cancer researcher, codirecting the Department of Orthopaedic Surgery's Musculoskeletal Oncology Laboratory, dedicated to the study of bone and soft tissue tumors.

"Kurt brought us up to speed on his research," says Mr. Garcia. "The question still looms: How does that cancer metastasize from bone to the lung or other parts of the body? He seems to be making headway on that."

Mr. Hardesty credits Mr. Garcia with coming up with the idea for them to create the Osteosarcoma Research Fund in Johnny's memory to support Dr. Weiss' research. The fund has been essential for Dr. Weiss' lab, which he codirects with Rebecca Watters, PhD, assistant professor of orthopaedic surgery.

"Dr. Watters and I had originally planned to save this donation for a rainy day," says Dr. Weiss. "Well, that was before COVID-19, and now it's raining! The pandemic has been difficult for everyone, and scientists are no exception. Thanks to the Hardesty and Garcia families, we have been able to keep the lights on in the lab. We are grateful beyond words for their friendship, kindness, and generosity."

"My wife, Cathy, and I are truly grateful for the physicians and care we have received at the University of Pittsburgh and UPMC over the years," says Mr. Garcia. "We have a great deal of appreciation for their work. It was great for me to see Dr. Weiss' research facility. When you walk through that lab and see what they're doing, you want them to have the best and be the best. That's what motivates us to help with these programs. Dr. Weiss is a special guy, and his staff truly reflect his passion. In my mind, it is not a coincidence that a conversation on a fishing trip with my friend Ken Marino regarding Dr. Weiss and Johnny reunited the families after all these years."

"We're praying that Dr. Weiss can find a cure for osteogenic sarcoma," says Mr. Hardesty. "Kurt has dedicated a significant amount of his life and time to doing research on a cancer that he and my son both went through. We're glad to be a part of supporting research." ●

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