UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE

REFLECTION

University of Pittsburgh
School of Medicine

2019 ANNUAL REPORT

REFLECTION

COVER: Alessandro Gottardo

A shooting star is said to reap good fortune — and, in reflecting upon the past two decades, Arthur S. Levine, MD, was in many ways a shooting star for the University of Pittsburgh.

In past years, annual report readers have been greeted on page one with a thoughtful column by Arthur S. Levine, MD, senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of the School of Medicine. However, this year is not a typical year because Dr. Levine will step down from his leadership positions, once his successor arrives in June 2020 (see below). So, in lieu of his column, the annual report leads off with the story of Dr. Levine's tenure, encapsulating quite a journey for him and for the University of Pittsburgh

In addition, the report is packed with news emanating from the School of Medicine and the achievements of its students and faculty.

All is worthy of reflection.

Anticipation

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. His start date is June 2020.

Shekhar joins Pitt from Indiana University, the nation's largest medical school, where he holds a number of leadership roles.

"Anantha's capacity to envision solutions, galvanize partnerships, and produce results is second to none," said Chancellor Patrick Gallagher. "I could not be more excited to welcome Anantha into our community."

Shekhar's career has been defined by innovation, transformation, and sweeping and successful collaborations across the private, public, and philanthropic sectors. In addition, he has received continuous funding from the National Institutes of Health for basic, clinical, and translational research since 1989 and has authored more than 200 articles in peer-reviewed publications.

"I am honored and inspired to be joining one of the most respected medical and research communities in the world," says Shekhar.

Once at Pitt, Shekhar will oversee all six health sciences schools, the work of more than 6,000 faculty and staff, and the academic success of approximately 5,000 students while working closely with the institution's clinical partner, UPMC.

Learn more: http://pi.tt/successor

A Job Well Done

Change is coming.

It's the kind of change that the University of Pittsburgh School of Medicine hasn't endured in more than 20 years. That change will be new leadership as Arthur S. Levine, MD, announced on January 23, 2019, his plans to step down as senior vice chancellor for the health sciences and John and Gertrude Petersen Dean of the School of Medicine, effective the day his successor sets foot in Scaife Hall.

On the day of Levine's decision, the University community learned of the news in an email from Chancellor Patrick Gallagher. In part, he wrote: "It's difficult to overstate the remarkable impact that Art has had on our School of Medicine, on our health sciences programs, on UPMC, and on the University of Pittsburgh."

Gallagher's remarks are not mere hyperbole. Since succeeding Thomas Detre, MD, in 1998, Levine has—by essentially every metric and ranking—shepherded the School of Medicine to the stratosphere occupied by only the most elite medical schools.

"...ART 'SKATED WHERE THE PUCK WAS GOING.' I THINK THIS IS AN APT DEFINITION OF ART'S ABILITY TO ANTICIPATE WHERE THE MOST IMPORTANT SCIENTIFIC DISCOVERIES WOULD COME FROM AND TO SUPPORT THE PEOPLE WHO WOULD MAKE THOSE DISCOVERIES POSSIBLE."

— DUANE ALEXANDER, FORMER DIRECTOR OF NICHD

"Now, you need to recruit a leader who really understands basic biology. We found that person in Art Levine."

— MARK NORDENBERG, CHANCELLOR EMERITUS, UNIVERSITY OF PITTSBURGH

One of his many admirers is Arthur H. Rubenstein, MBBCh, who, from 2001 to 2011, was executive vice president of the University of Pennsylvania Health System and dean of the Perelman School of Medicine. "Art has been an exemplary and inspiring leader and has built one of the truly great medical centers in the world," says Rubenstein, who today is professor of medicine in Penn's Division of Endocrinology. "Art's dedication to excellence has often shaped my own thinking."

Levine's dedication to excellence is evident in National Institutes of Health (NIH) funding, which is perhaps the most objective metric for assessing research-focused institutions. The University has been among the top 10 recipients since Levine arrived in 1998. In 2018 alone, the University received more than $577 million in funding — nearly 80% of which went to the School of Medicine. By contrast, in 1998, Pitt received $169 million.

But Pitt's Levine era is about much more than statistics or grants or groundbreakings. It's about people. Brilliant people. Creative people. People who dare to be great. Levine has recruited those people, brought them to Pitt, and — by their own accounts — given each of them the stage they needed for the benefit of biomedical research. Regionally. Nationally. Globally.

The big question is — what was it that enabled Pitt to lure Levine from NIH in 1998, where, by all accounts, he was a superstar?

It turns out Pitt was the right place at the right time for his professional trajectory.

Levine's career in medicine and science began with an MD in 1964 from the Chicago Medical School of the Rosalind Franklin University of Medicine and Science, followed by an internship and residency in pediatrics and then a fellowship in hematology and biochemical genetics at the University of Minnesota Hospitals, which he completed in 1967.

Immediately afterward, amid the Vietnam War, he began his military service at NIH, as a public health service clinical associate in the National Cancer Institute.

"Art's rise through the NIH ranks was nothing short of meteoric," points out Peter Strick, PhD, Thomas Detre Professor of Neuroscience, Distinguished Professor and chair of neurobiology, professor of psychiatry, and scientific director of Pitt's Brain Institute.

Strick's assessment is hard to dispute. Within 15 years, Levine catapulted from clinical associate in 1967; to senior staff fellow in 1969; to senior investigator in 1970; to head of the institute's Section on Infectious Disease, Pediatric Oncology Branch, in 1973; to branch chief in 1975; to scientific director of the National Institute of Child Health and Human Development (NICHD) in 1982.

Or, as Strick simply states: "Fifteen years after his arrival, he was running the place. Art is properly credited with transforming the intramural program of his institute from a moribund unit to one of the gems of the NIH system."

Concurring is Juan Bonifacino, PhD, associate scientific director for NICHD's Neurosciences and Cellular and Structural Biology Division: "Art Levine is a visionary leader who built the Intramural Program of NICHD into one of the best Intramural Programs — actually *the* best while he was here — of all 27 institutes that make up the NIH," says Bonifacino, whom Levine brought on board at NIH in 1997. "I remember that at Art's NIH retirement party, the director of NICHD, Duane Alexander, paraphrased Walter Gretzky, father of ice hockey great Wayne Gretzky, saying that Art 'skated where the puck was going.' I think this is an apt definition of Art's ability to anticipate where the most important scientific discoveries would come from and to support the people who would make those discoveries possible."

Levine remained NICHD's scientific director until 1998, when he became Thomas Detre's successor at the University of Pittsburgh.

Again, the question — why Pitt?

Levine explains that at the time he earned his medical degree, NIH was the only real option for aspiring physician-scientists. However, by the 1990s, with the proliferation of MD/PhD programs, physicians could become scientists without necessarily training at NIH. "I saw those programs, as well as the end of the doctors' draft, as having a weakening effect on NIH," he recalls. "I wanted to be at a place that, in fact, was going up rather than staying the same or going down."

But, not to be repetitive, why Pitt? Even he had to ponder the answer to that question.

"I'd already looked at jobs in many top-tier universities and turned them down," he admits. "I recalled turning down the Pitt search committee's phone call about seven times until someone at NIH told me I was being very rude, and I should at least answer the phone."

He did, and he says he quickly became intrigued. The school's trajectory had already begun to rise under the helm of Detre, the retiring senior vice chancellor.

"Tom felt that the next step had to be to strengthen fundamental science," says Levine, "and I believe I was chosen because I was a physician who could address clinical research and patient care, but at the same time I was a researcher who could begin to strengthen fundamental science."

Pitt's chancellor at the time, Mark Nordenberg, confirms Levine's recollection: "When Tom was preparing to step down as senior vice chancellor for the health sciences, he said to me, 'Mark, this psychiatrist has taken you as far as he can. Now, you need to recruit a leader who really understands basic biology.' We found that person in Art Levine, who was the first choice of virtually everyone involved in the search process, even though the pool of candidates was strong. Because of the importance of the position, I did some personal reference-checking, including a call to a Nobel Laureate, who had led NIH. The key assessments of Art were consistent: He has an extraordinary mind, incredibly high standards, and seemingly endless energy."

" You can't be a great medical center without academic leadership, and Dr. Levine has extraordinary standards."

— JEFFREY ROMOFF, PRESIDENT AND CEO, UPMC

Levine accepted the position and gave NIH nine-months' notice. During that time, he read all 2,000 CVs of every School of Medicine faculty member, and he contemplated what he wanted to accomplish in his new position. He hit the ground running:

"My first week at Pitt, I met with the admissions committee for the medical school. I told them, having thought a lot about what I wanted to do here, that we were going to have a different kind of medical school. There were a lot of medical schools in the commonwealth. I didn't think that we needed to produce more primary care physicians for Western Pennsylvania. We needed to address a dramatic decline in the number of physicians who also became scientists. We had to strengthen the scientific underpinnings of our education and, as the dean of the medical school, it was up to me to lead. So I told the admissions committee that we were going to recruit students who had the potential to be creative scientists as well as physicians."

Levine says his proposed paradigm shift was met with less than unbridled enthusiasm: "The admissions committee stared at me and said, 'If you force us to do that, then our applicant pool will dry up, and you better go back to NIH.' But, at least for that week, I was the boss, and they had to do what I told them to do, for better or worse."

Turns out, it was definitely for the better. In 1998, the School of Medicine received 4,720 applications for its first-year class of 148. In 2019, it received 7,013 applications for its first-year class of 148 students.

The medical school curriculum now includes basic sciences, patient/doctor relationships, a mandatory longitudinal research project, life-like simulation training (using whole-body simulators), small group (i.e., problem-based) learning, a fourth-year integrated life science program, standardized patient encounters (using trained actors to interact with students in a clinical setting), evidence-based medicine, addiction medicine and the opioid epidemic, and patient experiences (pairing each student with a patient throughout the course of the student's education).

Levine meets monthly with students in an informal "Lunch with the Dean," so he can learn what's on their minds. He greets student Meghan Wilson (above), who didn't let her quadriplegic disability end her dream of becoming a doctor. She graduated in 2013 with an MD and a PhD in neuroscience.

Levine, in reshaping the admissions standards and curriculum, was just getting started. He also set out to enhance the medical school's partnership with UPMC, one of the nation's most renowned and successful health systems.

"Dr. Levine had big shoes to fill succeeding Dr. Detre, who was an enduring presence," remembers Jeffrey Romoff, UPMC's longtime president and CEO, who worked closely with the late Detre, too.

"Clinical departments were already successful and had been significantly enhanced under Dr. Detre's regime, but Dr. Levine's focus was strongly on the basic sciences; and by upgrading the basic sciences, he was able to round out the excellence of the School of Medicine," says Romoff. "He and I worked hand in glove from the beginning—his focus was academic, while mine at UPMC was clinical. The transition was seamless, and it's worked out very well."

Romoff believes Levine's greatest strength is what he calls Levine's "exquisite academic taste and his capacity to recruit people who are top rung. His recruits, both in research and for clinical department chairs, have been people with excellent academic credentials and judgment. You can't be a great medical center without academic leadership, and Dr. Levine has extraordinary standards."

Much recruitment was needed because, under Levine's direction, multiple new School of Medicine departments were created—including Biomedical Informatics, Cardiothoracic Surgery, Computational and Systems Biology, Critical Care Medicine, Developmental Biology, Immunology, Plastic Surgery, Physical Medicine and Rehabilitation, Structural Biology, and Urology.

There were also new centers and institutes: Aging Institute, Center for Evolutionary Biology and Medicine, Center for Military Medicine Research, Center for Vaccine Research, Clinical and Translational Science Institute, Institute for Precision Medicine, Pittsburgh Institute for Neurodegenerative Diseases, University of Pittsburgh Brain Institute, University of Pittsburgh Drug Discovery Institute, and the Vascular Medicine Institute.

And there were new research and medical buildings that added to the synergy: Biomedical Science Tower 3, Bridgeside Point II, UPMC Children's Hospital of Pittsburgh Rangos Research Center, and the UPMC Vision and Rehabilitation Tower, as well as additions and renovations to the Graduate School of Public Health, Magee -Womens Research Institute, and Salk Hall, and breaking ground for Scaife Hall's revamped west wing.

Not unlike Romoff, Steven D. Shapiro, MD, marvels at how Levine filled all those buildings, centers, institutes, and departments with what Romoff called "top rung" professionals. Shapiro, UPMC's executive vice president and chief medical and scientific officer, even witnessed the magic firsthand because he frequently joined Levine on recruiting efforts.

Shapiro, himself, had been recruited by Levine to become chair of the Department of Medicine in 2005. He recalls one instance, as he began his new role with UPMC in 2008, when they were recruiting John Reilly, MD, to become his successor.

"I'm proud of what we've been able to accomplish in teaching and training as well as in research. …What really is important is our impact on the science of medicine and how we use that science to further promote health care."

— ARTHUR S. LEVINE, MD

The School of Medicine entered into an agreement with three world-renowned French research institutions in 2017, which focuses on collaborative research and education in the fields of medicine and biomedical sciences. Levine (far left) was among those signing the historic agreement.

Reilly had been affiliated with Brigham and Women's Hospital in Boston for more than two decades.

"Art, how long do you plan on doing this for?" asked Reilly, who clearly didn't want to make a move if Levine, who was 72 years old, had plans to retire in the near future.

"I come from a line of long-lived, short-statured Russians," replied Levine. "I don't have a fleck of calcium in my coronary arteries, and I have fire in my belly."

Reilly needed no more convincing. He came on board; and, ironically, after seven years at Pitt, he moved on before Levine. He is now vice chancellor for health affairs at the University of Colorado and dean of its medical school.

"It has been great fun working with Art," says Shapiro, adding, "it's not just the senior faculty who are important to him. When I first started as chair of medicine in 2005, I was still trying to figure out the names of my faculty. Art could give me a succinct summary of all of the research they did. When he says he wants to see your articles, he reads them."

Attesting to Levine's sincere mentoring interest is Barbara Barnes, MD, MS, associate vice chancellor for industry relations and continuing education, health sciences; and vice president for sponsored programs, research support, and continuing medical education, UPMC.

"I am most grateful for Dr. Levine's support and advocacy of my own career," she says. "In 1994, I was recruited to Pitt with a very unusual background for my role as assistant dean in the School of Medicine, having been a primary care physician and hospital administrator. Art, despite his strong interest in basic science, recognized how I could contribute to the core missions of the Schools of the Health Sciences and afforded me multiple opportunities to intellectually and personally grow and develop. Through his support, I have been able to take on so many different responsibilities, both internal and external to the University and UPMC, leading to an amazingly rich and rewarding career over the past 25 years."

Barnes is one of many to express her gratitude to Levine. With the announcement that he is stepping down, other colleagues—past and present—have conveyed heartfelt, appreciative accolades. For a sampling (or to submit an accolade), visit www.health.pitt.edu/accolades-job-well-done

Acknowledging all of the praise, Levine jokes that—while it's great fodder—no one should be writing his eulogy just yet. He makes clear that just because he is stepping down, it doesn't mean that—after celebrating his 83rd birthday on November 1—he'll be spending all his time with his wife, Linda, walking their Havanese doggie, Sasha, or going bike-riding or swimming (though he does enjoy the exercise!). Rather, he will spend chunks of his days hunkered down in a School of Medicine lab, building upon his research roots. Overall, he has already authored or coauthored more than 280 scientific publications during his career at NIH and Pitt.

As for future research, he says, "I want to become a quasi-neuroscientist. I want to do something about Alzheimer's; it's a horrible disease. It consumes 12% of our nation's health care economy. It's not a treatable disease. The latest clinical trials basically, in my view, are failures, like all of the other clinical trials. I don't think you can treat this disease once it's established. The only breakthrough in Alzheimer's was here in Pittsburgh—development of Pittsburgh Compound B that allows us to visualize amyloid in the brain, the telltale marker of Alzheimer's. We now know that patients with Alzheimer's develop their disease 10 to 20 years before they ever become symptomatic, and it's at that time that we have to understand the molecular roots of the disease and, hopefully, prevent them—just as in this institution we prevented polio, revolutionized organ transplantation, and revolutionized our sense of the biology of breast cancer."

For Levine, his Alzheimer's research will be about results, not about just staying busy. And he says it's the results achieved at Pitt, under his watch, which have helped make his career seem so worthwhile.

"I'm proud of what we've been able to accomplish in teaching and training as well as in research. It's not the amount of NIH funding, or the number of research and medical buildings, or the new centers or institutes. What really is important is our impact on the science of medicine and how we use that science to further promote health care."

Chancellor Gallagher, for one, is grateful for that impact, which he points out has been "nothing short of transformative for the University, the city of Pittsburgh, the region and, in many ways, the broader fields of medicine and health today."

It has been incumbent on Gallagher, along with the search committee, to select a worthy successor to Levine. But that's a story for another day. This much is known now. And it's what was known when Thomas Detre stepped down. The next dean, using Jeffrey Romoff's words, will have big shoes to fill.

Pitt and UPMC

Every day, significant health sciences research and clinical medicine outcomes rest on the bedrock of the University of Pittsburgh and UPMC. The essential partnership of these two legally separate but interdependent entities continues to set the standard for academic medical centers in the advancement of knowledge, education, and training of new scientists and health care professionals in Pittsburgh and worldwide.

University of Pittsburgh Research Funding

Funding from the National Institutes of Health (NIH) is a benchmark of overall stature among research-intensive academic health centers. Since 1998, the University of Pittsburgh has ranked among the top 10 recipients of NIH funding, driven by the School of Medicine. The University's faculty has been ranked fifth since 2010.

2018 NIH FUNDING

$577M

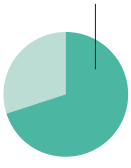
1,157 AWARDS

RANK 5

2019 OVERALL RESEARCH SPENDING

$819M

Nearly 70% of this amount was for research in the School of Medicine.



BRAVO! UPMC'S PARTNERSHIP IN PALERMO STILL GOING STRONG

It's been more than 20 years since the Italian government, Region of Sicily, and UPMC came together to establish the Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT) in Palermo.

Over the years, the hospital has become a center of international reference in the Mediterranean and helped to link Pitt's School of Medicine to important collaborative research opportunities in Italy through the Ri.MED Foundation, formed in 2006.

Ri.MED is a collaboration of the School of Medicine, UPMC, the Italian government, the Region of Sicily, and Italy's National Research Council. In June, the foundation became part of ISMETT's governance structure.

This successful partnership is continuing because in January 2019, a 10-year management agreement covering the premier transplant facility was renewed. The agreement also allocates a decade-long yearly investment of €100 million from the Region of Sicily and affirms the region's support for a new hospital to be built adjacent to the long-planned Biomedical Research and Biotechnology Center (BRBC) in Carini, Sicily. Groundbreaking for the BRBC and construction for the hospital will take place in 2020.

Like Pitt's Biomedical Science Tower 3 in Pittsburgh, the BRBC will house state-of-the-art research laboratories, centralized core facilities, and first-class equipment to support research in leading-edge disciplines like computational and systems biology, precision medicine, and others. Ri.MED fellows who have completed training in Pittsburgh are expected to act as core faculty once the facility is built.

The new hospital and research center are expected to further fuel scientific and medical excellence in southern Italy and, in collaboration with Sicilian universities, will provide training to health care professionals and biomedical scientists.

Construction of BRBC to begin in 2020

AAP

ASCI

From top, L–R, Gittes, Miller Morris, Shlomchik Berger

Elite Company

For their achievements in scholarship and research, several Pitt faculty members were 2019 inductees into two of the most elite professional societies—the Association of American Physicians (AAP) and the American Society for Clinical Investigation (ASCI):

Elected to AAP were:

George Gittes, MD, is Benjamin R. Fisher Professor of Pediatric Surgery, professor of surgery and of pediatrics, and director of the Richard King Mellon Institute for Pediatric Research.

Elizabeth Miller, MD, PhD, is Edmund R. McCluskey Professor of Pediatric Medical Education, professor of pediatrics and of clinical and translational science, and director of the Division of Adolescent and Young Adult Medicine, UPMC Children's Hospital of Pittsburgh.

Alison Morris, MD, MS, is UPMC Professor of Translational Pulmonary and Critical Care Medicine, professor of medicine, of immunology, and of clinical and translational science, and director of the Center for Medicine and the Microbiome.

Warren Shlomchik, MD, is Professor of Cancer Immunotherapy, professor of medicine and of immunology, and director of Hematopoietic Stem Cell Transplant and Cell Therapy and scientific director of the Hematopoietic Malignancy Program at UPMC Hillman Cancer Center.

Elected to ASCI were:

Rachel Berger, MD, MPH, is professor of pediatrics and of clinical and translational science, chief of the Division of Child Advocacy in the Department of Pediatrics, and director of child abuse research in the Safar Center for Resuscitation Research.

L–R, Stephen Emery, MD, Allee Mullen (holding baby Emery Greene), and Stephanie Greene, MD.

Innovative In Utero *Surgery*

Baby Emery Greene Mullen is healthier today thanks to surgical intervention to repair the most common and severe form of spina bifida. The surgery was done for the first time in Pittsburgh in the months before she was born.

A multidisciplinary team of specialists, including **Stephen Emery, MD**, associate professor of obstetrics, gynecology, and reproductive sciences, and **Stephanie Greene, MD**, associate professor of neurological surgery, operated on the 25-week-old fetus to close an open neural tube defect that her mother, Allee Mullen, learned about earlier in pregnancy.

"Research shows that babies who are closed *in utero* have better neurologic outcomes than babies treated after birth," says Emery.

Baby Emery Greene—named after her surgeons—was diagnosed with the most serious form of spina bifida, a myelomeningocele. The condition results when a portion of the spinal cord remains abnormally exposed during fetal development and causes differing degrees of disability. Spina bifida affects about 1,500 babies a year in the United States; most undergo surgical repair after delivery. So far, little Emery Greene is exhibiting near-normal leg function.

"RESEARCH SHOWS THAT BABIES WHO ARE CLOSED *IN UTERO* HAVE BETTER NEUROLOGIC OUTCOMES THAN BABIES TREATED AFTER BIRTH."

— STEPHEN EMERY, MD

Immunology Trailblazer

Developing more effective immunotherapies and treatments is the focus of a new interdisciplinary center at Pitt. Under the leadership of **Harinder Singh, PhD**, the Center for Systems Immunology will harness newly emerging experimental, computational, and engineering approaches to analyze the immune system in health and disease.

Singh is an international expert in the analysis of transcription factors and gene regulatory networks that regulate the development and functioning of innate and adaptive cells of the immune system. He has been a Howard Hughes Medical Institute investigator at the University of Chicago, director of Genentech's Department of Immunology Discovery, and director of the Division of Immunobiology at Cincinnati Children's Hospital Medical Center. He earned his PhD at Northwestern University and completed a postdoctoral fellowship at Massachusetts Institute of Technology.

Master Educator

Dedicated to mentoring and advising trainees from underrepresented groups, researcher **Doris Rubio, PhD**, has assumed new roles in 2019 as assistant vice chancellor for clinical research education and training, health sciences, and director of the Institute for Clinical Research Education (ICRE).

Among ICRE's offerings are programs in clinical and translational science, clinical research, medical education, and comparative effectiveness research, along with a number of career-development programs reaching more than 2,100 investigators at all stages of their careers.

Rubio has led the efforts to forge partnerships with minority-serving institutions to expand ICRE's impact on workforce diversity. She is a recipient of the Distinguished Educator Award from the Association for Clinical and Translational Science and a member of Pitt's Academy of Master Educators.

Presidential

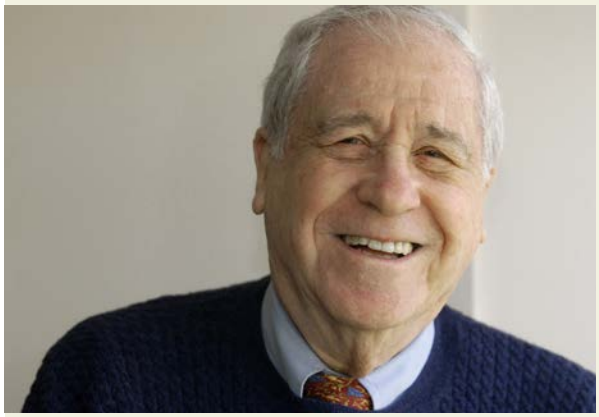
The Society for Biological Psychiatry's new president in 2020 will be **David A. Lewis, MD**, Distinguished Professor of Psychiatry. Lewis, who is also the Thomas Detre Professor of Academic Psychiatry and psychiatry department chair, will oversee the professional society, which is dedicated to research and education about the biological mechanisms of mental illness.

Esteemed Recognition

Anita Courcoulas, MD, MPH, chief of the Division of Minimally Invasive Bariatric and General Surgery, Department of Surgery, has been named the inaugural Anthony M. Harrison Professor of Surgery. The professorship honors the late Anthony Miller Harrison, MD, a respected professor of surgery at Pitt and UPMC surgeon.

Giselle Hamad, MD, has been appointed Charles G. Watson Professor of Surgical Education within the Department of Surgery and an advisory dean of students in the School of Medicine. Hamad is a lauded educator and mentor as well as a respected surgeon.

Remembering a Trailblazer in Cancer Research



"BERNARD FISHER WAS A TITAN. HIS RESEARCH IMPROVED AND EXTENDED THE LIVES OF UNTOLD NUMBERS OF WOMEN WHO SUFFERED THE SCOURGE OF BREAST CANCER. HIS WORK OVERTURNED THE DOMINANT PARADIGM OF CANCER PROGRESSION AND, TO THE BENEFIT OF ALL, DEMONSTRATED THE SYSTEMIC NATURE OF METASTASIS. WE ARE GRATEFUL FOR HIS INCALCULABLE CONTRIBUTIONS TO HUMAN HEALTH."

— ARTHUR S. LEVINE, MD

Bernard Fisher, MD, Distinguished Service Professor at the School of Medicine and a true pioneer in the field of breast cancer research, died on October 16, 2019. He was 101.

A role model for the surgeon-scientist, Fisher advanced understanding of the clinical biology of breast cancer and pioneered the design and implementation of large-scale multi-institutional randomized clinical trials.

A Pittsburgh native, Fisher earned a Bachelor of Science in 1940 and an MD in 1943, both at the University of Pittsburgh.

Following surgical training, he joined Pitt's faculty as the medical school's first full-time member of the Department of Surgery. In 1953, he established the first Laboratory of Surgical Research at the University, based on his firm belief that evidence gathered through scientific inquiry should serve as the basis for advancing patient care.

In this early part of his career, he contributed to the development of both transplantation and vascular surgery, performing the first kidney transplant in Pittsburgh in 1964 and directing surgical research at Pitt in liver regeneration, transplant rejection, and hypothermia.

Fisher's focus shifted to cancer research in 1958, and throughout his influential career, he elucidated the way in which breast cancer spreads and steered medicine away from radical mastectomy as treatment. Perhaps Fisher's most important contribution, however, has been the establishment of a scientific approach to the study of breast cancer. As a result of his pioneering research, women worldwide with breast cancer have a scientific basis to guide treatment that leads to improved quality of life and a greater chance of long-term survival. Moreover, his work resulted in the creation of the paradigm that not only governs the treatment of breast cancer but has shaped the landscape of cancer research more broadly.

Learn more: https://tinyurl.com/pitt-bfisher

EXCEPTIONAL PROMISE

It's the highest honor given by the U.S. government to scientists and engineers who are beginning their independent research careers. Recipients must demonstrate exceptional promise for leadership in science and technology.

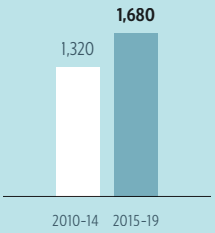
Among those chosen for the 2019 Presidential Early Career Award for Scientists and Engineers is **Walid Gellad, MD, MPH**, associate professor of medicine and of health policy and management, Graduate School of Public Health, director of Pitt's Center for Pharmaceutical Policy and Prescribing, and a VA Pittsburgh Healthcare System primary care physician/researcher.

Gellad's research interests focus on physician prescribing practices and policy issues affecting patient access to medications, including the use of machine learning to better predict opioid overdose risk. He is also a nationally recognized authority on prescription drug pricing and spending.

Accelerating Pace of Pitt Innovation

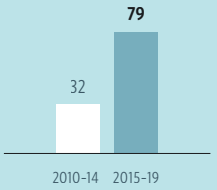
Invention Disclosures

+27%



Patents

+147%



Transactions

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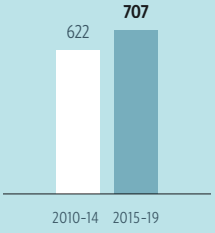
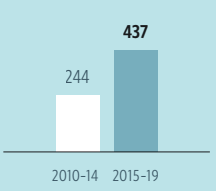


Startups

+79%



Pneumatically powered wheelchairs and scooters first used at Morgan's Wonderland, Texas, developed by Pitt's PhD student Brandon Daveler.

Licensed to Think Big

The hub for innovation and entrepreneurship at Pitt is its Innovation Institute, which assists faculty and staff with translating their breakthrough discoveries or ideas.

Based on technology licensed from Pitt, these fiscal year 2019 inspiring startup companies could make a tangible difference in people's lives:

ATIMIZE INC.

Brandon Daveler, a PhD student in Pitt's Human Engineering Research Laboratory (HERL), licensed technology he helped develop for pneumatically powered wheelchairs and scooters. The technology was first used at Morgan's Wonderland, a Texas waterpark whose builder was looking for a way to help children with physical challenges enjoy the park's attractions without risking damage to their wheelchairs' electronics. Daveler is now refining his prototypes and pursuing customers while taking part in The Forge, a student incubator program.

DEEPRX INC.

Xinghua Lu, MD, PhD, MS, and **Gregory Cooper, MD, PhD**, both faculty in the Department of Biomedical Informatics, have developed a clinical decision support platform that uses patient-specific data to provide targeted cancer immunotherapy and combination therapy recommendations.

VIVASC THERAPEUTICS INC.

Maliha Zahid, MD, PhD, assistant professor of developmental biology, has identified a peptide that targets heart muscle cells exclusively, making it an ideal molecular vehicle to deliver therapeutic and diagnostic agents. Its platform technology can deliver numerous elements, with the first one projected to be the anti-arrhythmic drug amiodarone.

Homecoming

Norman Wolmark, MD, noted surgeon and cancer researcher, has returned to Pitt and UPMC Hillman Cancer Center as director of National Cancer Institute (NCI) cooperative group clinical trials and professor of surgery.

Wolmark has published more than 400 manuscripts and serves on the editorial boards of the *Journal of Clinical Oncology*, *JAMA*, and *Lancet*. In addition, he is the 2019 recipient of the Gianni Bonadonna Breast Cancer Award from the American Society of Clinical Oncology.

Many of his early, groundbreaking cancer studies and clinical trials were conducted at Pitt alongside the late **Bernard Fisher, MD**, Distinguished Service Professor of Surgery and founding director of the National Surgical Adjuvant Breast and Bowel Project, an NCI-supported clinical trials cooperative group.

Caregiving Research, Education, and Policy

Nearly everyone will feel the weight of caregiving at some time in life. The severity of its stress on health, finances, and family dynamics is being brought into focus locally with the establishment of the Center for Caregiving Research, Education, and Policy, a collaboration of the University's Health Policy Institute, UPMC, the American Association of Retired Persons, the Alzheimer's Association, and the Hospital and Healthsystem Association of Pennsylvania.

Researchers will study the effects of caregiving on family members giving and receiving care, as well as developing strategies to strengthen the positive aspects of caregiving and develop policies to support caregivers.

The center is directed by **Richard Schulz, PhD**, Distinguished Service Professor of Psychiatry, and addresses caregiving across the lifespan. "We have a rich array of experts in childhood, midlife, and late-life caregiving, plus a depth of experience in the research-based evidence needed to affect policy changes," says Schulz.

In addition, the center provides resources and information for a variety of needs, including issues associated with veterans, mental illness, substance abuse, chronic illness, and elder care.

Diversity and Inclusion

Faculty diversity is of great importance to the Department of Medicine, which has appointed **Naudia Jonassaint, MD, MHS**, assistant professor of medicine, as its first vice chair for diversity and inclusion. Jonassaint, a hepatologist who also serves as medical director of hepatology at UPMC Presbyterian Hospital, will work to develop programs to enhance diversity and inclusion across the department.

Jonassaint earned her MD at Yale School of Medicine and MHS in clinical investigation at Johns Hopkins University, where she also completed her residency, chief residency, and fellowships in gastroenterology and transplant hepatology.

THE CONVERSATION

Pitt Faculty Are in The Conversation

Academics often say their work speaks for itself. A number of Pitt researchers have gone a step further, using *The Conversation*—an independent, nonprofit global newsgathering consortium—to communicate directly to the public about that work.

Founded in 2011 in Australia, *The Conversation* appreciates the vital role that academic experts can play in public discourse. Pitt became a sponsor institution in 2018. *The Conversation* U.S. draws about half of its funding from universities and research institutions and half from philanthropy.

Editors assist experts to write articles of varying lengths depending on subject matter, interest level, and timely news value. Each month, the website audience includes nearly 11 million people, and its articles reach more than 38 million through republication in news outlets worldwide. The organization is currently active in eight countries.

"I can't say enough about the physicians and researchers there who are willing to write [with the help of an editor] about this hard science for the lay public," says Lynne Anderson, *The Conversation* health and medicine editor. "Our collaboration with Pitt and UPMC has really been a model of the collaborative process for good, fact-based stories."

Anderson points out the popularity of *The Conversation* story, "Measles: Why it's so deadly, and why vaccination is so vital," by **Paul Duprex, PhD**, professor of microbiology and molecular genetics and director of Pitt's Center for Vaccine Research. The article was published by 54 news outlets, translated into French, and read more than 98,000 times in February 2019.

Another well-received *Conversation* article was by **Alejandro Soto-Gutiérrez, MD, PhD**, associate professor of pathology. In "How to grow human mini-livers in the lab to help solve liver disease," he explained his research to develop new treatments for liver disease. The article was published by 27 outlets and read more than 18,000 times in August 2019.

Throughout the past year, Pitt has contributed more than 70 articles to *The Conversation*, most of which were written by health sciences faculty.

Anderson remains in particular awe of trauma surgeon **Matthew (Macky) Neal, MD**, who—less than a week after treating people who were wounded in a mass shooting at Pittsburgh's Tree of Life synagogue—wrote: "'Stop the Bleed' training saved lives after shooting, but stopping the need must be next." His reflections in *The Conversation* were ultimately published by more than two dozen outlets, including *Time*, the *Washington Post*, *PBS*, *Quartz*, and *Salon*.

Each *Conversation* article is meant to contribute to public discourse, which pleases the authors and helps fulfill Pitt's mission of public service.

"OUR COLLABORATION WITH PITT AND UPMC HAS REALLY BEEN A MODEL OF THE COLLABORATIVE PROCESS FOR GOOD, FACT-BASED STORIES."

— LYNNE ANDERSON, *THE CONVERSATION* HEALTH AND MEDICINE EDITOR

PRECISION MEDICINE

Research Study with National Focus

To better understand how factors like lifestyle, environment, and genes influence health and disease, the *All of Us* program is helping researchers by gathering data from 1 million people across the country. The School of Medicine and the Clinical and Translational Science Institute (CTSI) are key partners in the program's regional affiliate.

All of Us Pennsylvania—headed by **Steven E. Reis, MD**, associate vice chancellor for clinical research, health sciences, Distinguished Service Professor of Medicine, and CTSI director—has already registered nearly 21,000 participants. Nationally, nearly 206,000 have been registered.

The massive study, launched in 2018 by NIH, is just one of the far-reaching, transformative projects of which CTSI is a part. The organization aims to recruit a projected 100,000 to 120,000 participants into the study, especially those from traditionally underrepresented populations.

"Studies can gather data from as many participants as they want, but if these data only apply to a specific group, then researchers could be missing out on important findings," says *All of Us* Pennsylvania co-investigator Mylynda Massart, MD, PhD, assistant professor of family medicine at Pitt.

While most studies focus on one specific disease or population, the findings from *All of Us* will function as a national research resource to inform thousands of future studies on various illnesses and groups.

Determining the impact of these factors will advance the practice of precision medicine—an emerging approach to health care where doctors and researchers more accurately predict which treatment and prevention strategies will work for which diseases in which groups of people. "Precision medicine is truly the future of health care," says Massart, "and every participant in *All of Us* will help to shape that."




National Spotlight

Two renowned national academies have been augmented in 2019 by Pitt faculty.

The U.S. National Academies recognizes distinguished and continuing achievements in original research, scholarship, and advancement of medicine, engineering, and the sciences. Inducted into the National Academy of Medicine:

Clifton W. Callaway, MD, PhD, Ronald D. Stewart Professor of Emergency Medicine Research (top, left)

Robert M. Friedlander, MD, MA, Walter E. Dandy Professor and chair of neurological surgery (top, right)

Amy J. Houtrow, MD, PhD, MPH, Professor of Pediatric Rehabilitation Medicine (above, left)

The National Academy of Inventors, honoring inventors in academia, inducted:

Stephen F. Badylak, DVM, PhD, MD, professor of surgery (above, right)

FACULTY HONORS AND AWARDS

School of Medicine faculty recognized in 2018–19 for their accomplishments include:

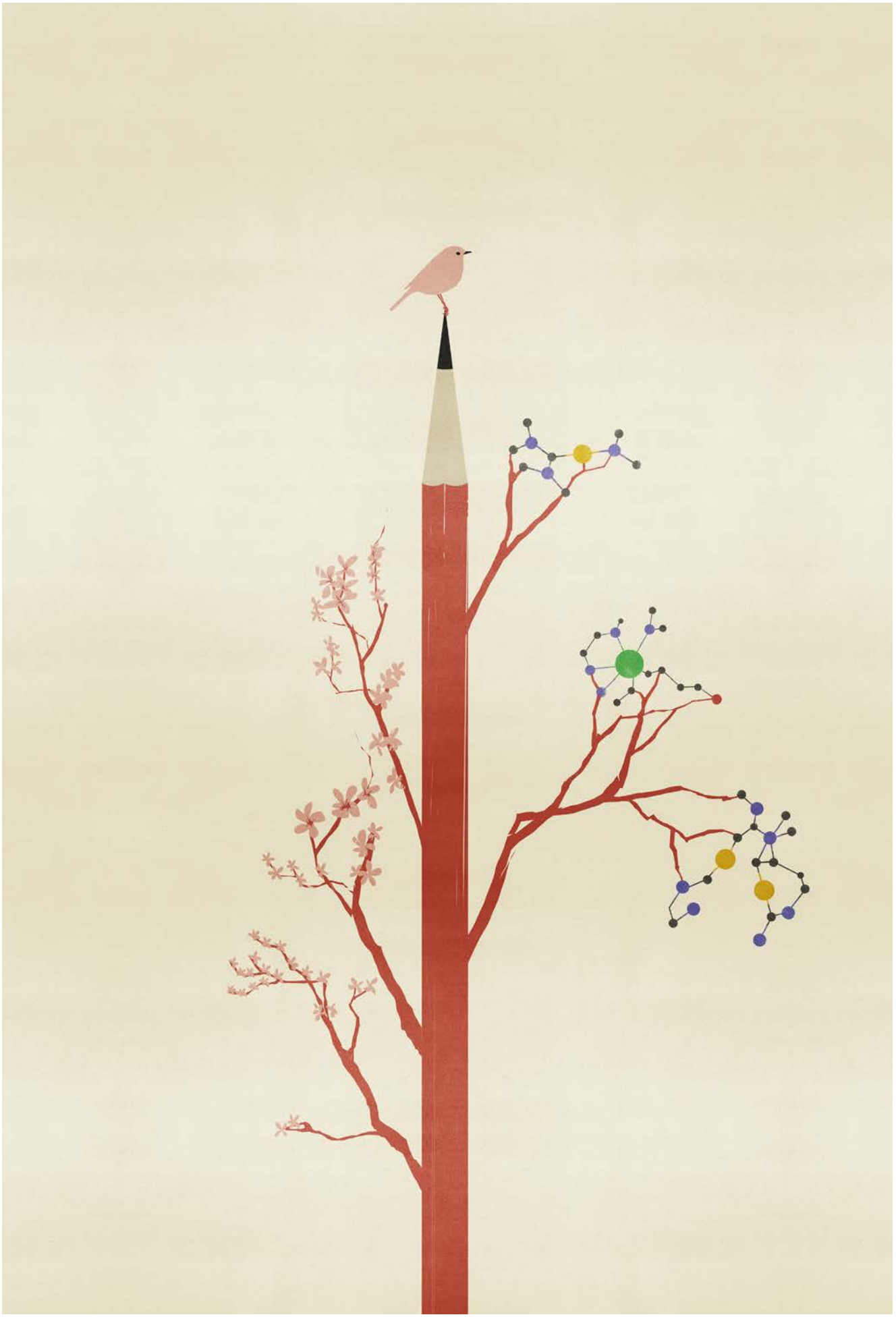
Beth Piraino, MD, associate dean of admissions and financial aid and professor of medicine, J. Michael Lazarus Award (National Kidney Foundation)

Mary Ganguli, MBBS, MPH, professor of psychiatry and of neurology, Distinguished Scientist Award (American Association of Geriatric Psychiatry)

Olivera J. Finn, PhD, Distinguished Professor of Immunology and professor of surgery, Richard V. Smalley Award (Society for Immunotherapy of Cancer); named a distinguished fellow (American Association of Immunologists)

Martica H. Hall, PhD, professor of psychiatry and of clinical and translational science, Outstanding Educator Award (Sleep Research Society)

Ann Thompson, MD, MCCM, vice dean and professor of critical care medicine and of pediatrics, Group on Women in Medicine and Science Leadership Award (Association of American Medical Colleges)



For more than two decades, under the leadership of Dr. Levine, we have striven to provide a unique education that is based in both science and compassionate care. The results speak for themselves as elite clinicians and scientists continue to emerge from the School of Medicine—advancing medical science and bettering the human condition.

Perfect Match

For Match Day 2019 last March, even the spacious Alumni Hall Connolly Ballroom on Pitt's campus could barely contain the excitement and energy. The graduating medical students had gathered there wearing "Yinz Matched" T-shirts, perfectly capturing the spirit and dialect of Pittsburgh.

Moments before finding out the life-changing news, a screen on stage in the ballroom shared students' photos and their favorite med school memories—making friends, Pitt Med's Halloween party, free coffee at the Medical Alumni Association office. As a timer on the screen counted down to noon and students tore into their envelopes, they found matches to virtually all of the top programs in the country.

All 139 students matched, including 30 who will remain in Pittsburgh to join UPMC's prestigious training programs. Overall, the largest match was in the primary care fields, which 58 students will pursue. Some other notable matches included 13 students in general surgery, 12 in psychiatry, and seven in anesthesiology. Nationwide, this year's match had more than 18,000 active participants.

With the matches revealed, students embraced family members, friends, and faculty members. Cellphones were busy, too, with the snapping of photos and hurried, high-volume calls home.

Addressing the crowd of students, family, friends, and well-wishers, Associate Dean for Student Affairs Joan Harvey, MD, reflected on the significance of this celebratory moment, on students' capacity for kindness, and on the opportunities ahead. She also spoke for all who played a part in the students' lives: "We couldn't be prouder of you."

"WE COULDN'T BE PROUDER OF YOU."

— JOAN HARVEY, ASSOCIATE DEAN FOR STUDENT AFFAIRS

Match Results Class of 2019

Anesthesiology

ALEXANDER ENG
Westchester Medical Center/
New York Medical College
*Westchester Medical Center/
New York Medical College

JAMIE HUYNH
UC San Diego Medical Center/
University of California, San Diego
*Scripps Mercy Hospital, California

SACHIDHANAND JAYAKUMAR
Yale New Haven Hospital, Conn.

FARIHA KAMAL
University of Michigan Hospitals

MATTHEW KOCHER
UPMC/University of Pittsburgh, Pa.

ZACHARY LIGUS
Strong Memorial Hospital/University of Rochester, N.Y.

RUDO MAKONZA GOTO
Vanderbilt University Medical Center, Tenn.

Dermatology

ALYCE ANDERSON
McGaw Medical Center/
Northwestern University, Ill.
*UPMC/University of Pittsburgh, Pa.

Emergency Medicine

JENNIFER AHN
UPMC/University of Pittsburgh, Pa.

BRIAN FRODEY
Albany Medical Center/Albany Medical College, N.Y.

JOSE MIGUEL JUAREZ
Mount Sinai Hospital/
Icahn School of Medicine, N.Y.

NADIA LEHTIHET
MedStar Washington Hospital Center/
Georgetown University, D.C.

ANASTASIA MARKOVTSOVA
Stanford University Programs, Calif.

DENZEL MASSEY
Madigan Army Medical Center, Wash.

ERIC RESELAND
Beth Israel Deaconess Medical Center/
Harvard University, Mass.

HARMONY YOURISH
UPMC/University of Pittsburgh, Pa.

Family Medicine

ELIZABETH CLARK
Thomas Jefferson University Hospital, Pa.

HARBIR DHILLON
St. Joseph's Medical Center, Calif.

CECILIA HUANG
Long Beach Memorial Medical Center, Calif.

HIBAA OUNIS
Kaiser Permanente Woodland Hills Medical Center/UCLA, Calif.

JOHN TAORMINA
UPMC St. Margaret/University of Pittsburgh, Pa.

Internal Medicine

ANDREW ABBOUD
Massachusetts General Hospital/
Harvard University, Mass.

MATTHEW ALLEN
University of Virginia Health System

VAIBHAV BIRDA
Beth Israel Deaconess Medical Center/Harvard University, Mass.

FREDERICK BROWN
Barnes Jewish Hospital/Washington University, Mo.

TRACY CAMPBELL
MedStar Washington Hospital Center/
Georgetown University, D.C.

HE CHANG
University of Iowa Hospitals and Clinics

ERICA CORREDERA
New York—Presbyterian Hospital/
Weill Cornell Medical Center

KATHERINE FAIR
University of Washington Affiliated Hospitals

RACHAEL GORDON
UPMC/University of Pittsburgh, Pa.

CLARK HATHEWAY
California Pacific Medical Center

JENNY HUANG
Scripps Clinic/Scripps Green Hospital Program, Calif.

POUYA JOOLHARZADEH
Barnes Jewish Hospital/
Washington University, Mo.

SPENCER KEIL
UPMC/University of Pittsburgh, Pa.

MICHAEL MACKLIN
UPMC/University of Pittsburgh, Pa.

LAURA McNAMARA
Beth Israel Deaconess Medical Center/
Harvard University, Mass.

AMANDA MORRISON
Vanderbilt University Medical Center, Tenn.

HIMA NAMBOODIRI
LAC+USC Medical Center/
University of Southern California

FELIX NGUYEN
Barnes Jewish Hospital/
Washington University, Mo.

ADRIANNA OH
UPMC/University of Pittsburgh, Pa.

NOLAN PRIEDIGKEIT
Brigham & Women's Hospital/
Harvard University, Mass.

DARVE ROBINSON
Yale New Haven Hospital, Conn.

PRIYA ROY
University of Wisconsin Hospital and Clinics

SAMUEL SESTITO
Vanderbilt University Medical Center, Tenn.

STEPHANIE SPEHAR
University of Michigan Hospitals

YICHENG TANG
UPMC/University of Pittsburgh, Pa.

PHILLIP WAGNER
UPMC/University of Pittsburgh, Pa.

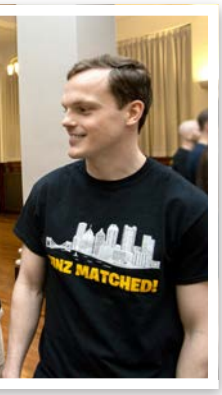
LINDA WANG
Beth Israel Deaconess Medical Center/Harvard University, Mass.

Internal Medicine/Pediatrics

MICHAEL AXLINE
Virginia Commonwealth University Health System Program

ALEXANDRA LINN
Hospital of the University of Pennsylvania

*Indicates location of transitional or preliminary year of medical or surgical training.



Internal Medicine/Psychiatry

GREGG ROBBINS-WELTY
Duke University Medical Center, N.C.

OLOLADE SALIU
University of Iowa Hospitals and Clinics

Internal Medicine/Women's Health

LEAH KOENIG
UPMC/University of Pittsburgh, Pa.

RACHEL PACE
UPMC/University of Pittsburgh, Pa.

Neurological Surgery

AHMED KASHKOUSH
Cleveland Clinic/Case Western Reserve University, Ohio

Neurology

ERICA JOHNSON
Mayo Clinic/Mayo Clinic School of Health Sciences, Minn.
*UPMC/University of Pittsburgh, Pa.

EVAN MADILL
*Stanford University Programs, Calif.

AMOL MEHTA
New York—Presbyterian Hospital/ Columbia University Medical Center

JIA-YI WANG
*Beth Israel Deaconess Medical Center/ Harvard University, Mass.

PAUL WECHSLER
New York—Presbyterian Hospital/ Weill Cornell Medical Center

Neurology—Pediatric

ROSS CARSON
Boston Children's Hospital/ Harvard University, Mass.

Obstetrics/Gynecology

SHIRLEY DONG
Ohio State University Medical Center

NOZOMI SAKAI
University of North Carolina Hospitals

LIBBY SZETO
Montefiore Medical Center/Albert Einstein College of Medicine, N.Y.

ISHA VASUDEVA
UConn Health/University of Connecticut

Ophthalmology

JUSTIN ARNETT
UC San Diego Medical Center/ University of California, San Diego
*Englewood Hospital, N.J.

NATHANIEL BLECHER
*Barnes Jewish Hospital/Washington University, Mo.

PETER JONES
*UPMC/University of Pittsburgh, Pa.

KEVIN KEPPEL
Cleveland Clinic/Case Western Reserve University, Ohio
*UPMC/University of Pittsburgh, Pa.

Oral/Maxillofacial Surgery

GREGORY BIRON
UPMC/University of Pittsburgh, Pa.

KRISTOPHER COOPER
UPMC/University of Pittsburgh, Pa.

Orthopaedic Surgery

SUMAIL BHOGAL
UPMC/University of Pittsburgh, Pa.

RYAN JUDY
Temple University Hospital, Pa.

KEVIN KOHUT
University at Buffalo, N.Y.

ADEL MAHJOUB
Cooper University Hospital/ Rowan University, N.J.

OBIANUJU OBIOHA
Rush University Medical Center, Ill.

FAVIAN SU
UCSF Medical Center/University of California, San Francisco

Otolaryngology

FASIL MATHEWS
SUNY Downstate Medical Center, N.Y.

Pathology

KIKUCHI, ALEXANDER
University of California, San Francisco Affiliates

Pediatrics

AKSHAYA ARJUNAN
UPMC Children's Hospital of Pittsburgh/University of Pittsburgh, Pa.

JONATHAN BERKEN
Lurie Children's Hospital of Chicago & McGaw Medical Center/ Northwestern University, Ill.

SAMUEL BRAYER
Cincinnati Children's Medical Center/ University of Cincinnati, Ohio

ILONA BRUECKMANN
Lurie Children's Hospital of Chicago & McGaw Medical Center/ Northwestern University, Ill.

CATHY CHEN
UC San Diego Medical Center/ University of California, San Diego

ANDREW HUGHES
Children's Hospital of Philadelphia/ University of Pennsylvania

RACHEL HUGHES
NYU Langone Medical Center & Bellevue Hospital

SABRINA KARIM
Boston Children's Hospital/ Harvard University, Mass.

KELSEY KOFF
University of Washington Affiliated Hospitals

MICHAEL MATT
Cincinnati Children's Medical Center/ University of Cincinnati, Ohio

JAMES MCAULEY
Comer Children's Hospital/University of Chicago Medical Center, Ill.

JENNIFER MENA
Montefiore Medical Center/Albert Einstein College of Medicine, N.Y.

ANDREA PARK
Riley Hospital for Children/ Indiana University

MONDIRA RAY
University of Washington Affiliated Hospitals

MARGARET RUSSELL
UPMC Children's Hospital of Pittsburgh/University of Pittsburgh, Pa.

Physical Medicine and Rehabilitation

CHRISTOPHER MANTIK
Casa Colina Hospital, Calif.

Psychiatry

BRITTANY ATUAHENE
Yale New Haven Hospital, Conn.

CLAIRE BECKER
Western Psychiatric Institute and Clinic/University of Pittsburgh, Pa.

MEGHAN BISBEY
Western Psychiatric Institute and Clinic/University of Pittsburgh, Pa.

IDA BROCKMAN
Western Psychiatric Institute and Clinic/University of Pittsburgh, Pa.

EVA CHERNOFF
Mount Sinai Hospital/Icahn School of Medicine at Mount Sinai, N.Y.

LAUREN GOLDSCHEN
Brigham & Women's Hospital/ Harvard University, Mass.

JOSHUA KRIVINKO
Western Psychiatric Institute and Clinic/University of Pittsburgh, Pa.

JULIA NGUYEN
UNM Psychiatric Center/ University of New Mexico

IHUOMA NJOKU
University of Virginia Medical Center

ERIC STROBL
Vanderbilt University Medical Center, Tenn.

EMILIE TRANSUE
Strong Memorial Hospital/ University of Rochester, N.Y.

ERIC ZIMMERMAN
UPMC Western Psychiatric Hospital/ University of Pittsburgh, Pa.

Psychiatry/Family Medicine

GILLIAN KRUSZKA
UPMC/University of Pittsburgh, Pa.

Radiation Oncology

POOJA KARUKONDA
Duke University Medical Center, N.C.
*University of North Carolina Hospitals

ARANEE SIVANANTHAN
University of Chicago Medical Center, Ill.
*UPMC/University of Pittsburgh, Pa.

PHILIP SUTERA
Johns Hopkins Hospital, Md.
*Allegheny General Hospital, Pa.

Radiology—Diagnostic

KYLE ATCHESON
Wake Forest University Baptist Medical Center, N.C.
*Presence Resurrection Medical Center, N.C.

JOSEPH MOULTON
Yale New Haven Hospital, Conn.
*UPMC/University of Pittsburgh, Pa.

Radiology—Interventional

ABDULLAH KHAN
UC Davis Medical Center/ University of California, Davis
*Santa Clara Valley Medical Center, Calif.

Research

SARA ERNST
UPMC/University of Pittsburgh, Pa.

Surgery—General

VINCENT ANTO
UPMC/University of Pittsburgh, Pa.

LAUREN BOULAY
Morristown Medical Center/ Mount Sinai School of Medicine, N.J.

JENNIFER DARBY
Loyola University Medical Center, Ill.

ASHLEY DONOVAN
Ohio State University Medical Center

BRIAN GRIFFITH
University of Michigan Hospitals

MIR SHANAZ HOSSAIN
Cleveland Clinic/Case Western Reserve University, Ohio

DYLAN KAHLER
Temple University Hospital, Pa.

ALEXANDER KREGER
University Hospitals Cleveland Medical Center/Case Western Reserve University, Ohio

BINGHAU LI
Creighton University, Neb.

ANNIE LIU
Duke University Medical Center, N.C.

THIAGARAJAN MEYYAPPAN
UPMC/University of Pittsburgh, Pa.

ANNA RAMOS
UPMC/University of Pittsburgh, Pa.

GLORIA SANIN
Wake Forest University Baptist Medical Center, N.C.

Surgery—Preliminary

DREW MICHAEL DONNELL
Ohio State University Medical Center

BEVERLY HERSH
Zucker School of Medicine at Hofstra/Northwell, N.Y.

RONAK JANI
Brigham & Women's Hospital/ Harvard University, Mass.

DANIEL LEWIS
UPMC Mercy/University of Pittsburgh, Pa.

SHIH-DUN STANLEY LIU
San Joaquin General Hospital, Calif.

MICHAEL LU
UPMC Mercy/University of Pittsburgh, Pa.

ELENA NIKONOVA
Shands Hospital/University of Florida

Surgery—Thoracic

BRYANT FISHER
UPMC/University of Pittsburgh, Pa.

Urology

AUSTIN LEE
University of Rochester Medical Center, N.Y.

JOHN MYRGA
UPMC/University of Pittsburgh, Pa.
*UPMC/University of Pittsburgh, Pa.

*Indicates location of transitional or preliminary year of medical or surgical training.

LONGITUDINAL RESEARCH PROJECT BY THE NUMBERS / CLASS OF 2019

Beginning in year one of medical school, students in the Class of 2019 embraced the opportunity to engage in research through the Longitudinal Research Project. As of graduation day, the fruits of their labor include:

148
med students completed a research project
84% of the class participated in summer research between their first and second years of med school

174
peer-reviewed publications
plus an additional 46 submitted and/or under review

346
presentations at national and international meetings

63
national or state awards

124
local awards

2019 O'MALLEY AWARD WINNERS

At Scholars Day 2019, four graduating MD students were individually honored with a Bert and Sally O'Malley Award for Outstanding Medical Student Research.

The awards are named for a pair of Pitt alumni: Bert earned his BS in 1959 and MD in 1963 and was awarded the 2007 National Medal of Science for his pivotal work on steroid hormone receptors. He is professor of molecular and cellular biology at Baylor College of Medicine. Sally (Johnson) earned her BS in education in 1959.

The O'Malley award recognizes outstanding scholarly projects in basic and clinical research.

4-Year Basic Science Research

IHUOMA NJOKU, MD

Effect of Galantamine on Attentional Set-Shifting Performance after Experimental Brain Trauma

Residency Match:
Psychiatry, University of Virginia

Mentor:
Corina Bondi, PhD, assistant professor of physical medicine and rehabilitation

4-Year Clinical Science Research

AMOL MEHTA, MD

Perioperative Stroke as an Independent Risk Factor for Mortality and Morbidity in Patients Undergoing CABG

Residency Match:
Neurology, New York Presbyterian Hospital-Columbia University Medical Center

Mentor:
Parthasarathy Thirumala, MD, associate professor of neurological surgery and of neurology

5-Year Clinical Science Research

JOSE MIGUEL JUAREZ, MD

Loss of Follow-Up After Failed Newborn Hearing Screening: Factors Influencing Parental and Primary Care Provider Awareness

Residency Match:
Emergency Medicine, Icahn School of Medicine at Mount Sinai

Mentor:
David H. Chi, MD, associate professor of otolaryngology

5-Year Basic Science Research

PHILIP SUTERA, MD

Bcl-xL Knockdown Sensitizes Glioma Cell Lines to Survivin Inhibitor YM-155

Residency Match:
Radiation Oncology, Allegheny General Hospital

Mentor:
Ian F. Pollack, MD, Distinguished Professor, Dr. A. Leland Albright Professor of Children's Neurosurgery, vice chair for academic affairs, and codirector of the Brain Tumor Program, Department of Neurological Surgery

MED SCHOOL DEMOGRAPHICS

7,013 students applied and **655 were interviewed** for the **148 available positions** in the medical school **Class of 2023**.

As of the **2019–20** academic year, **596 MD students** are registered in the School of Medicine, including **332 women (55%)** and **264 (44%) men**. Of these, **210 (35%) are Pennsylvania residents**; **approximately 18%** of Pitt medical students **are from groups that are underrepresented within the medical profession**.

There are **348 registrants in PhD programs** (including those in the Medical Scientist Training Program), **132 students in MS programs**, and **27 students in certificate programs**.

The School of Medicine has **2,350 regular** and **1,664 volunteer faculty members**. Of these, **70 are current members of the Academy of Master Educators**, an organization that recognizes and rewards excellence in medical education.

Tour de Force

As soon as the general internal medicine residents learned where they matched for 2019 fellowships, the news spread quickly, including to Arthur S. Levine, MD, senior vice chancellor for the health sciences, John and Gertrude Petersen Dean of Medicine, and professor of medicine and molecular genetics, School of Medicine.

"This list is truly exceptional," he remarked. "There could not be a better testament to what has been achieved here."

Agreeing with Levine was Mark T. Gladwin, MD, Distinguished Professor of Medicine, Jack D. Myers Professor of Internal Medicine, and chair, Department of Medicine: "Tour de force—the best residency fellowship match I've seen."

Also thrilled and proud of the residents was the director of the Internal Medicine Residency Training Program, Jennifer A. Corbelli, MD, MS, associate professor of medicine (Division of General Internal Medicine). Corbelli has worked extensively to help residents find mentorship and research opportunities, as well as to develop as educators.

"Our residents are strong," she says. "We're really able to recruit top people from medical school, which reflects the increasing competitiveness and caliber of our program and the growing infrastructure to support our residents' success and scholarship during their time here."

The School of Medicine's reputation as a top-tier academic medical center enables residents to conduct research in almost any area in which they are interested.

"What is unique about us is the size of our research enterprise," says Corbelli. "Our program is particularly impressive in the amount of funding and the scope of options; we just have so much going on from a research and innovation standpoint."

Two chief residents echo Corbelli's explanation for the impressive fellowship matches:

Joe Rocco, MD, (who matched at the National Institutes of Health for an infectious diseases fellowship), recalls telling his professor—Peter Veldkamp, MD, MS, professor of medicine, Division of Infectious Diseases, and associate dean for medical student research—that he had an interest in infectious diseases. By the next day, Rocco was connected with opportunities from three different researchers.

"I've been able to publish research, which isn't easy to do in residency and is almost impossible to do if your mentors don't prioritize you," says Rocco. "Here, everyone wants their mentees to be successful. If you look at academic medical centers in the country, lots of them make great researchers and clinicians, but not as many of them make good researchers, clinicians, and educators. I think Pitt does that better than anywhere else."

Anjali Rao, MD, (who's beginning a cardiology fellowship at UT Southwestern) adds: "One really big component is access to some of the best research opportunities out there. Our department gets so many NIH dollars that anything you want to do is at your fingertips."

She gives Pitt much credit for her match: "Pitt is a really supportive place. I feel as if the program has molded me in exactly the way I hoped it would; it has made me a better teacher, better doctor, better member of the team, and better at the job I've wanted to do for forever. It's the mentors, the training, our culture, my co-residents—a lot of different things that come together."

"TOUR DE FORCE—THE BEST RESIDENCY FELLOWSHIP MATCH I'VE SEEN."

— MARK T. GLADWIN, MD

RESIDENCY FELLOWSHIP MATCHES:

PGY 3 Residents

BRIAN AHN, MD
Pulmonary/Critical Care Medicine, University of Colorado

MICHAEL BASHLINE, MD
Cardiology, UPMC

RYAN BELECANECH, MD
Pulmonary/Critical Care Medicine, Johns Hopkins Hospital

DIVYA BHAMIDIPATI, MD
Infectious Diseases, Emory University

ROMA BHATIA, MD
General Internal Medicine, Harvard University

ANN CANTERBURY (PACENTA), MD
Cardiology, UPMC

SUMEDHA CHABLANI, MD
Endocrinology, NewYork-Presbyterian/ Weill Cornell Medical Center

ALIANA CHODOFF, MD
General Internal Medicine Education, Johns Hopkins Hospital

FURKAN ERTEM, MD
Gastrointestinal, UPMC

PETER FININ, MD
Infectious Diseases, National Institutes of Health

COLLEEN GAVIGAN, MD
Endocrinology, Johns Hopkins Hospital

KELLY GIBBS (ALLISON), MD
Gastrointestinal, University of Arkansas

KATRINA HAN, MD
Endocrinology, Barnes Jewish Hospital/Washington University in St. Louis

ALIZA HUSSAIN, MD
Clinical Cardiology and Atherosclerosis, Baylor University

NATALIE KLAR, MD
Hematology/Oncology, New York University

AARON KUNTZP, MD
Hospice and Palliative Care, University of Wisconsin

HELGE (IMMO) LEHMANN, MD
Cardiology, Massachusetts General Hospital/ Harvard University

YIJIA LI, MD
Infectious Diseases, Massachusetts General Hospital/ Harvard University

JACOB LIPKIN, MD
Gastrointestinal, UPMC

RICARDO NIEVES, MD
Cardiology, UPMC

OLUBUSOLA (BUSOLA) OLUWOLE, MD
Hematology/Oncology, University of Washington

NEETI PATEL, MD
Endocrinology, New York University

RACHEL RODENBACH, MD
Hospice and Palliative Care, UPMC

ADI SHAFIR, MD
Geriatrics, University of California, San Francisco

JESSE SOLOMON, MD
Hospice and Palliative Care, Beth Israel Deaconess Medical Center/Harvard University

MICHAEL SIMONSON, MD
General Internal Medicine, UPMC

BENJAMIN SMITH, MD
Critical Care Medicine, UPMC

SUNNY TAO, MD
Gastrointestinal, UPMC

GEORGIOS (GEORGE) TRIANTAFYLLOU, MD
Pulmonary/Critical Care Medicine, UPMC

YANTING WANG, MD
Cardiology, Yale University

XIE MAYLENE, MD
Allergy and Immunology, Yale University

RICHARD ZOU, MD
Pulmonary/Critical Care Medicine, Yale University

Med-Peds

GABRIELLE LANGMANN, MD
Hospice and Palliative Care, UPMC

Research Pathway

EDWIN CHEN, MD, PhD
Infectious Diseases, UPMC

AMIR GHAFFARI, MD, PhD
Gastrointestinal, UPMC

Chief Medical Residents

STEVE FOX, MD
Pulmonary/Critical Care Medicine, Cleveland Clinic

AGNES KOCZO, MD
Cardiology, UPMC

ANJALI RAO, MD
Cardiology, University of Texas Southwestern Medical Center

JOE ROCCO, MD
Infectious Diseases, National Institutes of Health

DIANA SAMBERG, MD
General Internal Medicine, UPMC

Former Grads

EILEEN ZHUANG, MD
Pulmonary/Critical Care Medicine, University of Maryland

Asian Consults

To improve the medical education and health care for the nearly 20 million people living in Central Asia's Republic of Kazakhstan, Nazarbayev University selected the University of Pittsburgh School of Medicine as its strategic academic partner to assist in the development of its medical school.

The partnership formed in 2012, the Nazarbayev University School of Medicine (NUSOM) enrolled its first class of students in 2015, and that inaugural class graduated in 2019.

Along the way, Pitt's School of Medicine has provided guidance on curriculum, teaching facilities, school leadership and faculty, policies, courses, and more—allowing the new school to stand out in the republic.

The commencement ceremony for NUSOM, alongside the rest of the university graduates, took place May 31, 2019. Out of 937 university graduates, 41 earned degrees at NUSOM. Core team members representing Pitt were Ann E. Thompson, MD, MCCM, vice dean and professor of critical care medicine and of pediatrics, School of Medicine; Margaret C. McDonald, PhD, MFA, associate vice chancellor for academic affairs and international programs, Health Sciences, and associate professor of epidemiology, Graduate School of Public Health; D. Michael Elnicki, MD, professor of medicine and director, international medical education programs, School of Medicine; and Saleem Khan, PhD, professor of microbiology and molecular genetics and associate dean for academic affairs, School of Medicine, and professor of communication science and disorders, School of Health and Rehabilitation Sciences.

The NUSOM partnership isn't Pitt Med's only Asian presence. The school also partners with Tsinghua University School of Medicine in Beijing, through which medical students from this renowned Chinese scientific institution undergo a rigorous, two-year mentored biomedical research training program in Pittsburgh. Initiated in 2012, Pitt's Tsinghua scholars work in the labs of some of Pitt's most accomplished biomedical researchers.

Pitt School of Medicine also initiated a collaboration with China's prestigious Central South University Xiangya School of Medicine in 2012. Under the agreement, Pitt provides two years of extensive biomedical research training to medical students, most of whom have already undergone six years of medical school, including clinical clerkships.

Well Trained

Some of the most significant breakthroughs in medicine come from physicians trained in clinical care and research. The University of Pittsburgh School of Medicine nurtures that exact group through the Medical Scientist Training Program (MSTP).

The program provides an opportunity for medical students interested in a biomedical research career to undertake doctoral work at either the University of Pittsburgh or Carnegie Mellon University in basic science, engineering, or public health. After two years of medical school, students complete PhD work before returning to medical training. Both degrees are completed in an average of seven to eight years. The program, funded by a grant from the National Institutes of Health (NIH) with support from the Office of the Dean, offers full tuition and a yearly stipend.

In 2019, Pitt said farewell to nine of these budding physician-scientists, who have matched to some of the most prestigious residency programs in the nation.

PITT'S 2019 MSTP GRADUATES AND THEIR RESIDENCY MATCHES:

ALYCE ANDERSON, MD, PhD
Residency Match:
Dermatology, UPMC Medical Education, University of Pittsburgh
Mentor:
David Binion, MD, professor of medicine, codirector, IBD Center-Translational Research, (Division of Gastroenterology, Hepatology, and Nutrition), Department of Medicine; and professor of clinical and translational science

RACHEL GORDON, MD, PhD
Residency Match:
Internal Medicine, UPMC Medical Education, University of Pittsburgh
Mentor:
Mark Shlomchik, MD, PhD, Distinguished Professor, UPMC Professor, and chair, Department of Immunology, and professor of pathology

ALEXANDER KIKUCHI, MD, PhD
Residency Match:
Pathology (Anatomic and Clinical), University of California, San Francisco
Mentor:
Satdarshan (Paul) Singh Monga, MD, Professor of Experimental Pathology, vice chair and chief, Division of Experimental Pathology, and professor of medicine (Division of Gastroenterology, Hepatology, and Nutrition); assistant dean and codirector, Medical Scientist Training Program; and director, Pittsburgh Liver Research Center

ANNIE LIU, MD, PhD
Residency Match:
General Surgery, Duke University Medical Center
Mentor:
Nathan Urban, PhD, professor and vice chair of neurobiology; codirector, Center for the Neural Basis of Cognition; associate director, University of Pittsburgh Brain Institute; and vice provost for graduate studies and strategic initiatives, University of Pittsburgh

J. RANDALL MCAULEY, MD, PhD
Residency Match:
Pediatrics, University of Chicago Medical Center
Mentor:
Peter Lucas, MD, PhD, professor of pathology (Divisions of Molecular Genomic Pathology and Experimental Pathology) and of pediatrics

NOLAN PRIEDIGKEIT, MD, PhD
Residency Match:
Internal Medicine, Brigham and Women's Hospital/Harvard University
Mentor:
Adrian Lee, PhD, Pittsburgh Foundation Professor of Precision Medicine, professor of pharmacology and chemical biology, director, Institute for Precision Medicine; professor of human genetics, Graduate School of Public Health

BENJAMIN ROTHRAUFF, MD, PhD
Residency Match:
Orthopaedic Surgery, UPMC Medical Education, University of Pittsburgh
Mentor:
Rocky Tuan, PhD, Distinguished Professor of Orthopaedic Surgery, executive vice chair of orthopaedic research, Department of Orthopaedic Surgery, School of Medicine; professor of bioengineering and of mechanical engineering and materials science, Swanson School of Engineering

ERIC STROBL, MD, PhD
Residency Match:
Psychiatry, Vanderbilt University Medical Center
Mentor:
Shyam Visweswaran, MD, PhD, associate professor of biomedical informatics, School of Medicine; of intelligent systems, Dietrich School of Arts and Sciences; and of clinical and translational science

ERIC ZIMMERMAN, MD, PhD
Residency Match:
Psychiatry, UPMC Medical Education, University of Pittsburgh
Mentor:
Anthony Grace, PhD, Distinguished Professor of Neuroscience and professor of psychology, Dietrich School of Arts and Sciences; and professor of psychiatry, School of Medicine

Award-Winning MSTP Research Projects

In addition to news of those MSTP matches, several of the program's students have caught the attention of NIH. Also known as the Ruth L. Kirschstein National Research Service Awards, F30 awards are NIH grants created for MSTP students who demonstrate the potential to become highly trained, productive, and independent physician-scientists. NIH's ultimate goal with the program is to increase the number of future investigators with both clinical knowledge and skills in basic, translational, or clinical research. In recent years, roughly half of Pitt's MSTP students have earned NIH grants.

F30 AWARDS TO CURRENT MSTP STUDENTS:

LLOYD HARVEY
HIV-Infected Macrophages Induce Endothelial Cell Dysfunction and Metabolic Reprogramming to Promote HIV-Associated Pulmonary Arterial Hypertension
Mentor:
Stephen Chan, MD, PhD, professor of medicine and associate fellowship director for research, Division of Cardiology

ANDREW LAMADE
Targeting Mitochondrial PARP1 in Neuronal Ischemia-Reperfusion Injury
Mentor:
Hülya Bayır, MD, UPMC Professor of Critical Care Pediatric Research, professor of critical care medicine, School of Medicine; and professor of environmental and occupational health, Graduate School of Public Health

STEPHANIE MYAL
(CMU grad student currently)
Sources of Cholinergic Modulation of Cortical Microcircuits

Mentor:
Alison Barth, PhD, Maxwell H. and Gloria C. Connan Professor in the Life Sciences and professor of biological sciences, Carnegie Mellon University

EILEEN NGUYEN
Cellular Basis for Morphine-Induced Itch

Mentor:
Sarah Ross, PhD, associate professor of neurobiology

MARYANNA OWOC
Cell-Based Approach for Increasing Central Auditory Inhibition

Mentor:
Karl Kandler, PhD, professor of neurobiology and of otolaryngology

OTHER NOTABLE AWARDS TO MSTP STUDENTS:

GAELEN DWYER, LAURA MOLINA
Chateaubriand Fellowship

(The Chateaubriand Fellowship is a grant offered by the Embassy of France in the United States. It supports outstanding PhD students from universities in the United States who wish to conduct research in France.)

MARIA LY
Ly was awarded a summer research fellowship with the Mallinckrodt Institute of Radiology at the Washington University School of Medicine in St. Louis.

ALEXANDER SCHUYLER
Sally Miller Award for Advocacy on Behalf of the Medically Underserved

(This award is given to a student who has demonstrated a keen awareness of the needs of patients and the obstacles they confront in accessing health care, has advocated on behalf of underserved patients or populations, and has expressed a key career interest in patient advocacy.)

Mentor:
Sally Wenzel, MD, Rachel Carson Professor of Environmental Health and chair, Department of Environmental and Occupational Health, Graduate School of Public Health; and professor of immunology, School of Medicine

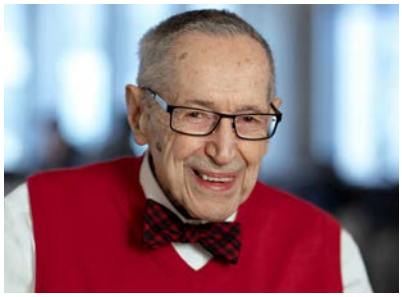
ZACHARY YOCHUM
Department of Medicine Graduate Student Research Award

Mentor:
Alan Wells, MD, DMSc, Thomas J. Gill III Professor of Clinical Pathology and executive vice chair, Department of Pathology, and professor of computational and systems biology, School of Medicine; and professor of bioengineering, Swanson School of Engineering

THE SCHOOL OF MEDICINE HAS A MISSION TO EDUCATE SCIENCE-BASED, SKILLED, AND COMPASSIONATE CLINICIANS PREPARED TO MEET THE CHALLENGES OF PRACTICING MEDICINE IN TODAY'S EVER-CHANGING WORLD.

Spotlight: Master Educator

ELMER J. HOLZINGER, MD



Wearing his ever-present bow tie, **Elmer J. Holzinger, MD**, is in Scaife Hall to interview University of Pittsburgh School of Medicine applicants — he's right at home.

Holzinger, professor emeritus of medicine, has trained thousands of medical students and medical residents and earned universal recognition for his passion and dedication to the medical profession during a clinical and teaching career that spans nearly six decades. Today, at 92, he has a well-deserved reputation as a master in the art of physical examination and is one of the School of Medicine's most beloved and respected clinical professors.

A Pittsburgh native and 1954 School of Medicine graduate, Holzinger has been affiliated with the School of Medicine faculty since 1960, when he joined the Pitt staff as a clinical assistant instructor in medicine after serving in the U.S. Navy. He became dedicated to teaching students and residents in 1970 and continued an active medical practice.

Every student who passes through Pitt's medical education program eventually has Holzinger as a professor. Noted for his kind, respectful demeanor with students, he has left a lasting impression on many of them.

D. Michael Elnicki, MD, professor of medicine and director, International Medical Education Programs, School of Medicine, says, "He embodies the concept of the clinician-educator in medical education. His immense fund of medical knowledge allows him to make clinical decisions quickly and guide learners through a diagnosis. He does this in a gentle, confidence-inspiring fashion, and students uniformly respond favorably to him because they see that he has their interests at heart. His ability to remediate struggling learners or to make good learners better has always amazed me."

Holzinger's career as a physician and educator has not gone unnoticed over the years. At Pitt, he received the 2014 Kenneth E. Schuit Award, the dean's award for master educator. In 2013, the UPMC Presbyterian Shadyside Internal Medicine Residency Program established the Elmer Holzinger Award, of which he was the first recipient, for an attending physician who emulates Holzinger's "love of patients, medicine, and teaching." In 2008, he became a Distinguished Member of the School of Medicine Academy of Master Educators. And, in 2004, the University honored Holzinger with the Chancellor's Distinguished Teaching Award.

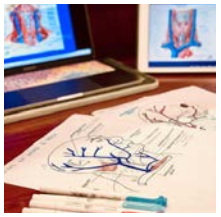
When asked to describe how he how he became a master educator, Holzinger looks to history: "Abraham Lincoln did some teaching, and he said the greatest way to success was persistence. I would add to persistence that you need to actively figure out how to get better. At the end of my meetings, I always ask, 'What do we need to change?' I knew I could be a little bit better the next day than I was today."

pittmed_students

Pitt Med Student Ambassadors Program

Current School of Medicine students, navigating their own journeys toward Match Day, are spotlighting their day-to-day experiences on social media. They post about everything from the best study spots on campus to their favorite class during M1. Follow six student ambassadors, introduced by the Office of Student Affairs and Diversity Programs, who share their stories at Instagram.com/pittmed_students and facebook.com/pittmedstudents

pittmed_students The MS1s have their first Intro to Physical Exam assessment this week, which means I practiced on every family member who would let me during Thanksgiving break. They loved it!



pittmed_students Stumbled across some drawings I made while studying anatomy. 💊 It reminded me of how much I enjoyed the course taught by one of the best professors, Dr. Schumann #PittMedHaniah #h2p #anatomy

pittmed_students Always good to spend time with my dogs. ✌🏻 Pittsburgh has so many beautiful parks within 30 minutes of downtown. Hartwood Acres in Hampton is one of my favorites. 👌🏻 #pittmed #PittMedJoe #H2P #ParkerTheBarker

pittmed_students Emma is our "Student of the Week!" She is an MS2 and was a neuroscience and psychology major at the University of Wisconsin at Madison. For a stress reliever as well as a paying job, Emma teaches a weekly kickboxing class to both undergraduate and graduate students at Pitt. "I'm so happy that I have a job where I can motivate people toward change and get a good workout and study break in at the same time." I personally took Emma's class and was very sore the next day. #pittmed #PittMedMaria

LIFE SAVER

When Paul Offit, MD, was a resident in the emergency department at UPMC Children's Hospital of Pittsburgh in the late 1970s, he had a patient—a 9-month-old infant—who died of rotavirus. He was shocked to realize that this common intestinal infection still killed children in the United States.

Some three decades later, in 2009, RotaTeq—a rotavirus vaccine codeveloped by Offit—was recommended by the World Health Organization to protect against the deadly infection, which was estimated to be causing as many as 500,000 deaths worldwide for children under the age of 5.

RotaTeq was the fruit of 25 years of labor for Offit, who is now a renowned expert in virology and immunology. He says he is "enormously proud" of helping develop the vaccine that is administered around the world.

His research has also led to his becoming a prominent defender of vaccines.

Sadly, he has also become a target for people who speculate that there is a connection between vaccines and autism. These accusations are scientifically unfounded, yet they are often widely publicized while, unfortunately, the epidemiological and other studies debunking any correlation between vaccines and autism don't receive the same kind of publicity.

To help disseminate factual information about vaccines to the public and media, Offit cofounded the Vaccine Education Center at Children's Hospital of Philadelphia in 2000. He has also written several books and newspaper articles on the topic, and he has taught an open online course on vaccines.

"The motivation for educating [the public] about vaccines and vaccine safety is because I don't want to have to watch children come into our hospital and suffer and die from diseases that are preventable," says Offit, who today is the Maurice R. Hilleman Professor of Vaccinology, professor of pediatrics, University of Pennsylvania Perelman School of Medicine, and director, Children's Hospital of Pennsylvania Vaccine Education Center.

Offit has been well recognized for his work in infectious diseases, vaccination, immunology, and virology, including by Pitt, where he received the Porter Prize from the Graduate School of Public Health.

However, his biggest reward, he says, has been helping save countless lives.

LGBTQ+ Patient Care

The LGBTQ+ community faces barriers when it comes to accessing and receiving health care, according to numerous studies, in addition to myriad health disparities.

One way to reduce the burden of health disparities is to appropriately train medical students in the health care needs of patients with diverse sexual orientations and gender identities.

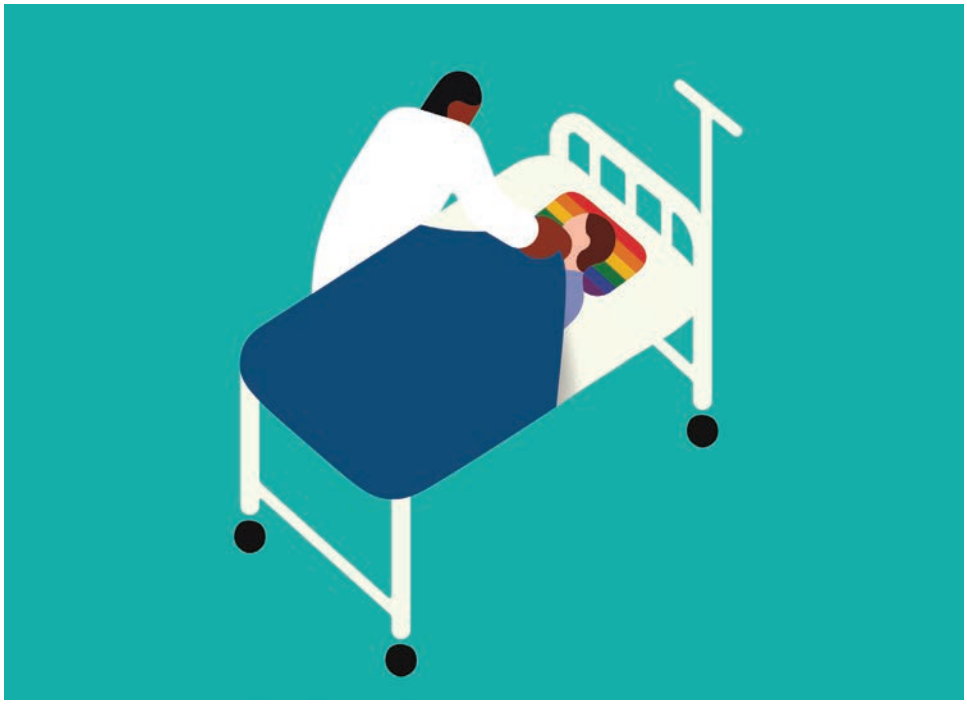
At Pitt, there is now the mini-elective "Diversity in Sexual Orientation/Gender Identity and Expression (SOGIE): Health and Health Care," which aims to give medical students the necessary training to provide responsible care to LGBTQ+ patients. This mini-elective is led by codirectors Dena Hofkosh, MD, MEd, professor and vice chair for faculty development, Department of Pediatrics; Kristen Eckstrand, MD, PhD, child and adolescent psychiatry fellow, Department of Psychiatry; Morgan Faeder, MD, PhD, assistant professor of psychiatry; and Eloho Ufomata, MD, assistant professor of medicine, in collaboration with medical students Alex Schuyler and Hannah Apfelbaum.

Students enrolled in the mini-elective receive an additional 14 hours of training in LGBTQ+ health care, including in-depth didactics and discussion in taking medical histories pertaining to sexuality and gender, gender-affirming hormone treatment, surgical options for masculinization and feminization, puberty suppression, caring for gender-diverse youths, interprofessional collaboration with mental health providers, and dispelling common excuses masking unethical treatments of LGBTQ+ persons (e.g., so-called conversion therapies). These sessions are provided by faculty who work with LGBTQ+ patients as well as patients who identify as LGBTQ+.

"The mini-elective is not meant to be an exhaustive course," says Hofkosh. "It's a complement to a very packed standard medical school curriculum. The hope is that the more we infuse the regular curriculum with examples of people just living their lives as members of the LGBTQ+ community, the fewer times those patients will be on their guard with a physician."

She hopes that the mini-elective can grow to a clinical elective and an area of concentration; a third-year clinical elective that emphasizes both clinical and community experiences is also in the works: "This material is relevant to every student," she says, "because everybody as a physician is going to have some experience taking care of patients from all different communities."

ONE WAY TO REDUCE THE BURDEN OF HEALTH DISPARITIES IS TO APPROPRIATELY TRAIN MEDICAL STUDENTS IN THE HEALTH CARE NEEDS OF PATIENTS WITH DIVERSE SEXUAL ORIENTATIONS AND GENDER IDENTITIES.



Since his arrival in Pittsburgh in 1998, Arthur S. Levine, MD, has aimed to bring about transformational change in medicine. He has done so by supporting an environment in the School of Medicine that cultivates exploration of the biological sciences in order to understand the human body at its most fundamental levels in both health and disease. The approach has led to substantive research outcomes, demonstrated in part through noteworthy scholarly articles and significant grants.

Grants of Note

SOLUTIONS FOR ANTIBIOTIC RESISTANCE

Solutions to the growing problem of antibiotic resistance could be right underneath our feet. Just scoop a handful of soil from the ground and inhale deeply. That fresh, earthy smell comes from the compound geosmin, a natural product produced by certain bacteria.

"When you smell soil, you're actually smelling a lot of geosmin, and it's mostly produced by these guys," says **Erik Wright, PhD**, gesturing toward a picture of bacteria from the genus *Streptomyces* hanging on his office wall. *Streptomyces* bacteria are everywhere, so much so that when Wright, an assistant professor of biomedical informatics, plucked a speck of soil from the backyard at the Bridgeside Point II research building, it contained thousands of *Streptomyces*. These ubiquitous bacteria may also be key to combatting the growing problem of antibiotic resistance, Wright says.

Geosmin isn't the only natural product that these bacteria emit; in fact, Wright says that some 50% of clinical antibiotics have been derived from the numerous compounds that *Streptomyces* produce. Wright, who recently received a **$2.3 million** NIH Director's New Innovator Award, is looking to develop innovative solutions to the problem of antibiotic resistance in part by studying how *Streptomyces* produce and use natural antibiotics.

Streptomyces have produced antibiotics for hundreds of millions of years in order to inhibit surrounding bacterial competitors, Wright says, yet they've managed to avoid widespread resistance to their antibiotics. Their versatility appears to be a key asset; *Streptomyces* can produce dozens of bacteria-killing compounds in doses that change depending on which bacterial neighbors surround them. "Every *Streptomyces* has a different set of antibiotics available to it," Wright says.

Wright and his colleagues will interrogate the *Streptomyces* genome and use genomic sequencing to identify new sets of genes that code for antibiotic molecules. The process will also shed light on which antibacterial natural products act synergistically and which compounds could then be harnessed for use together.

Ultimately, the goal is to develop new antibiotics and new combinations of drugs for the clinic based on *Streptomyces*' strategies, Wright says. Better understanding of *Streptomyces* could also lead to development of chemotherapy drugs, pesticides, and other agents that have all been derived from *Streptomyces*' natural products.

In the end, nature has found a way around antibiotic resistance while humans remain vexed by an increasing threat. While finding new compounds could lead to new antibiotics, bacteria will probably find a way around them, too, Wright says. Therefore, truly understanding how nature solves this problem is our best hope, he says, and, perhaps, the only sustainable solution.

NATURE HAS FOUND A WAY AROUND ANTIBIOTIC RESISTANCE WHILE HUMANS REMAIN VEXED BY AN INCREASING THREAT. TRULY UNDERSTANDING HOW NATURE SOLVES THIS PROBLEM IS OUR BEST HOPE.

"OFTENTIMES, RESEARCH DOES NOT INCLUDE DATA FROM RURAL POPULATIONS, MEANING THAT THE FINDINGS DON'T ALWAYS APPLY IN THE SAME WAY THEY WOULD TO AN URBAN POPULATION. THIS GRANT WILL HELP TO ENSURE THAT WE ARE ADDRESSING THE OPIOID EPIDEMIC IN A WAY THAT TRULY HELPS THOSE WHO ARE MOST AFFECTED."

— JANE LIEBSCHUTZ, MD, MPH

OPIOID EPIDEMIC FROM A RURAL PERSPECTIVE

Across the country, policy makers, practitioners, and community members are looking for evidence-based solutions to the devastating opioid epidemic. But for rural regions like Appalachia, part of the problem is that their populations are often overlooked during data collection for scientific studies, leaving certain findings with limited application to rural populations. Studies on the opioid epidemic, which has afflicted Appalachia, have been no exception.

"Historical and cultural factors have caused Appalachia to experience the negative consequences of the opioid epidemic at a disproportionately high rate, including overdoses, neonatal abstinence syndrome, and death," says principal investigator **Jane Liebschutz, MD, MPH**, UPMC Professor of Translational Medicine and Research and chief of the Department of Medicine's Division of General Internal Medicine. "Oftentimes, research does not include data from rural populations, meaning that the findings don't always apply in the same way they would to an urban population. This grant will help to ensure that we are addressing the opioid epidemic in a way that truly helps those who are most affected," she says, referring to a **$5.8 million** National Institute on Drug Abuse grant that will establish the Appalachian node of the National Institute on Drug Abuse Clinical Trials Network (CTN).

In a partnership with Pennsylvania State University and West Virginia University, Pitt's Division of General Internal Medicine will conduct opioid-related research in Appalachia over the next five years and work with individual clinical practices throughout Appalachia to enroll patients in opioid use and treatment studies. With the support of CTN, patients will be able to contribute much-needed data for understanding the opioid epidemic in Appalachia specifically.

To extend more advanced care into regions with limited resources, the CTN collaborators plan to use existing resources, including local pharmacies, peer navigators, and digital technology, to facilitate studies.

The findings and benefits from the Appalachian studies can also extend beyond the region, Liebschutz says. "The knowledge we obtain from this research will help not only the Appalachian region but also people across the country," she says.

SICKLE CELL TREATMENT TRIAL

Sickle cell disease (SCD) patients experience high rates of organ damage often leading to early death. While blood transfusions to treat SCD complications can cause iron toxicity due to the presence of excessive red blood cells, red cell exchange transfusion removes and replaces sickled red blood cells with normal ones. In a trial supported by a **$19.2 million** National Heart, Lung, and Blood Institute grant, Pitt researchers, including principal investigator **Mark Gladwin, MD**, Distinguished Professor and chair of medicine and Jack D. Myers Professor of Internal Medicine; coprincipal investigator **Darrell J. Triulzi, MD**, professor of pathology; and **Maria Mori Brooks, PhD**, principal investigator of the Data Coordinating Center at the Graduate School of Public Health, will seek to determine whether red cell exchange can lower death rates, reduce hospitalizations, and slow down or reverse development of organ damage. While red cell exchange requires more donor blood, takes longer, and is more expensive than blood transfusions, the multi-site Sickle Cell Disease and Cardiovascular Risk—Red Cell Exchange (SCD-CARRE) trial will help determine whether the process should be added to the standard of care.

INNOVATIVE CANCER IMMUNOTHERAPY RESEARCH

Supporting innovative cancer immunotherapy research is the goal of the Sy Holzer Endowed Immunotherapy Research Fund, and **Greg M. Delgoffe, PhD**, is the fund's first beneficiary. The fund, which provides **$150,000** for research, honors former PNC Bank president Sy Holzer and his philanthropic work and service as chair of the UPMC Hillman Cancer Center Council. Delgoffe, associate professor of immunology and a researcher with UPMC Hillman Cancer Center's Tumor Microenvironment Center, and his lab members study how cancer cells use fuel from their surrounding environment to starve and prevent infiltrating immune cells from attacking cancer cells.

COMBATING PARALYSIS

Groundbreaking brain computer interface (BCI) research conducted by **Andrew Schwartz, PhD**, Distinguished Professor of Neurobiology and Professor of Systems Neuroscience, and other Pitt researchers, has enabled three study participants with paralysis to control a robotic arm using only their thoughts. One even regained a sense of touch through stimulating the brain. Now, with the support of two NIH grants, the researchers are furthering their work. A **$7 million** Brain Initiative grant, led by **Michael Boninger, MD**, Research Professor of Physical Medicine and Rehabilitation, will expand Pitt and UPMC's BCI trial to include additional participants at Pitt and a second site at the University of Chicago. The goal is to advance restoration of hand function via the BCI. **Jennifer Collinger, PhD**, assistant professor of physical medicine and rehabilitation, is leading a **$1.2 million** Brain Initiative grant to study how the environment and context surrounding a task affect motor plans and sensory perception.

PRECISION MEDICINE

Helping researchers and clinicians uncover specific treatments and disease risks applicable to the individual patient has been the goal of the Institute for Precision Medicine at the University of Pittsburgh and UPMC. At the institute, which is directed by **Adrian Lee, PhD**, Pittsburgh Foundation Professor of Precision Medicine, a three-year **$2.8 million** grant from the Richard King Mellon Foundation will support three major initiatives: rapid genome sequencing for critically ill infants to improve efforts to quickly diagnose genetic errors and reduce infant mortality, genomics education for health care providers and front-line health care practitioners, and translating precision medicine findings to the market while advancing intellectual property protection, licensing, and new company creation.

TRANSFORMATIVE RESEARCH

Only nine researchers nationally received a five-year **$6 million** NIH Director's Transformative Research Award. Among them is **Peter Strick, PhD**, Distinguished Professor and chair of neurobiology and Thomas Detre Professor of Neuroscience. The award supports work that challenges fundamental paradigms. For Strick, it will help him advance a project aimed at establishing a structural framework for the brain-body connection, which explores how neural pathways enable specific areas of the brain to influence function of the heart, digestive system, and organs underlying immune function.

BREAST CANCER RESEARCH SUPPORT

Investigating breast cancer, everything from detection to treatment, is at the forefront of Pitt and UPMC Hillman Cancer Center research. Recently, four researchers received grants totaling nearly **$1 million** from the Breast Cancer Research Foundation as part of the foundation's $63 million investment to support the spectrum of breast cancer research at top academic and medical institutions worldwide. The recipients are: **Wendie Berg, MD, PhD**, professor of radiology, who seeks to improve breast cancer detection by using artificial intelligence to screen ultrasounds from women with dense breasts and using contrast-enhanced mammography in women with a history of breast cancer; **Leisha Emens, MD, PhD**, professor of medicine in the Division of Hematology/Oncology, who is advancing highly effective combination immunotherapies for breast cancer patients; **Adrian Lee, PhD**, Pittsburgh Foundation Professor of Precision Medicine, who is studying the insulin-like growth factor pathway in E-cadherin-deficient breast cancers; and **Steffi Oesterreich, PhD**, professor of pharmacology and chemical biology, who is investigating the unique features of invasive lobular breast cancer, the second-most common histological subtype of breast cancer.

MANAGING HIV PATIENTS' CHRONIC PAIN

HIV patients have very few chronic pain treatments that have been tailored to them, says **Jessica Merlin, MD, PhD, MBA**, associate professor of medicine in the Division of General Internal Medicine and of Infectious Diseases. To study HIV patients' use of behavioral therapy, as opposed to opioids, to manage chronic pain, principal investigator Merlin has received a National Institute of Mental Health grant providing more than **$3 million**. The funding will support the first full-scale behavioral therapy trial for HIV patients with chronic pain.

TARGETING OVARIAN CANCER

Developing an ovarian cancer treatment that blocks cellular interactions that promote cancer cells' growth and metastasis is the goal of the first grant received from the Mary Kay Foundation to UPMC Hillman Cancer Center. The **$100,000** grant, which supports research to better understand cancers that affect women, will advance research led by **Lan Coffman, MD, PhD**, assistant professor of medicine in the Division of Hematology/Oncology.

Publications of Note

SCIENCE TRANSLATIONAL MEDICINE

GENE MAY AFFECT ALL PARKINSON'S PATIENTS REGARDLESS OF MUTATION

JUL 2018 \ VOL 10 \ ISSUE 451

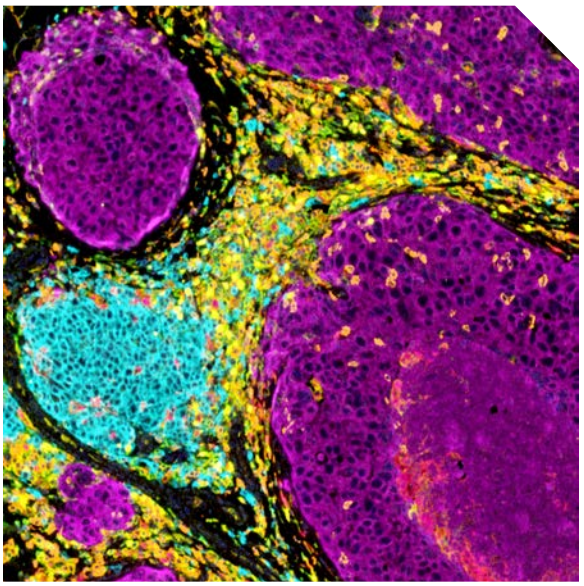
Mutations in the LRRK2 gene overactivate the LRRK2 protein, causing Parkinson's disease in 3 to 4% of affected patients. The gene was thought to cause Parkinson's disease only when mutated; but after researchers probed postmortem brain tissue from Parkinson's patients without LRRK2 mutations, they found that LRRK2 protein was highly active in the brain's dopamine neurons, indicating that LRRK2 overactivity may play a role in most or all people with Parkinson's disease regardless of mutation presence. The research team also found that the LRRK2 activation blocked cellular mechanisms that clear excess alpha-synuclein protein, which accumulates and forms Lewy bodies, indicators of Parkinson's. Further, a Parkinson's drug under development that blocks LRRK2 activity successfully prevented alpha-synuclein protein accumulation and Lewy-body formation in a rodent model. The findings suggest that therapies targeting a small group of people could benefit all Parkinson's patients, says senior author **J. Timothy Greenamyre, MD, PhD**, Love Family Professor of Neurology, and director of the Pittsburgh Institute for Neurodegenerative Diseases.

GUT

GENETIC TEST ACCURATELY SCREENS FOR PANCREATIC CANCER PRECURSOR

DEC 2018 \ VOL 67 \ ISSUE 12

PancreaSeq®, a UPMC-developed genetic test, screens pancreatic cyst fluid for 10 tumor genes associated with pancreatic cancer and can evaluate cysts before surgery instead of, as is standard, after surgery. During a clinical analysis, PancreaSeq was applied to 595 patients with pancreatic cysts. Of this group, 102 patients underwent surgical removal of their cysts (after the test and other determinants indicated tumor gene presence). Following post-surgical analysis of the removed cysts, PancreaSeq 100% correctly classified every patient with intraductal papillary mucinous neoplasm (IPMN), a pancreatic cancer precursor, based on mutations in the *KRAS* and *GNAS* genes. The test also analyzed mutations in three additional genes to accurately identify cysts that would become cancerous. A version of PancreaSeq that tests for additional tumor genes is being developed, says lead author **Aatur D. Singhi, MD, PhD**, assistant professor of pathology, and clinical guidelines may need to be revisited to explore incorporating tests like PancreaSeq.



NATURE IMMUNOLOGY

TUMOR-INDUCED CYTOKINES WORK TOGETHER TO SUPPRESS THE IMMUNE SYSTEM

JUN 2019 \ VOL 20 \ ISSUE 6

In the hunt for cancer cures, researchers have long targeted certain mechanisms that enable tumors to slip past the body's defenses — but maybe they've been focusing on the wrong targets. In the tumor microenvironment, regulatory T cells (Tregs), which normally help keep the immune system balanced, can release the inhibitory cytokines interleukin-10 (IL-10) and interleukin-35 (IL-35) to disable cancer-killing killer T cells, helping a tumor evade the body's immune defenses. Researchers at Pitt and the UPMC Hillman Cancer Center, including senior author **Dario A.A. Vignali, PhD**, Frank Dixon Professor of Cancer Immunology and professor of immunology, found that populations of Tregs could either make IL-10 or IL-35 but, surprisingly, not both at the same time. A cancer mouse model showed that tumors need Treg cells that can secrete both IL-10 and IL-35 to effectively suppress the immune system. Further investigation revealed that IL-10 and IL-35 together activate the transcription factor BLIMP1 that makes killer T cells express many types of inhibitory proteins, impeding the killer T cells from attacking cancer. Since many immunotherapies target just one or two inhibitory proteins, developing drugs that block IL-10 or IL-35 could lead to more widely applicable and effective therapies.

Populations of Tregs could either make IL-10 or IL-35 but, surprisingly, not both at the same time.

SCIENCE

GENOME 'DARK MATTER' MAY HOLD CLUES TO AUTISM AND OTHER DISORDERS

DEC 2018 \ VOL 362 \ ISSUE 6420

Dozens of the genes associated with autism spectrum disorder, most of them linked to protein-coding genes, have been identified. But by studying *de novo* mutations, newly arising changes to the genome found in children but not their parents, researchers are beginning to explore how these noncoding DNA sequences (the genome's so called "dark matter"), may contribute to the onset of psychiatric diseases like autism, bipolar disorder, and schizophrenia. Recently, a research team with members from Pitt — including **Bernie Devlin, PhD**, professor of psychiatry — Carnegie Mellon University, the University of California, San Francisco, the Broad Institute, and other institutions, identified tens of thousands of rare mutations that may influence autism onset.

The study is one of 13 released in the first round of results to emerge from the National Institute of Mental Health's PsychENCODE Consortium — a nationwide research effort that seeks to decipher how noncoding DNA contributes to psychiatric diseases. "We were particularly interested in the elements of the genome that regulate when, where, and to what degree genes are transcribed. Understanding this noncoding sequence could provide insights into a variety of human disorders," said Devlin.

The study used whole-genome sequencing to analyze data from nearly 2,000 families with an autistic child, and the researchers narrowed billions of nucleotides down to tens of thousands of functional categories for further study. Using machine learning, the research team then created statistical models to predict autism risk from a subset of families in the study. Applying this model to an independent set of families successfully predicted at-risk gene patterns in the noncoding genome. The technique and findings may advance genetically informed autism therapies and research on the variety of human disorders influenced by noncoding DNA.

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

PHENOTYPES FOR SEPSIS COULD HELP TAILOR TREATMENTS

MAY 2019 \ VOL 321 \ ISSUE 20

Pitt School of Medicine researchers revealed that, much like cancer, there are subtypes of sepsis, a potentially life-threatening condition. The study, led by **Christopher Seymour, MD, MSc**, associate professor of critical care medicine, included researchers from Pitt, Carnegie Mellon University, the University of Amsterdam, and other institutions. They identified sepsis as having four distinct phenotypes, which could help tailor therapies, as opposed to using one-size-fits-all treatments. Seymour and his colleagues used algorithms to analyze clinical variables in electronic health records of more than 20,000 septic UPMC patients. Alpha sepsis patients have the fewest abnormal laboratory test results and the least organ dysfunction. Beta patients are older, with the most chronic illnesses and kidney dysfunction. Gamma patients have elevated inflammation and pulmonary dysfunction. Delta patients, the most deadly subtype, often have liver dysfunction and shock. From these findings, the next step is to test therapies aimed at the specific types of sepsis.

SCIENCE

MARINE MAMMALS LACK GENE PRODUCT THAT PROTECTS AGAINST COMMON PESTICIDE COMPOUNDS

AUG 2018 \ VOL 361 \ ISSUE 6402

In humans and other terrestrial mammals, the gene *Paraoxonase 1 (PON1)* produces a protein that protects against oxidative damage in the bloodstream and also against organophosphates, compounds that make up common, neurotoxic pesticides. Marine mammals, however, lost the ability to generate the protective protein through the course of evolution, potentially putting them at risk from pesticide exposure. Former associate professor of computational and systems biology **Nathan Clark, PhD** (now at the University of Utah), and postdoctoral researcher **Wynn K. Meyer, PhD,** serendipitously came across the *PON1* gene while exploring genetic divergences in land and sea mammals. After analyzing DNA sequences from five species of marine mammals and 53 species of terrestrial mammals, the researchers found that *PON1* was always found intact in terrestrial mammals but was degraded in most marine mammals. Researchers are still investigating why marine mammals lost *PON1* function. The implications could support studies into how agricultural pesticide runoff can harm marine mammals and how *PON1* protects against heart disease in humans.

Marine mammals lost the ability to generate the protective protein through the course of evolution, potentially putting them at risk from pesticide exposure.

NEURON

TDP-43 PROTEIN CLUMPS TARGETED TO COMBAT NEURODEGENERATIVE DISEASES

APR 2019 \ VOL 102 \ ISSUE 2

Targeting genes that cause neurodegenerative disorders — such as ALS and Alzheimer's — has been the elusive goal of numerous studies. But **Christopher Donnelly, PhD**, assistant professor of neurobiology, and colleagues have taken aim at the proteins that clump together in nearly all such disorders, potentially opening up new therapy avenues. The protein TDP-43 forms toxic clumps that can cause neurodegeneration and is found in most cases of neurodegenerative diseases. Pitt researchers found that applying an oligonucleotide — a short strand of RNA — mimics the cell's natural protective mechanisms and prevents TDP-43 accumulation *in vitro*. After using optogenetics to genetically engineer the TDP-43 protein to clump when illuminated with blue light, the investigators found that the TDP-43 could form damaging clumps only when its RNA binding partners were missing. They then created TDP-43-targeting oligonucleotides that mimic the action of the RNA binding partners, which, when applied, successfully prevented protein clumping. Using this oligo treatment that protected against toxicity due to the TDP-43 clumping could lead to new therapies.

NEW ENGLAND JOURNAL OF MEDICINE

GIVING PLASMA TO TRAUMA INJURY PATIENTS INCREASES SURVIVAL ODDS

JUL 2018 \ VOL 379 \ ISSUE 4

Giving two units of plasma to traumatically injured patients with severe bleeding can increase survival odds by 10%, according to findings from the Prehospital Air Medical Plasma (PAMPer) trial. The national phase III randomized trial, led by Pitt's School of Medicine, involved 501 trauma patients who either received plasma while being transported aboard medical helicopters or received standard care. After 30 days, 76.8% of the patients who received plasma were still alive, compared to 67% of those who received standard care. The plasma patients' blood clotted faster, and they had less need for blood transfusions than the patients who did not receive prehospital plasma. The findings emphasize the importance of prehospital care as a vital component of patient transportation to the hospital, says colead author **Jason Sperry, MD, MPH**, professor of surgery.

JAMA INTERNAL MEDICINE

SEXUAL HARASSMENT AND SEXUAL ASSAULT NEGATIVELY AFFECT WOMEN'S PHYSICAL AND MENTAL HEALTH

JAN 2019 \ VOL 179 \ ISSUE 1

Previous studies have linked sexual harassment and sexual assault of women to poorer health outcomes but were limited by their reliance on self-reported health information — which could be affected by memory, mood, and health literacy — and lack of full consideration of the potential confounding effects of socioeconomic status and medication use. In a recent study involving 304 women between 40 and 60, **Rebecca Thurston, PhD**, professor of psychiatry, analyzed their history of sexual assault or workplace sexual harassment and physical and mental health parameters such as blood pressure, sleep, mood, and anxiety. Approximately one in five of the women reported being either sexually harassed or assaulted. The study found that assaulted women were almost three times more likely to have symptoms of major depression and more than twice as likely to have elevated anxiety. Sexual harassment was also associated with double the likelihood of hypertension, and both harassment and assault were associated with double the likelihood of poor sleep consistent with clinical insomnia. These effects on physical and mental health held true even when demographics, socioeconomic status, medication use, and medical history were taken into account.

JAMA CARDIOLOGY

BLACK PATIENTS ARE LESS LIKELY TO RECEIVE ORAL ANTICOAGULANT DRUGS

DEC 2018 \ VOL 3 \ ISSUE 12

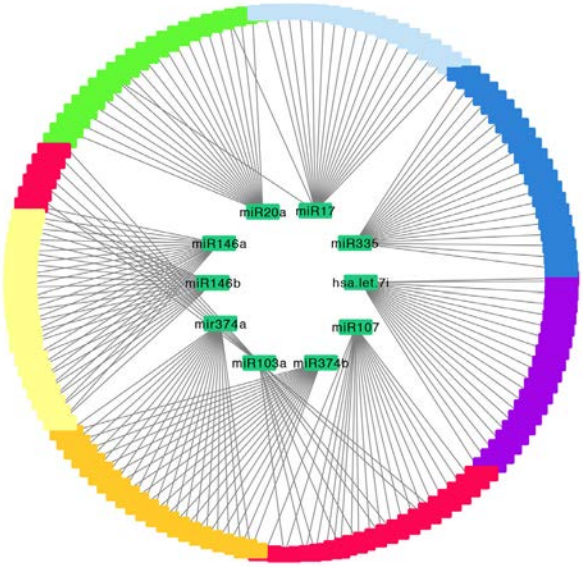
Addressing social determinants and reducing disparities could improve outlooks for African American atrial fibrillation patients, according to research by **Utibe R. Essien, MD, MPH**, assistant professor in the Department of Medicine's Division of General Internal Medicine, and colleagues. They found that black patients with atrial fibrillation had 25% lower odds of receiving oral anticoagulant drugs, which reduce risk of stroke, compared to their white and Hispanic counterparts. The results were based on data from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation II involving 11,100 white patients, 646 black patients, and 671 Hispanic patients from February 2013 through June 2016. The results, which controlled for clinical and sociodemographic factors, also showed that black patients had 27% lower odds of receiving the easier-to-use, safer, and more effective direct-acting oral anticoagulants. Factors like limited access to specialists, costs, medication adherence, and implicit bias could explain the disparities, but further research is needed.

BIOLOGICAL PSYCHIATRY

MECHANISMS OF CIRCADIAN PROTEIN AND BIPOLAR DISORDER EXPLORED

DEC 2018 \ VOL 84 \ ISSUE 11

To investigate the possible effect of circadian rhythm disruption on bipolar disorder risk, researchers looked at the protein CLOCK (circadian locomotor output cycles kaput) and its regulation of neurotransmitter monoaminergic systems and mood-related behavior. The team, led by **Colleen A. McClung, PhD**, professor of psychiatry, used a form of electrophysiology coupled with molecular techniques to find that *Clock*Δ19 mutant mice, compared to wild-type mice, had reduced excitatory synaptic responses within nucleus accumbens (NAc) medium spiny neurons. The mice, which modeled bipolar mania, also exuded decreased NAc surface protein levels and glutamate receptor 1 (GluR1) rhythms, which is consistent with reduced synaptic response. *Clock*Δ19 mice's medium spiny neurons exhibited a hyperpolarized resting membrane potential, which indicates lowered intrinsic excitability. Restoration of GluR1 in the NAc reversed the mice's manic-like behavior, suggesting that these changes in excitability represent a mechanistic connection between disrupted circadian rhythms and bipolar disorder.



BMC MEDICAL GENOMICS

NEW DEEP LEARNING MODEL BETTER REVEALS mRNA TARGETS

DEC 2018

Harnessing genetic data has enabled numerous insights into physiological processes and disease development — and has led to better tools for making these discoveries. While micro-RNAs (miRNAs) are key to gene expression regulation in health and disease states, using data-driven techniques to reveal the target messenger RNAs of miRNAs remains challenging, with sequence-based methods producing too many false positives and expression correlation analysis failing to demonstrate causality. Pitt researchers **Lujia Chen, PhD**, postdoctoral associate in the Department of Biomedical Informatics, and **Xinghua Lu, MD, PhD, MS**, professor of biomedical informatics, designed the miRNA causal deep net (mCADET) deep learning model to analyze and simulate transcription mechanisms underlying the co-expression of miRNA and mRNA. The model uses a deep neural network to uncover statistical relationships. Analysis of the model's results indicated that, when combining miRNA and mRNA expression data, mCADET can better capture high-order statistical structures in the data compared to conventional deep learning. mCADET also demonstrated better accuracy and a lower false-discovery rate compared to sequence-based and correlation-based methods.

The model uses a deep neural network to uncover statistical relationships.

JOURNAL OF INFECTIOUS DISEASES

SECRETIONS PROTECT AIRBORNE FLU VIRUS FROM HUMIDITY DEGRADATION

SEP 2018 \ VOL 218 \ ISSUE 5

The winter months tend to keep people indoors, enabling increased person-to-person spread of influenza amid the dry air of heated indoor spaces. Previous studies have demonstrated that moderate to high humidity degrades and inactivates aerosolized flu virus, fueling the belief that flu season's dry winter air protected the virus. However, researchers, including **Seema Lakdawala, PhD**, assistant professor of microbiology and molecular genetics and a researcher with Pitt's Center for Vaccine Research, have shown that mucus and other secretions expelled by coughing, talking, or exhaling appear to protect the airborne virus, keeping it intact regardless of humidity.

To mimic real-world conditions, the research team, which also included members from Virginia Tech University's Department of Civil and Environmental Engineering, combined samples of human airway secretions with the 2009 pandemic H1N1 flu strain in a rotating metal drum that suspends aerosols and maintains constant relative humidity. The device replicated real-world conditions to evaluate how long the influenza virus could be expected to survive in an indoor setting in a variety of humidity levels after being expelled via aerosols and droplets.

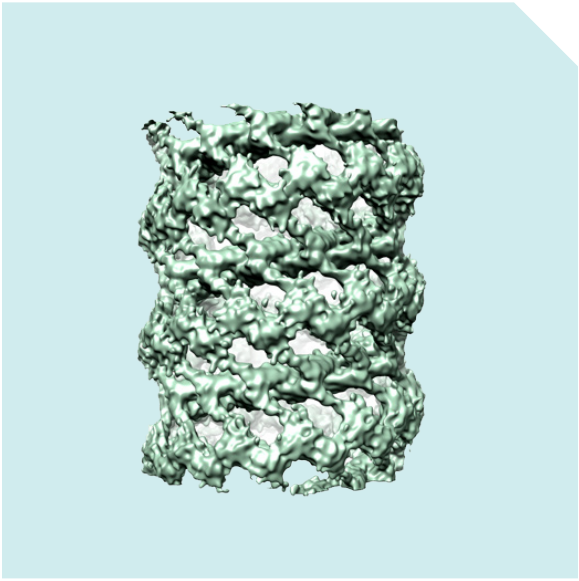
The team ran the drum for an hour, a typical length of time that air stays in homes and other buildings before moving outside. The virus remained equally infectious at all seven humidity levels tested; it did not fare better or worse at low humidity. The sustained infectivity was observed in both aerosols and in stationary droplets harboring the virus. "Our findings highlight the importance of mimicking real-world conditions when determining the infectivity of emerging viruses," Lakdawala says. While future research may involve testing other flu strains and pathogens to see whether they are also protected by airway secretions when airborne, the study's findings can inform public health efforts to impede the spread of flu virus and other infectious agents.

JOURNAL OF MEDICAL INTERNET RESEARCH

ANIMATIONS COULD HELP PATIENTS BETTER COMMUNICATE, DESCRIBE PAIN

AUG 2018 \ VOL 20 \ ISSUE 8

Patients' available methods to communicate pain involve using a 0–10 scale or selection of words and phrases to describe the pain. But many patients say that their pain cannot be measured on a 0–10 scale or easily described. The novel electronic assessment tool "Painimation" uses animations to assess patients' pain quality, type, and location. When a multidisciplinary team of psychiatrists, anesthesiologists, and developers issued Painimation to 202 patients with chronic pain, the patients used the mobile app alongside the standard questionnaires to characterize and relay their pain. More than 80% of the patients found the app to be beneficial, and the patients completed the Painimation assessment more quickly than the questionnaires. Lead author **Charles Jonassaint, PhD, MHSc**, assistant professor of medicine in the Division of General Internal Medicine, says that Painimation could allow patients to more accurately relay pain to medical care providers and could minimize barriers posed by language and literacy when relaying pain.



JOURNAL OF CELL BIOLOGY

RESEARCHERS SHED LIGHT ON PROTEINS KEY TO CELLULAR TRAFFICKING

OCT 2018 \ VOL 217 \ ISSUE 10

While proteins carry out key physiological processes, they're also prone to alteration that can exacerbate disease development and aging. Dynamin-related proteins (DRPs) are central to cellular functions like endocytosis, intracellular trafficking, and energy homeostasis, and, when mutated, are associated with aging and several human diseases. While DRPs self-assemble into helical structures to carry out their roles, Pitt researchers have studied how they adapt their shape for specific cellular functions and targets. The researchers, including **Marijn Ford, PhD**, assistant professor of cell biology, and **Peijun Zhang, PhD**, former associate professor of structural biology (now at the University of Oxford), demonstrated that Vps1, a fungal DRP, primarily localizes to and functions in the endosomal compartment within cells. Using cryogenic electron microscopy, the researchers determined the structure of Vps1 and found that its helix is broader and more flexible than the helix of dynamin, an enzyme critical to endocytosis and other processes. The researchers also observed a novel interface, which forms during Vps1 helical assembly, that, when disrupted, abolishes Vps1 function *in vivo*. These findings and observations shed light on how DRPs influence cellular membrane fission and fusion events critical to many physiological processes.

While DRPs self-assemble into helical structures... Pitt researchers have studied how they adapt their shape for specific cellular functions and targets.

NEW ENGLAND JOURNAL OF MEDICINE

COMBINING IMMUNOTHERAPY WITH CHEMOTHERAPY CAN BENEFIT WOMEN WITH TRIPLE-NEGATIVE BREAST CANCER

NOV 2018 \ VOL 379 \ ISSUE 22

Adding the checkpoint inhibitor immunotherapy drug atezolizumab to chemotherapy treatment improved the outcomes of women with metastatic or locally advanced triple-negative breast cancer, an aggressive form of breast cancer — which was demonstrated by a phase III clinical trial led by senior trial investigator **Leisha Emens, MD, PhD**, professor of medicine in the Division of Hematology/Oncology and a UPMC Hillman Cancer Center researcher. Atezolizumab targets the PD-L1 protein, which inhibits immune cells from combatting tumors. Nine hundred two patients who enrolled at 246 sites in 41 countries received either atezolizumab or placebo with a chemotherapy drug. Patients receiving atezolizumab and chemotherapy experienced no tumor progression for 7.2 months on average compared to 5.5 months with chemotherapy alone. Overall survival was 21.3 months in the combination group compared to 17.6 months in the chemotherapy-alone group. Patients whose tumors expressed PD-L1 survived an average of 25 months in comparison to 15.5 months for patients treated only with chemotherapy. Based on these trial results, atezolizumab combined with chemotherapy received accelerated approval for treating advanced triple-negative breast cancer in March 2019.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

CANCER-CAUSING VIRUSES EXPRESS MULTIPLE CIRCULAR RNAS

SEP 2018 \ VOL 115 \ ISSUE 37

Using RNase R-resistant RNA sequencing, Pitt researchers found that Epstein–Barr virus (EBV) and Kaposi's sarcoma herpesvirus (KSHV), which together cause approximately 2% of all human cancers, express multiple circular RNAs (circRNA), which perform critical physiological functions. After studying EBV and KSHV tumors and cell lines, the research team, including **Yuan Chang, MD**, Distinguished Professor of Pathology and UPMC Professor of Cancer Virology Research, and **Patrick S. Moore, MD, MPH**, Distinguished Professor of Microbiology and Molecular Genetics and Pittsburgh Foundation Professor of Innovative Cancer Research, found specific circRNAs expressed from both viruses. All evaluated EBV tumor latency forms expressed circular BamHI A rightward transcripts, or circBARTs, a family of mRNAs. Other circular RNAs, such as circBHLF1 and circLMP2, were more variably expressed. Primary effusion lymphoma cell lines of KSHV— which model a malignant B-cell lymphoma that forms no tumor mass — expressed circvIRF4, while the polyadenylated nuclear locus promiscuously generated variable, inducible, and bidirectional circRNAs. These newly identified circRNAs can be long lived, unique tumor biomarkers that, with further study, could shed light on how certain viruses cause cancer.

NATURE COMMUNICATIONS

KLOTHO IMPROVES SKELETAL MUSCLE HEALING IN OLD MICE

NOV 2018

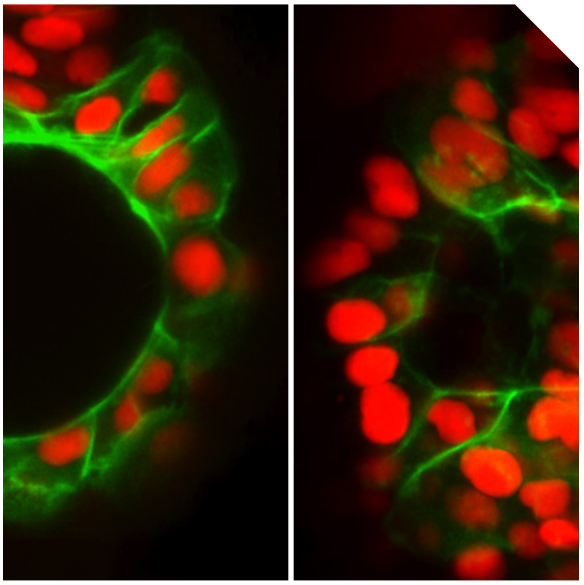
In young mice, Klotho expression soars after muscle injury; but in old mice, expression of Klotho, the so-called "longevity protein," remains flat. In a study of skeletal muscle healing, Pitt researchers targeted mitochondrial dysfunction — which is linked to Klotho expression — to restore aged skeletal muscle's regenerative abilities. The researchers, including lead author **Fabrisia Ambrosio, PhD**, associate professor of physical medicine and rehabilitation and a researcher with the McGowan Institute for Regenerative Medicine, gave Klotho-deficient animals the mitochondria-targeting drug SS-31, resulting in more muscle tissue growth at the injury site and strength restored to normal levels. The team also injected Klotho into older animals a few days after injury, which led to greater muscle mass and improved functional recovery. These results could translate to eventually help older adults recover after a muscle injury or damaging surgery. The timing, dosage, and treatment administration will first require further research, Ambrosio says.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

TARGETING NEURITE MITOCHONDRIAL PROTEINS MIGHT CURB HUNTINGTON'S EFFECTS

JAN 2019 \ VOL 116 \ ISSUE 2

Using lab-grown nerve cells, researchers at Pitt observed that when mitochondrial proteins at the ends of neurites (connective, finger-like projections from neuronal cells) degrade with wear and tear, newer proteins do not quickly replace them, unlike with mitochondria near the nucleus. This delay in replacement inhibits optimal functioning, prompting the "executioner" enzyme caspases to kill the degraded neurites. The researchers, including senior author **Robert M. Friedlander, MD, MA**, Walter E. Dandy Professor and chair of neurological surgery, dubbed this process "neuritosis." Because neurodegenerative diseases stress already vulnerable neurite ends, neuritosis may exacerbate cell death associated with these diseases, researchers believed. Knowing that mutations in the protein huntingtin — linked to Huntington's disease — also interfere with the protein replacement process in neuritosis, the researchers studied mice with mutated huntingtin proteins. The mice exhibited symptoms of Huntington's and had more pronounced effects of neuritosis, such as fewer and more dysfunctional mitochondria at neurite ends and increased cell death. Finding a way to keep mitochondria at nerve ends healthy might impede Huntington's and other neurodegenerative diseases, Friedlander says.



NATURE COMMUNICATIONS

INVESTIGATING THE GENETIC AND MECHANISTIC PROPERTIES BEHIND LEFT-RIGHT PATTERNING IN VERTEBRATE ORGAN DEVELOPMENT

AUG 2018

Just as young children must learn their left from their right, so too must young cells. During an organism's development, biological cues inform the proper arrangement of internal organs and the establishment of left-right asymmetry. In zebrafish, Pitt researchers, including the Department of Developmental Biology's **Cecilia Lo, PhD**, Distinguished Professor and F. Sargent Cheever Professor and chair, and **Michael Tsang, PhD,** associate professor, found that *myosin 1d (myo1d)*, a gene that is important for cell motility and cellular trafficking, is essential for establishing left-right asymmetry. Studying the zebrafish Kupffer's vesicle (KV), a fluid-filled ciliated organ, the researchers found that without *myo1d*, the KV fails to form a spherical lumen, preventing proper unidirectional flow. This disrupts the organism's assignment of left-right polarity. The team further identified an evolutionary conserved role for the protein myosin1C, derived from an ancient eukaryote *Acanthamoeba castellanii*, which can substitute for *myo1d* and its vacuole-trafficking roles. These findings shed light on mechanisms critical to left-right patterning in vertebrate organ development.

***Myosin 1d (myo1d)*, a gene that is important for cell motility and cellular trafficking, is essential for establishing left-right asymmetry.**

NATURE COMMUNICATIONS

HARNESSING A SYSTEMS BIOLOGY APPROACH TO DRUG DEVELOPMENT

FEB 2019

Drug development strategies often target specific single molecules or mechanisms *in vitro* without accounting for connectivity and other factors within a cell's signal transduction network. But a network-centric systems biology approach to drug discovery that simultaneously targets protein interactions in the context of disease-associated pathways and networks could be more effective for drug development and pharmacologic intervention in cellular signaling, researchers suggest. By combining cellular transcriptomes, structural, and live-cell dynamics analysis, Pitt Department of Computational and Systems Biology investigators, including **Carlos Camacho, PhD**, associate professor, and **Robin E.C. Lee, PhD**, assistant professor, harnessed a systems biology approach to uncovering new techniques for inhibiting the NF-kB protein complex, which is linked to inflammation and to cancer development when deregulated. The team identified two first-in-class small molecules that can prevent activation of the IKK complex, a central regulator of NF-kB activation.

JAMA PEDIATRICS

HOLDING POSITIVE OUTLOOKS ON THE FUTURE MAY PROTECT ADOLESCENTS FROM VIOLENCE

SEP 2018 \ VOL 172 \ ISSUE 9

Teens who have positive outlooks on their futures are more likely to be engaged in school and less likely to use drugs. According to new research, they're also less likely to report threatening or using a weapon against someone, indicating that a "positive future orientation" may protect adolescents from violence. Pitt and UPMC Children's Hospital of Pittsburgh researchers studied 866 teenage boys, ages 13 to 19, in under-resourced Pittsburgh neighborhoods. The teens were asked seven questions to gauge their thoughts about their futures. The researchers then examined how their answers and future orientations related to violence perpetration and actions like fighting or using a weapon. Adolescents with positive outlooks were less likely to report having threatened or injured someone with a weapon during the past nine months at the time of evaluation. Efforts to help adolescents develop positive outlooks on the future may play an important role in violence prevention, says lead author **Alison Culyba, MD, PhD, MPH**, assistant professor of pediatrics.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

BOLSTERING NEURON REPAIR COULD BE KEY TO BETTER RECOVERY AFTER STROKE

MAR 2019 \ VOL 116 \ ISSUE 10

In addition to using therapies to limit the extent of brain damage after a stroke, some Pitt researchers hope to improve nerve cell repair after stroke damage. In the brain, the enzyme UCHL1 helps to remove abnormal proteins. After a stroke, cyclopentenone prostaglandins (CyPgs), fatty acid molecules released in nerve cells, can bind to and impede UCHL1. In a mouse model with the UCHL1 gene made resistant to CyPgs, and after surgically modeling the effects of a stroke in these mice, the animals experienced decreased injury to their neurons' axons, which carry electrical signals, compared to mice with regular UCHL1 genes. In the modified mice with unimpaired UCHL1, the enzyme helped to preserve brain tissue and neuron function by activating cell-repair mechanisms that clean up damaged proteins. The study revealed that UCHL1 is essential to preserving axonal function and to decreasing white matter injury, which are both key to improved stroke recovery, says co-senior author **Steven H. Graham, MD, PhD**, Connolly Family Professor in the Stroke Institute and professor of neurology.

CELL REPORTS

ERASING MEMORY CUES COULD HELP PREVENT ADDICTION RELAPSE

JAN 2019 \ VOL 26 \ ISSUE 4

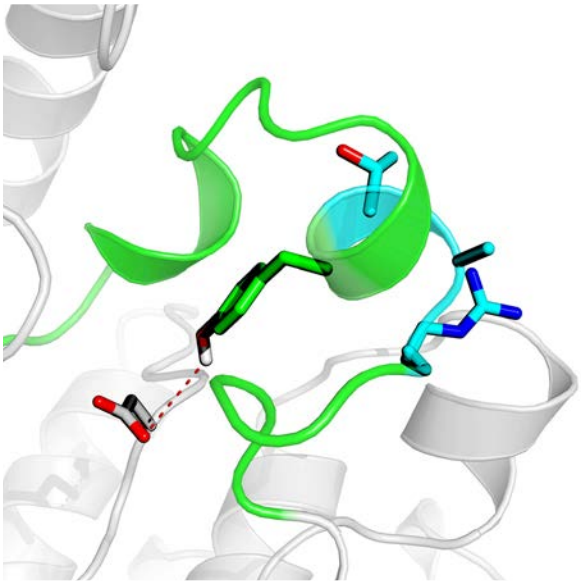
In a study on relapse and addiction, rats pressed a lever and subsequently received a bit of cocaine accompanied by a tone and light, cues that the animals learned to associate with the cocaine high. The study's researchers, including associate professor of psychiatry **Mary Torregrossa, PhD**, then repeatedly triggered the tone and light cues without providing the cocaine, eventually reducing the rats' drug-seeking behavior — demonstrating "exposure therapy." But shifting the rats to a different environment nullified this reduction. Humans mirror this phenomenon, which can explain why gains made in therapy falter after exposure to stimulating cues outside of a controlled environment. Using optogenetics, which uses light to control genetically modified neurons, the scientists erased the rats' cocaine-cue memories. As a result, the rats pressed the lever significantly fewer times after detecting the light and tone cues. This result remained even after the rats were moved to a different environment, suggesting that erasing cue-associated memories can overcome the challenges posed by a new environment and enhance exposure therapy to help prevent relapse.

PEDIATRICS

CHILDREN MORE COMMONLY PRESCRIBED ANTIBIOTICS DURING TELEMEDICINE VISITS

MAY 2019 \ VOL 143 \ ISSUE 5

Children were more commonly prescribed antibiotics for acute respiratory infections during direct-to-consumer telemedicine visits than during in-person primary care appointments, according to a health plan database analysis. This practice could add to the use of unnecessary antibiotics, which may cause side effects and bolster antibiotic resistance. Pitt and UPMC Children's Hospital of Pittsburgh researchers analyzed a national health plan database that covers more than 4 million U.S. children annually and found that children were prescribed antibiotics during 52% of direct-to-consumer telemedicine visits compared to 42% during urgent care visits and 31% during primary care provider visits. Antibiotics prescribed during telemedicine visits were less likely to be consistent with clinical guidelines. According to lead author **Kristin Ray, MD, MS**, assistant professor of pediatrics, an analysis of adult patients who used telemedicine visits did not show such differences in antibiotic prescribing rates, indicating the need for pediatric-specific attention to health care innovations and delivery.



SCIENCE SIGNALING

EXPLORING FGR'S ROLE IN ACUTE MYELOID LEUKEMIA AND OTHER BLOOD CANCERS

OCT 2018 \ VOL 11 \ ISSUE 553

Pitt researchers have uncovered a finding that could be key to understanding the rise of cancerous cells in certain blood cancers. The investigators, including first author **Kexin Shen**, a visiting Tsinghua University scholar, and **Thomas Smithgall, PhD**, William S. McEllroy Professor of Biochemistry and chair of microbiology and molecular genetics, investigated the oncogenic potential of Fgr, a Src family nonreceptor tyrosine kinase linked to acute myeloid leukemia (AML). Using Rat-2 fibroblast cells that do not express Fgr, they found that, *in vitro*, the kinase domain of Fgr functions independently of regulation by its noncatalytic SH3-SH2 region and that the activation loop of Fgr was distinct from that of all other Src family members. Because Src family kinase activity has been thought to be controlled by intramolecular interactions involving the SH3 and SH2 domains, the finding that Fgr's kinase domain is not governed by SH3-SH2 control indicates that overexpression of Fgr without mutation may contribute to the rise of cancerous cells in AML and other blood cancers.

The kinase domain of Fgr functions independently of regulation by its noncatalytic SH3-SH2 region and…the activation loop of Fgr was distinct from that of all other Src family members.

CELL METABOLISM

TARGETING mTOR PROTEIN TO ADVANCE LIVER CANCER TREATMENT

MAY 2019 \ VOL 29 \ ISSUE 5

Rapamycin, a common anti-rejection transplant medication, may be useful for treating certain liver cancers. Patients with liver cancers with mutations of the *beta-catenin* gene contain high levels of active mTOR protein, Pitt scientists observed. So, they created a liver cancer mouse model with mutations in both *beta-catenin* genes and in another gene called *Met*. The research team, which included **Satdarshan (Paul) S. Monga, MD**, Professor of Experimental Pathology, found that the intermediate enzyme glutamine synthase (GS), involved with the cancer cells' energy intake, prompted *beta-catenin* to activate mTOR. Fast-growing cancer cells, which consume abundant energy, showed high GS and mTOR activity. Since mTOR activation accelerates production of proteins that help cancer cells divide and grow, giving rapamycin — which inhibits mTOR — to the mutated mice decreased the size of their tumors. Further, adding a drug that targeted *Met* almost completely killed the tumors. These findings could advance precision treatment for the approximately 20–35% of liver cancer patients with *beta-catenin* gene mutations and for liver transplant patients hoping to stem cancer recurrence.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

NUCLEAR LAMINA MADE UP OF TWO DISTINCT MESHWORK LAYERS

MAR 2019 \ VOL 116 \ ISSUE 10

The nuclear lamina scaffolding encasing a cell's nucleus is formed by a meshwork of filaments made up of lamin A and B proteins. Using the super-resolution imaging technique "stochastic optical reconstruction microscopy" (STORM), research led by investigators from Pitt's School of Medicine, Graduate School of Public Health, and from Carnegie Mellon University found that cells actually contain two distinct lamin meshworks — a more loosely woven outer layer of lamin B and a tighter inner layer of lamin A. The team observed that, under pressure, the outer layer thins, allowing the inner layer to bulge out at the axes of the nucleus. This enables compression to relieve pressure on the nucleus when moving through a very thin blood vessel, for example. The senior authors, including **Yang Liu, PhD**, associate professor of medicine in the Division of Gastroenterology, Hepatology, and Nutrition and of bioengineering, and **Quasar Padiath, MBBS, PhD**, associate professor of human genetics, Pitt Public Health, and of neurobiology, believe that the findings could be key to understanding several genetic diseases, like autosomal dominant leukodystrophy with autonomic disease (ADLD), affecting the lamina.

JAMA PSYCHIATRY

NEW PREDICTION RISK SCORE IMPROVES ACCURACY OF PREDICTING SUICIDAL BEHAVIOR

JUN 2019 \ VOL 76 \ ISSUE 6

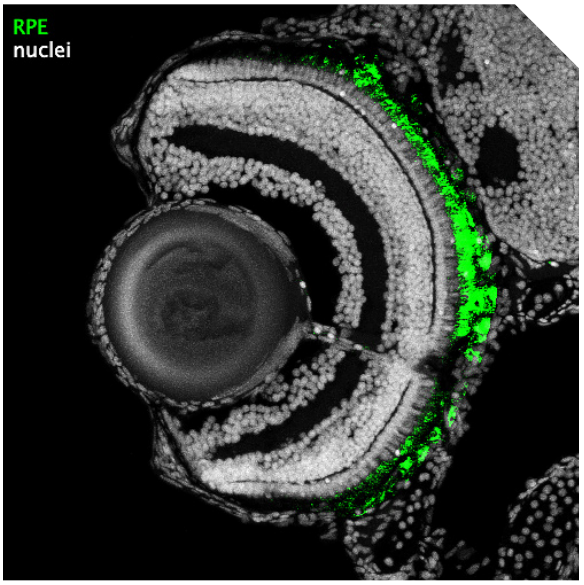
Physicians use psychiatric diagnoses to predict suicide risk, but predictive ability is often only slightly better than chance, and diagnoses are labels that do not change. Seeking a better predictive model, Pitt researchers, including **Nadine Melhem, PhD, MPH**, associate professor of psychiatry, and **David A. Brent, MD**, Distinguished Professor of Psychiatry and Professor of Suicide Studies, looked at 663 young adults deemed at high risk for suicidal behavior because their parents had diagnosed mood disorders. Over 12 years, the parents and their children were periodically evaluated; and, after analysis, the team found that having severe depressive symptoms and a high variability of those symptoms over time most accurately predicted suicidal behavior. By combining this measure of variability in depressive symptoms with factors like younger age, mood disorders, and personal and parental history of suicide attempts, the team developed a prediction risk score model. The model was precise when predicting suicide risk in high-risk individuals but will need to be tested independently, in different populations, and in conjunction with objective biological markers, the study's authors say.

THORAX

MACHINE LEARNING MODEL REDUCES FALSE POSITIVE LUNG CANCER DIAGNOSES

JUL 2019 \ VOL 74 \ ISSUE 7

The diagnosis of lung cancer is devastating news for patients — but what if the diagnosis is wrong? A low-dose CT scan is the standard diagnostic test for lung cancer for those at high risk, but it has a 96% false positive rate. Nationwide, about a quarter of the scans reveal shadows indicating possibly cancerous nodules in the lung — but fewer than 4% of these patients actually have cancer. Pitt and UPMC Hillman Cancer Center researchers, including **David Wilson, MD, MPH**, associate professor of medicine in the Division of Pulmonary, Allergy, and Critical Care Medicine, and **Panayiotis (Takis) Benos, PhD**, professor of computational and systems biology, gathered CT scan data from 218 high-risk patients who either had lung cancer or benign nodules. They created a machine learning model that calculates cancer probability by analyzing the number of blood vessels surrounding a nodule, the total number of nodules identified in the lung, and the number of years since a patient quit smoking. Comparing against the actual diagnoses of the 218 patients, the model's assessment identified approximately 30% of patients' benign nodules, all without missing a single positive case. Evaluating this technique in a larger population is the next step, the authors indicate.



PLOS GENETICS

ZEBRAFISH MODEL REVEALS REGENERATION OF THE RETINAL PIGMENT EPITHELIUM

JAN 2019

Given the many causes of blindness, approaches to therapies must be equally diverse. Degeneration of the retinal pigment epithelium (RPE), which is critical to visual system functioning, is a leading cause of atrophic age-related macular degeneration and of blindness worldwide. Therapies to replace RPE cells could one day stem from the work of Pitt investigators, including **Jeffrey Gross, PhD**, E. Ronald Salvitti Professor of Ophthalmology Research, professor of ophthalmology, and director of the Louis J. Fox Center for Vision Restoration. He and colleagues explored the process of endogenous RPE regeneration in a transgenic zebrafish model. The researchers destroyed large portions of the mature RPE, which resulted in rapid RPE and photoreceptor degeneration. Then, they observed that the remaining adjacent RPE exhibited a robust proliferative response; proliferative cells moved into the injury site and differentiated into new RPE cells, suggesting that they are the source of regenerated tissue. After applying pharmacological disruption to the repair process, the researchers demonstrated that Wnt signaling pathways may be involved in RPE regeneration. The study has established a versatile *in vivo* model for further studying RPE degeneration and repair mechanisms.

Therapies to replace retinal pigment epithelium cells could one day stem from the work of Pitt investigators.

AMERICAN JOURNAL OF PREVENTIVE MEDICINE

WAITING CAN IMPROVE INFLUENZA VACCINE EFFECTIVENESS BUT COULD DECREASE UPTAKE

APR 2019 \ VOL 56 \ ISSUE 4

The influenza vaccine is sometimes administered in August or September, but protection from the vaccine wanes over time. In contrast, the flu season typically peaks between December and April. So, researchers have asked whether the flu shot should be given later in the fall. In a recent study, Pitt researchers used a Markov model and influenza data from the U.S. Centers for Disease Control and Prevention to explore this question. The researchers, including **Mary Patricia Nowalk, PhD, RD**, professor of family medicine; **Kenneth Smith, MD**, professor of medicine, Division of General Internal Medicine; and **Richard K. Zimmerman, MD, MPH**, professor of family medicine and a researcher with Pitt's Center for Vaccine Research, found that delaying flu vaccine administration until October or later could prevent more than 11,400 influenza cases in older U.S. adults. However, if this compressed vaccination window decreases vaccine uptake, and if influenza comes early in the season, this positive effect would be negated, the study revealed. In probabilistic sensitivity analyses, a compressed vaccination window was never favored if it decreased absolute vaccine uptake by greater than 5.5%.

THE NEW ENGLAND JOURNAL OF MEDICINE

NEUROMUSCULAR BLOCKADE IN ARDS PATIENTS DOES NOT AFFECT MORTALITY RATES

MAY 2019 \ VOL 380 \ ISSUE 21

Treatment for ARDS, or acute respiratory distress syndrome, could be due for an update. A decade ago, a multicenter trial concluded that early administration of a 48-hour infusion of neuromuscular blockade in patients with moderate to severe ARDS resulted in lower mortality than treating with deep sedation without neuromuscular blockade. (Neuromuscular blockade induces paralysis of the affected skeletal muscles.) Recently, researchers at Pitt, including **Derek Angus, MD, MPH**, Distinguished Professor and Mitchell P. Fink Professor and chair of critical care medicine; **David Huang, MD, MPH**, professor of critical care medicine; and **Donald Yealy, MD**, professor and chair of emergency medicine, and at many other institutions reevaluated this finding in response to changing care practices. The original trial had compared neuromuscular blockade in patients to a patient group that underwent heavy sedation. In contemporary care, there has been a movement toward much lighter sedation in an attempt to keep critically ill patients more awake, says Angus. The researchers randomly assigned 1,006 moderate-to-severe ARDS patients to receive either a 48-hour continuous infusion of cisatracurium with concomitant deep sedation (the neuromuscular blockade intervention group) or usual care without neuromuscular blockade and lighter sedation. At 90 days, 213 of 501 patients (42.5%) in the intervention group had died before hospital discharge. In the control group, 216 of 505 patients (42.8%) had died. The trial was stopped for futility, concluding that there was no significant difference in mortality at 90 days in ARDS patients treated with early neuromuscular blockade.

HEPATOLOGY

LIVING IN COLD, DARK CLIMATES INCREASES ALCOHOL CONSUMPTION

MAY 2019 \ VOL 69 \ ISSUE 5

People living in colder, darker regions consume more alcohol than people in sunnier, warm regions both in the United States and globally, according to the findings of Pitt researchers, including **Ramon Bataller, MD, PhD**, professor of medicine in the Division of Gastroenterology, Hepatology, and Nutrition. These findings confirm a commonly held belief that, formerly, lacked scientific backing, and they implicate climate factors in rates of binge drinking and alcoholic liver disease. The researchers analyzed World Health Organization and World Meteorological Organization data, as well as data from all U.S. counties, to find a negative correlation between climate factors (measured as average temperature and sunlight hours) and alcohol consumption (measured as total alcohol intake per capita, population percentage that drinks, and binge drinking incidence). Even after controlling for confounding factors that influence alcohol habits, like religion, climate contributed to alcohol consumption and to the burden of alcoholic liver disease across countries worldwide. Findings from the study, which received broad media attention across platforms, suggest that health policy to curtail drinking should factor in climate and geographic location.

SCIENCE ADVANCES

MODELS OF RIFT VALLEY FEVER VIRUS REVEAL ITS POTENTIAL DANGERS TO FETUSES

DEC 2018 \ VOL 4 \ ISSUE 12

Rift Valley fever virus (RVFV) can go unnoticed during pregnancy, like Zika virus, but can cause significant, lethal damage to the placenta and offspring in a rodent model, according to a study by Pitt investigators. Newly established rodent and human tissue models of RVFV revealed that the virus passes through the placenta and can result in high rates of stillbirth with no outward disease symptoms during pregnancy. During the study, whose authors included **Carolyn Coyne, PhD**, professor of pediatrics, and **Amy Hartman, PhD**, assistant professor of infectious diseases and microbiology in Pitt's Graduate School of Public Health and a researcher with Pitt's Center for Vaccine Research, 65% of the pups from infected rats died, compared to 25% from uninfected rats. All of the pups of infected mothers contracted the virus. Using human placenta tissue, the research team found that, compared to Zika, RVFV is even better at dodging the placenta's antiviral defenses and evading the maternal-fetal barrier. The study results emphasize the importance of disease prevention for pregnant women and could advance RVFV vaccine development.

NATURE MEDICINE

BINDING BREAST MILK ANTIBODY TO BACTERIA KEY TO PREVENTING NEC

JUL 2019 \ VOL 25 \ ISSUE 7

Of the many benefits that breastfeeding provides, at least one of them could be lifesaving. In human babies, immunoglobulin A (IgA) antibodies, found only in breast milk, bind to *Enterobacteriaceae* bacteria, preventing the bacteria from taking over the gut microbiome and potentially causing necrotizing enterocolitis (NEC), a deadly intestinal disease that's more common among preterm infants. This finding reveals that whether the bacteria are bound to IgA, and not necessarily their quantity, can indicate the likelihood of developing NEC, says **Timothy Hand, PhD**, assistant professor of pediatrics. The researchers looked at fecal samples from 30 preterm infants with NEC and 39 age-matched controls. Overall, breast milk-fed babies had more IgA-bound gut bacteria than their formula-fed peers, and even among breast milk-fed infants, those who developed NEC had significantly less IgA-bound bacteria. To demonstrate causation between IgA and NEC, the researchers bred mice that couldn't produce IgA in their breast milk. Pups reared on IgA-free milk were as susceptible to NEC as their formula-fed littermates. Because breast milk has other benefits beyond IgA, donor milk that's tested for antibody content may be a better option than formula if breastfeeding isn't possible, Hand says.

MOLECULAR CANCER THERAPEUTICS

TAKING AIM AT NEW THERAPEUTIC TARGETS FOR CASTRATION RESISTANT PROSTATE CANCER

JAN 2019 \ VOL 18 \ ISSUE 1

Prostate cancer is the second leading cause of cancer death in American men (behind only lung cancer), according to the American Cancer Society. In developing new treatments, researchers have taken aim at the androgen receptor (AR) as a therapeutic target for androgen-sensitive prostate cancer, castration resistant prostate cancer (CRPC), and CRPC resistant to the AR-inhibiting drugs abiraterone and enzalutamide. Investigators, including **Zhou Wang, PhD**, UPMC Professor of Urological Research and professor of urology, sought to identify and characterize novel cofactors interacting with the AR N-terminal domain to uncover AR signaling targets in CRPC. After identifying the cofactor Hsp70, a protein key to folding, transport, and degradation processes, the team found that its inhibition indicated that the protein played an important role in the expression and transactivation of endogenous AR. Clonogenic assays demonstrated that an Hsp70 inhibitor alone, or in conjunction with enzalutamide, can inhibit proliferation of 22Rv1, a widely used enzalutamide-resistant CRPC prostate cancer cell line. These findings suggest that targeting Hsp70 could advance therapies for enzalutamide-resistant CRPC.

NATURE COMMUNICATIONS

LEVERAGING THE VACCINIA VIRUS AND INTERLEUKIN-2 ENABLES IMMUNOTHERAPY IN MOUSE TUMORS

NOV 2018

The body itself may possess the best weapons to fight cancer — but only if immunotherapy can unlock them. Oncolytic viruses that express immune-activating cytokines, spurring leukocytes to attack cancer cells, may be well suited to modify the immune microenvironment and improve antitumor effects. In a recent study, researchers at Pitt and the UPMC Hillman Cancer Center harnessed the tumor-selective oncolytic vaccinia virus to evaluate the use of various interleukin-2 (IL-2) cytokines. The investigators, including **David Bartlett, MD**, Bernard F. Fisher Professor of Surgery, found that a novel combination therapy effectively treated cancers previously unresponsive to immunotherapy. The research team used an IL-2 construct combining a glycosylphosphatidylinositol anchor with a rigid peptide linker, leading to functional IL-2 expression on the tumor cell surface and in the tumor microenvironment. In mouse tumor models, the virus construct acted in combination with PD-1/PD-L1 blockade to cure most mice that had a high tumor burden.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

INDUCIBLE NITRIC OXIDE SYNTHASE COULD BE TARGET FOR HEPATOCELLULAR CARCINOMA

OCT 2018 \ VOL 115 \ ISSUE 43

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer and one of the most common causes of cancer deaths worldwide. In pursuit of better treatments for HCC patients, Pitt researchers, including **Timothy Billiar, MD**, Distinguished Professor, George V. Foster Professor, and chair of surgery, studied how inducible nitric oxide synthase (iNOS) — originally cloned at Pitt by David Geller, MD, Billiar, and colleagues (PNAS, 1993) — is linked to more aggressive HCC. In HCC patients, expression of the stem cell markers CD24 and CD133 in tumors was associated with greater iNOS expression and worse outcomes. In CD24+ CD133+ liver cancer stem cells, the expression of iNOS promoted Notch1 signaling *in vitro* and *in vivo* and accelerated HCC tumor formation in a mouse xenograft model. The research team found that iNOS/NO led to Notch1 signaling through a pathway involving TACE/ADAM17 proteases. Targeting and further understanding how iNOS contributes to progression of CD24+ CD133+ HCC could enable therapeutic benefits for HCC patients.

SCIENCE

NONHUMAN PRIMATE BORN FOLLOWING CRYOPRESERVED TESTICULAR TISSUE GRAFT

MAR 2019 \ VOL 363 \ ISSUE 6433

When Grady was born in April 2018, she wasn't just any healthy female rhesus macaque baby. She was the first nonhuman primate born after grafted immature testicular tissue had been extracted, cryopreserved, and then implanted to produce the sperm that enabled her conception.

Grady's birth marked a milestone for fertility preservation and reproduction therapies, especially those aimed at boys with cancer, who can become infertile from chemotherapy and radiation treatments before reaching puberty.

During the study, researchers from Pitt and Magee-Womens Research Institute removed one testis from prepubertal rhesus macaques and cryopreserved the testicular tissue. As the animals approached puberty, the researchers removed the other testis and grafted the freshly isolated tissue as well as the thawed cryopreserved tissue under the skin. Entering puberty, the animals' testosterone levels increased, and the grafted tissue successfully produced sperm. Several months later, researchers extracted sperm cells in order to generate embryos that were then implanted into recipient females; Grady's birth followed.

Now that a nonhuman primate demonstrated successful conception and birth, testicular tissue grafting, as well as spermatogonial stem cell transplantation to restore fertility, could be ready for translation to the clinic. "We believe these technologies are ready for the clinic now," says senior author **Kyle Orwig, PhD**, professor of obstetrics, gynecology, and reproductive sciences. Since 2011, Orwig and colleagues at the Fertility Preservation Program at UPMC Magee-Womens Hospital had been collecting and cryopreserving testicular tissue from boys with cancer. Now, that preserved tissue could soon be used to restore fertility.

For the study's first author, **Adetunji Fayomi, PhD, DVM**, the study marked the capstone of his graduate training at Pitt. A former veterinary clinical researcher in Nigeria, Fayomi made the switch to basic science — a transition that requires a different mindset and isn't always easy, he says. "He struggled in the beginning, but he was really persistent," Orwig says of Fayomi. "Probably one of my very proudest teaching moments was watching Adetunji evolve into a great scientist, colleague, and mentor in the laboratory."

Currently, Fayomi is studying the *EGFL6* gene, which is linked to ovarian cancer progression.

"My current objective is actually to help people to increase reproductive efficiency and to solve reproductive problems," he says.

NATURE IMMUNOLOGY

INTERLEUKIN-17 AND PROLIFERATION OF LYMPH NODE STROMAL CELLS

MAY 2019 \ VOL 20 \ ISSUE 5

The proinflammatory cytokine interleukin-17 (IL-17) promotes inflammation and the recruitment of myeloid cells. But IL-17 has also been implicated in diseases that include proliferation of non-immune cells. Pitt researchers demonstrated a critical requirement for IL-17 in the proliferation of lymph-node stromal cells — non-myeloid cells — particularly fibroblastic reticular cells (FRCs). Using mouse models of experimental autoimmune encephalomyelitis and colitis, the research team, led by **Mandy McGeachy, PhD**, associate professor of medicine in the Division of Rheumatology and Clinical Immunology, showed that FRCs experienced cell cycle arrest and apoptosis in the absence of signaling via the IL-17 receptor. While IL-17 signaling in FRCs was not required for the development of TH17 cells (helper T cells), failed FRC proliferation impaired germinal center formation and antigen-specific antibody production, key features of autoimmune disease in humans. This finding sheds new light on IL-17's role in driving proliferation during pathologic tissue remodeling and fibrosis, avenues that the research team plans to explore in the future.

MOLECULAR CELL

TARGETING THE CRTH2 RECEPTOR TO TREAT INFLAMMATORY DISEASES

OCT 2018 \ VOL 72 \ ISSUE 1

New therapies for inflammatory diseases, like asthma, could draw from research by **Cheng Zhang, PhD**, assistant professor of pharmacology and chemical biology, and colleagues. Researchers know that blocking signaling of the G-protein-coupled receptor CRTH2 could enable new therapies for many inflammatory conditions, as it is key to a major pathway in type 2 inflammation. A number of CRTH2 antagonists, which impede the receptor's signaling, are being studied in the clinic, including the compound fevipiprant, which is currently in phase III clinical trials for the treatment of asthma. In a recent study, Pitt investigators defined the crystal structures of antagonist-bound human CRTH2. Structural analysis revealed a novel ligand-binding pocket with an uneven positive-charge distribution, which is key to impeding the receptor by antagonists, and suggested a novel mechanism for the binding of the endogenous lipid molecule PGD2. These structural insights into CRTH2 could facilitate drug development for many inflammatory diseases.

With all that is going on in today's world, now—more than ever—the School of Medicine understands the importance of community. Whether it's providing preventive care or responding to tragic events, we have generously offered our expertise throughout the years to help keep our neighbors healthy and our community vibrant.

Enhancing Community Health

To better understand and improve community behavioral health services, the School of Medicine's Department of Psychiatry and Pitt's School of Social Work have partnered to establish CiTECH, the Center for Interventions to Enhance Community Health.

This collaborative research center, a pioneering partnership between a school of social work and department of psychiatry, serves as a bridge to the community to conduct translational research on population behavioral health.

The overall mission of CiTECH is to enhance the quality and length of life of individuals living with behavioral health conditions. It plans to do so through innovative community-based interventions and will provide research infrastructure, mentorship, pilot awards, and community partnerships to support scholarly research on community-based interventions to improve behavioral health.

Priority areas include youth mental health, suicide, addiction, and psychosis, with faculty and community experts represented in each of these distinct areas.

CiTECH is directed by Shaun M. Eack, PhD, James and Noel Browne Professor, associate dean for research, and professor of social work, School of Social Work, and professor of psychiatry, School of Medicine, and David A. Brent, MD, Distinguished Professor of Psychiatry, Professor of Suicide Studies, and professor of pediatrics, School of Medicine; of epidemiology, Graduate School of Public Health; and of clinical and translational science.

THE OVERALL MISSION OF CiTECH IS TO ENHANCE THE QUALITY AND LENGTH OF LIFE OF INDIVIDUALS LIVING WITH BEHAVIORAL HEALTH CONDITIONS.

On the morning of October 27, 2018, a domestic terrorist stormed into Pittsburgh's Tree of Life synagogue and opened fire, using multiple firearms to murder 11 people and injure six others. Soon after the first 911 calls for help, University of Pittsburgh School of Medicine faculty members were a part of the immediate response—from SWAT first responders to physicians.

Stronger Than Hate

One year later, those Pitt responders have spent time evaluating their actions that day and, sadly, preparing for the possibility of another mass-casualty event.

One of the trauma surgeons who saved people's lives that day was Matthew D. Neal, MD, Roberta G. Simmons Assistant Professor of Surgery and assistant professor of critical care medicine.

NEAL DISCUSSES WHAT HAS CHANGED SINCE THE MASSACRE:

What has changed—I have a three-part answer to that question.

The first relates to how our clinical care has changed. I'm proud to say that—other than fine-tuning some details—not much has changed in our mass-casualty incident plan, which we've had in place for a long time and is something for which we do frequent practice drills. We learned that our delivery of the plan was well orchestrated, from the level of nurse to physician to operating room staff to housekeeping—top-to-bottom clinical care to administration, our plan worked well. It's hard to feel proud in the context of a massacre, but, with a blunted sense of pride, I'm immensely proud that everyone who left the synagogue alive that day is alive today.

The second part of the answer is how our Stop the Bleed program helped that day and how substantially the program has grown as a result of how it helped at Tree of Life.

[The Stop the Bleed program trains members of the public how to control traumatic bleeding until first responders arrive and places bleeding-control kits in public schools and a tourniquet on the belt of every police officer. The program grew out of the massacre at Sandy Hook Elementary School and surgeons' efforts to increase survival rates after mass-casualty events. In trauma care, the primary cause of preventable death is hemorrhage.]

Prior to the Tree of Life event, our region had the largest Stop the Bleed program in the country. We had done outreach and training at Tree of Life two months before the event and with law enforcement officers who responded that day; lives were saved as a result of that program. After that day in October, we've amplified Stop the Bleed efforts, and the number of requests we've received from community and religious organizations in the last year has been extraordinary. We're on a meteoric pace to educate the entire region on bleeding control and to make the bleeding-control kits as ubiquitous as AEDs. Unfortunately, we know how critically important it is for the general public to know bleeding control if and when similar events happen in the future.

The Tree of Life event, as all the other national tragedies of intentional mass injury, has also resulted in our trauma community developing a strong sense of advocacy for addressing the public health crisis that is gun violence, which is part three of my answer.

Many of us who were personally affected by our professional obligations on that day—in addition to grieving as community members—have had the perspective of having a personal connection with people who survived by being their physicians. We have partnered with Resolve Crisis Center to begin conversations about doing educational outreach that involves Stop the Bleed and an overall mission of working to end gun violence. We can have all the skill sets we want behind the closed doors of the hospital, but, if we're not out in the public, we're not going to make the impact we need to.

However, the Tree of Life tragedy didn't cause us suddenly to think that gun violence prevention was important. Horrific intentional mass-injury events are on a scale that gets a lot of public attention, but what doesn't get that same kind of attention is the gun violence that happens every single day. The Tree of Life tragedy was a catalyst in terms of what we're all facing in the public health crisis of our time; we, as University faculty and as clinicians, need to be leaders in trying to prevent this from happening again.

On a personal level, the connection to the community has been extraordinary. I don't know how you take a metric of this, but the relationship in Pittsburgh among our community of care providers, first responders, and people who were victims has taken a special tone. In the face of an anti-Semitic and violent event that is horrible and divisive, a tremendous sense of unity has evolved. I would rather never have anyone experience a mass-casualty event ever again. As much as I love my job and the challenge of what I do, I would rather the problem didn't exist. Just as oncologists who treat cancer every day say, we'll continue to strive to put ourselves out of business.

THE TREE OF LIFE TRAGEDY WAS A CATALYST IN TERMS OF WHAT WE'RE ALL FACING IN THE PUBLIC HEALTH CRISIS OF OUR TIME; WE, AS UNIVERSITY FACULTY AND AS CLINICIANS, NEED TO BE LEADERS IN TRYING TO PREVENT THIS FROM HAPPENING AGAIN.

During CEC's grand opening, its director, Daren Ellerbee, embraces Andrea Stanford, assistant county manager for Allegheny County.

Open Doors and Open Arms — Welcome!

Much welcomed health and wellness programs are coming soon for Pittsburgh's Homewood neighborhood.

It's all part of Pitt being a good neighbor, through the first of its Community Engagement Centers (CEC). The CECs are designed to be a front door to Pitt's programs and services for area residents, explains John Maier, MD, PhD, who is the School of Medicine representative on the CEC advisory board.

The CEC in Homewood, a partnership between the Homewood community and the University, opened last year. It already offers programs for children, adults, senior citizens, and families—everything from summer science camps and after-school support to career development opportunities and job fairs, says Maier, who is assistant professor and director of research and development, Department of Family Medicine. He expects multiple health and wellness programs to be available by 2020.

CECs were developed to "deepen the University's relationships within the community while collaboratively addressing the challenges of the area," says Daren Ellerbee, director of the CEC in Homewood and Pitt alumna. She gratefully points out that Pitt's CECs "are a front door to Pitt, which exemplifies the University's commitment to Homewood, a community with which our faculty, staff, and students have worked for decades."

It's a door that Pitt plans to keep wide open for years to come.

CECS WERE DEVELOPED TO DEEPEN THE UNIVERSITY'S RELATIONSHIPS WITHIN THE COMMUNITY WHILE COLLABORATIVELY ADDRESSING THE CHALLENGES OF THE AREA.

donors

With grateful appreciation for their generosity, we acknowledge the following individual, corporate, and foundation donors whose contributions of $1,000 or more to the University of Pittsburgh School of Medicine, UPMC Hillman Cancer Center, and UPMC Western Psychiatric Hospital between July 1, 2017, and June 30, 2019, have supported us in our academic, research, and clinical missions.

Thank you.

Family Tradition

On the fourth floor of Scaife Hall — where many of the University of Pittsburgh School of Medicine's classrooms are located — class photos line the hallway. The photos begin in 1899, with black and white shots of small numbers of people, and end in an adjacent hallway with more recent digital-color headshots.

Stewart Sell, MD, can walk down this hallway and find family members' photos. The first is of his great-uncle Milton from the class of 1908, and the second is of his father, Oliver Sell, who graduated in 1926 and was on the surgery faculty from 1945–55.

Recently, Dr. Sell returned to Pitt to celebrate a milestone moment for his family's connection to the School of Medicine. He was on campus at the Medical Alumni Association's annual luncheon to present the Sell Family Physician Scientist Award to its first recipient, Joshua Krivinko, MD, now a graduate of the Physician Scientist Training Program.

Considering how long Dr. Sell's family has been connected to Pitt Med, it's a well earned milestone to be supporting current graduate students.

A Pittsburgh native, Dr. Sell is a 1960 graduate of the medical school. During his years at Pitt, he studied immunology with Frank J. Dixon, MD, and published his first paper while still a medical student.

After training at Massachusetts General Hospital, the National Institute of Allergy and Infectious Diseases at the National Institutes of Health, and the University of Birmingham in England, he returned to Pitt to begin his career teaching in the pathology department.

Today, he is a senior scientist at the Wadsworth Center of the New York State Department of Health and professor of biomedical sciences at the State University of New York at Albany School of Public Health.

Dr. Sell's work includes some of the most pivotal studies in the history of stem cell research. Using an assay that he developed, he demonstrated that animals exposed to cancer-causing agents had elevated levels of alpha-fetoprotein (AFP) long before they exhibited liver cancer. In 1976, he identified stem cells in the adult liver as the source of the AFP and reported that these stem cells could promote liver cancer. In 2007, the American Association for Cancer Research cited his 1994 paper on malignant stem cells as a scientific landmark in cancer research.

In addition to his stem cell work, he has published multiple papers on immunopathologic mechanisms, and his book "Immunology, Immunopathology, and Immunity" was published in six editions. His review paper "How Vaccines Work: Immune Mechanisms and Designed Vaccines" was published in October 2019 in "Expert Reviews of Vaccines."

Pitt named Dr. Sell a Legacy Laureate in 2005 for his identification of AFP as a marker for liver cancer. Today, the AFP test he developed is used in prenatal screening to detect increased risk for Down syndrome, neural tube disorders, and other birth defects.

Of his career, he says, "I never thought I would be a pathologist. Who wants to sit around and look into a microscope all day? But at Pitt, it wasn't just looking at slides or making a diagnosis; it was thinking about how these things happened."

With such success in his career, he again looked to Pitt to see how he could help current medical students. He ended up creating the Sell Family Legacy Fund, which supports the Sell Family Physician Scientist Award and educational opportunities for students enrolled in the Physician Scientist Training Program.

His great uncle and father would be proud.

Stewart Sell, MD

INDIVIDUALS

Munira S. Abbasi, MD

*George Abramson

Brianna Acalotto

Tahsin O. Acarturk, MD

Venus A. Hadeed, MD, and Antonio A. Achkar, MD

Dr. Satoshi Aihara

Nancy L. Aitken

Suzanne R. Alexander

Gayle Martin and William C. Alexander

Nicholas J. Alfano

Nourah A. M. TH. Alghanem and Ebraheem J. Alghanim

Barbara A. Allen and David W. Allen

Nancy Allen and Jack B. Allen Jr.

Rachel and Nduka M. Amankulor, MD

*Bruce A. Americus

Patrice J. Americus and Robert L. Americus

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Explosive Research

Robert D. Wells was working with a dangerous reagent during the first summer of his graduate studies at the University of Pittsburgh School of Medicine.

Suddenly, there was an explosion.

He was knocked off his feet, and the Scaife Hall lab filled with smoke.

Crawling toward the door, he heard the crunching of shattered glass beneath him, the same glass that had already left cuts on his face, neck, and arms.

He made it to the doorway, where he was eye level with a pair of shoes he thought he recognized. Looking up, he saw his mentor and department chair, Klaus Hofmann, PhD, who rushed there to find out what happened.

Fortunately, the grad student wasn't seriously injured, and he now looks back on the drama as an "initiation" into his research career.

After that, work became less combustible for him. During his doctoral studies, from 1960–64, Dr. Wells worked with the noted Dr. Hofmann on peptide hormones, especially on the synthesis of ACTH, a shortened chain of the pituitary hormone adrenocorticotropin.

Nearly as challenging as his lab work was paying the bills after starting a family with his new wife, Dorothy ("Dotty") Wells. His graduate student stipend and her salary as a nurse at the Pittsburgh VA Medical Center didn't go far enough, but thankfully their parents lived nearby in their hometown, Uniontown, Pa. When the Wellses visited on weekends, their parents would stock them up with eggs, meat, and other food essentials for the week.

Dr. Wells earned his PhD at Pitt in 1964, and he and his family moved to the University of Wisconsin-Madison, where they finally could make ends meet. He joined Har Gobind Khorana, PhD, for postdoctoral research on the genetic code in humans. Khorana would go on to receive the Nobel Prize in Physiology or Medicine in 1968 for discovering how a DNA's genetic code determines protein synthesis, which dictates how a cell functions.

Throughout the years, Dr. Wells served in professorial and administrative positions at the University of Wisconsin-Madison, University of California, San Diego, Salk Institute for Biological Studies, University of Alabama at Birmingham Schools of Medicine and Dentistry, and Texas A&M University, where he was founding director of the Institute of Biosciences and Technology. He focused on research and published extensively in the area of unusual DNA structures and gene expression related to human diseases.

Since 2008, Dr. Wells has been the Welch Foundation and Regents Professor Emeritus, Institute of Biosciences and Technology, Texas A&M University System Health Science Center. During these years, Mrs. Wells has been a mother and grandmother, an art scholar, educator, docent at the Museum of Fine Arts, Houston, and volunteer at the MD Anderson Cancer Center. Their days of needing help for everyday groceries are long gone.

It was in 2014, when Dr. Wells was named a Legacy Laureate at the University of Pittsburgh, that he and his wife made a decision. After meeting other Legacy Laureates and hearing how they were supporting Pitt, Mrs. Wells decided that she and her husband could also help.

"Pittsburgh has always meant a lot to us—from the time I was a little girl, and we would go there to shop—and so has Pitt. We started our careers and family there," says Mrs. Wells. "It will always be a favorite of ours." To that end, their Wells Graduate Student Scholarship Fund supports doctoral students in the School of Medicine.

Few academics get into their careers for financial reward, adds Dr. Wells, but both he and his wife say that it's important to them that they give what they can to help today's students, just like their parents helped them.

"We want to grease the wheels," he says, which should help stock the refrigerators of the medical school's doctoral students.

Left, Dorothy ("Dotty") Wells and Robert D. Wells

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The Accidental Pathologist

William Zeiler never intended to specialize in pathology. By playing jazz piano to help pay for his education at the University of Pittsburgh, he earned both bachelor of science and medical degrees. He was finishing an internal medicine internship when his future career path was interrupted by the World War II draft.

After serving his country as chief of medicine at Eglin Air Force Base Hospital, he returned to Pitt, almost eligible to take the boards in internal medicine. But, as he later said in an interview with the College of American Pathologists: "I wanted to put in a year in the laboratory and reawaken my basic sciences. The result was that I never got out of the laboratory."

As Dr. Zeiler's life in pathology began, his personal life expanded, too. While completing a residency in anatomic and clinical pathology, he met his future wife, Geraldine, a cytologist trained at the Mayo Clinic, who helped build the cytology program at Pitt. Over the years, they had five children.

Despite his full life at home, Dr. Zeiler quickly became a leader in the field of pathology. A director of pathology at several Pittsburgh-area hospitals, he also created the Clinical Pathology Facility, an extension of local hospital laboratories meant to increase efficiency and ensure that a range of testing services would be available for reasonable prices. Because of his passion for excellent service, medical expertise, and vision for the field of pathology, the facility grew into a regional lab offering full pathology services. The lab was sold to MetPath Laboratories, which later became Quest Laboratories.

Dr. Zeiler went on to work with the College of American Pathologists (CAP), for which he served in many positions, including president. When he was CAP president, he addressed the American College of Physicians' controversial guidelines regarding clinical laboratory tests and the examination of surgical pathology specimens that were created without the input of pathologists. This action was responsible for the now-accepted general principle and practice that all specialties affected should be involved in the development of clinical guidelines.

In 1990, Dr. Zeiler received the CAP Pathologist of the Year award. He also served as president of the World Association of the Societies of Pathology and Laboratory Medicine, focusing on promoting education and best practices for patient evaluation and testing methods in areas of the world with limited resources.

Along with Dr. Zeiler's career accomplishments, he is known for devotion to his family. "He has spent his life taking care of generations of our family with boundless love and generosity. His every impulse is to do good," says Maura Frölich, one of his daughters. "He approaches everything with intelligence, curiosity, determination, and, occasionally, stubbornness, but that's probably what keeps him alive and well. At 98, he is the happy grandfather to 11 grandchildren."

Dr. Zeiler turned to philanthropy after his beloved Geraldine died from breast cancer at the age of 65. He has established many awards and programs in her memory. His gifts to Pitt's School of Medicine include general scholarships and the Geraldine and William Zeiler, MD, Fund for Pathology Research. He has supported the Department of Pathology and also its Summer Undergraduate Research Program.

All in all, it has been a remarkable career for a Pittsburgh pathologist who "never got out of the laboratory" and ended up having global reach.

William Zeiler with his 11 grandchildren

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Spine Chilling

Born in southeast Ohio and reared on a dairy farm, Orland Bethel decided to start his own business in 1956. He borrowed $4,000 from his parents and his in-laws and started an egg production and distribution company, Hillandale Farms.

"It began as a real quaint operation," Mr. Bethel says. "But today, we employ about 1,800 people scattered among 10 states with approximately 19.5 million chickens."

He credits his many years of success to "working and associating with good people."

Good fortune, however, whether it be personal or professional, doesn't always come without bumps in the road. In 2014, Mr. Bethel began to feel extreme pain in his hips and lower back. He learned that he had a bad case of spinal stenosis, which is the narrowing and squeezing of the nerves and spinal cord, causing pain and other symptoms. He consulted six different orthopaedic surgeons in search of treatment options. However, he didn't like the choices he received.

"Each and every one told me that they would need to cut a chunk of vertebrae out to put rods and mesh in," recalls Mr. Bethel. "I heard it was a relatively successful operation, but I also heard about cases where it wasn't."

He kept putting off surgery in hopes of a less-invasive option. At the time, his general manager of the Hillandale Farms' production facilities had a daughter who was attending the University of Pittsburgh School of Medicine. She offered to help Mr. Bethel seek another opinion, which led him to Joon Yung Lee, MD, professor of orthopaedic surgery.

At first, Dr. Lee told Mr. Bethel the same thing as the previous six surgeons—surgery to remove parts of the vertebrae would be the optimal treatment.

"That's what I've been told," Mr. Bethel said to Dr. Lee. "But that doesn't sound any good to me."

Dr. Lee looked over Mr. Bethel's records and spinal images one more time and made a proposition. He told Mr. Bethel that, if given the opportunity, Dr. Lee believed there was a 10–15% chance he would be able to do a less-invasive procedure. But Mr. Bethel had to give his consent to continue with the original operation if Dr. Lee found that it was necessary once he began the surgery.

"It's the best deal I'd ever heard," Mr. Bethel said.

Mr. Bethel scheduled the surgery, and, when he came out of the operation, he learned that Dr. Lee's plan worked. Mr. Bethel's lower-back nerves were chronically compressed from extensive bone spurs that had formed from wear and tear. In addition, he had developed mild scoliosis that potentially made his spine unstable. After carefully removing the bone spurs, the next decision was to determine whether his spine was stable enough to avoid the more extensive fusion procedure. Dr. Lee felt that fusion wasn't necessary, which turned out to be correct.

Some years later, though, Mr. Bethel came to Dr. Lee with another serious condition. His shoulder muscles were atrophied and weak; and, after some testing, it was determined that the spinal cord in his neck was being compressed. In this case, the situation was more urgent, as further damage to the spinal cord can mean quadriparesis, which can cause a temporary or permanent weakness in all four limbs. Mr. Bethel underwent another operation in his neck to remove compression on his spinal cord, restoring function to his shoulders.

"I have nothing but tremendous respect for Dr. Lee," says Mr. Bethel, ultimately deciding to show his appreciation through philanthropic support.

Mr. Bethel made a gift to the Ferguson Laboratory for Orthopaedic and Spine Research, of which Dr. Lee is clinical director, in support of Dr. Lee's work. The Orland Bethel Professorship in Spine Surgery will support the recruitment, salary, professional development, expenses, and scholarly activities of the faculty member who holds the professorship, as well as spine research and other key academic initiatives in the Department of Orthopaedic Surgery.

"I wanted the department to have anything and everything it wanted, so that they could be the very best in the world," says Mr. Bethel. "We strategically decided on a gift that would be of the most benefit to them. It will help the department foster what they believe in and allow Dr. Lee to decide, with the consultation of my children, where and how the endowment earnings can best be put to use."

"The gift from Mr. Bethel and his family is tremendous," says Dr. Lee. "His generosity will give us freedom to support projects in our laboratory that previously couldn't be funded, owing to the ever-diminishing National Institutes of Health resources. I'm most excited about the fact that we can now support undergraduate and graduate projects that were previously difficult to fund. Undergraduate and graduate students in our laboratory represent the next generation of scientists who may give us the most 'return on investment,' and educating them will be a lasting legacy for the Bethel family."

Today, Mr. Bethel lives in Florida with his wife, Dolly, and he also has a home in Greensburg, Pa. His children, Gary, Cynthia, and Susan, now own Hillandale Farms, but he says, thanks in large part to Dr. Lee, he remains involved in the daily operations.

"I feel," he adds, "that now, at 83 years of age, I can take on the world!"

L-R, Dr. Joon Yung Lee and Orland Bethel

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