



Vision

Vision

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Our Vision

It's no exaggeration to say that we have entered a new era of uncertainty in American health care. As a nation, we are faced with immense challenges related to the cost and quality of clinical care, not to mention access to such care. Ironically, these challenges have grown more pronounced at a time when we have the opportunity to take advantage of extraordinary leaps forward in science and medicine.

Despite current challenges, we at the University of Pittsburgh School of Medicine are optimistic, and we remain committed to achieving transformational change in medical education, patient care, and biomedical research in a culture of humanism.

As an educational and research-based institution, we also work every day to cultivate an environment that rewards creativity, collaboration, and innovation. As scientists, we encourage everyone to envision a world in which our civic leaders embrace the scientific method—a template for civil, disciplined, evidence-based, and sound discourse—to probe the problems that concern us all.

In that spirit of shared purpose, I am pleased to highlight our recent progress on the pages of this report. I invite you to explore it and discover for yourself how the University of Pittsburgh School of Medicine is constructing a compelling vision of the future every day.

ARTHUR S. LEVINE, MD

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

Come senators, congressmen please heed the call
Don't stand in the doorway, don't block up the hall
For he that gets hurt will be he who has stalled
There's a battle outside and it is ragin'
It'll soon shake your windows and rattle your walls
For the times they are a-changin'

BOB DYLAN / WINNER OF THE 2016 NOBEL PRIZE IN LITERATURE

News @ Achievements

Our Shared Ancestry

“UPMC was created out of the University of Pittsburgh [and] the two have risen together in national and international prestige,” Pittsburgh-area historian and author Mary Brignano notes in *Beyond the Bounds: A History of UPMC*. “UPMC’s founders followed one core principle: Research and clinical success are synergistic and interdependent. What is good for one is good for both.”

Together, the University and UPMC have grown into a model for the nation—one of the most successful examples of a health care system partnered with a medical school.

The vital collaboration between Pitt and UPMC drives a circular bond from research to clinical care and back to research. Having played a vital role in the transformation of Pittsburgh, the partners aim to play a similar role in the transformation of biomedical research, health sciences education, and clinical care across the globe.

Pitt 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.

2016 NIH FUNDING

UNIVERSITY OF PITTSBURGH

\$513M
1,090 AWARDS

RANK

5TH

SCHOOL OF MEDICINE

\$453M
846 AWARDS

RANK

5TH

2017 OVERALL RESEARCH SPENDING

UNIVERSITY OF PITTSBURGH

\$765M



for research in the
School of Medicine **\$513M**

National Institutes of Health Leader Recruited To Head Aging Institute

NHLBI Chief Toren Finkel, MD, PhD, Joined Pitt in September 2017



The new leader of Pitt's Aging Institute is **Toren Finkel, MD, PhD**, who was recently chief of the Center for Molecular Medicine at the National Heart, Lung, and Blood Institute (NHLBI) of the NIH.

"Toren Finkel is an exceptional physician-scientist," said Arthur S. Levine, MD, senior vice chancellor for the health sciences and Petersen Dean of Medicine. "Under his leadership, the Aging Institute will amplify its mission to include basic science investigations that focus on the aging process, with the ultimate goal of extending disease-free life."

Research into the biology of aging has undergone rapid evolution in recent years. Investigators are beginning to untangle the molecular pathways that regulate aging and identify therapeutic targets, Finkel observed. "And Pitt is just a phenomenal place that has a wonderful track record of translating therapies into patients," he said. "The combination of this commitment to build up the basic sciences of aging biology and having the infrastructure and knowledge to translate that to therapies is what is so attractive to me."

The Aging Institute will continue to tap expertise campus-wide to support the needs of older adults in Western Pennsylvania and throughout the region. Moving forward, a major focus will be the development of drugs to reinforce fundamental

mechanisms of resistance to age-related health complications such as heart disease, cancer, pulmonary fibrosis, and neurodegenerative disorders.

"Why and how we age is one of the great biological questions out there," said Finkel. "If we can slow aging down, rather than treating each individual disease of aging, we can have a way of treating all of them."

Investigations using Metformin—a diabetes drug shown to have an antiaging effect in epidemiological studies—are in the planning stages now at NIH, and Pitt's Aging Institute will attempt to discover other promising compounds, Finkel said.

His own commitment to basic science is longstanding. Finkel's team provided the first clear demonstration that reactive oxygen species (ROS) function as endogenous signaling molecules, an observation that established the field of redox signaling. He has described the regulation of mitochondrial and cytosolic ROS, identified cellular redox targets, and defined how ROS-regulated pathways contribute to normal aging and disease. Finkel's work spans animal models and human research participants, truly bridging bench to bedside.

Finkel, who is a professor of medicine in the Division of Cardiology, earned his MD and PhD in biophysics at Harvard Medical School. He completed an internal medicine residency at Massachusetts General Hospital and a cardiology fellowship at Johns Hopkins Hospital.

Finkel's lab has published nearly 200 manuscripts, many in high-impact journals like *Science*, *Nature*, and the *New England Journal of Medicine*. He is a member of the American Society for Clinical Investigation and the Association of American Physicians and is a fellow of the American Association for the Advancement of Science.

UPCI Gets New Name, New Director

Robert Ferris, MD, PhD, Leads UPMC Hillman Cancer Center



Robert L. Ferris, MD, PhD, an expert in immunotherapy and head-and-neck cancer specialist, has been named Hillman Professor of Oncology and director of the UPMC Hillman Cancer Center, the region's only National Cancer Institute (NCI)-designated comprehensive cancer center. Ferris, formerly UPMC Professor of Advanced Oncologic Head and Neck Surgery and clinical vice chair of the Department of Otolaryngology, Pitt School of Medicine, assumed the position on July 1. He succeeds Nancy E. Davidson, MD.

"Under Dr. Ferris's leadership, we expect that UPMC and the University of Pittsburgh will continue to lead the way locally, nationally, and internationally in the development of new therapies to treat and prevent the numerous forms of cancer," said Arthur S. Levine, MD, senior vice chancellor for the health sciences and Petersen Dean of Medicine.

The research institute and cancer network, established as the University of Pittsburgh Cancer Institute (UPCI) in 1985 under its late founding director Ronald B. Herberman, MD, was renamed to honor the late Henry and Elsie Hillman in May 2017. The Hillmans were longtime supporters of science and medicine whose vision and contributions were instrumental in making Pittsburgh a world leader in cancer care.

Ferris earned his MD and immunology PhD at the Johns Hopkins University School of Medicine. He was a surgical intern and otolaryngology resident at Johns Hopkins Hospital. As chief resident, he undertook subspecialty training in head and neck oncologic surgery.

He joined Pitt's faculty in 2002 and has held numerous roles within the School of Medicine since then, rising to the rank of professor in 2010, with a secondary appointment in the Department of Radiation Oncology. He has been coleader of UPCI's Cancer Immunology Program since 2007 and associate director for translational research and codirector of the Tumor Microenvironment Center since 2012.

Ferris is a fellow of the American College of Surgeons and co-chair of the NCI Steering Committee for Head and Neck Cancer. He was elected to the American Society for Clinical Investigation in 2008 and currently is chair of NCI's Tumor Microenvironment Study Section.

Ferris's research focuses on improving treatments for head and neck cancer. He was lead author on a seminal 2016 paper in the *New England Journal of Medicine* reporting the efficacy of Nivolumab (see story, page 47), an immune checkpoint inhibitor, for recurrent squamous cell carcinoma of the head and neck. His work extensively explores other treatments for high-risk head and neck cancer, including radiation, chemotherapy, and robotic surgery.

He is editor-in-chief of *Oral Oncology*, associate editor of the *Journal of the National Cancer Institute*, and a principal investigator of a large number of NCI-sponsored clinical trials.

Pitt School of Medicine Signs Collaborative Agreement with World-Renowned French Research Institutions



The University of Pittsburgh School of Medicine has entered into an agreement with three world-renowned French research institutions, the Université Pierre et Marie Curie of the Sorbonne Universités in Paris, the Institut National de la Santé et de la Recherche Médicale (Inserm), and the Centre National de la Recherche Scientifique (CNRS), to focus on collaborative research and education in the fields of medicine and biomedical sciences.

The agreement will enable researchers of all four institutions to cooperate on fundamental research, development of novel therapeutics, and clinical trials, with a focus on ophthalmology, vision, and neuroscience. Along with joint research, the agreement also emphasizes exchange of academic personnel, joint academic conferences, and of scientific, educational, and scholarly materials.

The agreement, signed on July 12 at the French Embassy in Washington, D.C., highlights an important partnership between Pitt and the French institutions that was spurred by the recent recruitment of **José-Alain Sahel, MD**, one of the world's top experts in retinal diseases, as the Eye and Ear Foundation Professor of Ophthalmology, chair of the Department of Ophthalmology, and director of the UPMC Eye Center. Sahel retained his connections to Paris as the founder and director of the Institut de la Vision in Paris and as a professor at the Université Pierre et Marie Curie of the Sorbonne Universités, a top-ranked medical school and the largest scientific and medical complex in France.

Inserm, the French National Institute of Health and Medical Research, is the only public research institution in France solely focused on human health and medical research and a leading



medical research agency worldwide; and CNRS, the French National Center for Scientific Research, is the largest governmental research organization in France and the largest fundamental science agency in Europe.

"This agreement will further strengthen the robust scientific and educational partnerships between Pittsburgh and Paris, bringing to bear our outstanding intellectual capacities to address some of the most significant diseases that lead to blindness and vision impairment through basic and translational research," said Sahel.

"Taking on an immense challenge like the quest to cure blindness requires that we not only have bold ideas but also the brightest minds to work on them. The University of Pittsburgh is proud to be a part of this international partnership that will bring together the world-class scientific community at Pitt with researchers from France under the able leadership of Dr. Sahel," said **Arthur S. Levine, MD**, Petersen Dean of Medicine.

Melanoma Expert Honored as 'Giant of Cancer Care'

John M. Kirkwood, MD, Sandra and Thomas Usher Professor of Melanoma, has been named a "Giant of Cancer Care" by OncoLive, the official website of the Oncology Specialty Group. Kirkwood is the second Pitt faculty member to receive this honor, following **Bernard Fisher, MD**, Distinguished Service Professor of Surgery, who was among the inaugural recipients in 2013.

Kirkwood's research interests include melanoma immunobiology, therapy, and prevention. He developed the first FDA-approved immunotherapy for melanoma in 1996 and is currently pioneering new approaches to assess the most recently approved immunotherapies and molecular therapies, which are anticipated to be the focus of the next decade of clinical and translational research.

Top left: Engaged in discussion at the French Embassy in Washington, D.C., are (left to right) Drs. Jean Chambaz of the Sorbonne, Yves Lévy of Inserm, and José-Alain Sahel of Pitt. Top right: Signing the historic agreement are (left to right) Drs. Sidney Wiener of CNRS, Arthur S. Levine and José-Alain Sahel of Pitt, Jean Chambaz of the Sorbonne, and Yves Lévy of Inserm.

Thanks to the extensive existing research infrastructure available through Pitt's Clinical and Translational Science Institute, PA Cares for Us was selected by the NIH to be the first of several sites to launch.

Research Effort Seeks Historic Levels of Participation

The University of Pittsburgh Clinical and Translational Science Institute and UPMC have launched the PA Cares for Us Research Program, a research participant enrollment effort that is a key part of the ambitious Precision Medicine Initiative introduced by President Barack Obama in 2015. PA Cares for Us is a part of the national All of Us Research Program, a long-term health research effort that aims to enroll 1 million or more research participants across the United States. The ultimate goal is to revolutionize our understanding of how and to what extent different factors like environment, DNA, and lifestyle affect long-term health.

Thanks to the extensive existing research infrastructure available through Pitt's Clinical and Translational Science Institute, PA Cares for Us was selected by the NIH to be the first of several sites to launch. The program enrolled the first volunteer research participant in the nation on May 31. Since then, PA Cares for Us has surpassed the 1,300 enrollee milestone and is responsible for more than 40 percent of the enrollment in the nation to date.

Over five years, the total amount awarded to Pitt is anticipated to top \$46 million. PA Cares for Us has the ambitious goal of forming one of the largest research cohorts in the history of medicine. The Pittsburgh program is looking for 150,000 participants from Western Pennsylvania, including populations historically underrepresented in research. For information, visit <https://pittplusme.org/>.

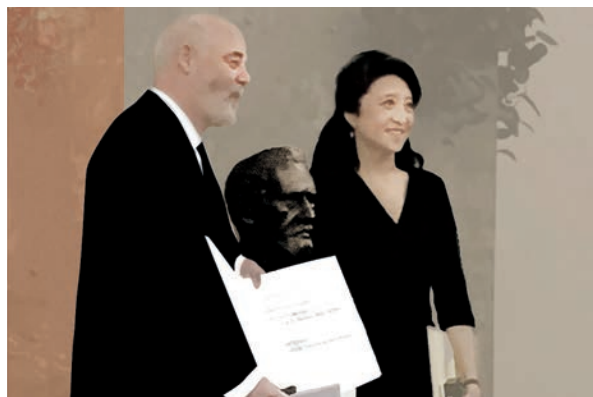
Hail to the Chief-Elect

Mary L. Phillips, MD, Pittsburgh Foundation-Emmerling Professor of Psychotic Disorders, has been named 2017-18 president-elect of the Society for Biological Psychiatry, an organization dedicated to advancing understanding, investigation, and treatment of psychiatric disorders. Phillips is also professor of psychiatry and of clinical and translational science.

She is internationally recognized as an expert in mood disorders research, affective neuroscience, and neuroimaging — particularly the use of functional magnetic resonance imaging to determine neural responses to emotional stimuli. Phillips is a fellow of the American College of Neuropsychopharmacology and was elected to the American Society for Clinical Investigation in 2014.

Pitt Cancer Researchers Honored

Yuan Chang, Patrick Moore Are Dual Prize Recipients



Two of the most prestigious awards in the field of medicine were presented to Pitt School of Medicine faculty members **Yuan Chang, MD**, and **Patrick S. Moore, MD, MPH**, in 2017—the Paul Ehrlich and Ludwig Darmstaedter Prize, in March, and the Passano Foundation Laureate Award, in May.

Given annually by the Paul Ehrlich Foundation, the Paul Ehrlich and Ludwig Darmstaedter Prize recognizes medical researchers who have made significant contributions in the fields of immunology, cancer research, microbiology, and chemotherapy.

Since 1945, Passano Foundation Laureates — more than 20 of whom have gone on to win the Nobel Prize — have been recognized for outstanding contributions to the advancement of medical science.

Chang and Moore, who were recruited to the University in 2002, are credited with discovering two of the seven known human viruses that directly cause cancer — Kaposi's sarcoma-associated herpes virus (1994) and Merkel cell polyomavirus (2008). Chang is Distinguished Professor of Pathology and UPMC Professor of Cancer Virology Research. Moore is Distinguished Professor of Microbiology and Molecular Genetics and Pittsburgh Foundation Professor of Innovative Cancer Research.

The two have been recognized with some of the highest national and international honors in medicine, infectious disease, and cancer, including the 2003 Charles S. Mott Award from the General Motors Cancer Research Foundation. Chang and Moore were elected to the National Academy of Sciences in 2012.

In Memoriam

Pittsburgh history includes a long list of innovators and leaders who've changed the world for the better. Many of those individuals made their greatest accomplishments in the fields of science and medicine. In 2017, the University of Pittsburgh bid farewell to three of the most accomplished and admired scientists of our time — all longtime School of Medicine faculty members whose legacies are writ large in the form of the longer, healthier, and more productive lives that are possible for all of us thanks to their accomplishments.



Herbert L. Needleman, MD

13 December 1927–18 July 2017

Herb Needleman's life's work demonstrated that environmental lead exposure — even at low doses — is linked to cognitive deficits and behavior issues. The pediatrician and emeritus professor of psychiatry at the University of Pittsburgh died in July 2017 in Pittsburgh at the age of 89.

He joined Pitt in 1981 after leaving Harvard University. Two years earlier, in 1979, he'd published a landmark study in the *New England Journal of Medicine* showing that Boston-area children with higher accumulations of lead also had, on average, five or six fewer IQ points than those with lower lead accumulations who were of the same neighborhood, ethnic background, and economic status.

"That study really changed the whole way the world thinks about lead poisoning," Philip Landrigan, MD, MSc, of Mount Sinai School of Medicine, a lead researcher who worked alongside Needleman, told *Pitt Med* magazine in 2001.

"He really made the world consider the possibility that subclinical exposure to environmental pollutants could have a serious societal impact," said David Bellinger, PhD, of Harvard University.

In 1996, Needleman conducted the first in-depth study on lead and delinquency. He measured bone lead levels in children and collected reports of aggression and delinquent behavior from the subjects, their parents, and their teachers. The results of this study showed an association between lead and delinquency.

The lead industry and experts it paid questioned his work. Yet he fought relentlessly for the health of children. For 40 years, through governmental committees, editorials, and other means, Needleman made the case against leaded gasoline, pushed for lead-free paint, and advocated for the remediation of houses with lead paint.

"The thing about lead toxicity is it's completely preventable," he said.



Thomas E. Starzl, MD, PhD

11 March 1926 – 4 March 2017

Thomas E. Starzl, Distinguished Service Professor of Surgery who performed the world's first successful liver transplant in 1967, died at age 90 in March 2017.

Starzl joined Pitt's School of Medicine in 1981 and launched the only liver transplant program in the nation at the time. Until he retired from clinical and surgical service in 1991, Starzl served as chief of transplantation services at UPMC Presbyterian, Children's Hospital of Pittsburgh of UPMC, and the Veterans Administration Hospital in Pittsburgh, overseeing the largest and busiest transplant program in the world. He then became director of the University of Pittsburgh Transplantation Institute, which was renamed the Thomas E. Starzl Transplantation Institute in 1996.

Starzl developed numerous immunosuppressive drugs to enable non-identical organ transplantation, and this work changed transplantation from an experimental procedure to an accepted form of treatment for patients with end-stage liver, kidney, and heart disease. In 1989, Starzl announced the first-time use of the immunosuppressive agent tacrolimus, which greatly improved survival rates for liver and other organ transplants and made intestinal transplantation possible for the first time.

A major focus of Starzl's later research was transplant tolerance and chimerism—the existence of cells from both the donor and recipient. His work contributed significantly to our understanding of transplant immunology, particularly with respect to how and why organs are accepted.

Starzl earned both a doctoral degree in neurophysiology and his MD from Northwestern University in Chicago, and he completed fellowship and residency training at Johns Hopkins Hospital in Baltimore.

Starzl was the recipient of more than 200 awards and honors, including the Lasker-DeBakey Clinical Medical Research Award, the National Medal of Science, and 26 honorary doctorates from universities around the world.



Julius Youngner, ScD

24 October 1920 – 27 April 2017

Julius Youngner was the last surviving member of the University of Pittsburgh team, led by Jonas Salk, that created the polio vaccine declared to be “safe, potent, and effective” amid international acclaim in 1955. Youngner, Pitt's Distinguished Service Professor of Microbiology and Molecular Genetics (emeritus), died in April 2017 at age 96. During his 60-year career, he witnessed the birth and growth of the field of virology and always seemed to be on the edge or in the middle of the “next big thing.”

After earning his doctorate in microbiology from the University of Michigan in 1944, Youngner was drafted into the U.S. Army and selected to work on the Manhattan Project studying the effects of uranium salts on human tissue. He then worked at the National Cancer Institute until 1949, when he was recruited to Pitt to join Salk in the quest for an effective polio vaccine.

As a member of Salk's team, Youngner developed trypsinization, a technique for culturing animal cells on a large scale. It made mass production of the killed-virus polio vaccine possible and ultimately changed the face of tissue culture investigation.

The virologist went on to chair Pitt's microbiology department from 1966–89. He became the first to demonstrate that nonviral agents could trigger interferon induction, which led to the idea that interferon could have important functions beyond its use as an antiviral. Interferon is now used in a variety of cancer therapies. His work on persistent viral infections made vaccines for type A and equine influenza possible.

Countless lives have been saved by Youngner's work.

Pitt Faculty Prominent at ASCI, AAP Roll Call

It's a pair of hat tricks for University of Pittsburgh medical faculty, with a cool half dozen tapped to join two important medical societies in 2017. Induction into these societies is considered among the highest honors in biomedical science.

Elected to the American Society for Clinical Investigation (ASCI) were:

Thomas G. Gleason, MD, UPMC Pellegrini Professor of Cardiothoracic Surgery and chief of the Division of Cardiac Surgery, Department of Cardiothoracic Surgery. He specializes in complex cardiac valvular repairs and surgery for thoracic aortic diseases. His research interest is in congenital bicuspid aortic valve and its associated aortopathy.

Ivona Pandrea, MD, PhD, professor of pathology, School of Medicine, and professor of infectious diseases and microbiology, Graduate School of Public Health. She is principal investigator on a \$3 million National Heart, Lung, and Blood Institute grant exploring the hypercoagulable state linked to HIV infection and non-AIDS comorbidities and on a \$2.7 million National Institute of Diabetes and Digestive and Kidney Diseases grant exploring the role of gastrointestinal dysfunction in AIDS progression.

Douglas B. White, MD, MAS, UPMC Professor for Ethics in Critical Care Medicine and vice chair, Department of Critical Care Medicine. He currently has more than \$7 million in grant support from the National Institute on Aging and the National Institute for Nursing Research to test interventions to improve surrogate decision making for incapacitated patients with advanced critical illness.

Elected to the Association of American Physicians (AAP) were:

Derek C. Angus, MD, MPH, Distinguished Professor of Critical Care Medicine and Mitchell P. Fink Professor and chair of critical care medicine. His research interests include clinical, epidemiologic, and translational studies of sepsis, pneumonia, and multisystem organ failure, as well as health services research of the organization and delivery of critical care services.

Charles F. "Chip" Reynolds III, MD, Distinguished Professor of Psychiatry and UPMC Professor of Geriatric Psychiatry (emeritus). His research focuses on the prevention and treatment of mood and anxiety disorders in older adults, treatment of complicated grief, and global mental health concerns.

Mark J. Shlomchik, MD, PhD, UPMC Professor and chair of immunology. In 2016, he received a 10-year, \$3.8 million MERIT award from the National Institute of Allergy and Infectious Diseases to support his research into autoimmune diseases and the body's immune response. Regarding lupus, Shlomchik's work was among the first to elucidate the roles of B lymphocytes and Toll-like receptors in promoting disease. Both of these are now targets of drugs that are either approved or in development to treat autoimmune disorders in patients.

ASCI is a medical honor society celebrating scholarly achievement among up-and-coming biomedical researchers, who must be 50 or younger at the time of their election. AAP selects 60 physicians each year for membership in recognition of their outstanding achievements in basic and clinical science and their application to clinical medicine.

AAP/ASCI



Left to right:
Gleason, Pandrea,
White, Angus,
Reynolds, Shlomchik

Chang Gets Leadership Nod

Judy C. Chang, MD, MPH, associate professor of obstetrics, gynecology, and reproductive sciences, and assistant dean for medical student research, has been accepted as a 2017-18 fellow in the Hedwig van Ameringen Executive Leadership in Academic Medicine (ELAM) program, a Drexel University College of Medicine fellowship for women faculty in schools of medicine, dentistry, and public health. Chang is the 10th Pitt faculty member selected for an ELAM fellowship.

The yearlong skill-building program equips participants to lead and manage in today's complex health care environment, with special attention to the unique challenges facing women in leadership positions. More than 1,000 ELAM alumnae hold leadership positions in institutions around the world.

New Pitt Center Targets Misshapen Proteins

Related Disorders Include Alzheimer's, Parkinson's, and Cystic Fibrosis

The University of Pittsburgh has established the Center for Protein Conformational Diseases — one of two such centers in the U.S.—to coalesce research efforts throughout the University that involve distorted proteins.

Headed by **Jeffrey Brodsky, PhD**, Avinoff Professor of Biological Sciences, Dietrich School of Arts and Sciences, the center includes faculty members from 15 academic departments and nine centers across Pitt's campus who seek to understand protein architecture and repair malformed proteins.

About 23,000 individual proteins work throughout the human body to maintain health. A protein's shape, or "conformation," governs its function; but proteins can be distorted as a result of metabolic stress, genetic mutations, and aging. A growing number of diseases are associated with malformed proteins, including Alzheimer's disease, Parkinson's disease, cystic fibrosis, certain cancers, and some kidney and liver diseases.

"Researchers in Pitt's School of Medicine and Dietrich School of Arts and Sciences have a long history of collaborative investigations into the biological mechanisms underlying these diseases," said Arthur S. Levine, MD, senior vice chancellor for the health sciences and Petersen Dean of Medicine. "It's very exciting that we now have a formal entity to support and accelerate these activities under the leadership of Dr. Brodsky, who is nationally recognized as a leading investigator of the basic biology of conformational diseases."

"It's very exciting that we now have a formal entity to support and accelerate these activities under the leadership of Dr. Brodsky."

— ARTHUR S. LEVINE, MD



Wagner Named National Academy of Inventors Fellow

With 19 patents and more than 40 patent filings to his name, University of Pittsburgh bioengineer **William R. Wagner, PhD**, has been named a fellow of the National Academy of Inventors (NAI). Election to the academy is a distinction accorded to academic inventors who have demonstrated a prolific spirit of innovation in creating or facilitating outstanding inventions that have made a tangible impact on quality of life, economic development, and societal welfare.

Wagner, who is director of the joint Pitt-UPMC McGowan Institute for Regenerative Medicine, is also professor of surgery, School of Medicine, and of bioengineering and chemical engineering, Swanson School of Engineering. In his most recent patent, Wagner and colleagues developed a temperature-sensitive polymer hydrogel that could be useful as a drug-delivery vehicle or as tissue-engineered scaffolding in heart muscle repair and other regenerative therapies. He is associated with six licenses or options of Pitt technologies, including three with the startup company Neograft Technologies (cofounded with **David Vorp, PhD**, Swanson School of Engineering associate dean for research), which is developing new treatment options for coronary artery bypass surgery and has begun clinical trials in Europe.

Wagner is the third Pitt faculty member to be named an NAI fellow, joining **Rory A. Cooper, PhD**, Distinguished Professor of Rehabilitation Science and Technology, School of Health and Rehabilitation Sciences (2014), and biotech entrepreneur **Mir Imran, MS**, adjunct faculty in the Department of Bioengineering, Swanson School of Engineering (2015). Wagner also serves as chair of the Tissue Engineering and Regenerative Medicine International Society (TERMIS)-Americas and chief scientific officer of the Armed Forces Institute of Regenerative Medicine. In addition, he is founding editor and editor-in-chief of *Acta Biomaterialia*, one of the nation's leading biomaterials and biomedical engineering journals.

*Charles F. Reynolds III, MD, Receives 2016
Pardes Humanitarian Prize in Mental Health*

Charles F. “Chip” Reynolds III, MD, Distinguished Professor of Psychiatry, UPMC Professor of Geriatric Psychiatry (emeritus), and former director of the Aging Institute, was awarded the 2016 Pardes Humanitarian Prize in Mental Health for his pioneering work in geriatric psychiatry and the prevention and treatment of late-life depression.

The Pardes Humanitarian Prize in Mental Health is given by the Brain and Behavior Research Foundation annually to recognize individuals whose contributions have made a profound and lasting impact in advancing the understanding of mental health and improving the lives of people suffering from mental illness. The prize is named in honor of Herbert Pardes, MD, a noted psychiatrist, outspoken advocate for the mentally ill, and the award’s first recipient.

Reynolds donated the cash that comes with the Pardes Prize to Sangath, a nonprofit organization in Goa, India, that improves mental health care in underdeveloped countries by teaching ordinary people to deliver front-line mental health care to address the unmet need for mental health services.

Shulkin Named U.S. Secretary of Veterans Affairs

David Shulkin, MD, whose nomination for Secretary of Veterans Affairs was confirmed in a unanimous Senate vote in early 2017, has a lot on his plate. Those who know Shulkin from his days in Pittsburgh say he is up to the task.

Persistent problems, including timely scheduling of veterans’ appointments, continue to plague the VA. In a White House briefing at the end of May 2017, Shulkin was candid in his assessment of the challenges remaining in efforts to overhaul the agency that provides health care to nearly 9 million veterans. With 300,000 employees, the VA is the nation’s second-largest agency after the Pentagon.

“I’m a doctor, and I like to diagnose things, assess them, and treat them,” he said.

Wishwa Kapoor, MD, MPH, Distinguished Service Professor and Falk Professor of Medicine, was the lone health services researcher on Pitt’s internal medicine faculty during Shulkin’s residency here in Pittsburgh. “He showed a lot of interest in the cost of health care and, even in those early days, saw increasing cost of care as unsustainable,” remembers Kapoor. “He was very forward-thinking about how cost of care affects the health system.”

During his last year of residency at what is now UPMC Presbyterian, Shulkin analyzed hospital diagnostic testing costs and was keen to study cost effectiveness, said Kapoor.

In the past, Shulkin has said he favors VA reforms like expanding patient access to outside providers but not system privatization. Writing in the *New England Journal of Medicine* in 2016, Shulkin supported opening the VA’s provider network to health care facilities run by other federal agencies and universities to increase patient access to care.

HOT TOPICS AND TOP SCIENTISTS

The School of Medicine, as one of the heavy hitters on campus, prides itself on attracting speakers of interest to the entire scientific community of Pittsburgh — from big names in the world of science to young guns on our own faculty. Here’s a sampling from the past year:

Dickson Prize in Medicine Lecture

As the high point of Science 2016, Pitt’s annual celebration of science and technology, **Jennifer A. Doudna, PhD**, a Howard Hughes Medical Institute investigator and University of California, Berkeley, faculty member, delivered the Dickson Prize in Medicine Lecture, “CRISPR Systems and the Future of Genome Engineering.” The School of Medicine honored Doudna with the \$50,000 Dickson Prize in Medicine for her breakthrough discoveries in genetics.

“Dr. Doudna’s discoveries have helped start the gene-editing revolution and, by elucidating the DNA-editing mechanisms of the CRISPR-Cas9 system, have given scientists the tools to add or delete genes in any type of cell,” said Arthur S. Levine, MD, Petersen Dean of Medicine. “In the near future, this technology might be used to eliminate mutated genes that cause conditions like sickle cell and a host of other diseases. It also could enable the genetic engineering of crops that resist disease and insect pests that fail to reproduce.”



Jennifer Doudna, PhD, receives the Dickson Prize in Medicine medal from Pitt Chancellor Patrick Gallagher, PhD.

“Dr. Doudna’s discoveries have helped start the gene-editing revolution and, by elucidating the DNA-editing mechanisms of the CRISPR-Cas9 system, have given scientists the tools to add or delete genes in any type of cell.”

—ARTHUR S. LEVINE, MD

Laureate Lectures

Since 2004, the Senior Vice Chancellor's Laureate Lecture series has brought scores of truly elite scientists from around the country to deliver lectures and meet with their scientific colleagues on Pitt's faculty. In 2017, four such talks were delivered to large audiences in Scaife Hall:

José-Alain Sahel, MD, Eye and Ear Foundation Professor and chair of the Department of Ophthalmology, University of Pittsburgh School of Medicine: "Sight Restoration: From Neuroprotection to Artificial Vision"

Subra Suresh, ScD, Henry L. Hillman President of Carnegie Mellon University (through June 2017): "Study of Human Diseases at the Intersections of Engineering, Sciences, and Medicine"

Lucy Shapiro, PhD, Ludwig Professor of Cancer Research in the Department of Developmental Biology at Stanford University School of Medicine: "The Regulatory Circuitry Controlling an Asymmetric Cell Division"

Zhijian "James" Chen, PhD, George L. MacGregor Distinguished Professor of Biomedical Science and professor of molecular biology at the University of Texas Southwestern Medical Center at Dallas: "Enemy Within: Immune and Autoimmune Responses to Cytosolic DNA"



12 at 12

There is a long tradition at Pitt of giving the best young scientists a platform to present their work that is equal to that provided for well-established, widely known researchers. The Senior Vice Chancellor's Research Seminar is the embodiment of that tradition. Each year, 12 Pitt scientists in the early stages of their careers are selected to present their work at lunchtime lectures in Scaife Hall. Most speakers are School of Medicine faculty, but many represent other health sciences schools, the Dietrich School of Arts and Sciences, and the Swanson School of Engineering. Whatever the topic, the speakers are invariably dynamic scientists who generate a great deal of interest across the campus community and demonstrate the exciting, interdisciplinary nature of research at Pitt.



A Toast to Diversity and Call to Action

At the Senator John Heinz History Center in Pittsburgh's Strip District, faculty members, students, trainees, and physicians gathered at the outset of the 2016-17 academic year for "A Toast to Diversity and Call to Action." Sponsored by the School of Medicine and UPMC Physician Services Division, the annual event highlights the strong community spanning Pitt and UPMC, made up of those who self-identify as members of groups underrepresented in the medical profession. A slideshow celebrating attendees' accomplishments from the past year ran throughout the evening, and guests from both institutions enjoyed the opportunity to connect and network.

"The theme was 'Celebrate, Connect, Catalyze.' We're trying to honor the achievements made and spark more activities and involvement in our community to help us recruit and retain faculty and trainees in a welcoming climate," says **Ora A. Weisz, PhD**, assistant vice chancellor for faculty excellence, health sciences; associate dean for faculty development and professor of medicine and of cell biology, School of Medicine; and vice chair for faculty development, Department of Medicine.



"The theme was 'Celebrate, Connect, Catalyze.' We're trying to honor the achievements made and spark more activities and involvement in our community to help us recruit and retain faculty and trainees in a welcoming climate."

—ORA A. WEISZ, PHD

The Pittsburgh-based biopharmaceutical company Complexa, which was formed to develop potent new anti-inflammatory drugs based on discoveries made here at the School of Medicine, announced a major step forward in July 2017. The company secured \$62 million in investment funding, which will enable phase II clinical trials of its experimental drug CXA-10.

The agent is an oral nitrated fatty acid compound with powerful anti-inflammatory properties. Years of combined biomedical and market research indicate that the drug has the potential to be a game-changer for a host of human diseases associated with fibrosis and inflammation; the most promising immediate targets are a **pair of rare diseases that cause a great deal of suffering but have few good treatment options.**

- **Focal segmental glomerulosclerosis leads to scarring in the kidney**, which reduces kidney function and causes up to 70 percent of patients to develop end-stage renal disease. Once these patients — 40,000 in this country alone — require dialysis, average life expectancy is only eight years. There are currently no approved therapeutic options, and patients often endure extensive treatment with steroids without responding. Complexa is investigating whether CXA-10 could replace steroid treatment in recently diagnosed patients.
- **Pulmonary arterial hypertension is a rare disease that leads to exercise intolerance, breathlessness, heart failure, and death.** After diagnosis, the mean survival is five to seven years. While there are approximately 25,000 treatable patients in the country, the therapies available to them are limited to vasodilators that do little to modify the disease course. In animal models of this disease, CXA-10 has shown some disease-modifying effects. Beginning in early 2018, the drug will be tested on top of existing standard of care.

Bruce Freeman, PhD, UPMC Irwin Fridovich Professor and chair of the Department of Pharmacology and Chemical Biology in the School of Medicine, is one of two scientific founders of Complexa. Freeman's lab has made seminal discoveries related to reactive inflammatory mediators. These insights have led to the identification of new drug strategies for treating metabolic diseases, fibrosis, and acute/chronic inflammatory disorders. His team pioneered the concept that nitric oxide has cell signaling and pathogenic actions modulated by a reaction with superoxide, yielding the oxidizing and nitrating species peroxynitrite. Of relevance to Complexa, Freeman's laboratory also discovered that metabolic and inflammatory reactions of unsaturated fatty acids yield products that manifest potent anti-inflammatory and tissue-protective signaling actions. His work has led to numerous patents and more than 250 peer-reviewed publications in basic science and clinical journals.

“Our planned partnership with Microsoft will help us transform the delivery of care and wellness in a way that was never possible before.”

—STEVEN D. SHAPIRO, MD

UPMC Is Microsoft's First Partner in Health Care Innovation Initiative

In early 2017, UPMC and Microsoft announced a strategic research partnership to develop transformative solutions and technologies to improve health and health care systems.

By combining Microsoft's expertise in artificial intelligence (AI), cloud computing, and business optimization tools with the clinical, research, and product development expertise of UPMC, the two expect to solve some of the most perplexing challenges facing the health care industry — from disconnected information systems and regulatory uncertainty to physician burnout and poor communication with patients.

“Despite UPMC's efforts to stay on the leading edge of technology, too often our clinicians and patients feel as though they're serving the technology rather than the other way around. With Microsoft, we have a shared vision of empowering clinicians by reducing the burden of electronic 'paperwork' and allowing the doctor to focus on the sacred doctor-patient relationship,” said **Steven D. Shapiro, MD**, Distinguished Professor of Medicine, chief medical and scientific officer of UPMC, and president of UPMC's Health Services Division. “Our planned partnership with Microsoft will help us transform the delivery of care and wellness in a way that was never possible before.”

Peter Lee, PhD, corporate vice president of Microsoft Research said, “This will be the first significant partnership in a new initiative that Microsoft is calling Healthcare NExT, which will deeply integrate greenfield research and health technology product development. Through these collaborations between health care partners and Microsoft's AI and research organization, our goal is to enable a new wave of innovation and impact.”

The two organizations intend to focus on projects that will empower both physicians and consumers and advance groundbreaking immunology research by using Microsoft's deep AI expertise and global-scale cloud. These new products are expected to be built with and piloted at UPMC, under the guidance of its innovation and commercialization arm, UPMC Enterprises, which already encompasses a broad portfolio of both homegrown and externally created technology companies.

“UPMC has a long history of applying technology the right way and bringing innovations to market,” said **C. Talbot Heppenstall Jr.**, president of UPMC Enterprises. “With Microsoft's vision and technological ingenuity, our planned, multi-year collaboration has the potential to help us deliver vastly better care and a better patient experience at a lower cost — the ‘Triple Aim’ of health care.”

Pitt's Focus:

DON'T WAIT, INNOVATE.

Today, Pittsburgh is... teeming with startup companies and is an internationally recognized research leader in medicine, robotics, advanced manufacturing, big data, and autonomous systems.

Pitt Chancellor Patrick Gallagher, PhD / *Science*, June 8, 2017

DATA, DATA EVERYWHERE AND BUSINESS PLANS TO SYNC

In April, the Pittsburgh Health Data Alliance (PHDA) hosted "The Next Big (Data) Thing," a conference that was both a presentation and celebration of progress for the University of Pittsburgh, UPMC, and Carnegie Mellon University partnership launched in 2015 to exploit rich streams of institutional data by creating practical applications that deliver better health, improved quality of life, and economic growth.

During breakout sessions, progress on projects spanning precision medicine and consumer health devices to biometrics and hospital risk management tools were reviewed to illustrate the breadth of PHDA-sponsored research at Pitt and Carnegie Mellon. Some highlights:

MEDivate is a personalized medication management application. A version is available through Giant Eagle pharmacies or individual download to monitor vaccine information.

Philip Empey, PharmD, PhD, assistant professor of pharmacy and therapeutics, School of Pharmacy, and associate director for pharmacogenomics, Institute for Precision Medicine, principal investigator

SPD: A computational cancer analytics company, Spatial Pathology Diagnostics, is developing software that enhances digital pathology practice and guides decisions on diagnoses, prognoses, and therapeutics. Studies in colon and breast cancers are under way to validate the approach.

Chakra Chennubhotla, PhD, associate professor of computational and systems biology, and **D. Lansing Taylor, PhD**, Allegheny Foundation Professor of Pharmacology, professor of computational and systems biology, and director, University of Pittsburgh Drug Discovery Institute, principal investigators

Tumor-Specific Driver Identification uses tumor-specific genomics to determine the genetic drivers of an individual patient's tumors, with the ultimate goal of enabling personalized treatments for cancer patients.

Xinghua Lu, MD, PhD, MS, professor of biomedical informatics, and **Gregory Cooper, MD, PhD**, professor and vice chair, Department of Biomedical Informatics, principal investigators

MEDICAL RESEARCH HELPS PITT SET PATENT RECORD

The U.S. Patent and Trademark Office issued 102 patents to University of Pittsburgh faculty and students in fiscal year 2017, ranking Pitt in the top third of universities issued United States patents. The figure surpasses a previous record of 80 patents set in fiscal year 2016.

"I think it's a metric of the innovative and entrepreneurial spirit of our faculty," said **Marc Malandro, PhD**, founding director of Pitt's Innovation Institute and, as of August 2017, vice president of operations for science at the Chan Zuckerberg Initiative in Palo Alto, Calif.

The National Academy of Inventors and the Intellectual Property Owners Association annually rank universities by the number of patents issued during the previous calendar year. So for 2016, Pitt ranked 27th, up from 35th in 2015. Pitt's internal record is for fiscal year 2017, which ended June 30.

Because of Pitt's relationship with UPMC, growth in the University's patents is predominantly due to life sciences-related inventions, said Malandro. Among patents issued during 2016 were an immunotherapy-based cancer treatment licensed by a Massachusetts company and an eye-disease treatment licensed by a startup called Ocugenix.

Since 2007, the Innovation Institute and its predecessor offices have generated more than \$110 million through more than 1,000 licenses, according to Malandro.

GENETIC CANCER TEST MAY LEAD TO SAFE THYROID-PRESERVING SURGERY

Pitt faculty and clinicians are conducting a first-ever clinical trial to determine whether a University-pioneered genetic test could spare some thyroid cancer patients from complete removal of the important hormone-regulating gland. Thyroid preservation surgery minimizes complications and can help patients to avoid lifelong thyroid hormone balancing medications.

In an innovative approach, the two-year trial is being funded entirely by philanthropy.

Researchers will investigate whether the Pitt-developed molecular genetic test ThyroSeq can correctly differentiate pre-operatively between cancers requiring complete thyroid removal and those likely to be less invasive that warrant a thyroid-preserving surgical approach.

More than a dozen of a projected 100 newly diagnosed thyroid cancer patients had been enrolled as of early summer 2017, said **Linwah Yip, MD**, associate professor of surgery and principal investigator.

According to the American Cancer Society, about 56,870 cases of thyroid cancer are diagnosed in the United States every year, and about 2,010 people die of the disease.

ThyroSeq, developed by a scientific team led by **Yuri Nikiforov, MD, PhD**, professor and vice chair of pathology, can simultaneously test 14 genes for 42 markers of thyroid cancer using just a few cells collected during initial biopsy.

The test has performed well at differentiating between cancerous and noncancerous thyroid nodules and has already spared patients from unnecessary operations.

PITT GETS TISSUE CHIP TESTING CENTER

The University of Pittsburgh Drug Discovery Institute (UPDDI) has been awarded a \$1 million-plus grant to establish a new Tissue Chip Testing Center (TCTC). The grant, led by **Mark Schurdak, PhD**, research associate professor of computational and systems biology, was awarded by the National Center for Advancing Translational Sciences at NIH.

More than 30 percent of drugs that show promise during early-phase trials are later abandoned because of toxicities, while approximately 65 percent of subsequent candidate drugs fail due to inadequate efficacy.

The initiative seeks to develop three-dimensional platforms on which living tissues and cells can be grown to serve as accurate human organ models for

experimental testing. Using a tissue chip system that more closely resembles human organ function will dramatically increase the speed and effectiveness of drug testing.

Data will be stored in a specially developed UPDDI database that is accessible to the broader research community.

The research team is currently awaiting regulatory approval by the Food and Drug Administration to begin a larger trial.

SEVERE BURNS SHOW DRAMATIC HEALING AFTER BEING SPRAYED WITH PATIENTS' OWN STEM CELLS

Six men with severe second-degree burns caused by scalding water, hot tar, gasoline, a chemical explosion, contact with a live electrical wire, and ignition of paint-can fumes have become the latest patients treated at UPMC Mercy Hospital with an innovative skin regeneration technology. To date, 45 people with burn injuries have undergone a procedure in which their own epidermal stem cells are isolated from healthy skin, then sprayed onto the burn to promote healing.

In an August 2016 edition of *Burns*, the journal of the International Society for Burn Injuries, **Jörg Gerlach, MD, PhD**, director of the Bioreactor Group at the McGowan Institute for Regenerative Medicine and professor of surgery and of bioengineering, and colleagues report astonishing degrees of recovery and full return of burn-injury affected function in all six patients.

PITT ENLISTS PARTNERS TO ACCELERATE RESEARCH TO REALITY

New software tools, statistical modeling, drug development, and a vast array of research efforts focusing on heart and brain health are on the University of Pittsburgh's agenda in partnerships announced over the past fiscal year.

Partner: Children's Hospital of Pittsburgh of UPMC

Project: Software for early detection of potentially catastrophic cardiac events among hospitalized children in intensive care

Participants: **Fuchiang "Rich" Tsui, PhD**, associate professor of biomedical informatics, and his team are using electronic health record data to build predictive models that give critical care staff real-time mortality warning indexes at Children's. **Ricardo Muñoz, MD**, professor of critical care medicine, is leading a team of pilot users.

Significance: Children with congenital heart disease account for more than 80 percent of the patients in cardiac intensive care. Current warning systems use a limited amount of available patient data and cannot discriminate risk associated with differing cardiovascular physiology.

Partner: Pfizer Inc.

Project: A computational model built from imaging, genetic, and clinical data to advance understanding of and treatments for schizophrenia, Alzheimer's disease, and related brain diseases

Principal Investigator: **Kayhan Batmanghelich, PhD, MSc**, assistant professor of biomedical informatics

Significance: Researchers aim to develop a statistical model that correlates brain imaging information to disease-related biomarkers that can potentially be used in precision medicine.

Partner: Bayer

Project: A master collaboration agreement to advance research for heart, lung, and blood diseases

Principal Investigator: **Mark Gladwin, MD**, Distinguished Professor of Medicine, Jack D. Myers Professor and chair, Department of Medicine; director, Vascular Medicine Institute

Significance: This broad collaboration spans concepts and early research studies to drug development and big data analyses, including real-world evidence studies. In addition to the research partnership, Bayer will be supporting an independent investigator-initiated clinical trial in sickle cell disease.

PITT INNOVATION CHALLENGE FUNDS NEW PROJECTS

A total of \$375,000 in funding grants were awarded in September 2016 to innovative School of Medicine-affiliated projects that address problems in health care during a Pitt Innovation Challenge (PlnCh) event. Three projects took home \$100,000 each, and three others received \$25,000 in an evening featuring live presentations and posters at the University Club.

PlnCh, now in its third year, is sponsored by the University of Pittsburgh's Clinical and Translational Science Institute, Office of the Provost, and Innovation Institute. To date, nearly \$1.7 million has been awarded.

\$100,000 awards:

Neurogel is an injectable solution containing a regenerative matrix that promotes healing of damaged nerve tissue. Team includes **Paul Gardner, MD**, associate professor of neurological surgery.

Esophagel is a minimally invasive treatment for Barrett's esophagus, a condition that can lead to esophageal cancer. Team led by **Stephen Badylak, MD, PhD, DVM**, professor of surgery and deputy director, McGowan Institute for Regenerative Medicine.

CardioTrak is a novel peptide that can deliver radioisotopes specifically to heart muscle, reducing radiation absorbed by the body during cardiac stress tests. Team led by **Cecilia Lo, PhD**, F. Sargent Cheever Professor and chair, Department of Developmental Biology.

\$25,000 awards:

Emotion Prosthetics is a wearable device that detects stress and noninvasively counters it through stimulating cranial nerves. Team led by **Greg Siegle, PhD**, associate professor of psychiatry.

EyeCures is an antibody technology-enabled eye drop formulation that delivers advanced biological drugs to the eye's surface. Team led by **Robert M.Q. Shanks, PhD**, associate professor of ophthalmology.

Ventriculo-Amniotic Shunt for Fetal Aqueeductal Stenosis is a device to drain excess fluid from the fetal brain and prevent progressive brain injury during pregnancy. Team includes **Stephen Emery, MD**, associate professor of obstetrics, gynecology, and reproductive sciences, and **Stephanie Greene, MD**, assistant professor of neurological surgery.



DAY: 1

DAY: 5

DAY: 25

CASE STUDY

Novel Stem Cell Spray for Burns

Photographs of a patient's burn injury taken before, five days after, and 25 days after being sprayed with a solution containing stem cells from his own skin.



**WHITE HOUSE FRONTIERS
CONFERENCE BRINGS
NATIONAL INNOVATION
CELEBRATION TO PITTSBURGH**

Poet John Keats said, "Touch has a memory." For Nathan Copeland, that memorable touch happened on a chilly afternoon in October 2016, during the Pittsburgh-hosted White House Frontiers Conference, when he shared a spotlight with President Barack Obama. Copeland, 31, has been wheelchair bound with tetraplegia since a car accident in 2004 and works with researchers at Pitt to manipulate a robotic arm and hand using only his thoughts, transmitted via cable from electrodes implanted in his brain. The president shared his own memory of their meeting later that day: "We shook hands. He had a strong grip, but he had kind of toned it down. Then we gave each other a fist bump. That's what science does. That's what American innovation can do... that's what this Frontiers Conference is all about — pushing the bounds of what is possible."

President Barack Obama fist-bumps Nathan Copeland during the October 2016 White House Frontiers Conference in Pittsburgh, which spotlighted scientific and technological innovation—the president noted the firm grip of Copeland's handshake.

Imagine a Machine Controlled by Your Thoughts

Pittsburgh's Brain-Computer Interface Team Forges Ahead

Nathan Copeland groans as the cylinder he's been trying to place on a table falls over for the fifth time. "I could do it yesterday," he insists.

"We're messing with you," **Robert Gaunt, PhD**, assistant professor of physical medicine and rehabilitation and of bioengineering, says with a grin as graduate students push buttons on a computer console that control whether — and what — Copeland may sense while manipulating the robotic arm and hand.

Pause for an eye-roll from Copeland. An aggrieved sigh drifts across the University of Pittsburgh's brain-computer interface (BCI) lab before Copeland settles himself for another attempt.

Now 31, Copeland was 18 when a car accident injured his spinal cord, leaving him paralyzed from the upper chest down, unable to feel or move his lower arms and legs. The college freshman had been pursuing a degree in nanofabrication following advanced science courses in high school. It was time to start over.

Copeland is the third person with tetraplegia to help researchers refine brain-computer interface technology developed at Pitt. Cables attach four electrodes embedded in the surface of his brain to a bank of computers, which, in turn, link to a robotic arm and hand. Three times a week for more than two years, Copeland has been moving items around with the arm, manipulating the wrist, hand, and fingers with a fluidity that often matches natural movement. He is expected to continue working on the BCI study for a total of five years.

After computer controls are adjusted to allow Copeland to resume full control of the arm, the cylinder moves across the table with uncommon grace and balances on its weighted end. "See, I *can* do it!" he crows.

Copeland's accomplishment differs from those of his predecessors because of the sensations he perceives when the robotic hand touches objects and Pitt researchers stimulate the electrodes implanted in his somatosensory cortex, a structure next to the motor cortex, which hosts the electrodes that allow him to move the arm and hand.

"Sometimes it feels like a tingle and sometimes like pressure or warmth," he says. The sensory feedback helps with grasping tasks, though gauging applied pressure is still tricky.

"We've been working on trying to tie together the motor control and sensory side of things," explains **Jennifer Collinger, PhD**, assistant professor of physical medicine and rehabilitation. "The mechanics of that are working. What we're trying to find out now is how to do that in the optimal way."

Researchers are currently pursuing additional neural signaling studies as well as investigating a "short cut" via machine learning with help from scientists at Carnegie Mellon University's Robotics Institute, says **Andrew Schwartz, PhD**, Distinguished Professor of Neurobiology and Professor of Systems Neuroscience. "It took 30 years of research to get this far," he says. "But what is really exciting now is the opportunity to learn something new."



Our mission is to educate science-based, skilled, and compassionate clinicians, as well as scientists whose biomedical research will better the human condition and advance our fundamental understanding of medical science.

education & training

Students Embrace Scholarly Research Project

It was a milestone year for the School of Medicine's Scholarly Research Project. In April, the Class of 2017 became the 10th class to complete the research requirement as a condition of graduation from the MD program. Introduced as an innovative (those less visionary called it "misguided") strategy to engage med students in mentored research throughout the course of their medical school experience, Pitt's Scholarly Research Project has

since become a model for other top medical schools attempting to incorporate a research component into the MD curriculum.

Arthur S. Levine, MD, dean of the medical school since 1998, recalls, "When I first suggested that every Pitt medical student should be required to do research, I was warned that, (1) applications to the medical school would plummet, (2) the quality of applicants would decline, and (3) I would not last long as dean. Well, none of those things has happened," Levine says, noting that admission to the medical school has become increasingly competitive. "And the fact that other top medical schools have followed our lead tells me we're doing something right."

The best medical students, it turns out, see the value of engaging in biomedical research. In fact, they increasingly recognize that their medical education would be incomplete without it. Medicine is rooted in science, after all. When an aspiring physician understands the importance of scientific rigor in research, it becomes obvious that scientific rigor is critical to patient care, as well.

Many Pitt med students report that their research experience really pays off when it comes to selecting and interviewing for residency programs.

"Early on, it's a good way to explore different specialties," said graduating med student William Wang. "When I started med school, I wasn't sure what I wanted to do. I was considering orthopaedic surgery, but I feel like I really discovered it doing research. Toward the end, I just couldn't see myself doing anything else."

Wang's classmate Mohini Dasari added that her research experience was a frequent topic of conversation during residency interviews, saying that program directors and others "definitely appreciate your ability to talk about research." She also noted that, with Pitt's Scholarly Research Project, mentorship is both well supported and structured, with clear expectations and milestones. "I found a mentor who was hands on but also allowed me the independence I needed to design the experiment, collect data, and analyze the results on my own."

At Scholars Day 2017, four graduating MD students, including Dasari and Wang, were individually honored with a Bert and Sally O'Malley Award for Outstanding Medical Student Research.

Introduced as an innovative (those less visionary called it "misguided") strategy to engage med students in mentored research throughout the course of their medical school experience, Pitt's Scholarly Research Project has since become a model for other top medical schools attempting to incorporate a research component into the MD curriculum.

SCHOLARLY PROJECT BY THE NUMBERS / CLASS OF 2017

Beginning in year one of medical school, students in the Class of 2017 embraced the opportunity to engage in research through the Scholarly Research Project.

132

med students completed a research project

89% (117) participated in summer research between their first and second years of med school

168

peer-reviewed publications

plus an additional 41 submitted and/or under review

241

presentations at national and international meetings

40

national or state awards

60

local awards

2017 O'MALLEY AWARD WINNERS

At Scholars Day 2017, four graduating MD students were individually honored with a Bert and Sally O'Malley Award for Outstanding Medical Student Research.

The best of the best from the Class of 2017:



MOHINI DASARI, MD

Barriers to Long-Acting Reversible Contraceptive (LARC) Uptake among Homeless Young Women

Residency Match:

General Surgery, University of Washington Affiliated Hospitals, Seattle

Mentor:

Elizabeth Miller, MD, PhD Professor of Pediatrics and Chief, Division of Adolescent and Young Adult Medicine; Professor of Behavioral and Community Health Sciences, Graduate School of Public Health



MARK DOYAL, MD

Promoter-Targeted Anti-Nociceptive HSV-1 Vectors Have Differential Effects on Pain Based on the Neuronal Population Targeted

Residency Match:

Emergency Medicine, Henry Ford Hospital, Detroit

Mentor:

William Goins, PhD Research Assistant Professor of Microbiology and Molecular Genetics



SOPHIE HAPAK, MD

Synapse Loss in Triple Mutant (PS1/APP/Kalirin +/-) Mice

Residency Match:

Internal Medicine, University of Minnesota Medical School, Minneapolis

Mentor:

Robert Sweet, MD UPMC Professor of Psychiatric Neuroscience, Department of Psychiatry, and Professor of Neurology



WILLIAM LIU WANG, MD

A Prospective Comparison of Diagnostic Tools for the Diagnosis of Carpal Tunnel Syndrome

Residency Match:

Orthopaedic Surgery, Thomas Jefferson University, Philadelphia

Mentor:

John Fowler Jr., MD Assistant Professor of Orthopaedic Surgery and Assistant Dean for Medical Student Research

CLASS OF 2021 / BY THE NUMBERS

15,872 students applied for the **148 available positions** for the medical school

Class of 2021, which is made up of **71 men** and **77 women**.

Members of the class are graduates of **82 different undergraduate colleges** and universities, and they hail from **29 states** and one foreign country. **Sixteen percent** come from underrepresented groups as defined by the Association of American Medical Colleges.

DEMOGRAPHICS

As of the 2017-18 academic year, **591 MD students** are registered in the School of Medicine, including **300** (51 percent) women and **291** (49 percent) men. Of these, **186** (31 percent) are Pennsylvania residents; approximately **16 percent** of Pitt medical students are **from groups that are underrepresented within the medical profession**.

There are **273 registrants in PhD programs** (including 82 in the Medical Scientist Training Program), **87 students in MS programs**, and **27 students in certificate programs**.

The School of Medicine has **2,264 regular** and **2,213 volunteer faculty members**. Of these, **81 are current members of the Academy of Master Educators**, an organization that recognizes and rewards excellence in medical education.

Team Twins



Identical twins Crystal (left) and Christy Taylor (both of the Class of '20) grew up in Florida, and each earned a bachelor's degree in biology and master's degree in public health from the University of Miami. While in grad school, Crystal taught biostatistics, and Christy epidemiology. Christy notes that their public health training will help them address the social determinants of health as they provide care.

The twins endured some difficult life changes themselves before entering the University of Pittsburgh School of Medicine. When they were in high school, one of their parents struggled with a debilitating condition. Christy and Crystal eventually moved in with their grandmother; and after college, they struck out on their own. They say it was the kindness of people here that drew them to Pittsburgh, 1,200 miles from their grandmother.

They attend many of the same classes, and both light up when asked what specialty they'll pursue.

"I hate dressing up," says Crystal, who is interested in surgery. "I remember watching TV like, 'Oh my gosh, doctors get to wear scrubs and sneakers? Sign me up!'"

"I hate dressing up, too," says Christy. "But I'm leaning toward cardiology."

And they'll continue supporting one another. "We really balance each other out. We don't really have anybody except each other," says Crystal.

Match Day rightfully commands the med school's attention each spring, but what about all the envelopes being opened at other schools? Who are the brand new docs coming to Pittsburgh?

Some impressive stats on the newest house staff: This year, 328 new residents said "Yes!" to Pitt and UPMC. Nationwide, more than 30,000 graduate medical positions were offered this year. At Pitt, 98.5 percent of spots offered were filled — more than two points higher than the national average.

UPMC's 2017 MATCH STATS

UPMC/Pitt is the

3rd Largest
training program in the country

328

New residents matched to UPMC/Pitt in 2016

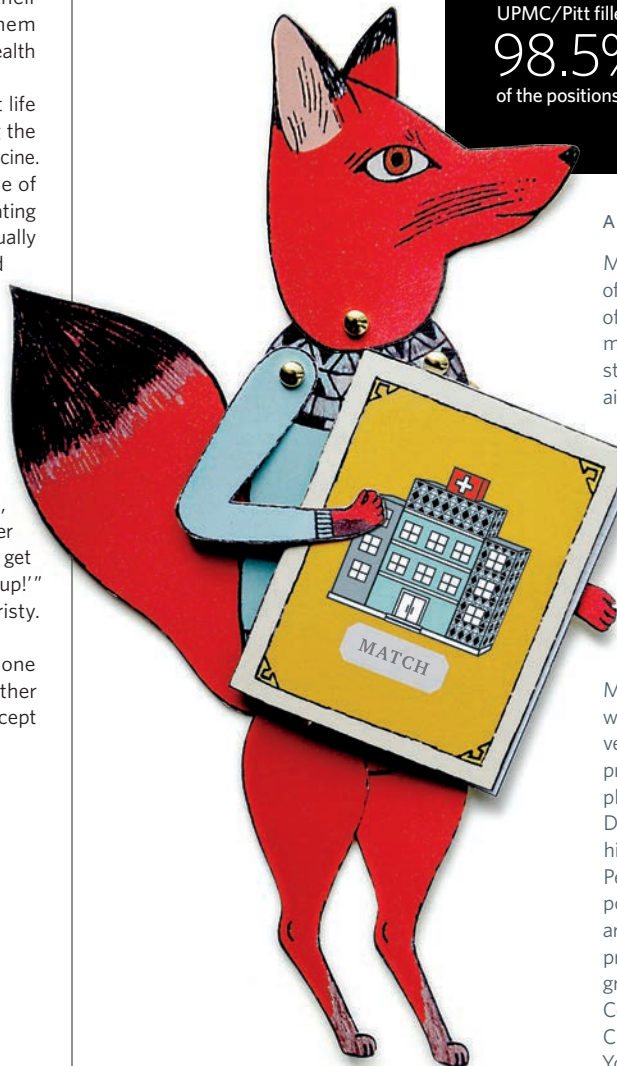
44

New trainees at UPMC/Pitt are graduates of Pitt's School of Medicine

UPMC/Pitt filled

98.5%

of the positions offered (national avg: 96%)



A MATCH MADE IN PITTSBURGH

Match Day 2017 at the University of Pittsburgh was a lively celebration of the hard work and accomplishments of our graduating med students. Held in the bright and airy Petersen Events Center lobby,

Pitt's Match Day festivities included dance music on full blast and a wall map of the United States, which students decorated with push pins after they learned where in the world they would begin their residency training.

Of the 18,000 graduating med students participating in the Match from across the nation, 149 were Pitt students, and they placed very well in this highly competitive process. Their residency assignments placed them in 30 states plus the District of Columbia — an all-time high. After the Commonwealth of Pennsylvania, the states most populated by Pitt's 2017 graduates are California and New York. The programs attracting the most Pitt grads, after UPMC, included Cornell, Columbia, Johns Hopkins, Harvard, Case Western Reserve, and New York University.



bedside to bench

New PhD Program's Audacious Goal: Build a Better Biomedical Scientist

Traditionally, medical schools have trained PhD students from the ground up. They'd begin with biochemistry and a thorough introduction to wet bench laboratory science. Upon that base, they'd build upward, systematically, to the physiology of living organisms. Eventually, students might get some exposure to clinicians and patients with conditions related to their chosen areas of research.

But science has changed dramatically in recent years, and the education of scientists must follow suit. Institutions around the world now understand that the scientists of the future will be thoroughly versed in biomedical informatics and computational biology. At the same time, they should feel empowered to explore the clinical realm—yes, even laboratory scientists must interact with clinicians and patients if they hope to understand and help cure human disease.

For a prospective PhD student, this may sound like a lot to ask of a single program, but faculty in Pitt's School of Medicine have prepared a long time for this. They've developed an approach that they believe is nothing less than a culture change in the education of biomedical scientists—the new Integrative Systems Biology graduate program.

Systems biology acknowledges that biological entities can't be reduced to linear representations of how their parts function. To study dynamic, complex living systems, systems biologists use technologies like genomics, bioinformatics, and proteomics, plus mathematical and computational models to describe and predict dynamic behavior.

First-year PhD students are introduced to biomedical science through extensive clinical coursework alongside Pitt physician-scientists.

The new Integrative Systems Biology program represents a culture change in how medical schools educate, train, and cultivate biomedical scientists.



COMPUTATIONAL BIOLOGY FOR LAB SCIENTISTS

Students in Pitt’s Integrative Systems Biology program are immersed in biomedical informatics and computational biology as soon as they arrive on campus—no prior experience required.

The program director of the ISB program, Neil Hukriede, PhD, associate professor and vice chair of developmental biology, says, “Bench scientists like myself, we struggle with the computation side because we weren’t trained as computational biologists. What we’re trying to do is to generate students who can do both.”

“That’s the thing that hooked me the most, I think,” says ISB student Ricardo DeMoya, “because I arrived with no computational background. In just one bioinformatics class, my knowledge has expanded beyond belief.”

“My undergrad advisor was in bioinformatics and he always said, ‘That’s the future of science. The future of science will be an amalgamation of computational skills and wet lab research.’”
—ISB student Alex Swain



CLINICAL BLOCKS FOR PHD STUDENTS

First-year ISB students are quickly placed in a clinic-focused course that is at the heart of the culture change that the program represents. “Bedside to Bench” is led by Gary Thomas, PhD, professor of microbiology and molecular genetics. Working closely with physician-scientists like Thomas Kleyman, MD, Pitt’s Sheldon Adler Professor of Nephrology Research and chief of the Renal-Electrolyte Division, Thomas created a course that puts PhD students in the clinical environment to foster deep understanding of human physiology and diseases that they might eventually help cure.

Students rotate through clinical blocks like endocrinology, cardiology, pulmonology, and infectious diseases. They meet patients who’ve survived breast cancer, undergone cardiac procedures, or live with diabetes. After each clinical block, they take part in a journal club in which they discuss recent research findings with clinicians.

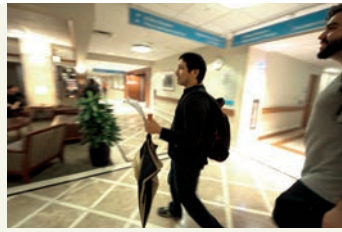
Thomas says this is the only such program in the nation introducing PhD students to biomedicine through extensive rotations through clinical areas. In their second year, students continue the course with six more blocks, ultimately covering 10 divisions of the Department of Medicine and two clinical departments.

Watching the students develop over the course of the year is incredible,” says Thomas. “By the middle of the course, they are becoming very savvy when it comes to understanding biology. The knowledge of a typical first-year grad student is usually narrow and shallow. This course gives them a much deeper and broader exposure to human physiology so that they can better understand the complex molecular pathways that drive disease.”



“The clinical perspective we get in this program — having the rotations and being in journal club with physician-scientists — is something that I don’t think I would be getting in any other program.”
—Sarah Munyoki

A DAY IN THE LIFE OF AN ISB STUDENT includes journal club at Bridgeside Point and a shuttle ride back to the heart of Pitt's campus, where students rotate through a dialysis clinic with faculty physicians from the Department of Medicine. The day concludes with a class that encourages them to apply what they've learned in clinic to basic research in the lab.



With extensive input from Pitt clinician-scientists Roderick Tan, MD, PhD, and Nate Weathington, MD, PhD, who are both assistant professors of medicine, this is the only program in the nation introducing PhD students to biomedicine through comprehensive clinical rotations.



ISB STUDENTS: IN THEIR OWN WORDS

"The most interesting part is the clinical blocks. In the endocrinology block, we met a person with diabetes. The experience really expanded my knowledge. For example, I thought that with type I diabetes, you only need to take insulin once or twice a day. But it's much more complex than that. Oftentimes, if you are diabetic you're on multiple other medications because you have complications like kidney failure and nerve loss. I thought it was kind of simple—now we have insulin, and it's very easy to manage. A patient being on 20 different medications a day is something I didn't think about before." — Sarah Munyoki

"I chose this program because I wanted to work with both clinical data and genetic data. I think it's really great that this graduate program is in a medical school and at a big medical center. My lab is in Children's Hospital, and we have exomes from around 500 patients. We can follow these patients very closely at the hospital, and that's a very useful resource to have as a graduate student. I can work with all of this data from a large population of patients, and that's what I want to do as a scientist." — Kyla Williams

RE-IMAGINE GRADUATE BIOMEDICAL EDUCATION

"We're really trying to change how graduate education is implemented. For example, we expect a student in the last year to have an externship experience. So, if your experiments are very much wet lab, you might spend three to six months in a lab that does more computation. It could also be off campus. We've made arrangements with venture capital firms, so a student could spend three to six months working in venture capital. We also have arrangements with the Beijing Genomics Institute in China, so a student could go there and do computational work on a different level. If your project has a clinical/translational bent, you might spend it in the clinical realm, where you have patient recruitment samples being obtained from patients. Or a student can do an externship experience with Pitt's Innovation Institute and learn about intellectual property. A student might learn what it takes to launch a successful company. We want to broaden students' horizons in terms of career choices so that it's not just 'one size fits all.'" — Cecilia Lo, PhD, F. Sargent Cheever Professor and chair of developmental biology; executive director, ISB program



In-Depth Study for Med Students

Through a raft of specialized programs, diverse research opportunities, and areas of concentration, med students at Pitt are able to explore their interests in depth. Many will take a year off at some point to earn a master’s degree in public health, biomedical ethics, or a related field; others will devote a full year to research through either the Clinical Scientist Training Program (CSTP) or the Physician Scientist Training Program (PSTP).

CSTP

The Clinical Scientist Training Program offers a leg up for medical students who show an interest in and a talent for clinical research. Select students whose mentored scholarly projects meet the NIH definition of clinical research are invited to delve deeper into their research during a fifth year of training. Interested students apply to CSTP in January of the year they plan to commit to full-time research (typically between the third and fourth years of medical school). Selected students are appointed as research fellows for the research year, during which they receive a living stipend, research funds, travel funds, health insurance, and tuition toward the graduate certificate in clinical research.

After successful completion of the fellowship year, they receive a CSTP scholarship toward the final year of medical school. By providing formal research training and partial tuition assistance, CSTP seeks to increase the number of Pitt graduates who choose clinical research careers and contribute to the vital work of translating biomedical science into clinical care.

Several members of the Class of 2017 are products of Pitt’s CSTP, having previously completed the research year.

PITT MED STUDENTS ARMED WITH A GUIDE TO 21ST CENTURY MEDICINE

Medical professionals have more knowledge at their disposal than at any time in history, but that doesn’t simplify practicing medicine. Physicians today need to consider the best use of complex biomedical information like a patient’s genome. While they personalize patient care based on such scientific data, they must also address the social determinants of health, including the societal and environmental conditions in which their patients are born, grow, live, work, and age.

To prepare fourth-year med students for the modern medical landscape, the Office of Medical Education introduced a course titled “Changing Science, Changing Society: A Guide to 21st Century Medicine.”

Topics covered include genomics, precision medicine, cancer risk prediction, opioid addiction, frontiers in neuroscience, the psychosocial and behavioral determinants of health, and the impact of the environment on health. The goal is to familiarize students with the very latest developments in basic and translational research that will influence how they provide care to a diverse population of patients.

CSTP GRADUATES AND THEIR RESIDENCY PROGRAMS:

UTSAV BANSAL, MD

Residency Match:
Preliminary Surgery and Urology, Baylor College of Medicine, Houston

Mentor:
Changfeng Tai, PhD, Associate Professor of Urology

CHRISTOPHER BECKER, MD

Residency Match:
Neurology, University of Michigan Hospitals, Ann Arbor

Mentors:
James Ibinson, MD, PhD, Assistant Professor of Anesthesiology
Michael Gold, PhD, Professor of Neurobiology, of Anesthesiology, and of Clinical and Translational Science

MOHINI DASARI, MD

Residency Match:
General Surgery, University of Washington Affiliated Hospitals, Seattle

Mentor:
Juan Carlos Puyana, MD, Professor of Surgery and of Critical Care Medicine

ZACHARY DONG, MD

Residency Match:
Pathology, University of Utah Affiliated Hospitals, Salt Lake City

Mentors:
Joel S. Schuman, MD, Adjunct Professor of Ophthalmology, School of Medicine; Chair, Department of Ophthalmology, New York University School of Medicine

Gadi Wollstein, MD, Adjunct Professor of Ophthalmology

NICHOLAS HESS, MD

Residency Match:
Thoracic Surgery, UPMC Medical Education Program/University of Pittsburgh

Mentors:
Inderpal Sarkaria, MD, Assistant Professor of Cardiothoracic Surgery

Arjun Pennathur, MD, Sampson Family Professor of Thoracic Surgical Oncology and Associate Professor of Cardiothoracic Surgery and of Critical Care Medicine

MARK EVANS, MD

Residency Match:
Obstetrics-Gynecology, University of California, Davis Medical Center, Sacramento

Mentor:
Sonya Borrero, MD, MS, Associate Professor of Medicine and of Clinical and Translational Science

KUNAL MEHTA, MD

Residency Match:
Vascular Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, N.H.

Mentor:
Arjun Pennathur, MD, Sampson Family Professor of Thoracic Surgical Oncology and Associate Professor of Cardiothoracic Surgery and of Critical Care Medicine

STEVEN PHAM, MD

Residency Match:
Pediatrics/Psychiatry, Cincinnati Children’s Hospital Medical Center, Cincinnati

Mentors:
David A. Brent, MD, Professor of Suicide Studies, Professor of Pediatrics and of Epidemiology

Nadine Melhem, PhD, Assistant Professor of Psychiatry

CAROLINE WEST, MD

Residency Match:
Pediatrics, University of Michigan Hospitals, Ann Arbor

Mentors:
Victor Morell, MD, Children’s Hospital of Pittsburgh Professor of Pediatric Cardiothoracic Surgery

Brian Feingold, MD, Professor of Pediatrics

Timothy Maul, PhD, Research Assistant Professor of Cardiothoracic Surgery

HADAS ZACHOR, MD

Residency Match:
Obstetrics-Gynecology, University of Chicago Medical Center, Chicago

Mentor:
Elizabeth Miller, MD, PhD, Professor of Pediatrics and Chief, Division of Adolescent Medicine; Professor of Behavioral and Community Health Sciences, Graduate School of Public Health

PSTP

The Physician Scientist Training Program (PSTP) is a five-year program for exceptionally talented students who, in addition to the regular curriculum, undertake two summers and a dedicated year of laboratory-based research training, as well as enrichment courses, to prepare for careers in academic medicine. Those selected for the program receive partial tuition assistance for the four years of medical school plus a stipend during the two research summers and the research year. The Class of 2017 included five graduating PSTP students, who matched to top residency programs in some of the most competitive medical specialties.

PSTP GRADUATES AND THEIR RESIDENCY PROGRAMS:

AHMED AL-KHAFAJI, MD

Residency Match:

Interventional Radiology,
UPMC Medical Education Program/
University of Pittsburgh

Mentor:

Allan Tsung, MD, Professor of Surgery

EFSTATHIOS KONDYLLIS, MD

Residency Match:

Neurological Surgery,
Cleveland Clinic, Cleveland

Mentor:

R. Mark Richardson, MD, PhD,
Associate Professor of
Neurological Surgery

ROBERT TISHERMAN, MD

Residency Match:

Orthopaedic Surgery,
UPMC Medical Education Program/
University of Pittsburgh

Mentor:

Gwendolyn Sowa, MD, PhD,
Physical Medicine and Rehabilitation
Professor and Chair of Physical
Medicine and Rehabilitation, Professor
of Clinical and Translational Science

ANIL VASIREDDI, MD

Residency Match:

Diagnostic Radiology,
UPMC Medical Education Program/
University of Pittsburgh

Mentor:

Alberto Vazquez, PhD,
Research Assistant Professor of
Radiology and of Bioengineering

WENDY YAU, MD

Residency Match:

Neurology, Brigham and Women's
and Massachusetts General
Hospitals, Boston

Mentor:

William E. Klunk, MD, PhD,
Levidow-Pittsburgh Foundation
Professor of Alzheimer's Disease
and Dementia Disorders,
Distinguished Professor of Psychiatry,
and Professor of Neurology



Tolani Olonisakin shares her research at a poster presentation during her HHMI fellowship.

put their medical school coursework on hold to immerse themselves in basic, translational, or applied biomedical research.

Pitt students have a strong track record in HHMI's fellowship program; successful students often credit the specialized grant writing course offered to PSTP students between the first and second years of med school. In addition to learning widely applicable keys to successful grant writing, the course provides very specific feedback on each student's HHMI proposal.

Med student Tolani Olonisakin's two years in the program inspired her to switch from the med school's PSTP to its Medical Scientist Training Program, where she is now working on her MD and PhD degrees. Her doctoral research is focused on the immune response to infection, particularly bacterial infection. Working with mentor Janet Lee, MD, professor of medicine, Olonisakin is searching for genetic factors that make people susceptible to infections — particularly bacterial infections — and aiming to discover ways to enhance the immune response to infection.

Olonisakin expected to benefit from HHMI's financial support and the protected research time, but the extent of the networking and social support was a revelation to her.

"At the first national meeting, you get to meet like 65 other students from across the country, and the whole point is collaboration. You make new friends at different institutions and talk about your research, and you get to identify people you want to work with in the future. Then there are meetings with junior faculty that are HHMI alumni. We met at Harvard Medical School, where we interacted with faculty from hospitals like Brigham and Women's and Mass General.

"What I realize now is that it's kind of a club," Olonisakin said. "HHMI wants to follow your career. If I go to a national meeting, I'll check in with HHMI, and they'll tell me who the HHMI med fellows are that I should look for at that meeting. When you're applying to residency, they'll send an e-mail asking, 'Where are you interviewing? What specialty are you interested in?' Then they'll search for HHMI fellows in that specialty or at that institution. It's a long-term relationship."

THE AWARD-WINNING PSTP STUDENTS AND THEIR PROJECTS:

FILIP ISTVANIC

Research Title/Topic:

Sonoreperfusion for
Microvascular Obstruction:
A Clinically Applicable Approach

Mentor:

Flordeliza Villanueva, MD,
Professor of Medicine in the
Division of Cardiology and Vice
Chair for Pre-Clinical Research,
Department of Medicine

AUDREY KINDFSATHER

Research Title/Topic:

Determination of the Methylation
of Gene Promoters in Lung Cancer
Cell Lines

Mentor:

Melissa Mann, PhD,
Associate Professor of Obstetrics,
Gynecology, and Reproductive
Sciences

PSTP Students Win Prestigious HHMI Fellowships for 2017-18

Two Pitt PSTP students were awarded highly coveted research training fellowships through the Howard Hughes Medical Institute (HHMI) Medical Research Fellows Program in 2017. The students will be supported through a one-year leave of absence, during which they'll dedicate themselves to their research projects and associated research training.

HHMI selected 79 top medical and veterinary students from 32 schools in the nation to conduct full-time biomedical research in its Medical Research Fellows Program. The \$3.4 million annual initiative is designed to develop the next generation of physician-scientists by giving the students a full year of mentored research training. For 2017, each HHMI fellow receives \$43,000 in grant support, and fellows are eligible to apply for a second year in the program. The fellows

MSTP Continues To Launch Physician-Scientist Careers

Match Day is a big deal for all graduating med students, but for those in the Medical Scientist Training Program (MSTP), Pitt's combined MD/PhD program, the anticipation has been building for an especially long time. Most classmates with whom they entered med school are long gone, because MSTP students begin with two years of MD training then break for a few years of PhD research before returning to complete the MD. While in the midst of their PhD research, they watch classmates they began med school with celebrate Match Day and move on to residency positions. Graduation for MSTP students typically arrives about seven to eight years after they begin medical school. In 2017, Pitt said farewell to 10 of these budding physician-scientists, who have matched to some of the most prestigious residency programs in the nation.

UNDER THE MICROSCOPE

Sara Whitlock, a student in the School of Medicine's Molecular Biophysics and Structural Biology Graduate Program, has put herself under the microscope. While jumping feet-first into her first year as a graduate student, she committed to documenting and sharing the experience as an occasional columnist for the science-themed news outlet STAT. This national publication produced by Boston Globe Media focuses on finding and telling compelling stories about health, medicine, and scientific discovery.

Over the course of her first year, Whitlock gained a steady readership as she produced roughly one column per month. In her first, she tackled the excitement and trepidation of starting grad school ("A new PhD student learns her first lesson: Certainty doesn't exist in science"). She wrapped up the academic year with a humorous and thoughtful retrospective ("Coffee and intellectual freedom: 5 things I learned from my first year of grad school"). Along the way, she provided her readers with a grad student's perspective on some of the most compelling scientific issues of the day, including research funding, activism, and the public's view of scientists.

Most important to Whitlock, the column documented what she calls "a highly successful" start to her grad school experience at Pitt. Read more of Whitlock's column at www.statnews.com/category/under-the-microscope/.

This is it. After a year of classes and research rotations and allnighters, I finally joined the lab where I'm going to get my PhD. This is a big deal — for the next several years this lab will be my home and the people in it my de facto family. ... Before long, I could be making exciting discoveries about how bacteria organize their innards using scaffolding proteins. I'm excited — I think it's the coolest project this side of the Mississippi. Along the way this year, I learned a few things about myself, about science, and about relationships...

— Sara Whitlock, writing for STAT

PITT'S 2017 MSTP GRADUATES AND THEIR RESIDENCY MATCHES:

ALEXIS CHIDI, MD, PHD

Residency Match:
General Surgery, Johns Hopkins Hospital, Baltimore

Mentors:

Cindy Bryce, PhD, Associate Professor of Health Policy and Management, Graduate School of Public Health

Michael Fine, MD, MSc, Professor of Medicine (General Internal Medicine), of Family Medicine, and of Clinical and Translational Science

MATTHEW L. HEDBERG, MD, PHD

Residency Match:
Pathology, Barnes-Jewish Hospital, St. Louis

Mentor:

Jennifer Grandis, MD, American Cancer Society Professor, Associate Vice Chancellor for Clinical and Translational Research, and Professor of Otolaryngology, University of California, San Francisco

NEIL J. KELLY, MD, PHD

Residency Match:
Internal Medicine, UPMC Medical Education Program/University of Pittsburgh

Mentor:

Steven D. Shapiro, MD, Distinguished Professor of Medicine

MARK T. LANGHANS, MD, PHD

Residency Match:
Orthopaedic Surgery, Hospital for Special Surgery, New York, N.Y.

Mentor:

Rocky Tuan, PhD, Distinguished Professor of Orthopaedic Surgery and Arthur J. Rooney Sr. Professor of Sports Medicine

RICARDO LONDONO, MD, PHD

Residency Match:
Postdoctoral Research Fellowship: McGowan Institute for Regenerative Medicine/University of Pittsburgh

Mentors:

Stephen Badylak, MD, PhD, DVM, Professor of Surgery

ELIZABETH A. OCZYPOK, MD, PHD

Residency Match:
Internal Medicine, UPMC Medical Education Program/University of Pittsburgh

Mentor:

Tim Oury, MD, PhD, Professor of Pathology

ROBERT G. RASMUSSEN, MD, PHD

Residency Match:
Preliminary Internal Medicine, UPMC Medical Education Program/University of Pittsburgh

Diagnostic Radiology, University of Texas Southwestern Medical Center, Dallas

Mentor:

Andrew Schwartz, PhD, Distinguished Professor of Neurobiology and Professor of Systems Neuroscience

DANIEL J. SIMMONDS, MD, PHD

Residency Match:
Preliminary Pediatrics/Neurodevelopmental Disabilities, Johns Hopkins Hospital, Baltimore

Mentor:

Beatriz Luna, PhD, Staunton Professor of Pediatrics and Psychiatry and Professor of Psychology, Dietrich School of Arts and Sciences

LAUREN BRILLI SKVARCA, MD, PHD

Residency Match:
Pathology, UPMC Medical Education Program/University of Pittsburgh

Mentor:

Neil Hukriede, PhD, Associate Professor of Developmental Biology

JOSHUA J. STURM, MD, PHD

Residency Match:
Otolaryngology, NewYork-Presbyterian Hospital, New York, N.Y.

Mentor:

Karl Kandler, PhD, Professor of Neurobiology, of Otolaryngology, and of Bioengineering, Swanson School of Engineering

RECENT ACCOMPLISHMENTS BY MSTP STUDENTS:

Class of 2017 graduate **Ricardo Londono, MD, PhD**, received the Society of Biomaterials' 2017 Student Award for Outstanding Research. Londono completed his PhD training in the laboratory of Stephen Badylak, MD, PhD, DVM, professor of surgery and deputy director of the McGowan Institute for Regenerative Medicine. Londono, whose clinical interest is regenerative medicine, is exploring how our bodies respond to implantable biomaterials. The goal of his research is to understand how the interaction of biomaterials and host cells leads to constructive remodeling of tissues. Londono has authored numerous peer-reviewed manuscripts and book chapters while a member of the MSTP, including a research paper in the *Annals of Biomedical Engineering* that was the journal's most highly cited publication of 2015.

A trio of past and current Pitt students authored a paper in *JAMA Internal Medicine* showing that women are significantly underrepresented as grand rounds lecturers in American medical schools and teaching hospitals. They found that roughly a quarter of speakers were women, while women currently make up 47 percent of medical students, 46 percent of residents, and 36 percent of medical faculty.

"When you don't see people who look like you, it can cause you to say, 'This doesn't look like a field I can thrive in,'" said the study's lead author, **Julie Boiko, MD, MS**, who graduated from Pitt's CSTP in 2015 and is currently a pediatrics resident at the University of California, San Francisco.

Boiko coauthored the paper with current MSTP students **Rachael Gordon** and **Alyce Anderson**. The publication reflects an interest the three share in encouraging women to pursue careers as physician-scientists, which is something they also do by example — Anderson explores intestinal bowel disease prevention; Boiko is training in pediatric hematology/oncology; and Gordon studies the immunology of lupus.

In December 2016, MSTP student **Nolan Priedigkeit** presented his study of brain metastases in patients with breast cancer at the San Antonio Breast Cancer Symposium, the largest national breast cancer meeting. The brain is a common and catastrophic site of metastasis for patients with breast cancer, but scientists and physicians have lacked a complete understanding of the genetic changes involved in these cancers. Priedigkeit and colleagues analyzed a cohort of nearly 8,000 breast cancers and showed that, despite the large degree of similarity between the initial breast tumor and the brain metastatic tumor, there were enough genetic alterations to support comprehensive genetic profiling of metastases to potentially personalize treatment for individual patients.

The research team includes corresponding author **Adrian Lee, PhD**, professor of pharmacology and chemical biology, director of Pitt's Institute for Precision Medicine, and director of the Women's Cancer Research Center at UPMC Hillman Cancer Center.



LONDONO

Londono is exploring how our bodies respond to implantable biomaterials.

"When you don't see people who look like you, it can cause you to say, 'This doesn't look like a field I can thrive in.'"

— JULIE BOIKO, MD, PHD



GORDON



ANDERSON

The brain is a common and catastrophic site of metastasis for patients with breast cancer, but scientists and physicians have lacked a complete understanding of the genetic changes involved in these cancers.



PRIEDIGKEIT

Publications and NIH Awards Indicate Success

On average over the past six years, MSTP students have each coauthored six scientific publications (three as first author) by the time they graduate. Other MSTP bragging points include Pitt's enviable success rate in winning F30 awards from the National Institutes of Health. Also known as Ruth L. Kirschstein National Research Service Awards, F30s are granted to MSTP students who demonstrate the potential to become highly trained, productive, and independent physician-scientists. NIH's ultimate goal with this 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:

MATTHEW AMDAHL

Novel Oxygen Carriers Based on Hexacoordinate Globins to Prevent Renal Toxicity

National Institute of Diabetes and Digestive and Kidney Diseases

Mentor:

Mark Gladwin, MD, Distinguished Professor, Jack D. Myers Professor, and Chair of Medicine

MICHAEL CHIANG

Understanding the Functional Role of Kappa Opioid Receptor Signaling in Somatosensory Neurons

National Institute of Neurological Disorders and Stroke

Mentor:

Sarah Ross, PhD, Assistant Professor of Neurobiology, of Anesthesiology, and of Clinical and Translational Science

KEVIN LEVINE

Combination FGFR4 and ER-Targeted Therapy for Invasive Lobular Carcinoma

National Cancer Institute

Mentor:

Steffi Oesterreich, PhD, Professor of Pharmacology and Chemical Biology

NOLAN PRIEDIGKEIT

Transcriptomic Profiling and Functional Characterization of Fusion Genes in Recurrent Ovarian Cancer

National Cancer Institute

Mentor:

Adrian Lee, PhD, Professor of Pharmacology and Chemical Biology and of Human Genetics, Graduate School of Public Health

ZACHARY YOCHUM

Determining the Mechanisms of TWIST1-Mediated Crizotinib Resistance in Met-Driven Non-Small Cell Lung Carcinoma

National Cancer Institute

Mentor:

Timothy F. Burns, MD, PhD, Assistant Professor of Medicine (Hematology/Oncology)

Graduate students have contributed directly to the success of these projects, and ongoing research is expected to lead to the next generation of immune-based therapies for human disease.

Debut of Combined PhD Program in Microbiology and Immunology

Pitt's tradition of excellence in microbiology and immunology goes back to Jonas Salk and the development of the polio vaccine on Pitt's campus in the 1950s. Today, Pitt research teams are investigating the molecular pathogenesis of a wide range of microbes and developing vaccines and novel therapies for HIV, tuberculosis, and cancer. To keep pace with the explosion of basic and applied research in these areas, Pitt's PhD programs in microbiology and immunology have made big changes.

For 20 years, PhD studies in these fields were separate tracks in the med school's Interdisciplinary Biomedical Graduate Program. In 2017, the immunology and microbiology tracks merged to form an independent PhD Program in Microbiology and Immunology (PMI). Because microbiology and immunology affect so many aspects of health and disease, PMI's 100-plus faculty members represent many academic departments, including immunology, microbiology and molecular genetics, medicine, ophthalmology, surgery, and pediatrics. Their affiliations also include the UPMC Hillman Cancer Center, the Magee-Womens Research Institute, the Center for Medicine and the Microbiome, and the Thomas E. Starzl Transplantation Institute. This diversity of expertise creates unique opportunities for students to explore cutting-edge research questions using multi-disciplinary approaches.

Faculty members are addressing a wide range of research topics, including innate and adaptive immunity, autoimmunity, tumor immunology, immunology of organ transplantation, basic bacteriology and virology, host-pathogen interactions, parasitology, viral and bacterial pathogenesis, and novel antimicrobial therapies. Recent clinical breakthroughs were made possible by the basic research of PhD students in PMI laboratories, and future graduate students will accelerate the development of the next generation of immune-based therapies for human disease.

Recent PMI accomplishments include papers in *Proceedings of the National Academy of Sciences* by 2016 alumna Becca Flitter, PhD, and mentor Jennifer Bomberger, PhD; in *Nature Communications* by student Lauren Kinner-Bibeau and mentor Robert Binder, PhD; in *Cell* by student Abigail Overacre-Delgoffe and mentor Dario A.A. Vignali, PhD; and in *mBio* by student Hannah Fox and mentor Neal DeLuca, PhD.

Including the 12 new students beginning their first year of medical school in 2017, Pitt's MSTP has 82 students currently – big enough to maintain a lively and diverse group dynamic. In the 2017–18 academic year, MSTP maintains its highest level of NIH support since its founding 30 years ago, with 20 Pitt MD/PhD students funded by NIH per year.



Offering
a Hand Up
for Students
from Under-
represented
Groups

The medical school environment can be stressful and competitive. For students from underrepresented racial and ethnic groups, it can be isolating as well. To create an environment in which these students can best develop and excel as clinical researchers, Pitt's Institute for Clinical Research Education offers the Career Education and Enhancement for Health Care Diversity Program for Medical Students (CEED II). Directed by

Sonya Borrero, MD, MS, associate professor of medicine and of clinical and translational science, the career development program reflects the School of Medicine's commitment to diversity and helps to develop the pipeline of investigators from underrepresented populations.

"Medical students have told me they feel isolated, so that isolation on top of usual medical school stress can be a real struggle," says Borrero. "This program, I hope, helps to offset some of the difficulties by offering a community in which students can discuss their day-to-day and career struggles. Also, the pragmatic tools and funding we offer are particularly helpful."

The one-year program geared toward third-year medical students offers a research stipend and didactic sessions on issues like productivity, negotiating difficult conversations with fellow researchers, scientific writing, and time management as a clinical researcher. Students gain access to mentoring, networking, and opportunities to disseminate research they

conduct for their Scholarly Research Projects. Students' feedback shows that the CEED II program is successful in offering students advice and examples from people who have experienced similar struggles.

Darvé Robinson first began to love research in high school. Now in his fourth year of medical school, Robinson found that his experience in CEED II has reaffirmed his desire to make biomedical research a substantial part of his career, one that he hopes will be in academic medicine in acute trauma.

"As an immigrant from the Caribbean, I'm very familiar with hard work," says Robinson, "but CEED II showed me how to work smart. I've learned how to 'talk science,' meaning I've always been able to speak with knowledge about science, but there's a special language and ethos in the field of science that I was lacking."

CEED II presentations about how to avoid common, early-career pitfalls and how to, as a junior clinical researcher, disseminate and advocate for one's own research have been especially helpful to Robinson. But the mentorship and real-time advice is, for him, the heart of his CEED II experience.

"As a young, African American future researcher, it's really beautiful to see other researchers from similar backgrounds at further stages in their careers," he says. "Some look like me, sound like me. They come from diverse places like I did, and they're accomplishing the things I want to eventually accomplish. It makes the dream a little closer to reality."

Members of the Class of 2021 kicked off their first year of med school with the White Coat Ceremony. In the presence of family and friends, they donned their first white coats as symbols of the trust bestowed on them as they enter the field of medicine.



Alumni of Note

Theresa Guise, MD

Theresa Guise, MD, the Jerry and Peggy Throgmartin Professor of Oncology at Indiana University School of Medicine, was honored with the 2017 Philip S. Hench Distinguished Alumnus Award, the highest honor given by Pitt's Medical Alumni Association.

For someone who hated swimming as a child, Guise has come a long way. After being persuaded to try scuba diving in adulthood, she became fascinated by underwater flora and fauna. Guise, who earned her MD at Pitt in 1985 and completed an internal medicine residency here in 1988, is now an award-winning underwater photographer in addition to a notable endocrinologist. Her photo of red whip coral, which resembles the skeletal muscle fibers she studies, was selected for a November 2015 cover of *Nature Medicine*. In that same issue, her lab at Indiana University published a paper identifying the unique mechanism by which bone, when destroyed by cancer, causes muscle weakness.

"That was my biggest career milestone, the marriage between my hobby and my work," Guise told *Pitt Med* magazine.

A recent project continues to go below the surface; she's developing a clinical trial to test drugs on cancer-associated muscle weakness.

Leon L. Haley Jr., MD, MHSA

Growing up in Pittsburgh, Leon L. Haley Jr., MD, MHSA, dreamed of becoming the first African American sportscaster on network television. "But that changed when I mixed basketball with a trampoline," he says. Having missed a slam dunk, young Haley wound up with a torn meniscus — and an awakening fascination with medicine.

As a med student at Pitt, he completed a summer program working afternoon shifts at the emergency department at St. Margaret's Hospital. The variety of injury and trauma cases that came through the door inspired him to pursue emergency medicine. After graduation in 1990, he completed his residency at Henry Ford Hospital in Detroit, followed by a master's in health services administration from the University of Michigan.

From there, Haley moved to Atlanta, where he rose through the ranks to professor of emergency medicine at Emory University, as well as the university's executive associate dean for clinical affairs for Grady Memorial Hospital. During his tenure there, he implemented a rapid medical evaluation process that shortened emergency medicine patient waiting times by 45 minutes and reduced the length of stay for the patients with the least pressing cases by three hours. The process also drastically decreased the number of patients who left without receiving care — by 50 percent.

In September, Haley was named dean of the College of Medicine, professor of emergency medicine, and vice president for health affairs at the University of Florida–Jacksonville.

As he looks to the future, Haley says teaching clinicians how to function in a digital environment will be critical. He emphasizes analytics, economics, and a push toward preventive medicine.

Jennifer R. Grandis, MD

In 2016, the Clinical and Translational Science Institute of the University of California, San Francisco, earned a renewal of its funding from the National Institutes of Health. The funding — \$85 million over five years — is both an endorsement of the institute's work to translate basic science discoveries to clinical care over its 10 years of existence, as well as a vote of confidence in its future direction.

Since 2014, the institute has been led by Jennifer R. Grandis, MD, professor of otolaryngology and associate vice chancellor for clinical and translational research. Grandis earned her MD at Pitt in 1987 and remained here for her otolaryngology residency and a fellowship in infectious diseases. Before joining UCSF, Grandis was Distinguished Professor of Otolaryngology at Pitt, vice chair for research in the Department of Otolaryngology, and leader of the head and neck cancer research program.

Grandis's own research focuses on signal transduction in head and neck squamous cell carcinoma. Her goal is to identify key pathways in cancer development and progression and target them for new therapeutic approaches. Her lab investigates mechanisms in preclinical models and conducts clinical trials to test these treatment strategies.

Dr. Grandis is an American Cancer Society Clinical Research Professor and a member of the American Society for Clinical Investigation, the Association of American Physicians, and the National Academy of Medicine.

Richard Pan, MD, MPH

In May 2017, California state senator Richard Pan, MD, MPH, who graduated from the School of Medicine in 1991, was the keynote speaker for the Class of 2017 graduation ceremony.

As a practicing pediatrician serving in the California State Senate, Pan has become widely known as an advocate for evidence-based legislation to advance public health.

In 2014, a single person who'd recently been exposed to measles virus visited Disneyland in California. One might think that measles would fail to get a foothold in this country, where the MMR vaccine is readily available. However, that's not what happened. More than

100 people became sick in the ensuing outbreak, which was possible only because a significant number of people had refused vaccination.

As the outbreak was brought under control, Senator Pan authored legislation mandating that school children in California would need a medical exemption to skip state-mandated vaccines, rather than a personal belief exemption. Pan took a lot of criticism for this position, and a petition drive was initiated to trigger a recall election and remove him from office—an effort that failed.

“Richard never backed down in the face of intimidation,” said Arthur S. Levine, MD, dean of the medical school. “In fact, he’s become more outspoken. He remains, to this day, a passionate advocate for public health, vaccination, and evidence-based medicine.”

Samuel Tisherman, MD

In November 2016, readers of the *New Yorker* were treated to a lengthy feature article on cutting-edge trauma research under way at the University of Maryland’s Shock Trauma Center. A clinical trial, led by Pitt alumnus Samuel Tisherman, MD (Class of 1985), will test an experimental trauma protocol known as “emergency preservation and resuscitation,” or EPR. It’s the culmination of nearly three decades of research, a great deal of it performed at Pitt by Tisherman and his mentor, the late Peter Safar, MD. EPR was designed to help save those patients who arrive at the trauma center with massive blood loss from traumatic injuries and die from exsanguination cardiac arrest before their injuries can be fully addressed. In many of these cases, surgeons simply need more time; EPR is an attempt to provide that time. Instead of blood, these patients will be given a cold saline solution that will drastically lower body temperature—so low that brain and heart activity will cease for up to an hour. After the traumatic injuries have been fixed, a heart-lung bypass will begin to replace the saline with blood and gradually warm the patient. The heart will be restarted.

If EPR works as the research suggests it will, it could reduce the number of people who bleed to death from fixable injuries (30,000–40,000 per year in the United States).

It’s been a long road to this point for Tisherman, who started working with Safar when he was a med student. He estimates it could be another two years before the results from the first few patients can be made public. But, as the *New Yorker* writer Nicola Twilley said of Tisherman, “He demonstrates boundless reserves of patience in the face of the endless delays that the trial has encountered, and his resolve seems to influence those around him.”



From top:
Guise, Haley,
Grandis, Pan,
Tisherman

We aim to bring about transformational changes in American medicine by exploring the most fundamental and important areas in biological science and clinical care.

research

High Risk, High Reward

*Pitt Faculty
Members Earn
Key NIH
Early-Career
Awards*

Platelet Biology Knowledge Boost

Doctors have long known that platelets drive blood clot formation, says **Matthew D. Neal, MD**, assistant professor of surgery. But it's more recent news that platelets help regulate the body's response to inflammation and act as immune cells. One indication of how intriguing platelets have become is that Neal, who earned his MD at the University of Pittsburgh School

of Medicine in 2006, is now the recipient of a **\$1.8 million** National Institutes of Health Maximizing Investigator's Research Award, which will further his lab's investigations into platelet biology and the mechanisms that regulate trauma patients' response to injury.

Trauma patients whose blood does not properly clot face life-threatening blood loss. Other trauma patients clot to excess, resulting in thrombosis, or a clotted blood vessel. Often, both conditions afflict the same patient. The NIH award will enable Neal to explore "the entire spectrum of disease," from the platelets' molecular signaling pathways that influence inflammation and thrombosis to the mechanisms that lead to blood clots following trauma. These avenues of research show a great deal of potential in several areas of medicine.

"Although the target is to devise strategies for early intervention in trauma, understanding some of the basic mechanistic response in platelets is going to have relevance to any disease where thrombosis plays a role, and that includes cardiovascular disease, cancer, sepsis, and many others," Neal says.

The NIH Director's New Innovator Award has been awarded to five Pitt investigators over the past 10 years.

Computing for a Rewarding Experience

Scientists recognize the rewards of good research, like publication in a top journal and recognition from their peers. But understanding how the human brain mechanistically computes the value of rewards isn't so clear. **William Stauffer, PhD**, assistant professor of neurobiology, received a prestigious **\$2.3 million** National Institutes of Health (NIH) Director's New Innovator Award in October 2016 to support his investigations into how the brain processes and makes choices based on rewards. (See story on page 48.)

Stauffer describes rewards as positive events that trigger repetition of a previous behavior or action. He says that the reward system in the human brain is connected to almost everything that we do. "Rewards play a huge role in determining the 'why' for a lot of what we do," he says. "There is an entire system in our brain that appears to be involved with processing rewards." While conducting postdoctoral research at the United Kingdom's University of Cambridge, Stauffer and colleagues demonstrated how the brain of a nonhuman primate tracks the subjective value of rewards. But he wanted to know more about the brain mechanisms that compute this value and how it's used to determine choice.

Now, he is employing optogenetics, among other tools, to identify the types of neurons involved in the rewards system and record their activity during demonstration of reward-based behaviors. Ultimately, he hopes to devise a paradigm that explains how the brain places value on rewards and then deliberates and exhibits more complex behavior based on this input. "If we can understand how reward circuits operate and go awry," Stauffer says, "we might enable new therapies for depression, drug addiction, Parkinson's disease, dystonia, and other disorders of those circuits." Biomedical research with such paradigm-shifting potential is identified and supported annually through the NIH Director's New Innovator Award, which has been awarded to five Pitt investigators over the past 10 years.

Grants of Note

PITT JOINS NETWORK AIMED AT IMPROVING TRAUMA CARE

Pitt's Schools of the Health Sciences, including the School of Medicine, are joining a nationwide network of schools and trauma centers aimed at improving military and civilian trauma care. The **\$10.8 million** project to establish the network is the first step in the Department of Defense (DOD) research initiative, which will eventually be funded with up to \$90 million. Led by principal investigator **Jason L. Sperry, MD, MPH**, professor of surgery and of critical care medicine, the Linking Investigations in Trauma and Emergency Services Network (LITES) will collect and analyze extensive data, from prehospital care through discharge and recovery, on thousands of trauma cases across the country in order to optimize trauma care for future soldiers. Pitt will lead and organize the network, which includes the University of Colorado, Oregon Health & Science University, and five other universities. Pitt will also lead a central institutional review board to address subsequent studies over the next decade.

“After approximately two years of accruing large amounts of data, we’ll be able to launch subsequent projects at the DOD’s request — including the gold standard: randomized clinical trials — to find out what approach to care works best to keep people who are injured by trauma from dying.”

— JASON L. SPERRY, MD, MPH

LONGITUDINAL STUDY WILL EXPLORE MATERNAL STRESS AND CHILD DEVELOPMENT

The National Institutes of Health will provide up to **\$14 million** to Pitt and University of Chicago researchers for a study that’s part of its Environmental Influences on Child Health Outcomes initiative. The longitudinal study will explore how a mother’s environmental stress, prior to her baby’s conception, can influence the child’s neurodevelopment. Study coprincipal investigator **Alison Hipwell, PhD**, professor of psychiatry, and colleagues will measure stress and nutrition biomarkers among a cohort of women who were exposed to family stress and violence. If and when these women become pregnant over the ensuing years, investigators will study their prenatal stress regulation and placental function and measure their children’s development up to age 3.

SIMPLE NASAL CELL EVALUATION COULD DETERMINE TREATMENT RESPONSE IN CYSTIC FIBROSIS PATIENTS

By developing mathematical models to map out and better understand liquid and ion transport in the lungs of cystic fibrosis (CF) patients, Pitt researchers are hoping to more effectively treat them. To support this project, the National Heart, Lung, and Blood Institute provided a **\$1.7 million** grant to researchers from Pitt’s Swanson School of Engineering and School of Medicine, including coprincipal investigator **Tim Corcoran, PhD**, associate professor of medicine in the Division of Pulmonary, Allergy, and Critical Care Medicine. After collecting cells from a patient’s nose, the team will employ nuclear imaging to measure how mucus and water move in the lungs. With that information, the researchers can create mathematical models to visualize patients’ physiology and predict how patients will respond to treatments.

NCI FUNDS CANCER EARLY DETECTION METHODS AND DRUG DEVELOPMENT RESEARCH

The UPMC Hillman Cancer Center could receive up to **\$10 million** over the next five years for the development of new cancer drugs under a contract from the National Cancer Institute (NCI). UPMC Hillman will conduct preclinical research and collect pharmacology data to determine the most effective means of delivery and dosage of prospective cancer drugs for use in human clinical trials. The contract solidifies UPMC Hillman’s roles in all five stages of NCI’s drug-development process: drug screening; preclinical research; and phase I, II, and III clinical trials.

As part of NCI’s Early Detection Research Network projects, UPMC Hillman is also receiving a portion of **\$15.5 million** over five years to ramp up cancer early-detection efforts. UPMC Hillman researchers will focus on advancing means of detecting cancer biomarkers in blood and other bodily fluids. New biomarker detection methods could replace more involved, invasive procedures like mammograms and colonoscopies. The ultimate goal is to detect cancer before patients even realize a problem. Better early detection techniques can also improve cancer progression monitoring.

NEW VACCINE-MONITORING ROLES FOR CHILDREN'S HOSPITAL OF PITTSBURGH OF UPMC

Pitt and Children's Hospital of Pittsburgh of UPMC continue to play critical roles in vaccine development by monitoring effectiveness and conducting surveillance. The University of Pittsburgh Vaccination Research Group (PittVax) received a **\$5.5 million** five-year grant renewal from the U.S. Centers for Disease Control and Prevention (CDC) to continue evaluating the annual influenza vaccine and the burden of respiratory syncytial virus (RSV) in adults. Since 2011, PittVax has been one of five U.S. Influenza Vaccine Effectiveness Network sites, which help steer public health officials' vaccine recommendations. The group works to assess flu vaccine effectiveness — compared to predicted success — after flu season begins. Children's Hospital has also competed to join a group of seven national academic children's hospitals that monitor communicable diseases in children and evaluate vaccine effectiveness. Through an additional **\$5million** CDC grant, the hospital will become a New Vaccine Surveillance Network site and focus on monitoring respiratory and gastrointestinal viruses within Allegheny County, among other surveillance duties.

“Active disease surveillance is necessary to establish the effectiveness of existing vaccines and provide the data needed to guide policymakers and pharmaceutical industries in the development of new vaccines.”

— JOHN V. WILLIAMS, MD
*Henry L. Hillman Professor of Pediatric Immunology
and chief, Division of Infectious Diseases*

AWARD FUNDS BLOOD AND MARROW TRANSPLANTATION RESEARCH

The American Society of Hematology awarded a 2017 Scholar Award to **Craig Byersdorfer, MD, PhD**, assistant professor of pediatrics in the School of Medicine and a physician in the Division of Blood and Marrow Transplantation and Cellular Therapies at Children's Hospital of Pittsburgh of UPMC. The **\$150,000** award will accelerate Byersdorfer's research on complications following blood and marrow transplants and ways to overcome them.

NEW STENT AIMS TO CURB BATTLEFIELD BLOOD LOSS

A retrievable stent that can be rapidly inserted by non-vascular physicians could be a literal lifesaver for service members, as well as civilian gunshot victims and others with blood loss from injuries. The U.S. Department of Defense has provided Pitt School of Medicine and Swanson School of Engineering researchers **\$2.5 million** to develop the stent, a prototype of which has already been developed and tested by UPMC. The stent uses radiofrequency tags and a handheld detector to guide and simplify placement, eliminating the need for bulky, often inaccessible X-ray equipment. Because noncompressible hemorrhage of the abdomen or chest requires more than just pressure to stop bleeding, the stent can control massive bleeding until patients reach a vascular surgeon and specialized care.

NEW UROLOGY RESEARCH CENTER TO INVESTIGATE INFLAMMATION AND COMMON UROLOGICAL CONDITIONS

The new O'Brien Urology Cooperative Research Center at Pitt is working to advance preventive and therapeutic treatments for benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS), two urological conditions that, while not generally life threatening, are costly to treat and affect most elderly men. The center, which will be led by **Zhou Wang, PhD**, UPMC Professor of Urological Research and director of urological research in the Department of Urology, is the result of **\$7.55 million** in NIH funding, primarily from the National Institute of Diabetes and Digestive and Kidney Diseases. Pitt's researchers will explore inflammation's role in the two conditions, specifically how prostatic inflammation affects the nerve and urothelial systems that connect the prostate to the bladder, leading to bladder sensitization, and on inflammation and luminal epithelial cellular junctions in BPH specimens. Researchers will also explore new approaches using nonsteroidal anti-inflammatory drugs to treat BPH and LUTS.

Hillman
Foundation
Gift Bolsters
Plethora
of Brain
Research
Projects

The in-depth, interdisciplinary research that's required to probe questions of neuronal function and dysfunction has received a **\$600,000** boost from the Henry L. Hillman Foundation to the University of Pittsburgh Brain Institute. After combining this lead gift with internal matching funds, the Brain Institute is distributing \$925,000 to several Pitt projects that explore pressing neurological questions and span Parkinson's

disease, paralysis, substance use, and other topics. "Collectively, these projects have the potential to significantly advance our understanding of brain function and shed light on disorders that affect millions of people," says Brain Institute scientific director **Peter L. Strick, PhD**, Thomas Detre Professor of Neuroscience and Distinguished Professor and chair of neurobiology. "These projects will enable us to better frame the national research agenda and compete more effectively for large-scale federal funding opportunities."

Modeling Movement Disorders

The collection of deep brain nuclei that make up the basal ganglia is associated with movement disorders like Parkinson's disease.

Robert Turner, PhD, professor of neurobiology, is establishing a model to determine how physiologic processes within the basal ganglia result in the movement-related symptoms characteristic of these disorders.

Adolescence and Addiction

The teenage brain is susceptible to developing substance abuse and sleep disorders. **Colleen McClung, PhD**, associate professor of psychiatry, will further her work exploring the effect of sleep and circadian rhythm disruptions on behaviors that could lead to addiction in young teenagers.

Investigating Obsessive-Compulsive Disorder

It's unclear what causes obsessive-compulsive disorder (OCD), which is a lifelong disability. **Susanne Ahmari, MD, PhD**, assistant professor of psychiatry, will investigate abnormal brain activity associated with OCD symptoms in both animal models and patients.

Neuron Variability: Why Results May Vary

Even when subjected to the same stimulus, neurons vary in response. This variability and unpredictable nature has functional consequences for certain brain computations and behaviors. **Matthew Smith, PhD**, assistant professor of ophthalmology, and **Brent Doiron, PhD**, professor of mathematics in the Dietrich School of Arts and Sciences, will seek to understand these functional consequences of variability, which is essential for understanding cognition and how the brain processes sensory signals.

Novel Neural Prosthetics

Andrew B. Schwartz, PhD, Distinguished Professor of Neurobiology and Professor of Systems Neuroscience, leads a team of scientists and engineers working to enhance the performance of neural prostheses. The researchers are further developing a robotic arm that's controlled by an individual's brain and uses an artificial intelligence component designed to predict an individual's movement. The project aims to significantly improve paralyzed individuals' dexterous abilities.

Brain Bank Boost

The Hillman funding supported expansion of the Brain Institute's brain bank, a valuable resource housing more than 1,000 brains and brain tissue samples for research. Recently, the brain bank has enabled research on a molecular marker of Parkinson's disease in human tissue, comparison of a human stem cell model of amyotrophic lateral sclerosis (ALS) and ALS-positive brain tissue, and other Pitt projects. The bank includes one of the largest collections of brain samples from patients who had ALS or Alzheimer's disease and is available to researchers worldwide. The recent expansion includes new resources for traumatic brain injury studies and the establishment of a bank for studying pediatric neurodegenerative diseases, says **Julia Kofler, MD**, assistant professor of pathology and the brain bank director.

THE BRAIN SPEAKS

R. Mark Richardson, MD, PhD, associate professor of neurological surgery and of neurobiology and member of Pitt's Brain Institute, is leading research to investigate speech control in the brain. With a **\$3.3 million** grant from NIH's National Institute of Neurological Disorders and Stroke, a multidisciplinary research team is studying Parkinson's disease patients while they undergo deep brain stimulation (DBS) surgery. Their goal is to better understand how neuronal activity in the basal ganglia helps to control articulation, volume, and other aspects of speech. In Parkinson's patients, DBS improves motor symptoms but often not speech. The researchers hope to gain insights that can advance treatments for speech disorders. The grant derives from NIH's BRAIN Initiative, a national, large-scale effort to advance understanding of the brain, launched by President Barack Obama in 2013.

Publications of Note

SCIENCE TRANSLATIONAL MEDICINE

NEWLY DEVELOPED PROTEIN COULD BE ANTIDOTE FOR CO POISONING

DEC 2016 \ VOL 8 \ ISSUE 368

Current treatment for carbon monoxide poisoning involves replacing CO with oxygen by administering 100 percent oxygen or using an oxygenated pressurized hyperbaric chamber to boost air pressure. After engineering a mutant version of the protein neuroglobin that binds and scavenges CO with very high affinity, Pitt researchers, including senior author **Mark T. Gladwin, MD**, Distinguished Professor, Jack D. Myers Professor, and chair of medicine, showed it was much more effective at removing CO from the blood than current treatments, hinting at the possibility of a game-changing antidote for CO poisoning. When testing red blood cells that are 100 percent saturated with CO, the mutant protein Ngb H64Q removed CO from the red blood cells in less than a minute, compared to more than 500 minutes when exposed to air alone. In a mouse model of lethal CO levels, seven of eight mice treated with Ngb H64Q survived, compared to 10 percent, or fewer, in control groups. While further safety and efficacy tests are needed, this work identifies a new paradigm for CO poisoning treatment.

The normal half-life of CO in humans after poisoning (time it takes for half of the CO to be eliminated from the body) is 320 minutes. Even with 100 percent oxygen therapy, that time is reduced only to 74 minutes. When the antidote therapy was tested in a mouse model of non-lethal CO poisoning, the CO half-life was reduced dramatically—to only 23 seconds.

AMERICAN JOURNAL OF PSYCHIATRY

METABOLIC ABNORMALITIES MAY CAUSE SOME TREATMENT-RESISTANT DEPRESSION

JAN 2017 \ VOL 174 \ ISSUE 1

Some 15 percent of patients with depression are unable to find a conventional treatment like antidepressant medication or psychotherapy to alleviate their symptoms. To help these patients, Pitt scientists teamed up to take an unconventional “metabolomics” approach. In a group of depressed young adults with treatment-resistant depression, they performed a very broad screen to look for metabolic abnormalities. The gambit worked so well that even the scientists were surprised. Sixty-four percent of the 33 participants with treatment-resistant depression were found to have a deficiency in neurotransmitter metabolism. The specific metabolites involved differed from patient to patient, but treating the deficiencies with what is essentially a nutritional supplement improved depression symptoms in most of these patients. Some patients experienced complete remission. Lead investigator **Lisa Pan, MD**, assistant professor of psychiatry, called it a “potentially transformative finding.”



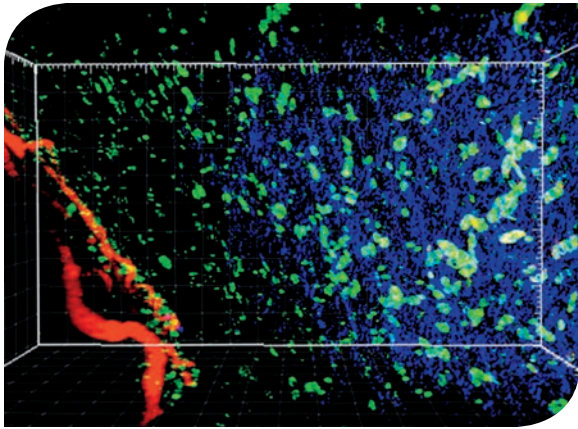
The patient who caused **Lisa Pan, MD**, to reconsider her whole career path nearly died of his depression. The teenager had a history of self-harm and unsuccessful suicide attempts. One day, he returned home to an empty house after telling his family he was going to school. He consumed 80-some pills, including narcotics. His stepfather returned home unexpectedly that day, and that’s the only reason the paramedics were called in time.

Pan, a psychiatrist with a focus on suicide prevention and a research interest in brain imaging, had treated this teen for years. He’d been on every drug available for his depression; he’d tried cognitive-behavioral therapy and electroconvulsive therapy, too, but nothing diminished his suicidal ideation. Feeling desperate after the patient had barely survived this latest suicide attempt, Pan asked biochemical geneticists **David Finegold, MD**, and **Jerry Vockley, MD, PhD**, if they could screen the patient for a narrow

range of neurotransmitters involved with serotonin activity. They proposed a screen for a variety of metabolic disorders known to contribute to neurologic dysfunction.

This “shotgun approach” yielded an unexpected answer for this one patient. The team found the patient was deficient in a chemical cofactor known as tetrahydrobiopterin, or BH4. After treatment with sapropterin, a replacement protein for BH4, the patient remarkably began to recover in a matter of weeks. Even though Pan was convinced this could be a real cure for this patient, she didn’t think it would necessarily apply to others with treatment-resistant depression. Then, the results of the small trial she and her colleagues ran with 33 similar patients became available. A significant number—21 out of 33—showed a metabolic disorder. Most of these showed improvement with replacement drug therapy.

Now, studying metabolic disorders of the nervous system has become an unexpected focus of Pan’s career. As this emerging field of medicine shows promise for treatment-resistant depression, it might benefit patients with other neurological disorders as well.



CELL

RESEARCHERS INVESTIGATE MECHANISMS TO INHIBIT TUMOR REGULATORY T CELLS

JUN 2017 \ VOL 169 \ ISSUE 6

Within tumor microenvironments, regulatory T cells (Tregs) are responsible for shielding tumors from the body's defenses. Previous research involving mice with tumors revealed that the surface protein neuropilin-1 (Nrp1) is vital to the function, integrity, and survival of Tregs within tumor microenvironments. In a more recent study, Pitt researchers demonstrated that impeding Nrp1 prevents the suppression capabilities of Tregs within the tumor microenvironment, thereby enabling the body to detect and attack tumors. "Interestingly, when Tregs lose Nrp1, they not only fail to suppress, they also become active participants in the anti-tumor immune response," said senior author **Dario A.A. Vignali, PhD**, Frank Dixon Professor of Cancer Immunology, vice chair of immunology, and coleader of the Cancer Immunology Program at the UPMC Hillman Cancer Center. Analyses showed that the secreted immune molecule interferon gamma (IFN γ) diminished Treg function and might be harnessed for development of future immunotherapy approaches.

"Interestingly, when Tregs lose Nrp1, they not only fail to suppress, they also become active participants in the anti-tumor immune response."

— DARIO A.A. VIGNALI, PHD

SCIENCE TRANSLATIONAL MEDICINE

ROBOTIC ARM SUCCESSFULLY RELAYS SENSE OF TOUCH

OCT 2016 \ VOL 8 \ ISSUE 361

After a car accident left Nathan Copeland with quadriplegia and unable to feel any sensation in parts of his body, he agreed to participate with Pitt researchers in the development of a "brain computer interface" aimed at using robotic prostheses to restore physical capabilities. Surgeons implanted microelectrode arrays in his brain, allowing Copeland to control a robotic arm and hand using only his thoughts. Now, he has become the first person to experience and regain the sensation of touch through a robotic arm. "The most important result in this study is that microstimulation of the sensory cortex can elicit natural sensation instead of tingling," said coauthor **Andrew Schwartz, PhD**, Distinguished Professor of Neurobiology and Professor of Systems Neuroscience. Microelectrodes were planted in Copeland's brain in the regions governing feeling in his fingers and palm. Copeland was able to determine which robotic finger was being touched and could, to an extent, distinguish the intensity of pressure applied. "The ultimate goal is to create a system that moves and feels just like a natural arm," said coauthor **Robert Gaunt, PhD**, assistant professor of physical medicine and rehabilitation. "This is a great start." (See story, page 17.)

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

NEW MOVEMENT-MEDIATING BRAIN REGION VALIDATED

APR 2017 \ VOL 114 \ ISSUE 16

Scientists have long believed that the signals instigating voluntary movement originate in the brain's frontal lobe. However, Pitt researchers revealed that a neural pathway in the posterior parietal cortex (PPC), a region separate from the frontal lobe, also influences voluntary movements. The researchers studied nonhuman primate models but believe humans contain a similar pathway. Although the presence of a movement control center in the PPC had previously been proposed, scientists believed that the PPC played a role only in associating sensory inputs and building a representation of personal space. The Pitt team confirmed the existence of this command apparatus and revealed the pathway connecting the PPC to spinal cord neurons that control hand movement. Using primate models, the researchers electrically stimulated the "lateral area 5" PPC region, resulting in finger and wrist movement in the primate models. When a protein marker and a rabies virus were injected into the hand, both traveled along routes that confirmed connection between the PPC and spinal cord neurons and between hand muscles and the PPC, respectively. The finding could influence therapies for patients with impaired motor function, among other implications.

"The findings break the hard and fast rule that a furrow in the brain called the central sulcus — a Mississippi River-like separation — splits up the areas controlling sensory and motor function."

— PETER L. STRICK, PHD

NATURE BIOTECHNOLOGY

CRISPR EDITING SUCCESSFULLY REDUCES
TUMOR SIZE IN MOUSE MODELS

JUN 2017 \ VOL 35 \ ISSUE 6

Using CRISPR-Cas9 genome editing technology, School of Medicine researchers manipulated cancer-causing fusion genes in mice, successfully reducing tumor size. When two separate genes fuse together, they can produce a cancer-promoting protein. The team, led by **Jianhua Luo, MD, PhD**, professor of pathology and director of Pitt's High Throughput Genome Center, used CRISPR-Cas9 to cut mutated DNA from these fusion genes and replace it with a gene that triggers cell death in cancer cells, leaving healthy cells untouched. Mice subjected to aggressive prostate and liver cancer showed a 30 percent reduction in tumor size after the intervention, which also produces significantly fewer side effects than treatments like chemotherapy. Researchers plan to test whether this technique could eradicate the cancer instead of diminishing it.

SCIENCE

REOVIRUS IMPLICATED IN CELIAC DISEASE

APR 2017 \ VOL 356 \ ISSUE 6333

Infection with reovirus, a common, generally harmless virus, can trigger an immune system response to gluten that may lead to celiac disease, according to new research using a mouse model at Pitt's School of Medicine and the University of Chicago. Celiac disease is a digestive disorder that damages the small intestine. There is no cure, other than eliminating gluten intake. The research team, which included coauthor **Terence S. Dermody, MD**, Vira I. Heinz Professor and chair of pediatrics and physician-in-chief and scientific director of Children's Hospital of Pittsburgh of UPMC, subjected mice to two similar but genetically different reovirus strains. Both strains induced protective immunity, but one strain caused an inflammatory immune response and loss of tolerance to dietary gluten. The study demonstrated that intestinal viruses can induce the immune system to overreact to gluten and lead to celiac disease development and suggests that other viruses can cause development of additional autoimmune disorders like type 1 diabetes. It also adds to the possibility of someday using vaccines to prevent these diseases.

"We have been studying reovirus for some time, and we were surprised by the discovery of a potential link between reovirus and celiac disease. We are now in a position to precisely define the viral factors responsible for the induction of the autoimmune response."

— TERENCE S. DERMODY, MD

GASTROENTEROLOGY

PITT TEAM LINKS GENE TO GUT MICROBES AND CROHN'S DISEASE

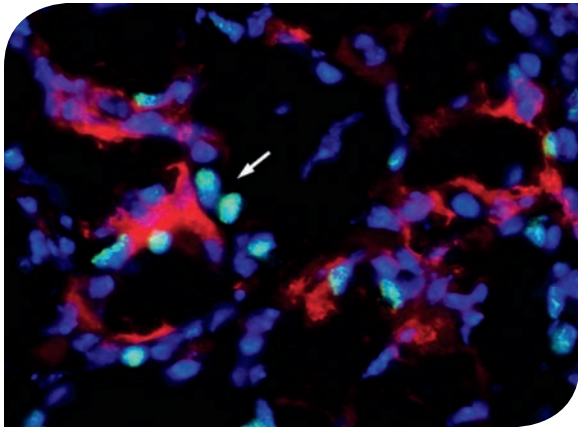
OCT 2016 \ VOL 151 \ ISSUE 4

A genetic variation linked to obesity, cholesterol levels, and schizophrenia is also associated with Crohn's disease and with changes in the gut microbiome, a team of Pitt-led researchers found. Patients with Crohn's disease, a chronic inflammatory condition of the gastrointestinal tract, have less microbial diversity in the gut microbiome. **Richard Duerr, MD**, Professor of Inflammatory Bowel Disease Genetics Research in the Department of Medicine, and fellow investigators identified an association between Crohn's disease and SLC39A8, a gene variant already linked to other microbiome-associated traits and phenotypes. They hypothesized that SLC39A8 may affect Crohn's disease susceptibility by altering the microbiome. "Our study found that there is a reduction in the abundance of hundreds of minor species of gut bacteria in healthy, overweight, and Crohn's disease-affected people who carry this genetic variant, suggesting that the genetic variant may increase risk for disease by altering the gut habitat," Duerr said. The finding enhances our understanding of bacteria that preserve good health and could advance Crohn's disease treatment and prevention.

One of the hottest topics at Pitt's Center for Medicine and the Microbiome involves potential connections between psychiatric disorders and the gut microbiome.

All Eyes on the Microbiome

Pitt's Center for Medicine and the Microbiome is a hub for collaborative investigations of the multitude of microbes that live in and on our bodies. Researchers from different disciplines and areas of expertise are exploring how the microbiome influences human health through the lenses of immunology, cancer biology, oral health, digestive disorders, and many other diverse perspectives. One of the hottest topics at the center involves potential connections between psychiatric disorders and the gut microbiome. This idea—that what's happening in a teenager's gut could have significant effects on anxiety and depression, for example—is stimulating some cutting-edge translational research that may open new avenues for cures and preventive medicine.



NATURE COMMUNICATIONS

DENDRITIC CELLS AS TARGETS FOR STOPPING ORGAN REJECTION

AUG 2016

An international, Pitt-led team of researchers found that targeting certain recipient cells reduced the risk of organ rejection in mice that received kidney and heart transplants. The team observed that the dendritic cells — which activate T cells — native to the heart or kidney grafts were rapidly replaced by the recipient's dendritic cells, which proceeded to spark T-cell activation within the graft and increase likelihood of rejection. "We demonstrated that dendritic cells not only exert a key role as antigen-presenting cells in graft-draining lymphoid organs but also play a critical function within the transplanted organs," said coauthor **Adrian E. Morelli, MD, PhD**, associate professor of surgery and of immunology. The study indicates that eliminating transplant-infiltrating dendritic cells reduces T-cell presence within the graft, prolonging transplant survival, he said. "The next step would be to devise methods to specifically target dendritic cells that have infiltrated transplanted organs," said coauthor **Fadi Lakkis, MD**, Frank and Athena Sarris Professor of Transplantation Biology and scientific director of the Starzl Transplantation Institute.

"We demonstrated that dendritic cells not only exert a key role as antigen-presenting cells in graft-draining lymphoid organs but also play a critical function within the transplanted organs."

— ADRIAN E. MORELLI, MD, PHD

JOURNAL OF CLINICAL INVESTIGATION

NEW DRUG TARGETS FOR PULMONARY HYPERTENSION

SEP 2016 \ VOL 126 \ ISSUE 9

Pulmonary hypertension (PH) is characterized by high blood pressure in the arteries of the lungs. The disease can lead to heart failure, but symptoms can go unnoticed for months or even years. Senior author **Stephen Y. Chan, MD, PhD**, associate professor of medicine, and colleagues, determined that stiffening of the lung's blood vessels — an early event in PH onset — activates the signaling molecules YAP and TAZ, which then activate a protein called GLS1 that controls how vessel cells produce and use energy. Chan and colleagues found that administering YAP and GLS1 inhibitor drugs improved PH conditions in rodent models. "The discovery offers us so many new ways to design drugs tailor made to stop pulmonary hypertension in its tracks," Chan says.

PLOS ONE

NEW SOFTWARE MAKES CANCER GENOME DATA WIDELY ACCESSIBLE

OCT 2016

New methods of cancer prevention, diagnosis, and treatment may be locked in the vast amounts of genomic data generated by cancer research. To exploit the data, Pitt researchers are working with the Pittsburgh Supercomputing Center to launch an open-source, free software program to process data stemming from the National Cancer Institute's Cancer Genome Atlas project, which seeks to map out and share certain cancers' complete sets of DNA. The software, called TCGA Expedition, will make these large data sets ubiquitously available to researchers, said lead author **Rebecca Jacobson, MD, MS**, adjunct professor of biomedical informatics. A key goal of the project is to make the data manageable despite the cumbersome size and complexity. "Right now, our institutions are choking on data," she says.

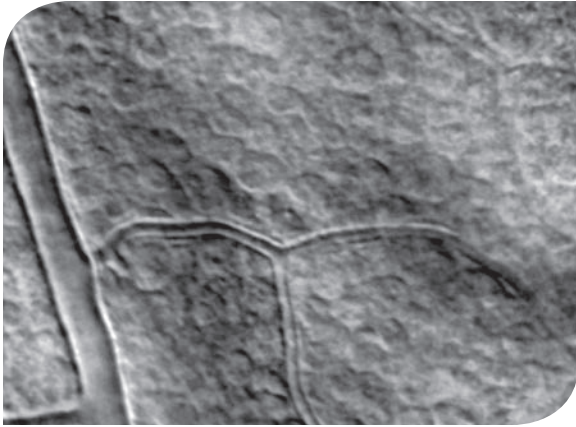
IMMUNITY

TUMOR MICROENVIRONMENT CRIPPLES IMMUNE CELLS' MITOCHONDRIA

AUG 2016 \ VOL 45 \ ISSUE 2

A budding tumor creates a microenvironment that keeps it nourished and protected as it siphons nutrients from the body. UPMC Hillman Cancer Center researchers found that this scenario also creates a nutrient-poor microenvironment for immune cells that the body sends to destroy the cancer. When T cells reach the tumor, their mitochondria begin to shrink and disappear, essentially leaving them without fuel. Senior author **Greg M. Delgoffe, PhD**, assistant professor of immunology, said that when researchers enhanced the immune cells' mitochondria, they could more effectively clear the tumor. He and his colleagues are testing various mitochondria-boosting techniques that could improve immunotherapy.





PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES
NEW TECHNIQUE MAY ENABLE EARLY GLAUCOMA DETECTION

JAN 2017 \ VOL 114 \ ISSUE 3

Ethan A. Rossi, PhD, assistant professor of ophthalmology, and colleagues developed a new technique to image individual retinal ganglion cells (RGCs) in the living eye. The approach may permit earlier detection of ganglion-cell loss in glaucoma. Glaucoma diagnosis currently involves assessing vision loss and measuring the thickness of nerve fibers connecting RGCs to the brain. Upon detecting a change in thickness, however, patients may already have lost tens of thousands of RGCs or more, with irreversible vision loss as a consequence. Detecting cellular changes before severe vision loss occurs may offer an earlier opportunity for therapeutic intervention.

Detecting cellular changes before severe vision loss occurs may offer an earlier opportunity for therapeutic intervention to prevent vision loss.

CELL REPORTS

ALT PATHWAY PROTEINS ARE POTENTIAL CANCER DRUG TARGETS

NOV 2016 \ VOL 17 \ ISSUE 7

By exploiting cells' alternative lengthening of telomeres (ALT) pathway, cancer cells hijack healthy cells' DNA repair processes and duplicate themselves. Telomeres, the protective endcaps of cells' chromosomes, shorten over their lifespan, leading to cell death. Yet cancer cells that sabotage the ALT pathway lengthen telomeres every time they shorten, tricking cells into dividing continuously and spreading tumors. Using a technique called BioID, senior author **Roderick J. O'Sullivan, PhD**, assistant professor of pharmacology and chemical biology, and other UPMC Hillman Cancer Center researchers identified 139 proteins unique to ALT-activated cells that are found near telomeres and could influence their lengthening.

NATURE CHEMICAL BIOLOGY

ENZYME COULD INHIBIT A TYPE OF CELL DEATH

JAN 2017 \ VOL 13 \ ISSUE 1

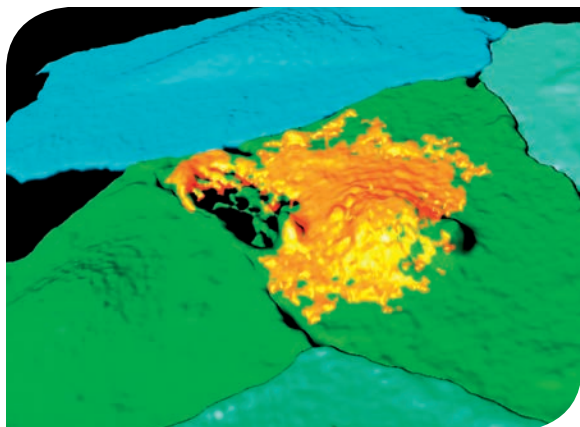
A team of researchers from Pitt and other institutions recently elucidated the processes behind a type of controlled cell death, ferroptosis. After analyzing hundreds of molecular combinations of oxidized lipids generated during ferroptosis, the team revealed that only four molecules—all phospholipids of a specific type, phosphatidylethanolamines—actually signal for a cell to die. Senior authors **Hülya Bayır, MD**, Professor of Critical Care Pediatric Research in the Department of Critical Care Medicine, and **Valerian Kagan, PhD, DSc**, professor of environmental and occupational health in the Graduate School of Public Health, believe that ferroptosis, which is associated with certain diseases, may also be behind radiation-induced cellular damage, which occurs prominently in the lining of the intestine. In back-to-back papers in the same journal issue, the researchers demonstrated in a mouse model that inhibiting ACSL4, an enzyme essential to ferroptosis onset, could be a viable therapeutic approach for treating ferroptosis-related conditions.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

THYROID CANCER OBSERVATION SUGGESTS
TREATMENT AVENUES FOR SEVERAL CANCERS

FEB 2017 \ VOL 114 \ ISSUE 9

Upon discovering a new genetic mechanism of thyroid cancer in tumor samples, Pitt researchers also noticed elevated levels of the protein IGF2BP3, a key component of the IGF1R protein signaling pathway, which is associated with tumor formation and growth. The team, including lead author **Yuri Nikiforov, MD, PhD**, professor of pathology and director of Pitt's Division of Molecular and Genomic Pathology, also examined other cancers, including those of the lung, pancreas, colon, and ovary, and found elevated IGF2BP3 in portions of each. After further research, administering IGF1R pathway-inhibiting drugs to patients with IGF2BP3 alterations could potentially block tumor growth, as demonstrated in cell culture and animal models, Nikiforov says.



PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES
 MICROBUBBLES AS A CELLULAR DRUG-DELIVERY SERVICE

SEP 2016 \ VOL 113 \ ISSUE 36

Using ultrasound energy coupled with microbubbles may provide an effective new technique to poke holes in cells and allow delivery of therapeutic agents for cardiovascular disease and cancer. This technique, called sonoporation, employs an ultrasound beam and gas-filled bubbles to precisely penetrate and access cells while sparing healthy tissue. With the aid of an ultrafast imaging camera, Pitt researchers, including lead author **Brandon Helfield, PhD**, a postdoctoral fellow at the Center for Ultrasound Molecular Imaging and Therapeutics, examined the biophysics of the technique and determined that microbubble-induced shear stress is the critical factor that permits sonoporation. By understanding its mechanics, researchers hope sonoporation will become an effective and clinically applicable drug-delivery tool, said senior author **Flordeliza Villanueva, MD**, professor of medicine and of clinical and translational science.

The combination of ultrasound energy and microbubbles may provide a new technique to penetrate cells and deliver therapeutic agents while sparing nearby healthy tissue.

MOLECULAR CELL

DNA-REPAIR PROTEIN'S MOVEMENT MADE VISIBLE UNDER THE MICROSCOPE

OCT 2016 \ VOL 64 \ ISSUE 2

Using a fluorescence microscope, researchers in the laboratory of **Bennett Van Houten, PhD**, Richard M. Cyert Professor of Molecular Oncology, observed Rad4 molecules tagged with light-emitting dots as they marched over strands of DNA, scanning for structural errors. The researchers found that Rad4, a DNA-repair protein, follows a "constrained motion" movement pattern to quickly scan lengths of DNA and detect structural errors caused by chemicals, ultraviolet light, or other agents. Rad4, working with another protein, Rad23, attempts to bend the DNA strand to examine its structure and find errors before exhibiting constrained motion to more carefully investigate smaller regions of DNA base pairs and calling in other DNA-repair machinery. Understanding these mechanisms may open new treatment avenues for cancer, especially cancers connected with UV light.

JOURNAL OF BIOLOGICAL CHEMISTRY

MYC GENE MAY BE TARGETED TO FIGHT PEDIATRIC LIVER CANCER

DEC 2016 \ VOL 291 \ ISSUE 51

Researchers from Pitt recently induced hepatoblastoma, a form of childhood liver cancer, in mice that either contained or lacked the Myc gene in liver cells. While both groups developed tumors, the group lacking Myc demonstrated slower tumor generation. Although Myc plays many roles in healthy cell division and metabolism, the researchers found that it boosts these processes to an even greater extent in tumors, thereby promoting tumor growth. Because normal cells are not dependent on Myc in the same fashion as tumor cells, a Myc inhibitor may be able to target cancer cells while sparing healthy ones, said lead investigator **Edward Prochownik, MD, PhD**, professor of pediatrics and director of oncology research at Children's Hospital of Pittsburgh of UPMC. This article was featured as a Paper of the Week by the *Journal of Biological Chemistry*.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

BACTERIA COMMON IN CYSTIC FIBROSIS PATIENTS
 EMIT INFLAMMATION-SUSTAINING ENZYME

JAN 2017 \ VOL 114 \ ISSUE 1

Pseudomonas aeruginosa, a bacterium that often infects cystic fibrosis (CF) patients, actually thrives after the body induces inflammation to fight foreign invaders. **Jennifer Bomberger, PhD**, assistant professor of microbiology and molecular genetics, found that *P. aeruginosa* secretes an enzyme called Cif that inhibits the body from making a molecule that can limit the inflammatory response. She and fellow researchers from Pitt and Dartmouth College analyzed CF patients' lung secretions and found that patients with higher Cif levels showed reduced ability to resolve inflammation, with increased levels of the inflammation marker IL-8 and reduced pulmonary function. Researchers are exploring therapeutic development to inhibit Cif or to artificially boost production of the molecule that reduces inflammation.

IMMUNOTHERAPEUTIC DRUG OUTPERFORMS
STANDARD THERAPY IN HEAD AND NECK CANCER

NOV 2016 \ VOL 375 \ ISSUE 19

Nivolumab, an immunotherapeutic drug, significantly increased survival rates in patients with recurrent head and neck cancer compared to standard therapy as demonstrated in a recent clinical trial led by the UPMC Hillman Cancer Center. The trial enrolled 361 patients with recurrent head or neck cancer that had progressed within six months of chemotherapy. After one year, 36 percent of the nivolumab patients were still living, compared to 17 percent of the patients receiving standard chemotherapy drugs. Significantly fewer nivolumab patients experienced quality-of-life-disrupting side effects compared to standard-therapy patients. "Due to our clinical trial, anti-PD-1 therapies like nivolumab are now the recommended treatment for patients with this very difficult, devastating cancer," said lead author **Robert Ferris, MD, PhD**, Hillman Professor of Oncology, professor of otolaryngology, and director of UPMC Hillman Cancer Center.

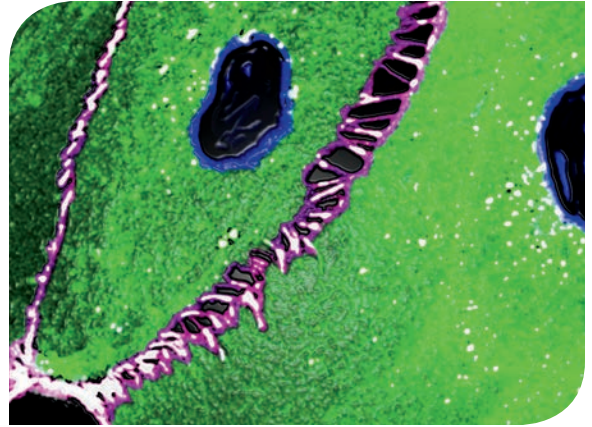
SKIN CANCER PATHOGEN HIJACKS CELLULAR
RECYCLING PROCESS TO STAY HIDDEN FOR YEARS

MAY 2017 \ VOL 114 \ ISSUE 20

Merkel cell polyomavirus (MCV), a pathogen that causes the most aggressive form of skin cancer, can lie dormant in the body for decades before cancer sets in. Pitt researchers **Yuan Chang, MD**, American Cancer Society Research Professor, UPMC Professor of Cancer Virology Research, and Distinguished Professor of Pathology, and **Patrick S. Moore, MD, MPH**, American Cancer Society Research Professor, Pittsburgh Foundation Professor of Innovative Cancer Research, and Distinguished Professor of Microbiology and Molecular Genetics — who together codiscovered MCV in 2008 — found in cell culture that the virus prolongs dormancy by hijacking molecules involved with cellular protein recycling. The virus tricks the cell into regularly degrading one of MCV's own proteins required for replication. MCV can then continue to exist within the cell for years until it senses adverse conditions like lack of nutrients, at which time it will permit protein replication and generate new viruses. If viral DNA breaks off during replication, it can merge with cellular DNA and cause Merkel cell carcinoma.

"Normally, viruses use elaborate measures to avoid being degraded by the cell so that they can infect a new host. But in a form of molecular jujitsu, MCV ensures that a key protein required for its replication is continually degraded so that the virus, retained as a naked piece of DNA, is not eliminated by the proteasome, which only degrades proteins."

— PATRICK S. MOORE, MD, MPH



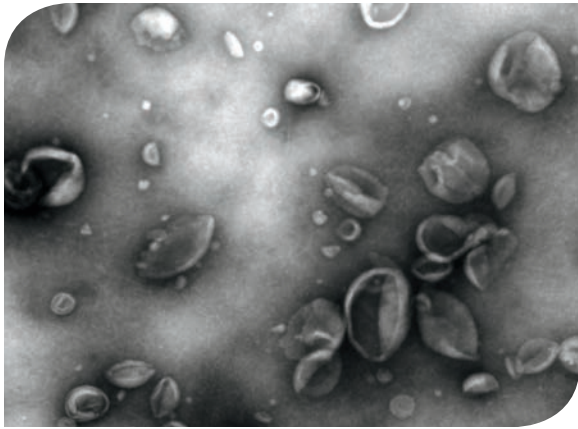
OLD-SCHOOL DRUGS MAY REDUCE ACUTE EDEMA

SEP 2016 \ VOL 17 \ ISSUE 1

Endothelial cells that line the capillaries are critical regulators of vascular permeability and, thereby, control whether fluid and immune cells can exit the bloodstream and occupy tissue, resulting in a condition known as edema. In excess, life-threatening consequences can result from edema. Pitt researchers investigated the enzyme MALT1 for its role in triggering endothelial permeability and whether its deactivation could lead to new therapies. For the study, researchers subjected mice that were genetically deficient in MALT1 enzymatic activity to a form of septic shock, which can lead to excessive fluid buildup in the lungs. The genetically deficient mice were protected from fluid accumulation, demonstrating MALT1's necessity for induced barrier leakiness. Researchers are now focused on using drugs to target MALT1. "We now understand that an old class of pharmaceuticals, the phenothiazines, are effective MALT1 inhibitors and might be quickly repurposed for a new therapeutic arena: the treatment of acute edema," said coauthor **Peter Lucas, MD, PhD**, associate professor of pathology and of pediatrics.

"We now understand that an old class of pharmaceuticals, the phenothiazines, are effective MALT1 inhibitors and might be quickly repurposed for a new therapeutic arena: the treatment of acute edema."

— PETER LUCAS, MD, PHD



SCIENCE ADVANCES

RESEARCHERS DISCOVER MYSTERY MECHANISM
BEHIND TISSUE REGENERATION

JUN 2016 \ VOL 2 \ ISSUE 6

Bioscaffolds made of extracellular matrix (ECM) derived from pig tissue have been used to promote tissue repair and reconstruction in the treatment of hernias, esophageal cancer, and injuries involving loss of bulk muscle tissue. But how ECM does this has remained a mystery. Researchers from the Pitt-UPMC McGowan Institute for Regenerative Medicine recently found that the ECM initiates tissue regrowth through “matrix bound nano-vesicles” or MBV—tiny, fluid-filled sacs that transfer nucleic acids and communicate with surrounding cells. Such vesicles, known as exosomes, were thought to be present only in body fluids, said lead investigator **Stephen Badylak, MD, PhD, DVM**, professor of surgery. The researchers, however, found these vesicles embedded in the solid ECM and discovered their role in stimulating tissue regrowth

Pitt and McGowan Institute for Regenerative Medicine researchers recently found that the ECM initiates tissue regrowth through “matrix bound nano-vesicles (MBV).”

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES

ENTEROVIRUS WORKINGS REVEALED THROUGH ‘MINI-GUT’ MODELS

FEB 2017 \ VOL 114 \ ISSUE 7

Pitt researchers grew stem cells from premature human small intestines into enteroids, or “mini-guts,” which contain the same cell types and tissue structures found in human intestines. The team, including senior author **Carolyn Coyne, PhD**, associate professor of pediatrics, then introduced a panel of enteroviruses, including echovirus 11 (E11), a virus linked to severe human disease, particularly in pediatric populations. Enteroviruses are common infectious agents associated with diseases and conditions ranging from flu-like symptoms to brain or heart inflammation, acute paralysis, and even death. In the mini-gut model, E11 induced significant damage to the enteroids. In actual human intestines, such damage could facilitate passage of the virus into the bloodstream. The team also found that different types of enteroviruses could target distinct types of cells within the gastrointestinal tract and that their effectiveness at infecting intestinal cells could vary. The results suggest that the mini-gut could be a powerful model system for exploring intestinal biology, diseases, and treatments.

CELL

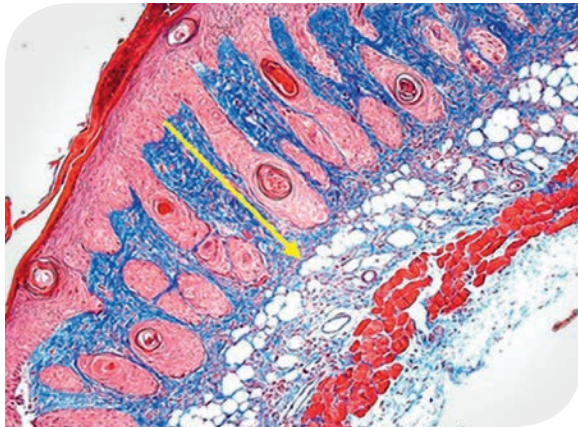
NEURON STIMULATION EVOKES NEW INSIGHT
INTO REWARD-BASED LEARNING

SEP 2016 \ VOL 166 \ ISSUE 6

Using optogenetics, scientists have explored new relationships and the connections between well-defined neurons and brain function in mice. However, researchers have not achieved the same cell-type specificity and understanding in nonhuman primates, which possess significantly greater neuroanatomical homology to humans and demonstrate more complex behaviors than mice.



William Stauffer, PhD, assistant professor of neurobiology — along with other researchers from Pitt and other institutions — recently demonstrated a method to induce cell-type-specific channelrhodopsin expression in Rhesus monkeys, a technique that permits modulating dopamine activity and behavioral choices. After using light pulses on target neurons to validate functional expression, the researchers demonstrated that adding optical stimulation boosted the monkey’s ability to learn behaviors driven by rewards. By demonstrating effective stimulation of dopamine neurons, researchers could apply the technique to other cell types in the monkey brain and shed new light on how neural reward systems facilitate behavior.



JOURNAL OF INVESTIGATIVE DERMATOLOGY

NEW THERAPY RELIEVES SKIN BURNS FROM RADIATION THERAPY

MAR 2017 \ VOL 137 \ ISSUE 3

Cancer patients who undergo radiation therapy can develop painful, irritating skin burns that can become infected. However, a new topical therapy developed by Pitt researchers and applied before or after radiation exposure has successfully prevented skin damage in animal models and in models using human skin. The therapeutic agent targets the formation of free radicals in the cell's mitochondria, thereby preventing inflammation and cell death, and may have applications for the prevention of skin cancer and skin aging. The researchers are optimistic about the therapy's future clinical development and the technology's licensing, said corresponding author **Louis D. Faló Jr., MD, PhD**, professor and chair of dermatology.

"During the course of radiation therapy, patients can develop irritating and painful skin burns. Sometimes they are so severe that patients must stop their treatment regimen. Our results show that topical treatment with this therapeutic agent prevents skin damage at the source."

— LOUIS D. FALO JR., MD, PHD

CANCER MEDICINE

JAN 2017 \ VOL 6 \ ISSUE 1

JOURNAL OF THE NATIONAL COMPREHENSIVE CANCER NETWORK

MAY 2017 \ VOL 15 \ ISSUE 5

PRECISION MEDICINE SHOWS PROMISE FOR PANCREATIC CANCER PATIENTS

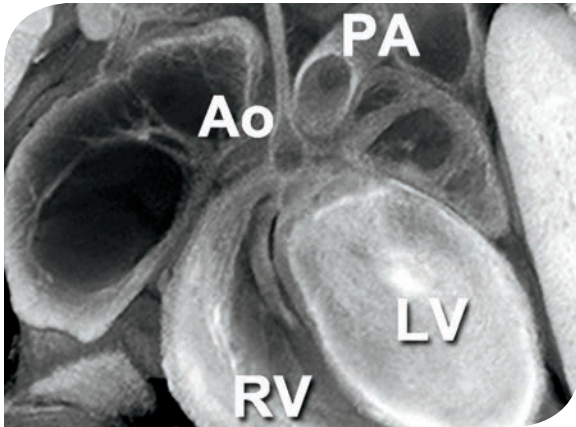
After employing DNA sequencing and finding gene changes in more than 100 gastrointestinal cancer samples from patients, Pitt researchers found that 14 percent of the patients met the criteria for a genomic-guided therapy. The team, led by **Nathan Bahary, MD, PhD**, associate professor of medicine and codirector of the UPMC Pancreatic Cancer Center of Excellence, found several mutations in each evaluated cancer type, including colorectal and pancreatic tumors. Half of the patients who received the genomic-guided therapy experienced improved outcomes and survival rates. In a separate study, researchers from Pitt and other institutions performed genomic profiling on 3,000 pancreatic cancer patients and found five with alterations in their anaplastic lymphoma kinase (ALK) gene. Among these, four received ALK-inhibiting drugs and three showed tumor shrinkage or other benefits. Patients with ALK mutations average just 38 years old at diagnosis, compared to 71 for other pancreatic cancers. These studies' findings suggest that using precision medicine and mutational analyses early in therapy may bring benefits not possible with standard therapies.

NATURE MEDICINE

NEW TEST DETECTS 'HIDDEN' HIV

JULY 2017 \ VOL 23 \ ISSUE 7

People who seem nearly cured of HIV may actually harbor dormant virus at an amount 70 times greater than previous estimates. A Pitt research team, including senior author **Phalguni Gupta, PhD**, professor and vice chair of infectious diseases and microbiology, Graduate School of Public Health; **Charles R. Rinaldo, PhD**, professor and chair of infectious diseases and microbiology, Pitt Public Health, and professor of pathology; and **Nicolas Sluis-Cremer, PhD**, professor of medicine, developed a new technique to detect "hidden" HIV. Most of the HIV DNA hiding out in the cells of patients receiving antiretroviral therapies is defective and can't restart infection. TZA, the Pitt-developed test, detects a gene that's turned on only in the presence of replicating HIV. This test produces a more accurate picture of the lingering HIV's potency, and it may help doctors determine whether someone being treated for HIV is actually cured. Compared to the quantitative viral outgrowth assay — the current best available test — TZA produces results at a third of the cost in one week instead of two, and with less labor and blood volume.



NATURE GENETICS

TWO GENES LINKED TO RARE BUT SEVERE CONGENITAL HEART DEFECT

JULY 2017 \ VOL 49 \ ISSUE 7

Pitt researchers uncovered two genes behind the rare but severe congenital heart defect known as hypoplastic left heart syndrome (HLHS). By screening mice with experimentally induced mutations for structural heart defects, the researchers found eight mouse strains with heart defects indicative of HLHS. After identifying several hundred mutations in the HLHS mutant strains, they demonstrated that mutations in multiple genes are required to cause HLHS. In one strain, they pinpointed two genes, *Sap130* and *Pcdha9*, that, when both are mutated, can cause HLHS. The heart cells in mice with these mutations harbored mitochondrial defects, had poor muscle development, and exhibited defects in cell proliferation. Thus, *Sap130* and *Pcdha9* could play a role in muscle progenitor expansion and regulation of cardiac muscle metabolic function. These findings indicate that HLHS may be associated with heart muscle defects that can severely compromise blood flow. As noted by **Cecilia Lo, PhD**, F. Sargent Cheever Professor and chair of the Department of Developmental Biology, these findings have important therapeutic implications.

After identifying several hundred gene mutations in mice born with structural heart defects, Pitt scientists from the Department of Developmental Biology pinpointed two genes that, when both are mutated, can cause the rare but severe heart defect known as hypoplastic left heart syndrome.

AMERICAN JOURNAL OF PSYCHIATRY

NEUROFEEDBACK AS TREATMENT FOR DEPRESSION

AUG 2017 \ VOL 174 \ ISSUE 8

A number of patients with depression experienced remission after they underwent brain imaging that allowed them to see a real-time visual representation of their own brain activity as they focused on positive memories. While inside an fMRI scanner, each patient was asked to concentrate on positive memories while looking at a “thermometer” on a computer screen that rose and fell in response to activity in the patient’s amygdala, a region of the brain that guides our response to both positive and negative emotional stimuli. The study, which was led by assistant professor of psychiatry **Kymerly Young, PhD**, showed that patients in the experimental group experienced increased blood flow to the amygdala relative to baseline and relative to a control group of patients. Some experienced a significant decrease in their depression and others experienced remission, suggesting that neurofeedback can help patients overcome depression.

NEW ENGLAND JOURNAL OF MEDICINE

SHORTENING ANTIBIOTIC TREATMENT FOR EAR INFECTIONS IN YOUNG CHILDREN CAN BE HARMFUL, NOT HELPFUL

DEC 2016 \ VOL 375 \ ISSUE 25

Reducing the course of antibiotics for treatment of middle-ear infection has worse clinical outcomes and doesn’t reduce the risk of antibiotic resistance, according to School of Medicine researchers. Led by **Alejandro Hoberman, MD**, Jack L. Paradise Professor of Pediatric Research and chief, Division of General Academic Pediatrics at Children’s Hospital of Pittsburgh of UPMC, the team conducted a trial including 520 children between 6 and 23 months old who received either a standard 10-day antibiotic treatment course or a shortened five-day course. Children in the 10-day group, compared with children in the five-day group, had fewer symptoms and overall better outcomes at the end of treatment. Furthermore, neither the rate of adverse events nor the rate of emergence of antimicrobial resistance was lower with the shorter regimen.

NATURE STRUCTURAL AND MOLECULAR BIOLOGY

RESEARCHERS SOLVE THE CRYSTAL STRUCTURE OF A COMPLEX KEY TO HIV INFECTION

OCT 2016 \ VOL 23 \ ISSUE 10

For HIV to successfully infect and spread within the body, the HIV-1 accessory protein Vpr must enable viral infection of macrophages and promote viral replication in T cells. Researchers from the Pittsburgh Center for HIV Protein Interactions, including **Angela Gronenborn, PhD**, Distinguished Professor, UPMC Rosalind Franklin Professor, and chair of structural biology; **Jinwoo Ahn, PhD**, assistant professor of structural biology; and **Guillermo Calero, MD, PhD**, associate professor of structural biology, elucidated the structural details behind Vpr’s role in seizing a key protein degradation pathway to antagonize the normal cellular response toward invading pathogens. To illuminate this process,

the researchers determined the crystal structure of the complex between the DNA repair enzyme UNG2, Vpr, and other components. The structure revealed how Vpr connects with the cellular substrate receptor DCAF1 to create a bridge for UNG2 attachment. As observed, Vpr uses similar regions to Vpx (another accessory protein) to bind the substrate receptor but different regions to target the specific cellular substrates. To recruit UNG2, Vpr inserts into UNG2's DNA-binding site, imitating the shape of DNA, thereby delivering a two-step punch, inhibiting the enzyme's active site, as well as steering it toward cellular degradation. Knowledge of the structure will help design strategies to interfere with Vpr's activities in the quest to curtail HIV infection.

CLINICAL CANCER RESEARCH

TUMOR SAMPLING SITE CAN AFFECT SCREENING RESULTS

NOV 2016 \ VOL 22 \ ISSUE 21

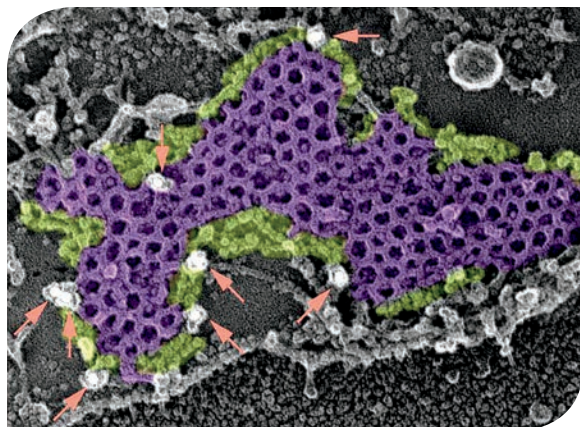
A tumor's physical and genetic makeup can vary within itself, meaning cells in one part of a tumor can be more aggressive than those in another. As described by UPMC Hillman Cancer Center researchers, including **Adrian V. Lee, PhD**, professor of pharmacology and chemical biology and director of Pitt's Institute for Precision Medicine, gene expression profiling — a test to determine which genes are active in a tumor's cells — can produce varying results and lead to different treatment plans depending on which part of the tumor is selected for testing. The researchers took 181 samples from various parts of 71 estrogen-receptor-positive breast tumors and found that, for 25 percent of patients, the risk of recurrence varied depending on which sample was processed. These results indicate that tumor sampling techniques may need to be refined to ensure that the most appropriate tumor sections are selected for testing.

SCIENCE IMMUNOLOGY

NEW MOLECULAR BASIS TO BLOCK THE IMMUNE SYSTEM, PREVENT ORGAN REJECTION

JUNE 2017 \ VOL 2 \ ISSUE 12

By uncovering the molecular steps behind organ transplant rejection, researchers from Pitt and the University of Toronto have potentially laid the groundwork for disrupting the process and preventing organ rejection. In mice, the researchers, including cosenior author **Fadi Lakkis, MD**, Frank and Athena Sarris Professor of Transplantation Biology in the Department of Surgery and scientific director of the Thomas E. Starzl Transplantation Institute, showed that the molecule SIRP-alpha leads to innate immune system activation and differs between unrelated individuals. When SIRP-alpha from transplanted tissue differs from that of the host tissue, it activates the CD47 receptor located on recipient innate immune cells, triggering the innate and eventually the adaptive immune system. Humans also express SIRP-alpha, so sequencing the gene and identifying similar donor and recipient pairs could reduce rejection. Impeding the interaction between SIRP-alpha and CD47 successfully blocked innate immune system activation in mice, opening the possibility for similar results in humans.



To resolve atomic structure, the team used a multitude of complementary imaging methods, including crystallography and three types of microscopy. Shown here is a deep-etch electron microscopy image.

DEVELOPMENTAL CELL

RESEARCHERS EXPLORE THE PASSAGE OF CELLULAR CARGO

JUN 2016 \ VOL 37 \ ISSUE 5

Clathrin-coated vesicles (CCVs) govern and relay the transport of cargo, such as proteins, from the plasma membrane to various cellular organelles. But how these vesicles are formed from the plasma membrane and capture the appropriate cargo remains unclear. Researchers from Pitt, including **Linton M. Traub, PhD**, associate professor of cell biology, and **Simon C. Watkins, PhD**, Distinguished Professor and vice chair of cell biology, employed structural and biochemical analyses to shed new light on these processes. The team observed a three-way interaction occurring among early-arriving clathrin-coat proteins Eps15/R and Fcho1/2 and the adaptor protein AP-2, which works to capture and internalize cargo. These proteins all work to decode arrayed Asp-Pro-Phe (DPF) peptides. However, Eps15/R decodes these peptides differently than Fcho1/2 and AP-2, the researchers showed. These interactions permit the AP-2 protein to assume an open conformation that enables cargo engagement. These studies provided insight into the molecular mechanisms of the early stages of endocytosis, a process critical for the regulation of cholesterol.



Pittsburgh is a vibrant city whose hills and hollows shelter close-knit neighborhoods and communities. As the city's medical school, we seek to identify areas of need, contribute our expertise and energy, and strengthen partnerships to make a most livable city even better.

community

Musical Medicine

Pitt med students Sae Jang and Pouya Joolharzadeh carefully put on tissue paper-thin yellow hospital gowns and bright blue gloves. They are outside the room of palliative care patient James Dorsey (not his real name). Dorsey has been at UPMC Presbyterian for almost a month.

But the med students aren't here for rounds. Jang picks up her cello, and Joolharzadeh gets his violin. They walk into the room, and Jang asks Dorsey if he'd like to hear some music. "Something from the '50s or '60s," he replies.

Jang sits in the corner of the room and starts playing "Yesterday" by the Beatles. Joolharzadeh follows with Bach while Jang stands close to Dorsey. Nurses gather outside the door. An infusion pump beeps nearby.

About three years ago, Jang started MusiCare, a program that gives medical students opportunities to perform for patients. Michael Chiang and Shawn Tahata helped formalize MusiCare in the Clinical Experiences curriculum and expand the program, which now brings students to play at UPMC Presbyterian and Children's Hospital of Pittsburgh of UPMC.

"I think that feeling of doing something positive for patients is really empowering as a medical student, especially in the first two years, when you are [mostly] studying from books and memorizing. It reminds us why we came to medical school," Jang says.

Across the hospital, Audrey Kindsfather is playing harp in the dialysis unit. Behind her, patients take videos of the performance on their phones. A man getting dialysis tears up. "I think it's beautiful," he says. "I just wish I was in a different situation."

Kindsfather, who joined MusiCare last year, co-coordinates the program with Joolharzadeh and Elena Nikonova. Kindsfather's harp wouldn't fit in the palliative care rooms, so

she and Jang expanded the program to the dialysis unit and to Children's with help from Jane Schell, MD, assistant professor of medicine. Kindsfather, who started playing piano at age 6 and took up harp at 12, sees the time she spends organizing the group and performing as self-care.

"It takes care of our mental health," she says.

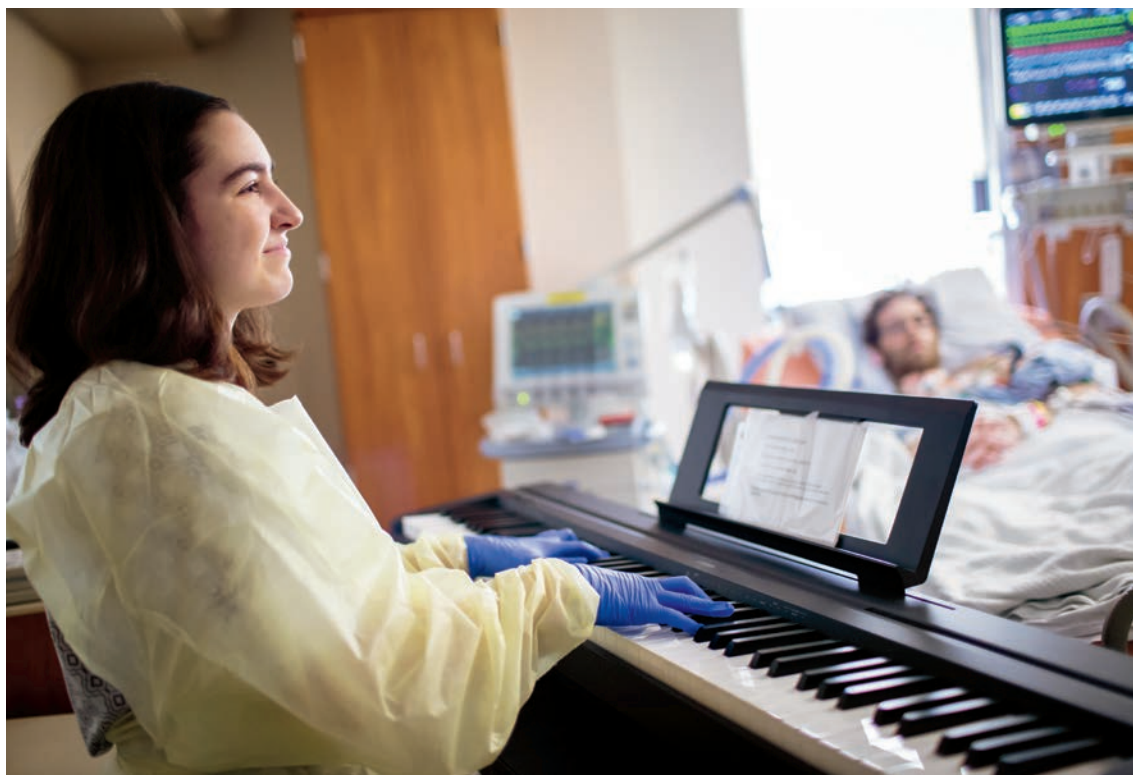
Schell, who is the faculty advisor for MusiCare and hosts informal musical get-togethers at her home, says this group of students is ahead of the curve.

"When we go into medical school, it's so easy to get focused on the physiology. It's very easy to become dehumanized in the medical setting. Our patients have a lot of suffering. ... Music helps our patients and our staff feel like humans. That, in and of itself, is therapeutic.

"That is the impressive thing, to see medical students really pick up on that piece," Schell says.

Now in her fourth year of medical school, Jang engages with patients directly as part of the curriculum. While she was doing her rotation in thoracic surgery, a patient caught her eye. She had seen the patient daily for weeks during rounds and decided she could deepen the connection by playing music for her.

"When we go into medical school, it's so easy to get focused on the physiology. It's very easy to become dehumanized in the medical setting. Our patients have a lot of suffering. ... Music helps our patients and our staff feel like humans. That, in and of itself, is therapeutic." — JANE SCHELL, MD



But when Jang brought her cello into the room, she realized the patient didn't recognize her. Because Jang had been focused on getting through the medical checklist when she saw her, they hadn't established a relationship.

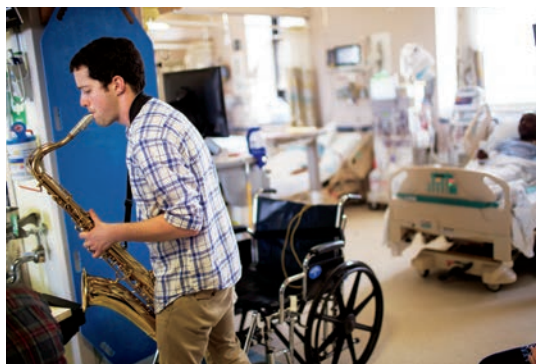
"I remember this incredible feeling of guilt. Since then I've really changed the way I talk to my patients. In my initial interviews, I've started to ask them, 'What's one thing that's really important to you as a person?'" Jang says.

Joolharzadeh has found that performing music in the hospital has changed not just how he sees patients but also how he sees music itself. While getting a bachelor's degree in music, he struggled with performance anxiety—his hands would shake to the point that he couldn't play.

"So far, playing for these patients has made that anxiety diminish, because it's not about me anymore," he says.

MusiCare is now among the variety of clinical settings where med students can volunteer for course credit. Nikonova, a pianist, would like MusiCare to grow to include residents and other physicians.

"Music itself bypasses everything and goes for the straight emotional appeal. For medical students it's cool because we can speak with residents and doctors and patients of all ages. Everyone will gather around a source of music when it's performed," Nikonova says. "There's nothing [else] that gives you that kind of room to breathe in the hospital."



Med students Natalie Nakles (top) and Jake Jerome perform for patients in the dialysis and intensive care units. Their catalogue of songs includes classical, original, and improvised pieces—even a selection from *The Legend of Zelda* video games.

Stop the Bleed

In 2013, after numerous mass shootings and casualties in the United States, including the devastating Sandy Hook Elementary School shootings, the American College of Surgeons created a committee to determine how to improve survival after intentional mass-injury events. The committee decided on a national protocol, referred to as the Hartford Consensus. Based on those recommendations, the White House

launched the Stop the Bleed campaign in 2015. In 2016, UPMC committed \$1.3 million over three years to implement the campaign in the region.

One of the goals of the community outreach program is to train bystanders to apply basic first aid to victims of severe blood loss as a result of trauma. Raquel M. Forsythe, MD, assistant professor of surgery and of critical care medicine, is one of the University of Pittsburgh faculty members directing the regional initiative.

“Uncontrolled bleeding is the most common preventable cause of death from trauma,” Forsythe said. “As trauma surgeons, we can only do so much by the time people get to the hospital. If we can get help earlier to people after they’re injured, by training lay people to respond, that’s an opportunity to save lives. Research shows that people’s willingness to step in and help increases significantly when they’ve had some training in how to help.”

The training is part instruction and part hands-on practice. Participants are taught three main techniques to control bleeding—direct pressure, wound packing, and tourniquet use—and practice them on training limbs with multiple wounds. Forsythe and colleagues use a train-the-trainer model to create the number of trainers needed to spread the knowledge throughout the region. In the initiative’s first six months, the program trained 806 trainers, 578 law enforcement officers, and 2,376 lay people.

Another goal of the program is to place hemorrhage-control kits in spaces for the general public to use, just as automatic external defibrillators are in place to assist in cardiac arrests. The kits include special clotting gel, gauze, and tourniquets.

“As we saw with the Boston Marathon bombings, people will jump in and try to help,” said Forsythe. “When people walk out of Stop the Bleed training, they feel empowered because they know how to help.”



Though no study has connected the exposure to e-cigarette aerosol to specific health issues, “We don’t have the luxury of waiting.”

—BRIAN A. PRIMACK, MD, PHD

The Evidence Supports a Ban on E-Cigarettes

Physicians and researchers from the University of Pittsburgh School of Medicine joined community officials in celebrating a recent ban on the use of electronic-cigarettes (e-cigarettes) in Allegheny County restaurants, stores, schools, sports stadiums, and public buildings. The regulation is meant to protect people from exposure to the dangers of secondhand e-cigarette aerosol mist.

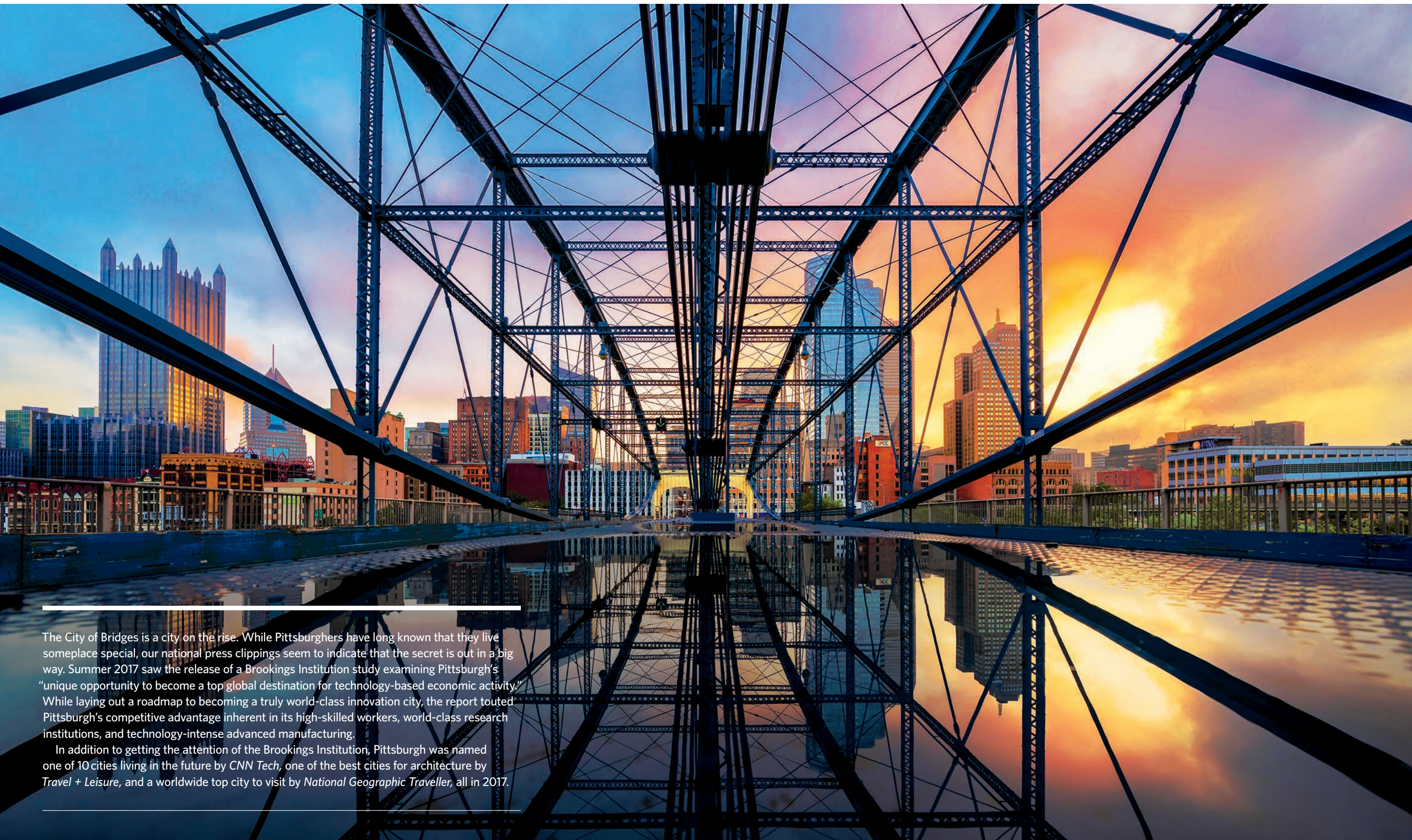
Though e-cigarettes are not fully regulated and, therefore, their ingredients are not always known, the aerosol from e-cigarettes is known to contain harmful compounds like nicotine, benzene, lead, tar, formaldehyde, ultrafine particles, and diacetyl, a flavoring chemical linked to serious lung disease, according to the Office of the U.S. Surgeon General.

Brian A. Primack, MD, PhD, dean of Pitt’s Honors College, professor of medicine, and director of the Center for Research on Media, Technology, and Health, supported the ban not only from a health standpoint but from a public health one. His own research has shown that e-cigarettes are a bridge to smoking tobacco for young people. The palatable flavorings of e-cigarettes and the addictive nicotine make the transition to smoking tobacco much easier, he posits. According to the Centers for Disease Control and Prevention, e-cigarette use surpassed conventional cigarette use among young people in 2014.

Though no study has connected the exposure to e-cigarette aerosol to specific health issues, Primack said, “We don’t have the luxury of waiting. The amount of toxic chemicals seen in blood studies is similar to levels associated with illnesses tied to secondhand cigarette smoke. It’s a matter of connecting the dots.”

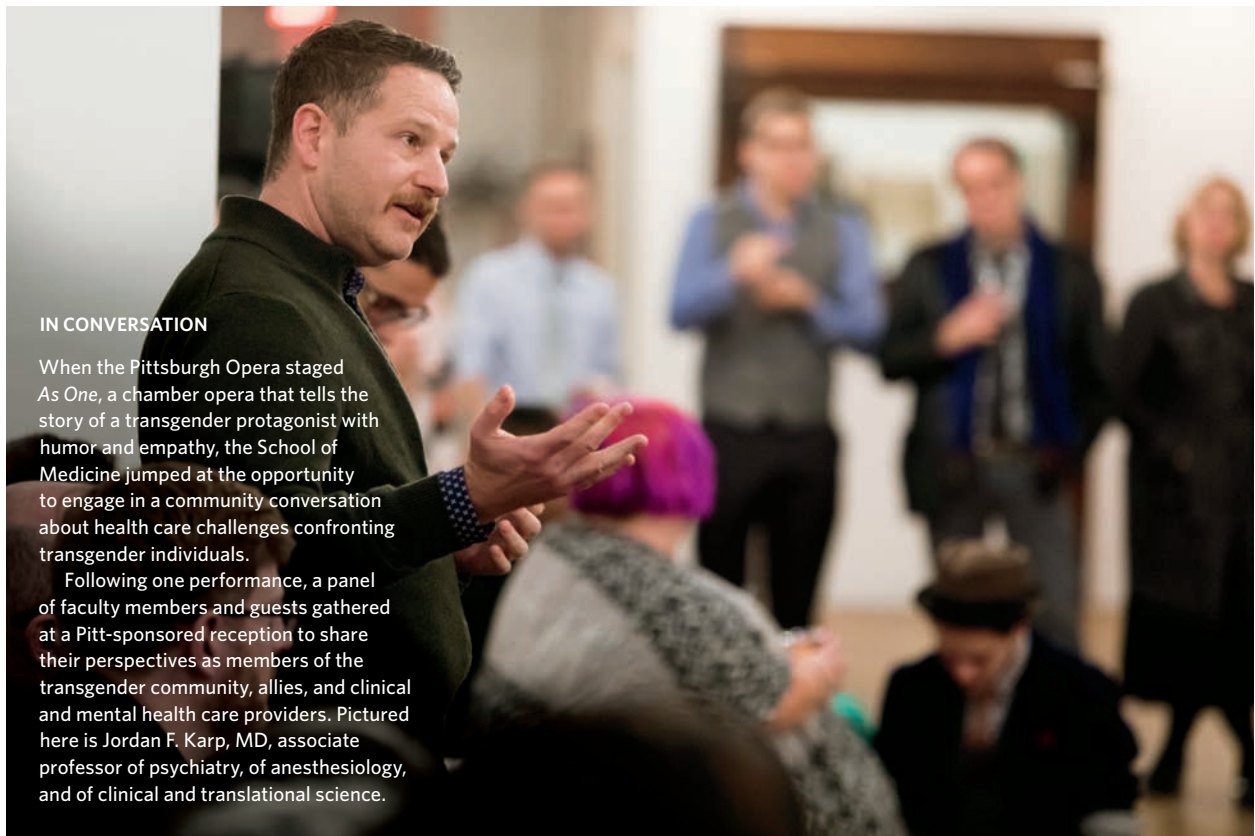
Smartphone App Aims To Curb Preterm Birth Risk

Rates of preterm birth, which is the leading cause of neonatal death or long-term disability, are disproportionately high among certain socioeconomic groups, including families living in poverty and among African Americans. With preterm birth rates rising, Magee-Womens Hospital of UPMC and Carnegie Mellon University scientists and specialists developed a personalized smartphone app that can more easily reach certain populations of pregnant women and provide accessible, personalized obstetric care and advice. The app queries users daily to assess preterm birth risk factors like weight gain, smoking, alcohol use, depression, and intimate partner violence and offers patient-specific feedback and recommendations. The research team, including Hyagriv Simhan, MD, professor of obstetrics, gynecology, and reproductive sciences, described the app’s success at mitigating preterm birth risk in a recent paper in the *Journal of Medical Internet Research mHealth and uHealth*. The next step is evaluating the app’s effects on behavioral and clinical outcomes, including adverse birth outcomes.



The City of Bridges is a city on the rise. While Pittsburghers have long known that they live someplace special, our national press clippings seem to indicate that the secret is out in a big way. Summer 2017 saw the release of a Brookings Institution study examining Pittsburgh's "unique opportunity to become a top global destination for technology-based economic activity." While laying out a roadmap to becoming a truly world-class innovation city, the report touted Pittsburgh's competitive advantage inherent in its high-skilled workers, world-class research institutions, and technology-intense advanced manufacturing.

In addition to getting the attention of the Brookings Institution, Pittsburgh was named one of 10 cities living in the future by *CNN Tech*, one of the best cities for architecture by *Travel + Leisure*, and a worldwide top city to visit by *National Geographic Traveller*, all in 2017.



IN CONVERSATION

When the Pittsburgh Opera staged *As One*, a chamber opera that tells the story of a transgender protagonist with humor and empathy, the School of Medicine jumped at the opportunity to engage in a community conversation about health care challenges confronting transgender individuals.

Following one performance, a panel of faculty members and guests gathered at a Pitt-sponsored reception to share their perspectives as members of the transgender community, allies, and clinical and mental health care providers. Pictured here is Jordan F. Karp, MD, associate professor of psychiatry, of anesthesiology, and of clinical and translational science.

Gender Care

The Gender and Sexual Development Program at Children’s Hospital of Pittsburgh of UPMC offers medical assistance and support for adolescent and young adult patients who wish for their bodies to match their gender identity. The adolescent medicine and endocrinology joint program was developed after two Pitt School of Medicine professors—Selma F. Witchel, MD (Pediatrics), and Elizabeth Miller, MD, PhD (Pediatrics, Behavioral

and Community Health Sciences), chief of the Division of Adolescent and Young Adult Medicine—recognized the need for expanded gender care for youths in Pittsburgh and the surrounding tristate area.

Patients can enter the program through two portals—pediatric endocrinology and adolescent medicine. The program serves children and youths (up to age 26) with concerns related to gender identity, gender nonconforming behaviors, gender expansive questions, and transgender care. The program provides thorough clinical assessments, promotes shared decision-making about available treatment options, offers

behavioral health support, and connects patients and families to appropriate resources and support in the community. Patients have access to a network of health care providers, including physicians, nurse practitioners, psychologists, social workers, surgeons, and nurses.

“This holistic care team provides a gender-affirmative approach,” says Witchel. “They work to help families appreciate gender-expansive behaviors and understand the distress of gender dysphoria. In addition, our team assesses for potential comorbidities such as severe depression or concomitant medical disorders.”

Another important role for pediatric and adolescent health care providers involves the use of “hormone blockers” to prevent the development of puberty incongruent with the individual’s gender identity. These medications can also be used to prevent menstrual cycles for youths who were assigned female but identify as male.

The team approach recognizes that patients benefit from individualized care to identify their strengths and help with their specific challenges. Available research data indicate that comprehensive multidisciplinary programs lead to significantly less gender dysphoria and improved quality of life.

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 Western Psychiatric Institute and Clinic of UPMC between July 1, 2015, and June 30, 2016, have supported us in our academic, research, and clinical missions.

Thank you.

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ELSIE AND HENRY L. HILLMAN

Hillman Family Foundations

In the spring of 2017, the University of Pittsburgh lost a dedicated philanthropist and longtime friend when Henry L. Hillman died at the age of 98. He was a nationally prominent business leader with many interests; but he and his wife, Elsie Hilliard Hillman (who died in 2015), are probably best known for their extensive philanthropy in medicine, education, arts, and human and social services. The Hillmans are known as some of the most generous donors in Pitt's history; their support of the School of Medicine alone has been far reaching and will influence the scope of its work well into the future.

Even a quick glance at Pittsburgh reveals the Hillmans' legacy in the region. Mr. Hillman built upon his family's industrial-era iron, coal, chemicals, and river transportation businesses and transformed them into a diversified global enterprise investing in commercial real estate and business and corporate holdings. He graduated from Princeton University and began military service the day after the attack on Pearl Harbor, eventually serving as a U.S. Navy pilot to the end of World War II. He and Mrs. Hillman married in 1945, and she became an influential civic leader and philanthropist in her own right during their 70-year marriage. (He was known to joke that people knew him best as "Mr. Elsie Hillman.") When Pittsburgh's industrial foundation crumbled in the 1980s, the Hillmans became integral architects of the city's revival, preparing it not only to survive but to thrive.

The Hillman family has had a long-term commitment to philanthropy and personal involvement in the Pittsburgh community. In the years since Mr. Hillman's father created the Hillman Foundation in 1951, the Hillmans have donated \$425.5 million to a variety of institutions and projects, \$71 million of which has been directed to health care and biomedical research in the region. The Hillmans' support of the School of Medicine has done more than help it thrive. Their generosity has helped to advance biomedical research at Pitt and make it a world leader in cancer care. In 1993, the Hillmans established an endowment at what was

then called the University of Pittsburgh Cancer Institute (UPCI) to support its director and to bolster research and clinical care in oncology. In another move to reinvent Pittsburgh as a first-class destination for medicine and education, the Hillmans granted \$10 million to build the Hillman Cancer Center, which became the flagship facility of UPCI and the UPMC CancerCenter network. (To honor the Hillmans' vital contributions to cancer care, UPCI and UPMC CancerCenter were recently renamed the UPMC Hillman Cancer Center.)

In 2004, the Henry L. Hillman and Hillman Family Foundations gave \$20 million to establish the Hillman Fellows for Innovative Cancer Research program to support scientists and foster the development of novel cancer treatments. At the time, it was the largest single grant in Pitt's history. Most recently, the Henry L. Hillman Foundation announced a \$30 million commitment—\$3 million per year for 10 years—to greatly expand the fellows program. This is the single largest gift to have been given to the University of Pittsburgh and UPMC for a medical initiative. The new funds will be used to accelerate high-priority scientific research, such as linking novel cancer genomics and immunology to personalized patient care.

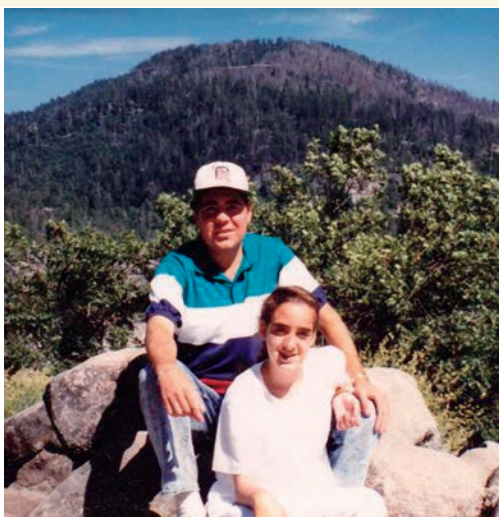
"The program has accelerated the move of cancer research from the bench to the bedside and helped to establish the UPMC Hillman Cancer Center as a model for others around the world," said Stanley Marks, MD, clinical professor of medicine and chair, UPMC Hillman Cancer Center. "We have been able to recruit world-class cancer researchers and financially support their groundbreaking efforts, all because of the vision of Henry and Elsie Hillman."

Additional support the School of Medicine has received from the Hillmans includes a grant to establish the Elsie Hilliard Hillman Chair in Women's and Infants' Health Research, currently held by Yoel Sadovsky, MD, Distinguished Professor of Obstetrics, Gynecology, and Reproductive Sciences and director, Magee-Womens Research Institute (MWRI). Reflecting Mr. Hillman's keen interest in technology and innovation, the Henry L. Hillman Foundation provided a grant to the Department of Emergency Medicine to adopt a smartphone app called PulsePoint, which alerts volunteer CPR responders to nearby cardiac arrest events. The foundation also supported Pitt, MWRI, and Carnegie Mellon University researchers' development of the MyHealthyPregnancy app, designed to reduce the incidence of preterm birth among high-risk mothers.

In ways both large and small, the Hillmans have positively influenced the lives of people in the Pittsburgh region and throughout the world. Their thoughtful, strategic approach to philanthropy ensures that many people will benefit from this legacy for generations to come.

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Gloria and Thomas Kitchen Memorial Foundation

In 1996, Gloria Kitchen was on a mission to raise money for cystic fibrosis research. Her older brother, Thomas, had died from complications of organ rejection following a double-lung transplant that he had received three years earlier because of the disease. Only seven months before, she, too, at age 17, had been given a new set of lungs because of her own struggles with cystic fibrosis. Gloria began her fundraising efforts modestly, walking into local shops and restaurants and asking for donations. Her sister, Stephanie Listman, remembers how well people responded to Gloria.

“She was shy, but people just opened up their wallets for her,” said Stephanie. “Gloria worked very hard at fundraising, and people were very generous when they heard what she had been through.”

Gloria raised an astounding \$25,000 for her first bowl-a-thon supporting the Cystic Fibrosis Foundation.

After her successful double-lung transplant, Gloria knew from Thomas’s experiences that, even though she could now live life without oxygen tubes and constant coughing, she was trading one set of problems for another.

“People think—even I did—that lung transplants will cure everything,” said Stephanie. “But Gloria was on so many medications afterward that ravaged her body. Her kidneys were shot.”

Despite her health problems, Gloria tirelessly raised funds for the Cystic Fibrosis Foundation for 14 years, eventually raising more than half a million dollars for research. In 2010, she created the Thomas Kitchen Memorial Foundation in honor of her brother. Unfortunately, chronic rejection of her double-lung transplant set

in soon after she launched the foundation. It became clear that her lungs were failing. The physicians who performed the transplant and managed her care told Gloria that they couldn’t do anything else for her.

“She had lived for an amazing 15 years after her double-lung transplant, but she wanted another shot; she wanted new lungs,” said Stephanie. “We went to a few other health care systems—some said they also couldn’t help her, and some didn’t respond. But Pitt did. They took her in, gave her hope, and started working with her. We have great feelings toward Pitt because they were compassionate with her and wanted to help.”

Unfortunately, Gloria lived only another six weeks. Soon after, the renamed Gloria and Thomas Kitchen Memorial Foundation made the first of its numerous gifts to the University of Pittsburgh. Per Gloria’s wishes, it went to the University of Pittsburgh Cystic Fibrosis Research Center (CFRC), led by Raymond A. Frizzell, PhD, professor of pediatrics and of cell biology. CFRC works to understand the basic mechanisms of cystic fibrosis, with the goal of translating that understanding to better treatments, quality of life for, and lifespan of people with the disease. Part of Dr. Frizzell’s focus with CFRC is the anion channel CFTR, whose mutation produces cystic fibrosis. Specifically, the Kitchen Foundation funding has permitted CFRC scientists to explore the mechanisms by which rarer mutations in CFTR cause disease and to identify which of the currently available drugs is optimal for increasing anion transport activity for these variants. These are the first steps in seeing that the available drugs are effective in reaching the greatest number of patients, and these studies will be continued as new reagents are made available.

“Gloria was the catalyst and got [the foundation] going,” said Stephanie. “Our motivation is simply to extend the lifespan and quality of life for people affected by cystic fibrosis. I keep hearing about people who are living longer with the disease, and that’s what keeps us going. We know the gifts are doing what they’re supposed to do and that the research is working.”

Thomas and Gloria Kitchen
(age 29 and 16) in Yosemite
National Park, 1994

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Richard King Mellon Foundation

Many urban areas in the United States have high rates of infant mortality. Though its rate is not the highest in the country, Allegheny County has a problem with infant mortality, and many people are working to solve it. The Allegheny County Health Department reports 6.65 infant deaths per 1,000 live births from 2008–12 (the national rate was 5.82 over a similar period, according to the Centers for Disease Control and Prevention, the highest infant mortality rate among similarly developed countries). The county also reports that the disparity between white infant deaths (average rate of 4.75) and African American infant deaths (average rate of 13.73) for the same time period is unacceptably large.

The good news is that Allegheny County's infant mortality rates are declining. Local organizations and health care providers are addressing the problem. Even better, the Richard King Mellon Foundation is bolstering these efforts with a \$5 million grant to the Magee-Womens Research Institute and Foundation to better understand infant mortality and reduce the disparities in the county's infant mortality rates.

"Realizing that the most common conditions associated with infant mortality occur before birth, it is clear that a healthy pregnancy is key to preventing infant death or disease," says Yoel Sadovsky, MD, Distinguished Professor of Obstetrics, Gynecology, and Reproductive Sciences, Elsie Hilliard Hillman Professor of Women's and Infants' Health Research, and director, Magee-Womens Research Institute. "We know what is commonly associated with infant mortality—premature delivery, maternal diseases, congenital abnormalities, accidents in the home, etc.—and these are important to understand. Now we're trying to take the next step and identify a period that has not been thoroughly investigated so far—pre-delivery—not only to enrich our knowledge but also to develop predictive models that will enable better therapy and prevention."

A portion of the grant—\$1 million—will be dedicated to general research projects on pregnancy and fetal development. The remaining \$4 million will be used to expand the Magee Obstetrical Maternal Infant Database, which is a repository for patient information from births at Magee-Womens Hospital of UPMC since 1995. The grant will expand the collection of clinical data—including weight gain, chromosomal defects, imaging data, maternal lifestyle, and other social indicators—to provide a comprehensive record of maternal health and environment prior to birth. A biobank will be created to store pregnancy-related specimens for deeper research. The \$5 million gift is a part of a larger \$10 million grant from the foundation, which will also support the Magee Prize and Summit. Every year, Magee-Womens Research Institute will award \$1 million to a researcher anywhere in the world who makes the most significant contribution to women's health research, with the intent of funding collaborative scientific inquiry based on the winning research. The recipient will be honored at the Magee Summit, an international conference on women's health research to be held in Pittsburgh.

The University of Pittsburgh and RAND Corporation also received grants from the Richard King Mellon Foundation to create algorithms that predict or score infant mortality risk. The new tool will identify those at risk and enable physicians to connect patients with appropriate and effective interventions tailored to them, with the long-term goal of sharing the information with other areas in the country where infant mortality is a public health issue.

Researchers aim to create a robust continuum of data that starts early in pregnancy and goes all the way through adulthood and allows health care professionals to direct patients to the right intervention at the right time.

"The goals of understanding and preventing infant mortality are embedded in these projects," says Dr. Sadovsky. "The bigger picture is understanding the population from the very beginning and across the lifespan to identify the future of wellness for people prior to birth and provide road maps that can guide better health and wellness. And that begins with a healthy pregnancy; it's the prelude to a healthy life."

The Richard King Mellon Foundation aims to improve infant mortality through supporting the efforts of the Magee-Womens Research Institute, which is led by Yoel Sadovsky, MD.



The Pittsburgh Foundation

Several years ago, leaders at the Pittsburgh Foundation wondered if the organization’s funding relationship with the University of Pittsburgh School of Medicine needed a change. Pitt has worked successfully for years with the community foundation, which provides individuals, families, organizations, and corporations with an avenue for their charitable giving and has more than 2,000 funds worth more than \$1.2 billion. But Jeanne Pearlman, PhD, senior vice president for program and policy, and Edith L. Shapira, MD, chair of the board of directors, began to reevaluate the medical grant-making partnership to see if they could make it even stronger.

“Dr. Shapira and I thought about how we measure the funding’s impact,” says Dr. Pearlman. “We met with different people at Pitt to help us better understand how we could meet the needs of researchers as well as carry out donor intent. They said they needed to continue attracting and retaining the highest level of talent that could be found internationally.”

Drs. Pearlman and Shapira decided they could best meet the needs of donors, physicians, and scientists by funding endowed chairs and making larger, more focused grants. Both sides of the medical grant-making process consider the strategy a success. In recent years, the Pittsburgh Foundation has established endowed chairs in research areas like personalized medicine, Alzheimer’s disease, cancer research, and psychiatry.

“Endowing a chair is just part of putting together the apparatus for good research,” says Maxwell King, chief executive officer and president of the Pittsburgh Foundation. “A \$25,000 grant for one or two years is not meaningful compared to endowing a chair that could support a great scientist for a significant period of time. Making progress in biomedical research and clinical innovation takes a long time, so we’re making a long-term bet.”

The foundation is making these bets with confidence and a great deal of donor support. It recently created another endowed chair—the Richard S. Caliguiri Chair for Amyloidosis and Heart Failure. Mr. Caliguiri, beloved mayor of Pittsburgh from 1977 to 1988, is credited with helping to spur urban renewal and economic growth following the decline of the American steel industry. After Mr. Caliguiri’s death from heart failure brought on by the rare disease amyloidosis, his family worked with the Pittsburgh Foundation to create a fund in his memory to support amyloidosis research in the hope of finding a cure and helping patients and families dealing with the disease.

Dr. Pearlman says quantitatively measuring the impact of the endowments is easy. “Has our funding leveraged other funding? The answer from all of our endowed professors is ‘yes,’” says Dr. Pearlman. “Qualitatively, endowed professors also report that their work is attracting new, talented researchers from around the world. I’ve thought about how hard it would be if we were doing this in a city that didn’t have a world-class institution like Pitt.”

“We didn’t set out to give a lot of money to Pitt,” says Mr. King. “It’s the recipient of these grants because we’re an organization that favors high-potential expertise, and we have that expertise right here in our community at Pitt. It’s logical.”

With the success of this endowment model, foundation leaders expect to be able to routinely create new endowed chairs in important research areas. That is good news because the need for biomedical research, as well as the needs of donor families, continues to grow. For Dr. Pearlman, understanding why donors want to support medical research drives her work.

“When I inherited this portfolio, I read the files of all the donors who had set up funds for medical research,” she says. “I read these heartbreaking stories about people who lost someone they loved so much to some dreadful disease, and the only thing that gave them any comfort was to try and make a difference in another family’s life so they wouldn’t have to go through the same experience. They made this investment; their wishes will be carried out forever.

“Then, I met the researchers—the finest minds in the world working on these diseases. I saw how determined they are, and I know they’re going to have a breakthrough. This partnership is so important.”

In 2017, the Pittsburgh Foundation and the School of Medicine honored the late Richard S. Caliguiri (fifth from right), former mayor of Pittsburgh who founded the city’s Great Race in 1977.

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