RISK AND REWARD

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Risk and reward. We all find ourselves face-to-face with these two eventually. Taking action involves strategy and forethought; but when the stakes are high, true risk doesn’t feel like a game.

In American health care, we now find ourselves in a time of enormous upheaval—a time in which the risks and potential rewards are greatly magnified. Hanging in the balance are assets of great value—our health, the future of the medical profession, our national economy, and our standing as a world leader in scientific discovery and innovation. Every day at the University of Pittsburgh School of Medicine, we strive to lead the way toward solutions to these challenges.

Academic medical centers like ours are part of a long tradition that binds teaching, research, and patient care—each leg of this tripod is equally responsible for holding up the entire enterprise. The academic medical enterprise, in turn, supports both public health and—through scientific discovery and innovation—the economic vitality of the nation. Today, each leg of the tripod is under a great deal of pressure—more than at any other time in living memory.

Institutions that wish to thrive in this environment require strategic thinking, innovation, entrepreneurship, and no small amount of risk—smart, calculated risk with the potential of significant reward for all. At Pitt—having experienced a meteoric, decades-long rise in the standing of our educational, research, and clinical programs—we are not content to hunker down and hold our ground. We intend to help lead the way out of these challenging times in American health care.
Here are just a few of the ways in which we are shaping the future of biomedicine:

- In medical education, we’ve introduced interaction with real patients into the earliest parts of the first-year curriculum—reminding many students why they chose medicine and inspiring them to make the direct connection between their basic science courses and the patients in the clinic. We’ve simultaneously crafted a popular and successful research requirement for all medical students. [See pages 17–19.] Our educational partnerships with new and developing medical schools at Tsinghua University in Beijing, China, and Nazarbayev University in Astana, Kazakhstan, are prime examples of how Pitt’s School of Medicine is setting the standard for academic medicine in the 21st century. [See pages 25–29.]

- When it comes to the national priority to improve the quality and lower the cost of patient care, our collaboration with our clinical partner, UPMC, puts us in a better position to contribute than perhaps any other academic medical center in the nation. Our students are immersed in teaching hospitals that house some of the top training programs in the nation. The clinical research environment at UPMC, one of the leading nonprofit health systems in the nation, contains endless possibilities for advancing scientific knowledge and improving patient outcomes. Our shared initiatives—including those in clinical and translational science and transferring “Big Data to Knowledge”—are second to none. [See page 7.]

- In biomedical research, the University of Pittsburgh currently ranks fifth out of more than 2,000 institutions receiving funding from the National Institutes of Health. But in these challenging economic times, even the leading institutions for biomedical research must do more with less, innovate, and be entrepreneurial. At Pitt, we have a campus-wide culture of innovation and multidisciplinary collaboration. In addition to our leadership in NIH-supported research, we are forging partnerships with industry and empowering scientific investigators with great ideas to blaze their own trails to discovery more rapidly than they might through traditional channels.

In all our initiatives, we refuse to be confined by the way things have always been done. We seek game-changing opportunities, and we take a global view of the future. I invite you to join us and learn more about our efforts on the pages of this report.

ARTHUR S. LEVINE, MD
Senior Vice Chancellor for the Health Sciences and
John and Gertrude Petersen Dean of Medicine
Solid Bonds Strengthen Pitt and UPMC

Confined to the pages of a scientific journal, medical research—no matter how elegant—does little to change anyone’s prognosis in the face of disease, disability, or traumatic injury. But without the constant work of discovery in medicine, today’s healers might still be using leeches to balance a patient’s humors.

Every day, Pitt’s School of Medicine and UPMC (University of Pittsburgh Medical Center) generate the multidisciplinary teamwork of caring physicians and visionary scientists across the biomedical spectrum to deliver scientific, clinical, and economic advancement throughout the region—and the world.

Although legally distinct and separate entities, the School of Medicine and UPMC share an alliance and commitment to excellence in education, research, clinical care, and entrepreneurship.

UPMC touts the University’s longtime status among the top 10 research institutions receiving funding from the National Institutes of Health, which drives the biomedical research that brings the latest developments from bench to bedside. Pitt’s NIH funding has increased from $25 million in 1980 (36th) to $456 million today (fifth). The faculty of the medical and public health schools also ranks fifth, with total funding of more than $390 million.

Even so, persistent constraints on federal funding for biomedical research, including NIH support, have kept government funding for research essentially flat for the past 10 years—with actual purchasing power diminished by inflation and Congress-mandated cuts to nondefense spending.

Today, only one in six NIH grant applications is successfully funded (typically at a lower level than requested), whereas one in three grants was approved before 2005.

Over the past three years, however, Pitt’s Schools of the Health Sciences have received nearly $500 million in biomedical research support from UPMC and nearly $400 million in funding for educational programs to foster the next generation of physicians, nurses, pharmacists, lab technicians, and other health care professionals. Nearly 1,800 residents and fellows train in UPMC hospitals and programs every year.

“Academic medical centers like Pitt and UPMC are of singular importance to the communities they serve as the best option for people with the most complex and challenging illnesses and injuries,” says Arthur S. Levine, MD, Petersen Dean of Medicine. “Seeking new scientific answers for those people is at the core of our shared mission.”

For its part, UPMC calls good science one of its “organizational pillars,” along with smart technology, new models of care, and sound finance—all concepts fully embraced throughout the University of Pittsburgh School of Medicine.

“The relationship we have forged over the years—and continue to strengthen—is hugely important to UPMC, to Pitt, and to the entire community,” says UPMC President and CEO Jeffrey A. Romoff.
The University of Pittsburgh and UPMC have entered into a new agreement designed to accelerate the commercialization of intellectual property arising from the research activity of University faculty. The partnership is intended to speed the commercialization of new medical technologies and services—bringing medical advances to the public more rapidly and supporting new business startups, with the accompanying economic benefits for the region.

The agreement builds on Pitt’s core mission of bettering society through knowledge. It also supports UPMC’s longstanding strategy of commercializing innovation to improve patient care while generating revenue to reinvest in research, its world-class health care services, and local communities. In addition, the collaborative effort draws on the strengths of both institutions in commercializing new technologies and extends the robust research collaboration between Pitt and UPMC.

With the new agreement, the terms of each type of commercialization (e.g., licensing, royalty arrangements, equity in new companies) have been negotiated in advance, allowing for a smoother transition from research to commercialization. Representatives from both partners will meet regularly to discuss research projects underway and medical needs based on clinical experience.

Pitt Chancellor Patrick Gallagher noted that this agreement is an example of Pitt’s increased emphasis on collaboration. “We have to work with others around us to be in a position to make the biggest difference in our community, our region, and ultimately, the world,” Gallagher said. “This expanded partnership with UPMC is a good example of how collaboration of this type can accelerate the beneficial health care aspects of our research for the community, while at the same time having a positive impact on our region’s economy.”

UPMC President and CEO Jeffrey Romoff endorsed Chancellor Gallagher’s remarks. “Our partnership is another example of how medicine and education—or ‘meds and eds’—continue to drive the economic revitalization of Western Pennsylvania,” Romoff said. “Collaborating with world-class academic and industry partners is also part of UPMC’s strategy for diversifying revenues in the face of a changing, value-driven health care landscape.”

The first technology to be licensed by UPMC Enterprises under the agreement is a genetic discovery that is leading to a highly accurate test for aggressive prostate cancer and could identify whether treatment is needed, Pitt and UPMC announced in February 2015. Prostate cancer is the second most common cancer among men.

UPMC Enterprises, the arm of UPMC responsible for identifying and commercializing health care technologies and services, will work closely with Pitt’s Innovation Institute to collaboratively translate Pitt research in the earliest stages into new products and companies. The agreement is not limited to any particular research area, nor is it exclusive for either partner.

Pitt’s Innovation Institute is the University’s hub for activities that promote and foster innovation and entrepreneurship on campus and throughout the Pittsburgh region. The goals of the institute are to encourage and support innovation and entrepreneurship on campus and in the community.
Pittsburgh is a city that will surprise you,” Mayor Bill Peduto says in the opening moments of a video tribute produced by Time Inc. and released online in July 2015. As the mayor talks, sunset-drenched images of people enjoying Point State Park are followed by an often-showcased yet no less dazzling glamor shot: the Fort Pitt Tunnel reveal of downtown Pittsburgh with its rivers and bridges.

The 10-minute video highlights Pittsburgh’s transformation from an aging industrial center to a superpower of clinical medicine, biomedical research, computer science, and biotech innovation. In addition to Peduto, the video features commentary from leaders and faculty from Pitt, UPMC, and Carnegie Mellon University (CMU), as well as other longtime observers of Pittsburgh’s economic ascendance.

“This is a city that captures the sophistication of the East Coast and retains the civility of the Midwest,” notes a smiling Arthur S. Levine, MD, Petersen Dean of Medicine.

To view Pittsburgh: The Comeback, visit http://time.com/pittsburgh/?xid=tcoshare
“Over time, the focus on ‘eds and meds’ and high knowledge really has taken off,” says UPMC Executive Vice President Steven D. Shapiro, MD, who is also a Pitt Distinguished Professor of Medicine.

Recent developments mentioned in the video include the Pittsburgh Health Data Alliance (see page 7) that, Levine explains, will mine petabytes of accumulated electronic information to further advance research and patient care.

“Lots of patients I care for have diseases that are incurable,” says Edward Burton, MD, DPhil, a neurologist who uses zebrafish models of neurodegenerative disease for his laboratory studies. “For them, research means hope.”

*Pittsburgh: The Comeback* also features a deep-dive look into robotics and computer science advancements coming out of CMU, making it clear that there is much to look forward to for the whole region. We’re told that even the hardened New York-based filmmakers were impressed by the ‘Burgh. A *Time* senior producer reportedly described Levine as “Shakespearean” and promised to return for more stories of Pittsburgh’s biotech bonanza.
The Clinical Research Forum was established in 1996 to provide leadership to the national clinical and translational research enterprise and promote understanding and support for clinical research and its impact on health and health care.
In recognition of its strong commitment to economic engagement, the University of Pittsburgh has been designated as an Innovation and Economic Prosperity University by the Association of Public and Land-grant Universities (APLU).

The designation acknowledges universities working with public and private sector partners in their states and regions to support economic development through a variety of activities, including innovation and entrepreneurship, technology transfer, talent and workforce development, and community development.

Pitt and Pennsylvania State University were the only Pennsylvania institutions named among the 14 public universities so honored by APLU in 2014.

Pitt was recognized for initiatives like the Pittsburgh Life Sciences Greenhouse; neighborhood revitalization projects in Oakland and other city neighborhoods, as well as in the communities of its regional campuses; and workforce development efforts that have stimulated Pittsburgh’s “eds and meds” economy, which now accounts for more than 20 percent of the region’s total employment.

Since 1995, Pitt has attracted more than $9 billion of sponsored research support into the region, and research has played a key role in the foundation for such future-oriented, technology-based economic development initiatives as the Pittsburgh Digital Greenhouse, the Pittsburgh Robotics Foundry, and the Technology Collaborative.

Founded in 1887, APLU is North America’s oldest higher education research, policy, and advocacy organization.

Yuan Chang, MD, Distinguished Professor of Pathology and UPMC Professor of Cancer Virology Research, has been appointed to a five-year term on the National Cancer Advisory Board of the National Cancer Institute (NCI).

In this role, Chang will advise the president and leadership of the U.S. Department of Health and Human Services and NCI on issues relevant to the national cancer program, including NCI operations. Her term is set to expire in 2020.

Chang, a member of the Molecular Virology Program at the University of Pittsburgh Cancer Institute, works to develop new techniques for discovering pathogens that cause human disease, particularly cancers. She is perhaps best known for her work to identify two of the seven known human cancer-causing viruses — Kaposi’s sarcoma-associated herpes virus and Merkel cell polyomavirus.

Chang was elected to the National Academy of Sciences in 2014. She received her MD from the University of Utah College of Medicine. Prior to joining the Pitt faculty in 2002, Chang was professor of pathology at Columbia University.
Seven School of Medicine faculty members have been tapped to join the prestigious Association of American Physicians (AAP) and the American Society for Clinical Investigation (ASCI) in 2015. Induction into these societies is considered among the highest honors in biomedical science.

New AAP members are J. Timothy Greenamyre, MD, PhD, Love Family Professor of Neurology and director, Pittsburgh Institute for Neurodegenerative Diseases; George Michalopoulos, MD, PhD, Maud L. Menten Professor of Experimental Pathology and Distinguished Professor and chair of pathology; John Kirkwood, MD, Sandra and Thomas Usher Professor of Melanoma, Department of Medicine; Juan Celedón, MD, DrPH, UPMC Niels Jerne Professor of Pediatrics; and Yoel Sadovsky, MD, Elsie Hilliard Hillman Professor of Women’s and Infants’ Health Research and Distinguished Professor of Obstetrics, Gynecology, and Reproductive Sciences.

Founded in 1885, AAP is dedicated to the pursuit of medical knowledge, experimentation and discovery in basic and clinical science, and the application of new findings to clinical medicine. Each year, 60 individuals are selected for AAP membership.

ASCI inductees are Pawel Kalinski, MD, PhD, professor of surgery and of immunology, and Jeremy Kahn, MD, MS, associate professor of critical care medicine and of medicine. Kalinski also holds an appointment in the Swanson School of Engineering. He and Kahn hold additional appointments in the Graduate School of Public Health.

The two join 49 other Pitt colleagues on the membership rolls of ASCI, an organization of more than 2,800 physician-scientists who have achieved notable success by age 50 or younger.
Pitt’s G. Bard Ermentrout, PhD, Distinguished University Professor of Computational Biology, Department of Computational and Systems Biology, is one of two U.S. recipients of the 2015 Mathematical Neuroscience Prize conferred by Tel Aviv-area-based nonprofit organization Israel Brain Technologies. The $100,000 prize was given in recognition of Ermentrout’s classic work in mathematical biology.

Ermentrout, who is also professor of mathematics, Dietrich School of Arts and Sciences, is a faculty affiliate of the Center for the Neural Basis of Cognition and the McGowan Institute for Regenerative Medicine. His research focuses on the applications of nonlinear dynamics to biological problems, particularly as they relate to patterns of activity in neuronal networks.

AMERICAN PSYCHIATRIC ASSOCIATION HONORS LEWIS

David A. Lewis, MD, Thomas Detre Professor and chair of psychiatry, is the 2014 recipient of the American Psychiatric Association’s most significant research award, the APA Award for Research in Psychiatry. First given in 1949, the award recognizes a single, distinguished contribution or lifetime body of work that has substantially influenced the field or changed psychiatric practice.

A noted expert on schizophrenia, Lewis studies the neural circuitry of the prefrontal cortex and related brain regions and alterations of this circuitry in mental illness. His other areas of research interest include the effects of cannabis and psychotropic medications on neural circuitry.

IT’S AN HONOR, DR. BILLIAR

Timothy Billiar, MD, George V. Foster Professor and chair of surgery, has been awarded the 2015 Medallion for Scientific Achievement, the highest honor conferred by the American Surgical Association.

“This is a much-deserved and singular honor for a physician-scientist who has excelled in his profession,” said Arthur S. Levine, MD, Pitt’s Petersen Dean of Medicine. “Dr. Billiar is a stellar researcher who has made invaluable contributions to our understanding of critical molecular pathways in shock, sepsis, cardiovascular disease, and much more.”

The Medallion for Scientific Achievement is given periodically to a surgeon who has served in his or her field with unusual distinction. Awarded 27 times in the past 45 years, the honor has previously been awarded to two other Pitt surgeons, Bernard Fisher, MD, (2000) and Thomas E. Starzl, MD, PhD (1990).

Billiar joined the Pitt faculty in 1992, after serving as chief surgical resident for two years and completing three years as a research fellow at the School of Medicine. He was named chair of the Department of Surgery in 1999. He received his medical degree from the University of Chicago Pritzker School of Medicine.

Billiar also holds the title of Distinguished Professor of Surgery and was elected in 2006 to membership in the Institute of Medicine.
Angela M. Gronenborn, PhD, Distinguished Professor of Structural Biology, has been elected to the German National Academy of Sciences. Known as the Leopoldina and founded in 1652, the organization is the world’s oldest continuously existing academy for medicine and the natural sciences.

Gronenborn, who is also UPMC Rosalind Franklin Professor and chair of structural biology in the School of Medicine, combines nuclear magnetic resonance spectroscopy with biophysics, biochemistry, and chemistry to investigate cellular processes at the molecular and atomic levels to advance knowledge of human disease. Currently, her work focuses on gene regulation and HIV pathogenesis. The Gronenborn team has solved the structures of a large number of medically and biologically important proteins, including cytokines and chemokines, transcription factors and their complexes, and various HIV- and AIDS-related proteins.

Gronenborn received her PhD in organic chemistry from the University of Cologne, Germany. She completed postdoctoral training in molecular pharmacology at the National Institute for Medical Research in London, U.K., and formerly served as chief of the Structural Biology Section at the National Institute of Diabetes and Digestive and Kidney Diseases. She is a member of the National Academy of Sciences and a fellow of the Royal Society of Chemistry.

Nancy E. Davidson, MD, Distinguished Professor of Medicine, Hillman Professor of Oncology, and director of the University of Pittsburgh Cancer Institute and UPMC CancerCenter, has been chosen as president-elect of the American Association for Cancer Research (AACR) and will assume the presidency in 2016.

Davidson’s work focuses on clinical and translational breast cancer research, cancer biology and treatment, and the role of apoptosis and mechanisms of epigenetic regulation of gene expression of the estrogen receptor alpha gene in breast cancer treatment. She is one of only two women elected to serve as president of both AACR and the American Society of Clinical Oncology in the past 50 years.

Thomas E. Starzl, MD, PhD, Distinguished Service Professor of Health Sciences and Distinguished Service Professor of Surgery, has received the Anthony Cerami Award in Translational Medicine in recognition of his groundbreaking research in organ transplantation and alloengraftment mechanisms. Conferred by the peer-reviewed, open-access journal Molecular Medicine and the Feinstein Institute for Medical Research, the $20,000 award honors Starzl’s many achievements, including the development of key surgical techniques during liver transplantation, the discovery of microchimerism, and the development of medications and strategies to enhance immunological transplant tolerance. The award is named for Aramis Pharmaceuticals CEO Anthony Cerami, PhD, an entrepreneurial biomedical investigator who has led research programs into genetic, metabolic, and infectious diseases.
**NEW FACES**

**Warren Shlomchik, MD**

**TITLE:** Professor of medicine and of immunology; director, Hematopoietic Stem Cell Transplantation and Cell Therapies, Division of Hematology/Oncology; scientific director, Hematopoietic Malignancies, University of Pittsburgh Cancer Institute

**BACKGROUND:** MD, University of Pennsylvania; internal medicine residency, Cornell/New York Hospital; hematology/oncology fellowship, Penn; former professor of medicine and of immunobiology at Yale University

**RESEARCH:** Immunobiology of allogeneic stem cell transplantation relevant to graft-versus-host disease; understanding basic principles of antigen presentation and T cell activation/effector function

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**James G. Herman, MD**

**TITLE:** Visiting professor of medicine, Division of Hematology/Oncology; coleader, UPCI Lung Cancer Program; associate director, Hematology/Oncology Fellowship Program

**BACKGROUND:** MD, Johns Hopkins University; internal medicine residency, Duke University Medical Center

**RESEARCH:** Internationally noted epigenetics researcher (developed methylation-specific assay used to characterize DNA methylation patterns); principal investigator, Lung Cancer Specialized Program of Research Excellence (SPORE), University of Pittsburgh Cancer Institute
Howard B. Gutstein, MD

**TITLE:** Professor and chair, Department of Anesthesiology

**BACKGROUND:** MD, Johns Hopkins University School of Medicine; general surgery internship/residency and pediatric anesthesiology fellowship, University of California, San Francisco

**RESEARCH:** Developing novel analytical methods and technologies to identify proteomic biomarkers, signaling mechanisms, and epigenetic changes relevant to addiction, opioid tolerance, and cancer pain; the role of RTK signaling in opioid tolerance, supported by the National Institute on Drug Abuse

Bernhard Kühn, MD

**TITLE:** Visiting associate professor of pediatrics; director of research, Division of Cardiology, Department of Pediatrics; associate scholar, Richard King Mellon Foundation Institute for Pediatric Research

**BACKGROUND:** MD and PhD-equivalent doctor of medicine, Freie Universität, Berlin; postdoctoral training, Harvard Medical School; pediatric residency, Yale-New Haven Children’s Hospital; pediatric cardiology fellowship, Boston Children’s Hospital

**RESEARCH:** Basic mechanisms of cellular growth and regeneration; novel approaches and molecular targets to enhance cardiomyocyte regenerative potential

John V. Williams, MD

**TITLE:** Professor of pediatrics and chief, Division of Pediatric Infectious Diseases

**BACKGROUND:** MD, Medical College of Virginia/ Virginia Commonwealth University; pediatrics residency, Children’s Hospital of Pittsburgh of UPMC; infectious diseases fellowship, Vanderbilt University Medical Center; former associate professor of pediatrics, of pathology, of microbiology, and of immunology, Vanderbilt

**RESEARCH:** Immunopathogenesis and epidemiology of respiratory viral infections, particularly human metapneumovirus

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**THAI GOVERNMENT HONORS D.A. HENDERSON**

Donald A. (D.A.) Henderson, MD, MPH, 21st Century Professor of Medicine and Public Health, is a 2014 recipient of the Prince Mahidol Award, one of the highest honors bestowed by the Royal Family of Thailand for achievement in medical science.

Established in 1992 to commemorate the 100th anniversary of the birth of Prince Mahidol of Songkla, the $100,000 award honors outstanding achievement in medicine and public health. Henderson becomes the third individual with Pitt ties to be so honored, joining Thomas E. Starzl, MD, PhD, Distinguished Service Professor of Surgery, and Herbert L. Needleman, MD, emeritus professor of psychiatry.

Henderson is known for leading the World Health Organization’s global program to eradicate smallpox—considered the first and only deadly disease to be eliminated worldwide. He is a distinguished scholar at the UPMC Center for Health Security.

Henderson received the Presidential Medal of Freedom, the highest civilian U.S. honor, in 2002 and has received commendations from 19 countries. He is the recipient of the National Medal of Science and the National Academy of Sciences Public Welfare Medal.

Henderson has written more than 200 articles, scientific papers, and book chapters, in addition to a 2009 memoir, *Smallpox: The Death of a Disease.*

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**A PRIZE FOR POLLACK**

Ian F. Pollack, MD, A. Leland Albright Professor of Neurological Surgery, is the 2015 recipient of the H. Richard Winn, MD, Prize, the highest honor of the Society of Neurological Surgeons.

The international award recognizes a neurosurgeon for outstanding achievement in basic and clinical neuroscience research.

Pollack, who is also chief of pediatric neurosurgery and director of the Brain Tumor Program at the University of Pittsburgh Cancer Institute, currently leads numerous National Institutes of Health-funded investigations to identify novel brain tumor therapies and molecular markers of tumor prognosis. He has published more than 310 papers in peer-reviewed journals, written more than 60 book chapters, edited two books on childhood brain tumors, and coedited the *Principles and Practice of Pediatric Neurosurgery* textbook.

Pollack received his MD from Johns Hopkins University School of Medicine. He completed a surgical internship and neurosurgical residency at Pitt; during part of this same time, he was also a neuropathology and neurobiology fellow.

Pollack is the second Pitt faculty member to be so honored by the neurological surgeons’ society, following Robert M. Friedlander, MD, MA, Walter E. Dandy Professor and chair of neurological surgery, who received the Winn Prize in 2012.
GLADWIN TAKES CHARGE

When friends and colleagues describe Mark Gladwin, MD, chair of Pitt’s Department of Medicine since March 2015, many of the same words crop up—“enthusiasm,” “imagination,” and “brains.”

Gladwin, Distinguished Professor of Medicine and Jack D. Myers Professor of Internal Medicine, will need to tap all those qualities and more to lead the largest of the School of Medicine’s 31 departments, with 983 clinical, research, and affiliated faculty in 10 divisions—not to mention educational programs that encompass postdoctoral trainees, residents, fellows, and medical students.

“This is a historic time for departments of medicine,” Gladwin says, leaning forward, gaze direct. “We’re probably at the most productive time in terms of translational scientific discovery.”

Landmark opportunities to explore molecular biology and health care delivery—areas in which Pittsburgh is poised to contribute—are right in front of us, he explains.

“I joke that we’re Johns Hopkins married to the Cleveland Clinic but with fewer silos and more people who have a foot in both worlds than any other place in the nation,” Gladwin says, pointing out the manifest opportunity inherent in Pitt’s “incredible foundation” of basic science combined with UPMC’s clinical expertise and big data-based discovery potential. “We’re probably better poised to do real translational research than anybody. We have to play to our strengths.”

The road from lab experiment to patient care innovation is one that Gladwin, also director of Pitt’s Vascular Medicine Institute, knows well. Before joining the University in 2008, he was chief of the National Heart, Lung, and Blood Institute’s Pulmonary and Vascular Medicine Branch, where his research coalesced around nitrite and nitric oxide (NO) in vascular medicine.

Among his major scientific discoveries is the finding that nitrite is a biological signaling molecule that regulates physiological and pathological hypoxic responses, blood pressure and flow, and dynamic mitochondrial electron transport. His 2003 Nature Medicine paper on proteins that regulate NO production has been cited more than 1,000 times and has led to the development and licensing of intravenous, oral, and inhaled nitrite as a human therapeutic agent, currently in clinical trials—focusing sessions for each division during which faculty members have just five minutes to present an overview of their science—among the best of this group, as an individual who provides an example not only of his enthusiasm for leadership but also of his depth of knowledge, O’Donnell says.

Gladwin’s creation of departmental mini-retreats—intense, focused sessions for each division during which faculty members have just five minutes to present an overview of their science—provides an example not only of his enthusiasm for leadership but also of his depth of knowledge, O’Donnell says.

The renal-electrolyte and rheumatology and clinical immunology divisions have had retreats and others are scheduled, he says, explaining that, during these retreats, Gladwin considers each research presentation as a starting point to make connections between faculty members with similar scientific interests who may not normally interact because they focus on different diseases.

“But he remembers people by their science. He can talk Western blots, cell signaling, and everything from phase 2 clinical trials to epidemiology,” says O’Donnell. “We’ve only been on the job a few months, and it’s ‘all hands on deck.’”
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.
PREPARING MEDICAL STUDENTS FOR 21ST-CENTURY MEDICINE

The best physicians have a solid grounding in the scientific method. They don’t have to be scientists, but they understand how research works and how the latest scientific discoveries can lead to better health for their patients. At Pitt, we challenge medical students to contribute to scholarly research during their med school years. In each graduating class, without fail, there are med students who seize this opportunity and produce extraordinary results.

Pitt’s innovative Scholarly Project requirement was introduced more than a decade ago. At the time, some said it would drive away applicants (who didn’t want to do research, presumably), but the opposite has proven true. Today, admission is more competitive than ever. Pitt graduates are increasingly sought after by top residency programs, partly because of their research experience. Even more telling, some of the nation’s other elite medical schools now emulate Pitt’s Scholarly Project.

A few key features developed over the years have greatly enhanced the success of the program, according to Donald B. DeFranco, PhD, associate dean for medical student research and professor and vice chair of pharmacology and chemical biology. “What is unique to Pitt, I think, is the direct connection to preparatory coursework. Methods and Logic in Medicine is a small-group, mentor-led class that prepares them to do research, and it happens in the fall and winter of their first year.”

Following that course, every med student is invited to take part in summer research between the first and second years of med school. “We are close to an all-time high,” DeFranco notes, “with about 85 percent of the class doing summer research.”

For the Scholarly Project, students are paired with established scientists, including some of Pitt’s most accomplished faculty members. Program organizers have created a culture in which there is a clear focus on providing guidance and tools for mentors. The mentor-student relationship is structured and supported from beginning to end.

Depending on their interests, med students delve into everything from wet-bench laboratory research to computational biology; some formulate clinical research projects with clinician mentors; others explore the subtleties of the doctor-patient relationship or mine public health data for new insights into disease trends. In these and scores of other ways, med students build their own scientific knowledge and develop skills that will help them to become clinicians who can make difficult diagnoses and help patients make decisions based on evidence.
2015 O’MALLEY AWARD WINNERS

At Scholars Day 2015, 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 2015:

BRIAN NOLEN, MD
The Use of Urine Protein Biomarkers in the Early Detection of Cancer
RESIDENCY MATCH: Internal Medicine, UPMC Medical Education Program/University of Pittsburgh
PEER-REVIEWED PUBLICATIONS: Cancer Prevention Research, PLOS ONE, Cancer Causes and Control, Cytokine, Expert Opinion on Medical Diagnostics
MENTOR: Anna Lokshin, PhD, Professor of Medicine, Pathology, and Obstetrics, Gynecology, and Reproductive Sciences

REGINA TRIPLETT, MD
Executive Function and Connectivity in Pediatric Epilepsy
RESIDENCY MATCH: Child Neurology, St. Louis Children’s Hospital/Washington University in St. Louis
PEER-REVIEWED PUBLICATIONS: Pediatric Neurology, Neuropsychologia, Epilepsia
MENTOR: Miya R. Asato, MD, Associate Professor of Pediatrics and of Psychiatry

DIANE LING, MD
Hospitalizations in Patients Who Receive Definite and Adjuvant Therapy for Head and Neck Cancer
RESIDENCY MATCH: Radiation Oncology, UPMC Medical Education Program/University of Pittsburgh
PEER-REVIEWED PUBLICATIONS: JAMA Otolaryngology, Neurosurgery, Practical Radiation Oncology, Head and Neck, Radiation Oncology
MENTOR: Dwight E. Heron, MD, Professor of Radiation Oncology and of Otolaryngology

SCHOLARLY PROJECTS BY THE NUMBERS

151 peer-reviewed publications (plus an additional 41 submitted)

331 presentations at national or international meetings
Twelve faculty members from across the School of Medicine were inducted into the school’s Academy of Master Educators (AME) in 2015. This special recognition comes with both tangible rewards and prestige. Directed by Jamie Johnston, MD, professor of medicine and clinical director of the Renal-Electrolyte Division in the Department of Medicine, the academy recognizes and rewards excellence in education, while striving to advance medical education through innovation and professional development. Members are nominated by their peers. Those elected to the academy help other faculty members develop their teaching skills, and they are supported and encouraged to cultivate their own passion for teaching amid the many demands of a faculty position.

Newly elected AME members for 2015:

Chung-Chou H. (Joyce) Chang, PhD
Professor of Medicine, School of Medicine, and of Biostatistics, Graduate School of Public Health

Marie C. DeFrances, MD, PhD
Associate Professor of Pathology

Stephanie B. Dewar, MD
Associate Professor of Pediatrics

Ankur A. Doshi, MD
Assistant Professor of Emergency Medicine

Scott Herrle, MD, MS
Assistant Professor of Medicine

Jenifer E. Lee, MD
Associate Professor of Medicine

Julie B. McCausland, MD, MS
Associate Professor of Emergency Medicine and of Medicine

David G. Metro Jr., MD
Professor of Anesthesiology

Charissa B. Pacella, MD
Associate Professor of Emergency Medicine

Tetsuro Sakai, MD, PhD
Professor of Anesthesiology

Reed W. Van Deusen, MD, MS
Assistant Professor of Medicine

Shanta M. Zimmer, MD
Associate Professor of Medicine
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 one of the following specialized programs: the Clinical Scientist Training Program (CSTP), and 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 the 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, the 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.

After leading the program for 12 years, Amber E. Barnato, MD, MPH, MS, associate professor of medicine and of clinical and translational science, stepped down as CSTP director in 2015. Margaret B. Conroy, MD, MPH, associate professor of medicine and of epidemiology, Graduate School of Public Health, will lead the program going forward. Conroy, who is also assistant dean for medical student research, plans to formalize a CSTP peer mentoring program and further strengthen the continuity between the Scholarly Project and the research that CSTP students conduct during the research year.

Several members of the Class of 2015 are products of Pitt’s CSTP, having previously completed the research year.

CSTP graduates and their residency programs:

ALEXANDRA DREYZIN, MD
RESIDENCY MATCH: Pediatrics, UPMC Medical Education Program/University of Pittsburgh
MENTOR: Ira J. Fox, MD, Professor of Surgery

CYNTHIA GRADY, MD
RESIDENCY MATCH: Obstetrics-Gynecology, Louisiana State University School of Medicine, New Orleans
MENTOR: Sonya B. Borrero, MD, MS, Associate Professor of Medicine

EDUARDO NUÑEZ, MD
RESIDENCY MATCH: Internal Medicine, Rhode Island Hospital/Brown University, Providence
MENTORS: Amber E. Barnato, MD, MPH, MS, Associate Professor of Medicine and of Clinical and Translational Science; Charles Reynolds III, MD, UPMC Professor of Geriatric Psychiatry and Professor of Neurology, School of Medicine; Professor of Neuroscience, Dietrich School of Arts and Sciences; Professor of Behavioral and Community Health Sciences, Graduate School of Public Health; Professor of Clinical and Translational Science

SEBASTIAN SHTERENTAL, MD
RESIDENCY MATCH: General Surgery, North Shore–LIJ Health System, New York
MENTOR: Marc A. Simon, MD, Assistant Professor of Medicine

REGINA TRIPLETT, MD
RESIDENCY MATCH: Child Neurology, St. Louis Children’s Hospital/Washington University in St. Louis
MENTORS: Miya R. Asato, MD, Associate Professor of Pediatrics and of Psychiatry; Beatriz Luna, PhD, Staunton Professor of Psychiatry and Pediatrics, School of Medicine; Professor of Psychology, Dietrich School of Arts and Sciences

Many MD students will take a year off to earn a master’s degree in public health, biomedical ethics, or a related field. Others devote a full year to research through the CSTP or 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 2015 included six graduating PSTP students who matched to top residency programs in some of the most competitive medical specialties. Collectively, these six graduates have published 21 papers (nine as first author), received 11 regional, national, or international awards (best poster, best talk, or travel awards), earned two Howard Hughes Medical Institute (HHMI) research fellowships, given 26 national or international presentations, and coauthored a successful Investigational New Drug application through the U.S. Food and Drug Administration.

Several members of the Class of 2015 are products of Pitt’s PSTP, having previously completed the research year.

**PSTP graduates and their residency programs:**

**ELLEN CAPAROSA, MD**

**RESIDENCY MATCH:** General Surgery, Thomas Jefferson University, Philadelphia

**MENTOR:** Robert M. Friedlander, MD, MA, Walter E. Dandy Professor and Chair of Neurological Surgery

**LEO CHEN, MD**

**RESIDENCY MATCH:** Urological Surgery, Stanford University, Palo Alto

**MENTOR:** Angus W. Thomson, PhD, DSc, MS, Distinguished Professor of Surgery, Professor of Immunology, of Microbiology and Molecular Genetics, and of Clinical and Translational Science

**BRITTANY DULMAGE, MD**

**RESIDENCY MATCH:** Dermatology, McGaw Medical Center/Northwestern University, Chicago

**MENTOR:** Larsa Geskin, MD, Associate Professor of Dermatology, Columbia University College of Physicians and Surgeons

**ERICA NAKAJIMA, MD**

**RESIDENCY MATCH:** Internal Medicine, Vanderbilt University Medical Center, Nashville

**MENTOR:** Bennett Van Houten, PhD, Richard M. Cyert Professor of Molecular Oncology, Department of Pharmacology and Chemical Biology, and Professor of Computational and Systems Biology

**CAROLINE RIESER, MD**

**RESIDENCY MATCH:** General Surgery, UPMC Medical Education Program/University of Pittsburgh

**MENTOR:** Jennifer Condon, PhD, Associate Professor of Obstetrics and Gynecology, Wayne State University

**SAMEER SHAKIR, MD**

**RESIDENCY MATCH:** Plastic Surgery, Hospital of the University of Pennsylvania, Philadelphia

**MENTOR:** Gregory M. Cooper, PhD, Assistant Professor of Plastic Surgery

**STUDENTS WIN PRESTIGIOUS HHMI FELLOWSHIPS**

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

**The award-winning students and their projects:**

**TOLANI OOLONISAKIN**

Identifying Small Molecule Compounds that Enhance the Host Innate Immune Response to Infection

**MENTOR:** Janet S. Lee, MD, Associate Professor of Medicine, Division of Pulmonary, Allergy, and Critical Care Medicine

**XIAO ZHU**

Identifying Molecular Mechanisms within Preglomerular Vascular Smooth Muscle Cells that Contribute to Enhanced Renal Vascular Resistance in Spontaneously Hypertensive Rats

**MENTOR:** Edwin K. Jackson, PhD, Professor of Pharmacology and Chemical Biology and of Medicine

HHMI selected 68 top medical and veterinary students from 37 different schools in the nation to conduct full-time biomedical research in its Medical Research Fellows Program. The $2.8 million annual initiative is designed to develop the next generation of physician-scientists by giving the students a full year of mentored research training with some of the nation’s top biomedical scientists.

The HHMI Medical Research Fellows Program allows medical, dental, and veterinary students to pursue biomedical research at academic or nonprofit research institutions anywhere in the United States except on the NIH campus in Bethesda, Md., or with other federal agencies. The fellows put their medical school coursework on hold and spend a year immersed in basic, translational, or applied biomedical research. For 2015, 187 students from 76 institutions applied to the program. Each student applied with a mentor and submitted a research proposal.

Out of 65 fellows in the 2014 class, six were selected by HHMI for an additional year of support, including one Pitt medical student:

**JOHN BUI**

Reversal of HIV-1 Latency by Activation of Patient-Derived CD4+ T Cells Results in Clonal Expansion and Sustained Production of Infectious Virus from a Subset of Cells

**MENTOR:** John W. Mellors, MD, Professor of Medicine and of Pathology and Chief, Division of Infectious Diseases
Match Day is a big deal for all graduating med students, but for those in the Medical Scientist Training Program (MSTP), our 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 most of the MD students they entered with celebrate graduation and move on to residency positions. Match Day for MSTP students typically arrives about seven years after they begin medical school. In 2015, Pitt said farewell to 10 of these budding physician-scientists.

“In 2015, our graduating students matched into top-tier programs around the country,” said Richard Steinman, MD, PhD, associate dean for the MSTP and associate professor of medicine and of pharmacology and chemical biology. “More notably, the academic programs that they chose for residency training have a tradition of supporting physician-researchers. Across the board, our graduates will continue both their clinical and scientific training with guidance from outstanding role models at their new institutions.”

**Pitt’s 2015 MSTP graduates and their residency matches:**

- **ALLISON BEAN, MD, PHD**
  - **Residency Match:** Physical Medicine and Rehabilitation, Icahn School of Medicine at Mount Sinai, New York
  - **Mentor:** Rocky Tuan, PhD, Distinguished Professor and Arthur J. Rooney Sr. Professor of Sports Medicine, Department of Orthopaedic Surgery, Professor of Clinical and Translational Science, and Professor of Bioengineering, Swanson School of Engineering

- **LAUREN FRAZER, MD, PHD**
  - **Residency Match:** Pediatrics, University of North Carolina Hospitals, Chapel Hill
  - **Mentor:** Toni Darville, MD, Professor of Pediatrics, University of North Carolina School of Medicine

- **RACHELLE (STOPOCYNSKI) GUPTA, MD, PHD**
  - **Residency Match:** Pediatrics, University of North Carolina Hospitals, Chapel Hill
  - **Mentor:** Kathryn M. Albers, PhD, Professor of Neurobiology and of Medicine

- **GIL HOFTMAN, MD, PHD**
  - **Residency Match:** Psychiatry, UPMC Medical Education Program/University of Pittsburgh
  - **Mentor:** David A. Lewis, MD, Thomas Detre Professor of Academic Psychiatry and Chair of Psychiatry

- **LOLITA NIDADAVOLU, MD, PHD**
  - **Residency Match:** Internal Medicine, Rhode Island Hospital/Brown University, Providence
  - **Mentor:** Saleem A. Khan, PhD, Professor of Microbiology and Molecular Genetics and Assistant Dean for Academic Affairs, School of Medicine

- **BRIAN ROSBOROUGH, MD, PHD**
  - **Residency Match:** Internal Medicine, Massachusetts General Hospital/Harvard University, Boston
  - **Mentor:** Angus W. Thomson, PhD, DSc, MS, Distinguished Professor of Surgery, Professor of Immunology, of Microbiology and Molecular Genetics, and of Clinical and Translational Science

- **JEFFREY WONG, MD, PHD**
  - **Residency Match:** Internal Medicine, Brigham and Women’s Hospital/Harvard University, Boston
  - **Mentor:** Pawel Kalinski, MD, PhD, Professor of Surgery and of Immunology, School of Medicine; Professor of Infectious Diseases and Microbiology, Graduate School of Public Health; Professor of Bioengineering, Swanson School of Engineering
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, 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, nearly two-thirds of Pitt’s MSTP students have been successful in their F30 applications. Our most recent awardee:

JARED MOREINES
Afferent Circuitry of Dopamine Dysregulation in Depression

INSTITUTE: National Institute of Mental Health

MENTOR: Anthony A. Grace, PhD, Distinguished Professor of Neuroscience, Dietrich School of Arts and Sciences; Professor of Psychiatry, School of Medicine

Pitt’s MSTP has 72 students currently—big enough to maintain a lively and diverse group dynamic. In the 2015–16 academic year, the MSTP boasts its highest level of NIH support since its founding 30 years ago, with 20 Pitt MD/PhD students funded by NIH.

As usual, students in the program welcomed an influx of fresh faces at the start of the academic year. The “Second Look” event in early 2015 was one of the largest in recent history, with 32 MSTP applicants traveling to Pittsburgh to learn more about a program in which they might spend the next seven to nine years. The research interests of the prospective class reflect a few of the many research strengths of the University, ranging from biomedical informatics to molecular genetics, with several prospects focusing on immunology, biomedical engineering, and neuroscience. It was a talented group as well, with interests including Irish dance, rock piano, and brewing beer.

“The 15 new students who make up this year’s incoming class stood out from the 419 applicants for their research accomplishments and their smart plans for how they would use our program to further develop their already outstanding skills,” said Steinman. “They were drawn to Pittsburgh by specific faculty members and research programs that buoy our national reputation in biomedical science.”
In addition to the approximately 600 students in the four-year MD program, there are nearly 300 students pursuing PhD degrees in 12 programs that include neuroscience, biomedical informatics, computational biology, molecular biophysics and structural biology, and clinical and translational science. The breadth and depth of research activity at the University are extensive enough that graduate students in a wide range of disciplines receive training that allows them to conduct research at the cutting edge of biomedical science.

New in 2015, the School of Medicine’s longstanding program in integrative molecular biology has been updated to reflect the rising importance of integrative systems biology and also to improve the experience for graduate students. The goal of the Integrative Systems Biology (ISB) program is to train students in emerging transformative methodologies that emphasize genomics, proteomics, complex cellular pathways, and the dynamics of cellular and organismal function. By collaborating with Carnegie Mellon University on the program, Pitt enables ISB students to explore the exciting interface between basic bench-top biology, computational analysis of big data sets, and the emergence of 21st-century clinical translation. One of the highlights of the revamped program is that students can graduate with a PhD in as few as four years.

“This program really is accelerated—students can begin dissertation research as early as January of the first year,” says John P. Horn, PhD, professor of neurobiology and associate dean for graduate studies. “It’s a special opportunity for well-prepared, self-motivated, and accomplished students. They are very well supported, and because the work is so interdisciplinary, they can choose to have more than one faculty mentor.”

In a traditional integrative studies graduate program, students begin by reviewing basic biology in an overview course and completing other required courses. For as much as the entire first year, students take part in extended laboratory rotations. In this way, they are exposed to multiple disciplines and potential mentors before deciding on a research project. The downside of this approach is that it delays entry into a dissertation research laboratory by a full year. The comprehensive exam is taken during the second or third year, and the total time to get a PhD is approximately five to six years.

First-year ISB students take Approaches in Systems Biology, a core course that teaches students how to attack complex problems using integrated, multidisciplinary approaches. Early in that first year, students also begin six-week rotations through research labs, which translates to a faster progression to their dissertation research and, ultimately, to the PhD.

Outside of dissertation research, the ISB curriculum is designed for flexibility and rapid completion of requirements. Students are able to tailor their own education by choosing from dozens of electives in courses that reflect the full range of research under way at the School of Medicine. (Elecctive courses offered include Developmental Neurobiology, Viral Pathogenesis, Molecular Pharmacology, and Historical Perspectives in Neuroscience.)

**FOUR MED STUDENTS WIN NBME CENTENNIAL PRIZE**

A team of four Pitt med students came out on top in a national competition to identify the best innovation aimed at the future assessment of health professionals. Their winning proposal is called TOPCATS (Trainee-Oriented Patient Communication Assessment System), a phone app they developed to provide crucial patient feedback to medical students and instructors. Sponsored by the National Board of Medical Examiners (NBME), the Centennial Prize Competition also garnered entries from medical professionals, academicians, and business leaders. Ideas were evaluated on the extent to which they addressed a need for future health professionals, the potential impact on assessment of health professionals, and the feasibility of the idea developing into a viable, useful product.

The TOPCATS team, made up of third-year med students Myung Sun Choi and Jennifer Hu and first-year med students Abby Koff and Devan Patel, received $5,000 in cash, a pledge that NBME will include the concept in its new product development, and an invitation to participate in the development process as NBME Centennial Fellows. The app allows students and patients to evaluate their encounters in real time. Immediately after a clinical encounter, both the med student and the patient will receive surveys asking them to reflect on objective skills (Did the student wash her hands? Did he introduce himself?) and subjective skills (Did she listen to the patient? Was he empathetic?). After a few patient responses, the student will receive feedback through the app in an anonymous, randomized set of response data. Data on how a cohort of students is doing as a whole can also be sent to medical educators to identify trends in the development of particular skills and proficiencies.

“TOPCATS represents everything we hoped for when we put the call out for next-generation assessment ideas that would move our discipline forward,” said NBME President Donald Melnick. “The fact that the winning team, chosen by a panel of judges, along with the NBME members, staff, and volunteers, is a team of students who have applied their first-hand experience to a concept that will improve their education makes us even prouder.”
In August 2015, the Republic of Kazakhstan’s Nazarbayev University welcomed the first class of students to the Nazarbayev University School of Medicine (NUSOM), with a Pitt adjunct professor of pathology as its founding dean.

Massimo Pignatelli, MD, PhD, a distinguished pathologist and biomedical scientist whose research focuses on cellular adhesion molecules, previously served as head of the School of Medicine at the University of Glasgow in Scotland. “My hope is that NUSOM will become a model for every medical school in the nation,” said Pignatelli. “This is the goal of the project: to create the hub of medical education and biomedical research in Central Asia. The project has all the necessary components, including infrastructure, resources, and political stability.”

Since 2013, Pitt experts have assisted NUSOM as it institutes a U.S.-style medical curriculum. Under the partnership, Pitt’s medical faculty have helped to design and develop teaching facilities, plan organizational and administrative details, and develop courses, syllabi, and clinical experiences with the participation of NUSOM’s locally and globally recruited faculty.

Joshua Morra, MD, PhD, studies the neurophysiology of how drug reward cues differ from those of natural signalers like food or water. As a psychiatry resident at UPMC, he participated in the development of a method to probe the neuronal encoding of drug-related cues in the primate brain using experimental neuroscience techniques. For this work, he received the 2014 National Institute of Mental Health Outstanding Resident Award.

During his final year in Albany Medical College’s MD/PhD program, Morra visited Pitt’s Department of Psychiatry as recipient of the Dr. Thomas Detre Senior Medical Student Award in Psychiatry. The award led to the opportunity to train with Pitt faculty and furthered his interest in human motivation and the pathological processes of addiction. Under the mentorship of addiction-related behaviors expert Charles W. Bradberry, PhD, professor of psychiatry, Morra will use his project to further his goal of becoming a leader in addiction psychiatry.

Second-year med student Arpan Prabhu earned a Global Changemaker Legacy Award from the Foundation for Global Scholars in 2015. The Colorado-based foundation helped support Prabhu’s cross-cultural education when he was a Pitt undergrad taking courses in Spain and living with a host family. Hooked on broadening his horizons through that experience, Prabhu successfully applied to Pitt’s Latin American Studies program for funding to conduct an independent research project in Bolivia the summer before he began med school. His project was a qualitative study exploring the intercultural challenges faced by both Bolivian and foreign physicians in a country where more than two-thirds of the population identifies as indigenous.

The $1,000 award will support Prabhu’s additional independent research projects, which are advanced for a second-year student. Working with Barton F. Branstetter, MD, professor of radiology, Prabhu was first author on a paper in the American Journal of Neuroradiology in 2015. Their retrospective study examined radiological images from 700 patients to determine the frequency of residual cervical thymus in adults — a normal finding in computed tomography that is most often seen in children and young adults and exponentially declines with age. Prabhu presented the work in April 2015 at a national neuroradiology conference, where he was regularly mistaken for a radiology resident. Then a first-year student, Prabhu says that he saw only one other med student at the conference.

Recently, Prabhu has been working with Simion Chiosea, MD, associate professor of pathology and of otolaryngology, investigating sampling techniques performed in treating oral tongue cancer. Their paper, “Early Oral Tongue Squamous Cell Carcinoma: Sampling of Margins from Tumor Bed Correlates with Worse Local Control,” was recently accepted by JAMA Otolaryngology-Head & Neck Surgery.
In the past few years, beginning in 2012, Pitt’s School of Medicine has developed highly successful collaborations with two premier institutions of higher learning in the People’s Republic of China. After four years, these programs are maturing and thriving.

Through the School of Medicine’s partnership with Tsinghua University School of Medicine in Beijing, medical students at this most prestigious of Chinese scientific institutions undergo a rigorous, two-year biomedical research training program in Pittsburgh. More than 50 Tsinghua students have completed the program and returned to Beijing to finish their medical education. As of August 2015, 28 Tsinghua scholars were on campus in Pittsburgh, working in the labs of some of Pitt’s most accomplished biomedical researchers.

The 2015 edition of the annual Pitt-Tsinghua Joint Symposium was held in Pittsburgh, and it included 46 scientific poster presentations by Tsinghua scholars. Several Tsinghua faculty members made the journey from Beijing. They gave keynote presentations alongside their peers at Pitt, toured laboratories, and visited with the Tsinghua scholars to get a taste of their experiences in Pittsburgh. The 2016 joint symposium will be held in Beijing.

Also in 2012, the School of Medicine initiated a collaboration with China’s renowned Central South University Xiangya School of Medicine. Under the five-year agreement, Pitt provides two years of rigorous biomedical research training to medical students, most of whom have already undergone six years of medical school, including clinical training. As of August 2015, more than 20 Xiangya medical students are on campus in Pittsburgh. In 2014, spurred on by the success of this global collaboration between universities, Xiangya Hospital formed a partnership with UPMC to establish an international medical center that will improve access to high-quality care for patients within the region.
A stute observers of all things China knew it was a big deal when it was reported that Chinese Vice Premier Liu Yandong would visit the University of Pittsburgh in summer 2015. A buzz of excitement percolated through the first several floors of Scaife Hall, and it was not limited to those involved in the Tsinghua Scholars Program. Such a visit is a clear indicator that Pitt’s global collaborations are attracting attention in high places.

Mme. Liu is one of four Chinese vice premiers—the highest ranking officials in China after the premier. Just like an overseas visit by a sitting American vice president or secretary of state, Vice Premier Liu’s visit to the University of Pittsburgh was meticulously planned, scripted, and scheduled down to the minutest detail. Security officials from the U.S. State Department and the Chinese government were involved throughout the process and were on campus for the duration of the visit. A large contingent of Tsinghua University’s academic and scientific leaders also made the trip from Beijing.

In addition to meetings with Pitt Chancellor Patrick Gallagher, Mme. Liu’s delegation toured clinical and laboratory facilities on campus and met with several Pitt scientists. The vice premier saw a powerful demonstration of the Pitt-developed brain imaging technology HDFT (high definition fiber tractography), even meeting with a young woman who overcame a serious brain condition with the help of HDFT-guided neurosurgery.

In the middle of these carefully orchestrated tours and meetings, several participants were surprised when Mme. Liu suddenly broke from the schedule to talk at length with Pitt’s Tsinghua Scholars. She explained that she was very moved by the dozens of bright, young students who had traveled halfway around the world to pursue a unique educational experience in Pittsburgh. A Tsinghua graduate herself, the vice premier told the scholars that she felt like she was one of them, and she took this unscheduled opportunity to have her photograph taken with them.
The University of Pittsburgh was honored to host a summer 2015 visit from the leaders of Tsinghua University in Beijing. Standing at center, amid Pitt’s Tsinghua scholars and members of his leadership team, is Tsinghua University President Qiu Yong.
ALUMNI OF NOTE

DeAngelis is perhaps best known as the first pediatrician and the first woman to be editor-in-chief of *JAMA*.

Catherine DeAngelis, MD, MPH

In recognition of her distinguished service in the field of pediatric medicine, Catherine DeAngelis, MD, MPH, was awarded the 2015 Howland Medal of the American Pediatric Society, one of the field’s highest honors. At Johns Hopkins University School of Medicine, DeAngelis, who goes by “Dr. De,” was the founding director of the Division of General Pediatrics and is a Distinguished Service Professor Emerita. A 1969 graduate of Pitt’s School of Medicine, DeAngelis became a wildly acclaimed pediatrician, educator, researcher, and thought leader in medicine. DeAngelis’ honors include election to the Institute of Medicine and a lifetime achievement award from the Association of American Medical Colleges. She spent nine years as vice dean for academic affairs and faculty at Hopkins, where she advocated increased representation for women in academic medicine and boosted hands-on training for medical students. DeAngelis is perhaps best known as the first pediatrician and the first female editor-in-chief of the *Journal of the American Medical Association*. Her tenure (2000–11) was marked by an increase in *JAMA*’s impact through a jump in citations and strong editorial stances regarding conflict of interest in medical research.
Shetty’s work and the efforts of the International Medical Corps were lauded by President Barack Obama during the 2015 State of the Union address.

Pranav Shetty, MD, MPH

As a medical student at Pitt, Pranav Shetty, MD, MPH, Class of 2007, did his share of lab research. Perhaps his most formative experience, however, came from his work in disaster relief overseas. Shetty is now global emergency health coordinator for International Medical Corps, a nonprofit organization that provides health and emergency services globally. During the unprecedented Ebola outbreak of 2014, he traveled to West Africa to train responders and establish two treatment units in Liberia. His experience in public health emergencies comes from deployments to Haiti, Libya, South Sudan, Jordan, Iraq, and the Philippines. Shetty’s work and the efforts of the International Medical Corps were lauded by President Barack Obama during the 2015 State of the Union address. Shetty, seated next to First Lady Michelle Obama, was an invited guest of the Obamas representing all the military and civilian health care workers deployed to West Africa to combat Ebola. Shetty completed a residency in emergency medicine at Harbor-UCLA Medical Center and a fellowship in global health and international emergency medicine at the University of Maryland, where he also received his Master of Public Health degree. As the outbreak wore on, Shetty said he remained guardedly optimistic, adding that it would require not just international health care workers but the work of communities, governments, and local doctors and nurses to end the epidemic.
Schwartz has been recognized with a MERIT and a Mentor of Excellence award from NIH.

Nancy Schwartz, PhD

In a distinguished career at the University of Chicago Pritzker School of Medicine, Nancy Schwartz, PhD, has made significant contributions to our understanding of genetic abnormalities and the mechanisms that lead to their manifestations as childhood diseases. Her lab discovered the PAPS synthetase gene family and identified mutations that lead to diseases of malformed cartilage in humans and animals.

Schwartz, who is professor of pediatrics and of biochemistry and molecular biology, directs the University of Chicago’s Joseph P. Kennedy Jr. Intellectual and Developmental Disabilities Research Center, which was established to promote collaborative research into the causes, prevention, and treatment of mental retardation and developmental disabilities.

The members are a multidisciplinary group of scientists with active research programs in areas related to understanding brain function and the causes of developmental abnormalities. The center’s research under the general rubric of mental retardation and developmental disabilities currently focuses mainly on studies of mechanisms of neurodegeneration that affect brain development and function, skeletal dysplasias that affect growth and maturation, and signaling pathways that affect cell migration and differentiation.

Among the group’s many research endeavors is the use of nanoparticles to treat disorders associated with intellectual disability caused by abnormal folding of proteins. For many years, Schwartz has maintained continuous R01 research funding from NIH, which has also recognized her work with both a MERIT and a Mentor of Excellence award. Schwartz is also the postdoctoral dean at the Pritzker School of Medicine.

Bruno studies how the neocortex, the outer few millimeters of the surface of our brains, mediates sensation and perception.

Randy Bruno, PhD

Randy Bruno, PhD, once aspired to be a computer scientist studying artificial intelligence, but he switched to neuroscience when he realized a need to understand the human brain first. After receiving his PhD in neurobiology from Pitt in 2002, he conducted postdoctoral research on neural connectivity underlying sensory perception with Nobel Prize winner Bert Sakmann, PhD, at the Max Planck Institute for Medical Research in Heidelberg, Germany. Now a tenured associate professor in the Department of Neuroscience at Columbia University, Bruno studies how the neocortex, the outer few millimeters of the surface of our brains, mediates sensation and perception. His latest work shows that sensory signals from our environments are copied to both the upper and lower layers of the neocortex. Surprisingly, these two halves do not always communicate with one another about incoming sensory signals despite being densely interconnected. Bruno has published these studies recently in Nature Neuroscience, Neuron, and Science. His laboratory is now investigating when the upper and lower halves of cortex interact and how their interactions contribute to normal behavior. According to Bruno, this information may be important in identifying treatments for human neurological and psychiatric disorders.
Deborah Gilboa, MD

As a former sign language interpreter, Deborah Gilboa, MD, Class of 2000, wanted to focus on treating patients with disabilities when she entered med school. She took advantage of Pitt’s collaborative and creative approach to the curriculum, which is routinely updated and improved, with students deeply involved in the process. Gilboa worked with the Office of Medical Education to launch an area of concentration in disabilities medicine. “Some of the things I really learned, in addition to medicine, were about creativity in education,” Gilboa recalls. “There’s always a way to personalize and make something more specific to your own goals.” Gilboa went on to practice family medicine and has become a leading voice on parenting and childhood development. Branding herself “Dr. G,” she has appeared on Good Morning America and is a contributor on the CBS morning show Pittsburgh Today Live. In 2014, she published her latest book, Get the Behavior You Want Without Being the Parent You Hate. Through offering parenting advice, Gilboa has identified an effective way to improve the health of children in her practice and beyond. “What I’ve discovered in my clinical practice is that when parents are effective, kids get healthier.”

Bertram Lubin, MD

Bertram Lubin, who earned his MD at Pitt in 1964, is well known for his research on sickle cell anemia, his public health initiatives regarding screening newborns for hemoglobin disorders, and his success in starting one of the first national cord blood banking programs for families with blood disorders. In 1984, Lubin became the director of medical research at Children’s Hospital Oakland. Under his leadership, basic, clinical, and translational research activities expanded. He transformed the hospital’s small research program into a highly successful enterprise called Children’s Hospital Oakland Research Institute (CHORI), which became one of the top 10 NIH-funded children’s hospital programs in basic, clinical, and translational research. In addition to his leadership of CHORI, he authored some 250 research papers during a long career. Lubin is now president and CEO of Benioff Children’s Hospital Oakland, part of the University of California, San Francisco Medical Center. He received Pitt’s Hench Distinguished Alumnus Award in 2007. He’s now focused on political advocacy for underserved populations and building a bridge between the technology sector and medicine. Lubin, who serves on an engineering advisory board for the University of California, Berkeley, says that engineering innovations can help distribute health care more broadly and address income and health disparities.

He once thought he might become a jazz drummer instead of a doctor. In Pittsburgh, he played jazz clubs in the Hill District; now, he still breaks out the kit on occasion to drum up support for a worthy cause.
“People’s brains age at different rates. If we can determine what governs brain aging rates, we can take steps to prevent age-related neurological diseases.”

Christin Glorioso, MD, PhD

By the time we’re 90, we have a 50/50 chance of having Alzheimer’s disease, notes Christin Glorioso, MD, PhD. A postdoc in the Paul F. Glenn Center for the Science of Aging Research at Massachusetts Institute of Technology (MIT), she mines data to find smart ways to identify genes that determine our brain’s health. Examining tissue from human brains of all ages, Glorioso looks at genes and their levels of expression to identify master regulators. “People’s brains age at different rates—a person may be 45 but age 40 at the molecular level. If we can determine what governs brain aging rates, we can take steps to prevent age-related neurological diseases.”

Glorioso earned her PhD in neurobiology in 2010 and her MD in 2011. Her postgraduate success supports the “apple doesn’t fall far from the tree” axiom. (Her father is Joseph C. Glorioso III, PhD, a pioneer in the design and application of herpes simplex virus gene vectors for the treatment of nervous system diseases like chronic pain. He chaired Pitt’s Department of Microbiology and Molecular Genetics for 20 years and remains a full professor since stepping down in 2009.)

In 2013, the younger Glorioso was awarded a postdoctoral fellowship in aging research by the Ellison Medical Foundation and the American Federation for Aging Research. Her research explores the sirtuin family of genes, which are activated by the resveratrol compound found in the skins of red grapes. Though the genes have been associated with extended lifespan and slowed brain aging in laboratory mice, more research is needed into the function of sirtuins in human brain aging. Glorioso’s research strategy is to identify variations in all genes that are associated with altered rates of normal human brain aging using a transcriptome-based biosignature. The team uses cellular models to identify the mechanisms underlying these associations and also compares brains aging normally with Alzheimer’s brains.

Jim Withers, MD

Withers was named one of CNN’s Top 10 Heroes for 2015 for his work delivering health care to the homeless.

Jim Withers, MD, Class of 1984, first began visiting patients in 1992—not in hospitals but on the streets of Pittsburgh. He dressed as a homeless person and carried a backpack with medical supplies. In the process, he pioneered street medicine—a term he coined—that encompasses all aspects of medical care to the homeless, a population often too alienated to visit shelters or clinics despite prevalent health issues.

Withers’ operation has come a long way since his initial late-night, dark-alley excursions. As Withers’ efforts picked up momentum, he formed Operation Safety Net in Pittsburgh, an organization to centralize and expand efforts to ensure that nobody would die on the streets. Other cities around the world have also begun organized efforts in street medicine. To serve as a central body for this network, Withers and others launched the Street Medicine Institute in 2008. The institute helps communities adopt street medicine and holds an annual, international symposium, the 10th of which was held in Dublin, Ireland, in 2014. Withers, a Pitt clinical assistant professor of medicine, has been taking advantage of Pittsburgh’s low rent by helping the homeless find housing; to date, his organization has helped find housing for more than 1,200 of the city’s homeless. Even with the strides that Withers and others have made, most nights he continues to search under Pittsburgh’s bridges and in other likely spots for those who need not just a doctor but an advocate.
Nima Sharifi, MD

Almost every man who dies of prostate cancer dies with castration-resistant prostate cancer. Nima Sharifi, MD, who holds the Kendrick Family Chair for Prostate Cancer Research at the Cleveland Clinic’s Lerner Research Institute, published in Cell his discovery of a genetic mutation that allows this deadly form of cancer to make its own supply of androgens, which fuel prostate tumor growth, regardless of treatments that target the body’s ability to produce it. Sharifi, who graduated from Pitt’s School of Medicine in 2001, was recognized with the 2014 American Association for Cancer Research Outstanding Achievement in Cancer Research Award. Since then, he has received $1 million in support from the Prostate Cancer Foundation, which he aims to use to develop a prognostic test to identify patients with the genetic mutation that predisposes them to the disease. In June 2015, Sharifi and colleagues authored a paper in Nature describing their discovery that a metabolite of an FDA-approved drug for metastatic prostate cancer appears to be more effective than the actual drug. The steroid inhibitor abiraterone is converted into a more physiologically active state in both patients and animal models with prostate cancer after receiving the drug. Sharifi and his colleagues showed that the metabolite, D4A, is more effective at killing aggressive prostate cancer cells, suggesting that some patients may benefit from direct treatment with D4A. “More studies are needed to uncover the exact mechanisms involved,” said Sharifi, “but we predict that direct treatment with D4A could prolong survival in some patients with metastatic prostate cancer. Further studies will also help us develop a potential biomarker profile to predict which patients will respond.”

Ryan McGarry, MD

The frenetic, high-pressure atmosphere of emergency departments has long set the stage for television shows looking to present intense, moving drama. For Code Black, a feature-length documentary about a Los Angeles hospital emergency department, the real-life drama it portrayed caught the eye of CBS, which in September premiered Code Black as a scripted television series on its Wednesday-night primetime lineup. The documentary film, written and directed by Ryan McGarry, MD, Class of 2009, immerses viewers in the Los Angeles County General Hospital ED, the busiest in America. When McGarry attended a clerkship and research rotation there as a med student, he decided to pick up his camera on a creative impulse; he later returned for his residency and continued shooting. His filmmaking debut saw breakout success, as Code Black won Best Documentary at the 2013 Los Angeles Film Festival and received praise from The New York Times and The Wall Street Journal. The show follows a hospital staff confronting medical and moral challenges amid the commotion of an urban ED. McGarry, an assistant professor of emergency medicine at Cornell University who practices at New York-Presbyterian Hospital, is an executive producer of the new CBS series.
What’s it like to be the only cardiologist in a landlocked nation of 15 million that’s among the poorest in the world?

“Busy,” said Anil Purohit, MD, a third-year cardiology fellow in the University of Pittsburgh’s Department of Medicine. Purohit practiced in the African country of Malawi for 10 months as part of the National Institutes of Health-funded Fogarty International Center Global Health Program for Fellows and Scholars. The prestigious fellowship (Purohit is one of just 20 clinicians selected nationwide) gives postdoctoral fellows with an interest in global health an opportunity to work in a developing country.

“The life expectancy in Malawi is 40 to 45,” Purohit said via Skype from the capital, Lilongwe, shortly before his return to Pittsburgh in July 2015. “Infections like HIV, malaria, and tuberculosis are major problems, and infection-related heart issues are becoming more prevalent.”

One in three HIV-positive patients taking antiretroviral (ARV) drugs has biomarkers of heart disease, he added, explaining that his Fogarty research project, “Cardiovascular Risk in HIV Patients on ARV Therapy,” focuses on using aspirin to possibly modify disease risk.

Beyond research and patient care, Purohit used his time in Malawi to train the next generation of heart specialists at the 780-bed Kamuzu Central Hospital, a facility that serves more than 4 million. “Our role at the end of the day is not to take over. It’s to teach and transfer these skills so that the Malawians can be in charge...
of their own health,” said Purohit, whose mentors in the Department of Medicine—Steven E. Reis, MD, associate vice chancellor for clinical research, professor of medicine and of emergency medicine, and director of Pitt’s Clinical and Translational Science Institute, and Joon Sup Lee, MD, associate professor of medicine and chief of the Division of Cardiology—supported his Fogarty application and encouraged his interest in global health.

Clinic days, which Purohit described in an online blog, were often challenging. The limited availability of medicines, supplies, and equipment far too frequently resulted in deaths that would be preventable in Pittsburgh.

“Wednesday was a disaster,” he wrote within weeks of his arrival. “I showed up at 8 a.m. to the outpatient unit and was met by at least 50 patients waiting in the hall. Apparently, news that a cardiologist was working spread like wildfire, and I had patients from all around the region (as far as four hours away) showing up in clinic.”

In November 2014, he gave a three-day lecture series at the Malawi College of Medicine, teaching medical students and clinical officers (similar to physician assistants) how to interpret electrocardiograms. “Teaching these students, I felt that I was actually able to make a difference,” said Purohit.

He is also working to found a nonprofit cardiac care hospital, Mheart, in cooperation with the Malawian government. Purohit has a proposed site, but he must seek philanthropic donations and other partnerships to advance his vision.
We aim to bring about transformational changes in American medicine by exploring the most fundamental and important areas in biological science and clinical care.
Here’s an example of a health problem that cries out for an innovative, paradigm-shifting approach: Heart disease is the leading cause of death in the United States. Approximately 5 million Americans are living with heart failure, with roughly 500,000 new cases each year. Because heart tissue has a limited ability to regenerate, end-stage heart failure is irreversible. Heart transplantation is the ultimate treatment strategy for those patients, but it’s far from a perfect solution. In fact, approximately 50,000 people die each year due to the limited availability of donor hearts for transplant.

An innovator might suggest we put aside heart transplants for a moment and ask, What if we found a way to regenerate heart tissue? That’s exactly what Lei Yang, PhD, assistant professor of developmental biology and of clinical and translational science, aims to do. In 2014, he received an NIH New Innovator Award for his proposal to use regenerative medicine to develop an approach that could ultimately make it possible to generate an entire bioartificial human heart. The experimental approach developed by Yang and his colleagues is to strip a mouse heart of all of its cells, leaving the extracellular matrix behind. This ghostly structure maintains the architecture of the heart and functions like a scaffold. Yang and colleagues then seed the structure with human pluripotent stem cells, which differentiate into the required cardiomyocytes, smooth muscle cells, and endothelial cells. The team has succeeded in generating a heart that spontaneously beats, though it has further to go to produce one that does so strongly enough to function like the real thing.

With five years of funding through the New Innovator Award, Yang is in a good position to advance this innovative line of research and gather experimental data that could help him secure his first NIH R01 grant—the gold standard for an independent, NIH-funded researcher. This is exactly what the New Innovator Award, introduced in 2007, was designed to do. Young scientists with potentially transformative ideas are often in a pinch. Lacking a long track record of funding and laboratory results, it’s difficult for them to get the financial support to fully commit to an idea that nobody has ever explored before. Established investigators who patiently and painstakingly built their own careers over many years might say that’s simply the reality of a career in biomedical research. But NIH has prioritized the identification of risky, innovative science that has the potential to catalyze dramatic leaps forward in health care. Yang is the third Pitt investigator to earn a New Innovator Award since its introduction.
One might not expect a serious academic physician to count a computer gaming company among her most important collaborators, but that’s exactly the case for Deepika Mohan, MD, MPH, assistant professor of critical care medicine and of surgery. Mohan’s professional mission is to improve the care of trauma patients, and she is working on what some would call an entirely unexpected way of doing so. Her innovative approach to this lifesaving mission is to create computer games—“serious games,” as they are called when used for such purposes—to help physicians understand why they make the decisions they make and to help them make better ones.

When a person suffers severe traumatic injury, he or she is often sent to the nearest emergency department (ED), but not all EDs are equipped for trauma. The American College of Surgeons provides guidelines for identifying severely injured patients who should be transferred to a designated trauma center, but only one-third of such patients at nontrauma centers are transferred. In a 2014 research paper in *PLOS ONE*, Mohan and colleagues tested their serious game to see whether it was a valid tool for understanding and improving decision making in the busy, stressful, and rapidly changing environment of the ED. In their study, Mohan and her colleagues demonstrated that, in the context of the game, ED physicians made decisions consistent with actual practice. Furthermore, when the team manipulated the cognitive load of individual players by adding realistic conditions such as an increased caseload, frequent interruptions, and reminders about additional patients, they found that players relied increasingly on intuition and pattern recognition for answers rather than guidelines, as predicted by cognitive theory. In other words, the team’s computer game appears to hold up to scrutiny as a viable model for replicating and understanding decision making in the ED. Mohan’s next step is to use serious games to improve decision making. The approach has the potential to create a paradigm shift in the drive to improve outcomes in trauma care.
Prosthetic arms and hands that can “feel” like natural ones by mimicking the sensation of touch could help amputees have better dexterous control and improve their ability to perform everyday tasks. While developing such prostheses, Robert Gaunt, PhD, assistant professor of physical medicine and rehabilitation, along with a multidisciplinary research team from Pitt and other institutions, hopes to test them in patients’ homes within four years. Funding from the Defense Advanced Research Projects Agency (DARPA) has helped spur the project. The first phase of the project will study whether stimulation of sensory nerves near the spinal cord can allow amputees to detect sensations of touch. Researchers will also insert fine-wire electrodes into participants’ forearm muscles to study the signals coming from remaining muscles, which will be used to control the prosthetic hand (a product of the Johns Hopkins University Applied Physics Laboratory) using biomimetic algorithms that should allow opening and closing of the thumb and individual fingers. “To make the most of these new capabilities, we have to integrate the prosthesis into the remaining neural circuitry so the patient can use it like a regular hand that, for example, can pick up a pen, gently hold an egg, or turn a doorknob,” Gaunt said. Pitt’s research team includes engineers, scientists, and clinicians from the School of Medicine Departments of Physical Medicine and Rehabilitation, Plastic Surgery, and Neurological Surgery, as well as the Departments of Occupational Therapy and Rehabilitation Science and Technology from the School of Health and Rehabilitation Sciences. An award from the BRAIN Initiative, a White House program seeking to accelerate understanding of the brain, also provided project funding. Michael Boninger, MD, Physical Medicine and Rehabilitation Professor, chair of physical medicine and rehabilitation, and professor of clinical and translational science, is codirecting the project.
**Grants of Note**

**PITT LEADS NATIONAL CENTER OF EXCELLENCE TRANSLATING BIG DATA TO KNOWLEDGE**

In late 2014, NIH awarded the University of Pittsburgh an $11 million, four-year grant to lead a Center of Excellence for Big Data Computing, which will help scientists capitalize more fully on large amounts of available data and make data science a more prominent component of biomedical research.

The highly competitive process for grants under the new NIH Big Data to Knowledge initiative — known as BD2K — attracted applications from 136 institutions around the nation. Pitt’s Center for Causal Modeling and Discovery, one of only 11 such centers to be funded, aims to develop new tools and approaches to turn the tremendous amount of information available to physicians and scientists — including data from electronic health records, digital images, and molecular analyses of genes, proteins, and metabolites — into discoveries that will benefit human health.

Led by principal investigator Gregory F. Cooper, MD, PhD, professor of biomedical informatics and of computational and systems biology, School of Medicine, the center represents a partnership among data scientists from Pitt, Carnegie Mellon University, and the Pittsburgh Supercomputing Center. The center seeks to develop highly efficient causal discovery algorithms that can be practically applied to very large biomedical datasets. Their goals are to, first of all, conduct research projects addressing three distinct biomedical issues (cancer driver mutations, lung fibrosis, and the brain cause) as a vehicle for algorithm development and optimization; to disseminate causal discovery algorithms, software, and tools to the larger research community; and to train data scientists and biomedical investigators in the use of these tools.

**DEFENSE DEPARTMENT FUNDS WHOLE-EYE TRANSPLANT RESEARCH**

Pitt researchers are leading a multidisciplinary consortium aimed at establishing the nation’s first whole-eye transplant program. While corneal transplants are routinely performed, whole-eye transplantation involves overcoming immune rejection and reestablishing optic nerve connectivity. The U.S. Department of Defense, which is providing Pitt $1.25 million for the project, says that up to 40 percent of blast injuries to soldiers wounded in combat affect the eyes. The Whole Eye Transplant Consortium established at Pitt marks the first cross-disciplinary, systematic approach to exploring whole-eye transplantation, along with long-distance optic nerve regeneration, retinal cell survival, and other topics. The consortium includes researchers from Harvard, Stanford, Johns Hopkins, and other universities nationally and globally. “This is a very aggressive program with very high-risk and high-reward scenarios,” said Joel S. Schuman, MD, Eye and Ear Foundation Professor, Distinguished Professor and chair of ophthalmology, and director of the UPMC Eye Center. “By solving one facet of the problem at a time, the long dreamed-of goal of whole-eye transplantation may be possible.”

**PITT RECEIVES $5.8 MILLION NIH GRANT TO CONSTRUCT 3D LIVER MODEL**

To better study physiology, drug toxicity, and disease interaction in the liver, Pitt researchers are developing a microfluidic 3D model that replicates the liver’s function, anatomy, and design. With a $5.8 million grant as part of NIH’s Tissue Chip for Drug Screening Program, Pitt’s team will develop a liver replica as part of the program’s multi-institutional effort to refine and combine 3D human tissue chips into a system that mimics complex functions of the human body. Using a variety of cell types, the team is creating models of the functional unit of the liver, called the acinus, to analyze acute and chronic toxicity effects. Principal investigator D. Lansing Taylor, PhD, Allegheny Foundation Professor of Computational and Systems Biology and director of Pitt’s Drug Discovery Institute, said the model will provide new opportunities to study treatment efficacy for conditions like nonalcoholic fatty liver disease, liver cancer, and immune-mediated toxicology and fibrosis.

**COLLABORATIVE TBI RESEARCH FUNDING PREPS CLINICAL TRIALS**

Pitt is part of a national “dream team” of universities, companies, and organizations working to improve treatment for traumatic brain injury (TBI) that will receive $17 million in funding from the U.S. Department of Defense as part of its TBI Endpoints Development initiative. Pitt’s Graduate School of Public Health will analyze data from previous TBI studies to determine the effectiveness of current TBI-measuring methods. Using the results, David Okonkwo, MD, PhD, professor of neurological surgery and clinical director of the Brain Trauma Research Center at the School of Medicine, will collate the selection of patients for clinical application of chosen TBI endpoints through the NIH-funded project Transforming Research and Clinical Knowledge in TBI. “If we can more accurately identify and quantify these injuries, we will be better able to select appropriate patients for clinical trials and to evaluate the success or failure of our therapies,” Okonkwo said. The team intends to overcome the difficulty of demonstrating the effectiveness of TBI drugs and medical devices. More than 2.5 million people in the U.S. seek TBI care each year, yet no TBI treatment has proved effective and no drug has been approved to treat this condition.

**EARLY REHABILITATION PROTOCOLS STUDIED IN CHILDREN WITH ACUTE BRAIN INJURY**

A $1.24 million grant from the Patient-Centered Outcomes Research Institute, or PCORI, is funding a multi-center randomized clinical trial of an early rehabilitation protocol (ERP) versus usual care in children with acute brain injury (ABI). Ericka Fink, MD, MS, associate professor of critical care medicine and of pediatrics, is studying ERP in the pediatric intensive care unit at Children’s Hospital of Pittsburgh of UPMC and Lurie Children’s Hospital in Chicago with site principal investigator, Craig Smith, MD. Instead of usual care, which entails physical, occupational, and speech therapy in the ICU if and when physicians consult patients, ERP provides a comprehensive program to begin these consultations early in ICU admission to address functional, cognitive, and emotional needs of critically ill children. Children with ABI are at high risk for developing multiple disabilities, Fink said.

**FUNDING PREPS CLINICAL TRIALS**

**COLLABORATIVE TBI RESEARCH**

**DEFENSE DEPARTMENT FUNDS**

**WHOLE-EYE TRANSPLANT RESEARCH**

**PITT RECEIVES $5.8 MILLION NIH GRANT TO CONSTRUCT 3D LIVER MODEL**

**PITT LEADS NATIONAL CENTER OF EXCELLENCE TRANSLATING BIG DATA TO KNOWLEDGE**

**EARLY REHABILITATION PROTOCOLS STUDIED IN CHILDREN WITH ACUTE BRAIN INJURY**
ECG DATABASE WILL IMPROVE CPR EVALUATION, PRACTICE

Of Americans who experience sudden cardiac arrest outside the hospital, fewer than 7 percent survive to hospital discharge. To improve cardiopulmonary resuscitation (CPR) evaluation and performance, Pitt researchers are creating a database of electrocardiogram (ECG) information based on data from upward of 16,000 ECG reports. To launch the project, Pitt received $1.8 million from the National Heart, Lung, and Blood Institute. “We will make use of this information to better understand how the quality of CPR might change the ECG patterns and then link that to the outcomes of the patient all the way to discharge. If we can see what works best, we can further refine CPR interventions and save more lives,” said lead investigator James Menegazzi, PhD, Department of Emergency Medicine Professor of Resuscitation Research. Collected data can better guide real-time decision making surrounding CPR.

NIAID GRANT FURTHERS SEVERE ASTHMA RESEARCH

The continuing study of severe asthma by Pitt researchers has been bolstered by an $8 million, five-year grant from NIH’s National Institute of Allergy and Infectious Diseases. In June, researchers launched a new project to expand studies of the immune response and genetic roots of severe asthma in 120 patients and in animal models. The research team comprises Pitt and UPMC scientists, immunologists, and clinicians to further their bench-to-bedside and bedside-to-bench work, said Sally Wenzel, MD, professor of medicine, of immunology, and of clinical and translational science and director of the University of Pittsburgh Asthma Institute at UPMC. “It’s the unmet need of asthma,” Wenzel said. “This is one of the first true opportunities to integrate top-tier immunologists with translational clinical science. To find the many different mechanisms involved, you need a team effort such as this one.” Grant coprincipal investigators include Anuradha Ray, PhD, professor of medicine and of immunology, and Wenzel, with core leaders Jay Kolls, MD, professor of pediatrics and of medicine and director of the Richard King Mellon Foundation Institute for Pediatric Research, Children’s Hospital of Pittsburgh of UPMC, and Timothy Oriss, PhD, research assistant professor of medicine.

ENGAGE PITT

At Pitt, innovation is applied to both scientific research and, lately, the very funding of it. Dwindling federal support for research necessitates new sources of funds, and the University has responded by launching EngagePitt, an online crowdfunding platform that generates money for Pitt-related student activities, community outreach, and research projects. Crowdfunding has been successfully used around the world for everything from movie productions to culinary ventures. At Pitt, it’s already shown success for scientific pursuits.

In January 2015, Christopher W. Seymour, MD, MSc, assistant professor of critical care medicine and of emergency medicine, and other researchers launched the ThinkSepsis project on EngagePitt. The project sought to outfit ambulances with technology to recognize and relay sepsis symptoms to awaiting hospitals. Sepsis can be deadly, but it often goes unrecognized. The pilot project will provide new opportunities for sepsis research, and the results may even shed light on other time-sensitive conditions and symptoms first observed in the ambulance. “There are a number of innovative and new ideas that just aren’t mature enough for NIH, which may be looking for projects that are more fully developed,” Seymour said. “A campaign like this is really ideal for these new, high-risk, high-reward project ideas.”

ThinkSepsis raised $2,000 during its two-month run on the site, and the research team is seeking additional funding for an implementation study. “As primary researchers, in our funding climate, seeking alternative ways to fund our projects is important,” Seymour said. “To be successful, we need to explore all avenues.”
$1.5 MILLION NATIONAL TRIAL TO ADDRESS ANTIBIOTIC OVERUSE

The leading reason for antibiotic use in post-acute and long-term care facilities is to treat suspected urinary tract infections (UTI), and the medications are often administered before making a correct diagnosis. Used inappropriately, antibiotics can kill good bacteria, cause allergic reactions or side effects, and allow harmful, drug-resistant bacteria to flourish. To examine methods to reduce unnecessary antibiotic use in such facilities, the School of Medicine will lead a $1.5 million national trial. The U.S. Department of Health and Human Services Agency for Health Care Research and Quality will fund the three-year study, which will update and disseminate guidelines and tools for the management of UTIs in the nursing-home setting. “Antimicrobial resistance is a hot-button issue in health care nationally and internationally — and inappropriate overutilization of antibiotics is the single largest culprit,” said primary investigator David A. Nace, MD, MPH, associate professor of medicine and director of long-term care and influenza programs, Division of Geriatric Medicine.

AMERICAN SOCIETY OF TRANSPLANTATION RECOGNIZES MENTOR AND MENTEE WITH TWO AWARDS

The American Society of Transplantation’s (AST) 2015 Achievement Awards and Faculty and Fellowship Grants included two Pitt recipients. The awards recognize achievements and contributions made to AST and to the field of transplantation.

Héth R. Turnquist, PhD, assistant professor of surgery and of immunology, received the Basic Science Career Development Award for identifying a previously unknown regulatory capacity of interleukin-33. This finding furthers our understanding of the immunological mechanisms supporting transplant tolerance and could help eliminate the persistent problem of chronic rejection after solid organ transplantation. Benjamin Matta, PhD, a postdoctoral fellow in the Turnquist lab, received a $100,000 Astellas Basic Science Fellowship Research Grant to support his research. His studies will lead to new targets enabling augmentation of the regulatory capacity of interleukin-33 after transplantation.

GRANT SUPPORTS RESEARCH ON BLADDER CANCER

Rahul Parikh, MD, PhD, assistant professor in the Division of Hematology/Oncology, Department of Medicine, received the Stephen Hale Gushée Young Investigator Award in June. The $100,000 grant from the Bladder Cancer Advocacy Network will further Parikh’s research on a genetic abnormality that permits certain bladder cancer cells to survive radiation and chemotherapy. His current study examines the role of this genetic change in the development of resistance to radiation and chemotherapies used for bladder cancer.

CTSI AWARDS $160,000 IN PAIN RESEARCH CHALLENGE

In spring 2015, the University of Pittsburgh Clinical and Translational Science Institute (CTSI) sponsored a competition to generate new ideas for research projects focused on pain relief. Called the “30, 300, 3000 Pain Research Challenge,” the competition offered awards totaling $150,000 through an endowment fund established in 2009 by the estate of Virginia Kaufman to support pain-focused research.

Fifty multidisciplinary groups of faculty and students from throughout the University of Pittsburgh and collaborators from other academic institutions entered the challenge. Six teams won $25,000 each to advance their projects. One entry picked up an additional $10,000 of CTSI funding as a “People’s Choice” poster winner.

Organizers looked for research solutions to address the dynamics of pain, causes and alleviation of pain, and treatment to prevent and mitigate pain (including, but not limited to, pain associated with post-herpetic neuralgia, cancer, or arthritis). Solutions were to target a specific problem such as mechanisms, treatments, modalities, or effects of acute and chronic pain, including associated psychological and physiological factors.

“Pain is the number-one reason people seek health care. It affects more Americans than diabetes, heart disease, and cancer combined,” said Steven E. Reis, MD, associate vice chancellor for clinical research, health sciences, and CTSI director. “We were very excited to see the variety of ideas and research approaches that were suggested to try to make a difference for people with acute or chronic pain.”

Winning projects are:

Expressive Painimation
As an alternative to the traditional “one to 10” scale, Charles Jonassaint, PhD, assistant professor of medicine, and his team are building an application that allows patients to describe the quality and intensity of their pain using dynamic animation.

Understanding the Amplification of Pain
Sarah Ross, PhD, assistant professor of neurobiology, and her team are pursuing studies to determine novel mechanistic insight into wind-up, the abnormal amplification of peripheral pain signals by the spinal cord.

A Novel Twist on IBS Pain
Michael Gold, PhD, professor of anesthesiaology, and his team are targeting chronic pain associated with irritable bowel syndrome, which affects more than 30 million people in North America.

Sit Less for Less Back Pain
Bethany Gibbs, PhD, assistant professor of health and physical activity, School of Education, and her team have designed a project to study the effect of using an adjustable-height desk and activity monitor to prompt movement as elements of a strategy to combat low-back pain.

TRIPOND-Z
Paul Kinchington, PhD, professor of ophthalmology, and his team are working on models of trigeminal pain and ocular neurological disease to study ways to treat pain.

HeadTrack (“People’s Choice” poster winner)
Kelly Beck, a first-year doctoral student in the School of Health and Rehabilitation Sciences, and her team will work to continuously track potential triggers and prodromal symptom activity in people with chronic migraines to better define the therapeutic window.
Combine Pitt's reputation as a medical and technological powerhouse with a dash of Steelers football, and you'll get a new sports-medicine startup aiming to drive Pitt-developed technologies to market. Philanthropist and former Steelers quarterback Charlie Batch forged a partnership with Pitt and its Innovation Institute this past year to launch Impellia, a company created to advance technologies surrounding human performance, wellness, rehabilitation, and injury prevention.

The School of Medicine, along with the UPMC Center for Sports Medicine, the Pitt–UPMC McGowan Institute for Regenerative Medicine, and other partners, has long been a leader in sports medicine and rehabilitation. The creation of Impellia adds a powerful force to commercialize scientific and clinical advancements to improve the health of the general public.

For Batch, who benefited from access to the best clinicians in sports medicine and rehabilitation during his 15-year NFL career, Impellia is an exciting development. “What we see in these technologies is the ability for us to bring innovation available to elite athletes out to everyday people,” he says.

Impellia kicked off its efforts in 2015 with three Pitt-developed technologies that enhance rehabilitation and diagnosis:

**interACTION** is a joint-function monitoring tool that uses wearable sensors to collect motion data during physical therapy. The data allow doctors to precisely monitor progress and personalize therapy.

**PIVOT** is designed to simplify and improve one of the most commonly used sports-injury diagnostics—the pivot shift test—by placing sensors at precise points on the knee and connecting them to the PIVOT app for accurate diagnosis of anterior cruciate ligament tears.

**VISYTER** (Versatile and Integrated System for Telerehabilitation) is a software platform to develop telerehabilitation applications, allowing far-flung patients to benefit from sports-medicine experts, no matter where they are. It incorporates videoconferencing, electronic health records access, remote camera control, and other features to remotely assess patients and monitor their recovery.
Publications of Note

JOURNAL OF CLINICAL INVESTIGATION
JUL 2015 | VOL 125 | ISSUE 7
INHIBITING PROTEIN COULD PREVENT PARKINSON'S DEVELOPMENT

The presence of Lewy bodies, which are clumps of the protein α-synuclein within neurons, is characteristic of Parkinson’s disease. By thwarting production of α-synuclein through gene therapy, Pitt researchers successfully prevented development of Parkinson’s symptoms in rats. The team used a harmless virus called AAV2 to deliver a piece of genetic code that blocks α-synuclein production to the neuron. The researchers then exposed AAV2-treated rats to the pesticide rotenone to reproduce many features of Parkinson’s, including movement problems, Lewy bodies, and loss of dopamine neurons and mitochondrial function. The treated rats did not exhibit any Parkinson’s-like symptoms, while a control group experienced loss of dopamine neurons and other symptoms. Researchers plan to investigate the molecular pathways that enable α-synuclein’s influence on mitochondria and other mechanisms and potentially translate the α-synuclein-reduction approach into human clinical trials. The research team included Edward A. Burton, MD, DPhil, associate professor of neurology and of microbiology and molecular genetics, and J. Timothy Greenamyre, MD, PhD, Love Family Professor of Neurology, professor of clinical and translational science, and director, Pittsburgh Institute for Neurodegenerative Diseases.

PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES
MAY 2015 | VOL 112 | ISSUE 20
ZINC’S UNCOVERED PATHWAY OPENS NEW NEUROLOGICAL RESEARCH AVENUES

Zinc and the neurotransmitter glutamate are present in the brain’s synapses. While glutamate is the brain’s major excitatory neurotransmitter, zinc’s role has been less understood beyond its action as a cofactor for enzyme and regulatory proteins. Pitt researchers conducted a study with researchers at the Massachusetts Institute of Technology that used an agent that fluoresced when bound to zinc, allowing the team to measure and track the element’s movement. After zinc diffused, it could bind to and, therefore, inhibit extrasynaptic glutamate NMDA-type receptors. By uncovering zinc’s pathway and observing these actions, researchers gained insight into mechanisms that may play a role in Alzheimer’s and other diseases. “Glutamate acts like an accelerator of neuronal activity, while zinc behaves like a brake that fine tunes that signal,” said Thanos Tzounopoulos, PhD, Auditory Physiology Professor in the Department of Otolaryngology. “The receptors that zinc influences are thought to play a role in neurodegenerative diseases, so these findings could open new research avenues in the field.”

SCIENCE SIGNALING
JAN 2015 | VOL 8 | ISSUE 361
ED DRUGS MAY COMBAT SEPSIS DAMAGE

Drugs for treating erectile dysfunction may also be effective at protecting the liver from sepsis-caused damage, according to Pitt researchers. Tumor necrosis factor (TNF) is a protein produced during sepsis that is harmful at high levels. In a mouse model, researchers found that sildenafil, or Viagra, increased the liver’s production of the signaling molecule cyclic GMP, causing cells to shed TNF receptors, reducing TNF signaling and preventing liver damage. Experiments with human liver cells also resulted in damage prevention. “Our study suggests that increasing the bioavailability of cyclic GMP might be beneficial in ameliorating the inflammation associated with sepsis,” said senior investigator Timothy Billiar, MD, George V. Foster Professor, Distinguished Professor, and chair of surgery, and professor of clinical and translational science. “Sildenafil and other ED drugs might be a good approach to try early in the course of the illness to forestall organ damage.” Sepsis, a systemic inflammatory response to infection, can cause whole-body inflammation resulting in damage to the liver, kidney, and other organs and even death. Researchers plan to further test their findings using a large animal model.

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY
FEB 2015 | VOL 59 | ISSUE 2
NEW TREATMENT COMBATS DRUG-RESISTANT BACTERIA, INCLUDING ‘SUPERBUGS’

Drug-resistant bacteria infect almost 2 million people in the United States each year and cause about 23,000 deaths. Among these, the “superbugs,” which are resistant to almost all existing antibiotics, pose special threats to hospitals and nursing homes. However, a new treatment developed at Pitt’s Center for Vaccine Research has inhibited growth of many drug-resistant bacteria and superbugs in the lab. Researchers developed synthetic peptide sequences called engineered cationic antimicrobial peptides, or “eCAPS,” to counter the growth of drug-resistant bacteria. They tested the eCAPS against a naturally occurring antimicrobial peptide and against an antibiotic, colistin, which is administered as a last resort against multidrug-resistant bacteria. The existing agents inhibited growth of about 50 percent of sample strains while the eCAPS blocked about 90 percent of test strains. Senior author Ronald C. Montelaro, PhD, professor of microbiology and molecular genetics and of medicine, and other researchers also tested the eCAPS against Pseudomonas aeruginosa, a highly infectious pathogenic bacterium; it took 25 to 30 days for the bacterium to develop resistance to the eCAPS compared to as few as three days for traditional drugs. “We were very impressed with the performance of the eCAPS,” Montelaro said. “However, we still needed to know how long the eCAPS would be effective before the bacteria develop resistance.”
A Pitt research team—one of a growing number at the University exploring genomic stability and DNA repair mechanisms—has discovered a novel, RNA-based homologous recombination mechanism that protects the genome from strand breaks at transcriptionally active sites during the G0/G1 phase of the cell cycle. The group’s data suggest that a deficiency in this repair mechanism might explain why neurodegeneration and tumorigenesis may occur in cell populations that, in this phase of the cell cycle, appear otherwise fully differentiated and stable.

DNA damage at transcriptionally active sites is expected to be more deleterious than elsewhere in the genome because the integrity of regions that code for proteins is likely to be compromised. But repair mechanisms at these sites during the G0/G1 phase have been largely unknown to this point. An intriguing finding is that the newly described mechanism is dependent on CSB (Cockayne syndrome protein B), which is known to counter radiation-induced DNA damage in cell and zebrafish models; the team’s discoveries may shed light on the clinical manifestations of Cockayne syndrome, a rare autosomal recessive neurodegenerative disorder characterized by growth failure, impaired neurodevelopment, vision, and leads to increased cell death in many organs and tissues, especially in neurons.

The team, including Li Lan, MD, PhD, assistant professor of microbiology and molecular genetics, Arthur S. Levine, MD, dean of the medical school and professor of medicine and molecular genetics, and Leizhen Wei, PhD, visiting research associate in the Department of Microbiology and Molecular Genetics, carried out the research using a novel method they developed (the DART system) in which the protein KillerRed is positioned directly on DNA to induce localized damage at that targeted site on the genome. They accomplish this by taking advantage of KillerRed’s ability to generate damage-inducing superoxide when excited by exposure to visible light. The research paper, “DNA damage during the G0/G1 phase triggers RNA-templated, Cockayne syndrome B-dependent homologous recombination,” appeared in a July 2015 issue of the Proceedings of the National Academy of Sciences.
Mechanism Targets Mutated Cells to Prevent Intestinal Polyps

Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) have long been known to lower the risk of developing intestinal polyps, which can become cancerous. While the reasons behind this reduced risk have been unknown, Pitt researchers have identified a biochemical mechanism that could explain the preventive effect: The NSAIDs induce cell suicide pathways in intestinal stem cells that have a certain mutated and dysfunctional gene, preventing them from becoming cancerous. “These findings could help us design new drugs to prevent colorectal cancer, which is the third-leading cause of cancer-related deaths in the country,” said senior investigator Lin Zhang, PhD, professor of pharmacology and chemical biology. In both animal models and tumor samples, researchers found that NSAIDs activate a “death receptor” pathway in cells with the mutation, while leaving healthy, nonmutated cells unaffected.

EXTRA OXYGEN COULD SHRINK TUMORS

The blood supply of a tumor often doesn’t match the pace of the cancer’s growth, which leads to areas that are ischemic and oxygen deprived, or hypoxic. Hypoxia triggers a biochemical cascade leading to the production of adenosine, a molecule that not only promotes tumor survival but also can act as a shield against immune system cells that would otherwise attack the cancer.

Pitt researchers, in collaboration with a team lead by Michail Sitkovsky, PhD, at Northeastern University, demonstrated through a study with animal models that simply breathing more oxygen could thwart the adenosine surge, explained coauthor Edwin K. Jackson, PhD, Pitt professor of pharmacology and chemical biology. In both animal models and tumor samples, researchers found that extra oxygen hypoxia attacks can be reduced.

Stem Cells Present in Esophagus

The esophageal lining must regularly renew as cells slough off into the gastrointestinal tract; to do so, cells in the deeper layers of the esophagus divide to produce the specialized cells. It was previously thought that, because all the cells were dividing rather than being quiescent, all the deeper-layer cells could be the same and that stem cells were not involved, explained senior investigator Eric Lagasse, PhD, PharmD, associate professor of pathology and director of the Cancer Stem Cell Center at the McGowan Institute for Regenerative Medicine. But researchers from Pitt have shown that stem cells are present in the esophagus. “Our findings reveal that there, indeed, are esophageal stem cells; and rather than being quiescent, they divide slowly compared to the rest of the deeper-layer cells,” said Lagasse. Researchers used esophageal tissue from mouse samples to examine different cells in the basal layer and found cells exhibiting marked stem-cell traits, thus confirming their presence. Esophageal stem cells and their abnormalities could help explain conditions like Barrett’s esophagus, a disease in which the lining of the esophagus alters to resemble that of the intestine.

Text-MESSAGE Intervention Reduces Binge Drinking in Young Adults

When a computer program interacts with young adult drinkers through text messaging, the young adults successfully reduce their alcohol consumption, particularly concerning binge drinking, according to a study by Pitt researchers. Up to half of young adults who visit the emergency room each day in the United States have hazardous alcohol-use patterns, said lead author Brian Suffoletto, MD, assistant professor of emergency medicine. Without sufficient resources to personally counsel all of those at risk for alcohol misuse, researchers designed and tested an interactive text message program to change drinking behaviors in young adults in a randomized controlled trial of 765 18- to 25-year-olds discharged from emergency departments in Western Pennsylvania hospitals. One group of participants engaged in brief, two-way text message dialogue sessions each Thursday and Sunday for 12 weeks to increase awareness regarding weekend drinking intentions and set goals to reduce weekend consumption. After three months, those who received the texting intervention reported one to two drinking occasions per month compared to three to four previously and consumed around one drink fewer per occasion. “There’s a lot of talk about mobile health intervention but not a lot of evidence. This is one of the first studies to test a simple mobile intervention and demonstrate the small but important impact it can have in helping patients make healthier choices,” Suffoletto said.
Despite the high occurrence of prostate cancer — one in seven men will develop the disease — only a small portion of men diagnosed develop metastases, and even fewer die from the cancer. This difference can lead to treatment being more harmful than the disease itself, said Jianhua Luo, MD, PhD, professor of pathology. However, Pitt research has revealed that prostate cancer patients with a certain genetic mutation have a 91 percent chance of the cancer recurring. After sequencing the genomes of prostate tissue samples, researchers found that those who experienced recurring cancer had specific genetic fusion transcripts in common. “Being able to say, with such certainty, that a patient is nearly guaranteed to see a recurrence of his prostate cancer means that doctors and patients can elect to be more aggressive in treating the cancer,” Luo said. “This could lead to a cure for prostate cancer through genetic therapy. With this discovery, we’re at the tip of the iceberg in terms of possibilities for improving patient outcomes.”

Older adults who have major depression are more than twice as likely to develop dementia as those who have never had the disorder. That was one finding from a Pitt study showing that those who develop depression and mild cognitive impairment (MCI) after age 65 are more vulnerable to accelerated brain aging. “Our study represents a significant advance because it provides a more comprehensive and integrated view of the neurobiological changes related to mild cognitive impairment in late life,” said senior investigator Meryl A. Butters, PhD, associate professor of psychiatry. “Better understanding of the neurobiology of cognitive impairment in depression can provide new targets for developing more specific treatments.” By studying blood samples and brain scans of older adults in remission after being treated for major depression, including some with MCI, the researchers found biological and brain imaging markers that indicated a greater likelihood of accelerated brain aging and cognitive impairment. “If we can understand what happens in the brain when people are depressed and suffer cognitive impairment, we can then develop strategies to slow or perhaps stop the impairment from progressing to dementia,” Butters said.

When envelopes containing anthrax spores were mailed to major U.S. media offices and two U.S. senators in 2001, it marked the worst bioterrorism attack in U.S. history, leaving five dead and 17 infected. That was 14 years ago. Since then, the scientific and medical communities have learned a great deal about anthrax and other potential bioterror agents. With the threat of both natural and intentional outbreaks still very real, the New England Journal of Medicine deemed the topic important enough for a thorough review. In March, the journal published “Clinical Management of Potential Bioterrorism-Related Conditions,” authored by Amesh A. Adalja, MD, clinical assistant professor in the Departments of Critical Care Medicine and of Emergency Medicine and adjunct instructor in the Division of Infectious Diseases in the Department of Medicine, and Thomas V. Inglesby, MD, associate professor of medicine and of environmental and occupational health, Graduate School of Public Health. Both Adalja and Inglesby, along with coauthor Eric Toner, MD, are affiliated with the UPMC Center for Health Security in Baltimore.

The report includes only those agents and preventions demonstrating the greatest need for concern and preparedness. The authors discuss and share new knowledge on anthrax, botulism, pneumonic plague, smallpox, and tularemia. For some of these threats, treatments remain relatively unchanged; others have seen new vaccines and treatments emerge: To treat anthrax, a monoclonal antibody has been developed; a heptavalent antitoxin can now be used to treat botulism; and experimental antivirals have been developed for smallpox. The review provides guidelines for cautiously assessing conditions and symptoms of the diseases. Pneumonic plague, for example, shows the same signs as regular pneumonia in its early stages. For each agent, the article emphasizes proper clinical and laboratory diagnosis. Above all, the review highlights that, since most of the associated conditions can occur naturally, bioterrorism awareness depends on clinicians maintaining alertness to unusual patterns of symptoms. The authors underscore that, even with clinical vigilance, collaboration between clinicians and public health officials must be emphasized for an effective response.
Premature ovarian failure, which occurs when a woman’s ovaries stop working before age 40, affects about 1 percent of women. Aside from infertility, the condition is linked to high risk of osteoporosis and heart disease. Pitt researchers at Magee-Womens Research Institute identified genetic mutations in two genes connected to premature ovarian failure, which could help pinpoint the condition’s cause and guide treatment options.

After conducting genome sequencing on blood and skin samples, researchers found that two genes, MCM8 and MCM9, that repair damaged DNA in ovarian cells that eventually become egg cells contained the newly discovered mutations. It’s an example of the power of whole genome sequencing, said senior author Aleksandar Rajkovic, MD, PhD, Marcus Allen Hogge Professor of Reproductive Genetics, Department of Obstetrics, Gynecology, and Reproductive Sciences, and professor of pathology. “Most women with premature ovarian failure don’t know why they can’t reproduce, and it can be devastating for them,” Rajkovic said. “Our findings indicate that genetics may play a strong role in this condition and raise the prospect of one day developing therapies to delay the early onset of menopause.”

Cardiac surgery is often life-saving for infants born with heart muscle disease, but currently there is no way to replace heart muscle other than heart transplantation. However, it may be possible to spur regeneration of heart muscle. Researchers at Pitt and at Children’s Hospital of Pittsburgh of UPMC studied the growth factor neuregulin-1 (rNRG1) and its ability to stimulate growth of heart muscle cells (cardiomyocytes). Researchers injected rNRG1 into newborn mice with induced heart muscle defects and found that cardiomyocytes divided, heart function improved, and scarring was significantly reduced. The application of rNRG1 to heart muscle samples obtained from infants undergoing cardiac surgery boosted cardiomyocyte production. In clinical trials, adult medicines were ineffective for pediatric heart disease, and the need for pediatric-specific heart failure therapies has become more recognized, said Bernhard Kühn, MD, visiting associate professor of pediatrics and director of research in the pediatric cardiology division. “Delivering agents early on that encourage the heart to make new cardiomyocytes could help the heart perform normally and reduce the risk of developing heart failure later in life.”

The cancer protein mTOR was thought to control a critical protein-production process in cancer cells called cap-dependent translation. However, a study by University of Pittsburgh Cancer Institute researchers showed that a different protein, CDK1, can also play a role in the process. Researchers studied this interaction while observing a viral oncoprotein that allows a typically harmless virus to transform healthy cells into cancer cells. Scientists have long believed that cap-dependent protein synthesis was disabled during cell division. Yet the study showed that the process could be enabled and that CDK1 can substitute for mTOR. Lead author Masahiro Shuda, PhD, assistant professor of microbiology and molecular genetics, used a technology known as flow cytometry and special fluorescent tags to identify and observe cells undergoing division. After mTOR was inactive, Shuda saw that CDK1 was still present and able to permit protein synthesis and further cell division and tumor growth. The finding could mean that developing drugs targeting not only mTOR but also CDK1 could be in store. “Now, we still can’t say that this process involving CDK1 contributes to cancer — that’s something we’ll tackle with future research,” said Patrick S. Moore, MD, MPH, senior author and American Cancer Society Professor, Pittsburgh Foundation Professor of Innovative Cancer Research, and Distinguished Professor of Microbiology and Molecular Genetics. “But it does point toward a fundamental control mechanism in cell biology and leads to the interesting possibility that creating or combining cancer drugs, so that they inhibit both mTOR- and CDK1-related protein synthesis, could be a very useful therapy to pursue.”
LIFESTYLE AND GENETIC VARIANT MAY AFFECT CHRONIC PANCREATITIS RISK

Smoking and drinking are risk factors for a range of diseases, including chronic pancreatitis. A Pitt study found that a genetic variant coupled with these factors further increases risk. Acute pancreatitis, characterized by inflammation causing nausea, vomiting, and severe pain in the upper abdomen, is often triggered by excessive drinking or gallbladder problems, said senior investigator David Whitcomb, MD, PhD, Giant Eagle Foundation Professor of Cancer Genetics; professor of cell biology; chief of the Division of Gastroenterology, Hepatology, and Nutrition, Department of Medicine; and professor of human genetics, Graduate School of Public Health. If chronic disease sets in, the organ becomes scarred from inflammation. Still, some heavy smokers and drinkers don’t develop the disease. By examining the CTRC gene, which protects pancreatic cells from a digestive enzyme inside the pancreas, researchers found a variant that may fail to protect against this enzyme, resulting in pancreatic inflammation and scarring.

“This finding presents us with a window of opportunity to intervene in the disease process,” Whitcomb said. “When people come to the hospital with acute pancreatitis, we could screen for this gene variant.” The variant’s presence, along with heavy smoking and drinking habits, may indicate an opportunity to offset chronic disease by changing behavior and perhaps further reduce risk through targeted therapies.

LACK OF ENZYME DISTORTS MITOCHONDRIA AND CAN LEAD TO IPF

Old age is a risk factor for a number of diseases, including idiopathic pulmonary fibrosis, or IPF. When researchers at Pitt examined cells from the scarred lungs of IPF patients, they found misshapen, dysfunctional mitochondria, leading them to explore a potential connection. “Other chronic and progressive diseases we see with aging, such as Parkinson’s disease, have been recently associated with mitochondrial abnormalities, so we wondered if that was occurring in IPF,” said senior investigator Ana L. Mora, MD, assistant professor of medicine in the Division of Pulmonary, Allergy, and Critical Care Medicine. “It was a simple question, but it hadn’t been asked before.” IPF is characterized by progressively scarred lung tissue, leading to breathing problems and even death. In patients, researchers found lower expression levels of the enzyme PINK1, which influences mitochondrial shape and function, and mice lacking PINK1 were susceptible to pulmonary fibrosis. Low PINK1 is associated with increased age, which helps explain why older adults are prone to IPF, Mora said.

HIGH STRESS LEVELS AFFECT TREATMENT RESPONSE IN PUERTO RICAN CHILDREN WITH ASTHMA

Children exposed to psychosocial stressors like violence or poverty more often suffer from long-term health problems, ranging from cancer to depression to asthma. In a recent study of Puerto Rican children, researchers from Pitt and other institutions demonstrated that high childhood stress levels are associated with reduced bronchodilator response (BDR), resulting in decreased effectiveness of short-acting, inhaled agents aimed at preventing asthma morbidity. The study further showed that a polymorphism in ADCYAP1R1, a gene that regulates anxiety, is associated with reduced BDR. Researchers also showed a connection between high maternal stress levels and BDR reduction. “This is the first demonstration of a link between stress or anxiety and reduced response to bronchodilators, as well as a potential pathway for this association,” said senior investigator Juan C. Celedón, MD, DrPH, UPMC Niels Jerne Professor of Pediatrics; chief of the Division of Pulmonology, Allergy, and Immunology, Department of Pediatrics; and professor of medicine.
Levels of human Y-box binding protein 1 (YB-1) have been shown to correlate with drug resistance and poor patient outcomes in a variety of cancers. Pitt researchers have uncovered a strong link between YB-1, a known prognostic biomarker for breast cancer and a believed prostate-cancer-progression agent, and two new classes of RNAs. This link could reveal new pathways to combat cancer. The team found that YB-1 is associated with many small RNAs, or microRNAs, as well as with thousands of RNAs that were never before known. “We conducted functional assays on one of these RNAs and found that it had the ability to suppress cancer cell growth when it interacted with YB-1,” said senior author Donald B. DeFranco, PhD, professor of pharmacology and chemical biology, School of Medicine. He added that more work must be done to understand the influence of the new RNAs on cancer progression and, potentially, other diseases.

**RNA**

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**PROTEIN’S LINK TO NEW CLASSES OF RNA COULD PREDICT NEW CANCER PATHWAYS**

**ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH**

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**YOUTUBE VIDEOS DEPICTING DRUNKENNESS OFFER ONE-SIDED PORTRAYAL TO PEERS**

The most-viewed videos on YouTube that depict drunkenness offer a one-sided portrayal to peers. The most-viewed videos on YouTube that depict drunkenness offer a one-sided portrayal to peers. The most-viewed videos on YouTube that depict drunkenness offer a one-sided portrayal to peers.

**ANNALS OF NEUROLOGY**

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**CORD BLOOD TRANSPLANTATION PREVENTS BRAIN DAMAGE FROM INHERITED DISEASE**

Hurler syndrome is a rare, severe neurodegenerative disease in children who lack an enzyme needed to break down complex sugars, resulting in organ deterioration, brain damage, and death in childhood. However, a Pitt and Children’s Hospital of Pittsburgh of UPMC study that followed 31 children with Hurler syndrome for several years showed that umbilical cord blood transplantation from unrelated donors can stop the disorder’s progression if administered before 9 months of age. Stem cells from the cord blood provide a source of the enzyme for the deficient cells. Normal cognitive development typically follows if a child is treated before 9 months; those treated at 12 to 25 months showed moderate to severe cognitive delays, indicating that they had too much brain damage even at this early age. “Unfortunately, early diagnosis is often difficult, as their initial symptoms may be common in the general population,” said Maria Luisa Escolar, MD, MS, director of the Program for the Study of Neurodevelopment in Rare Disorders, Children’s Hospital of Pittsburgh of UPMC, and associate professor of pediatrics. “There is a need for newborn screening for Hurler syndrome and similar neurodegenerative diseases.”

**JOURNAL OF CLINICAL INVESTIGATION**

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**PRESERVING LIVER FUNCTION COULD BE POSSIBLE WITH GENE THERAPY**

After observing that not all who develop cirrhosis, or scarring of the liver, progress to liver failure, Pitt researchers found that gene function could affect whether liver failure develops. The research team used rat models of liver disease after noting scar tissue development associated with cirrhosis. Even with large amounts of scar tissue, there are often enough cells to carry on normal liver function, said Ira Fox, MD, professor of surgery, School of Medicine, and director, Center for Innovative Regenerative Therapies at Children’s Hospital of Pittsburgh of UPMC and the McGowan Institute for Regenerative Medicine. Previously, Pitt researchers found that liver cells taken from animals with cirrhosis, but without liver failure, functioned properly when transplanted into another animal. Cells transplanted from animals with cirrhosis and liver failure, however, did not function normally at first. In this group, researchers noted low activity in the genes that control proteins affecting liver function and a decline in a factor called HNF4. After restoring production of HNF4, liver cells resumed normal function in both lab tests and in the rats. The investigators found that if HNF4 could be re-expressed in animals with end-stage cirrhosis, liver failure and hepatic scarring could be reversed. If this work could be applied to humans, it would ultimately reduce the need for liver transplants and help those too sick for a transplant. Investigators are now exploring means and drugs that could block pathways to HNF4 failure for clinical trials.
RESEARCHERS IDENTIFY MUTATIONS LEADING TO CONGENITAL HEART DISEASE

In 2009, the National Heart, Lung, and Blood Institute of the National Institutes of Health launched the "Bench to Bassinet" program as a national effort to learn about the formation of the cardiovascular system and pinpoint the genetic determinants of structural heart disease. At Pitt, principal investigator Cecilia Lo, PhD, Dr. F. Sargent Cheever Professor and chair of developmental biology and professor of pediatrics and of clinical and translational science, and fellow researchers used mouse models to identify and describe the core set of genes responsible for structural heart defects. Through the six-year effort, the team identified mutations associated with congenital heart disease in 94 genes, many not previously known to cause the disease. Researchers used fetal ultrasound exams on more than 100,000 mice that were exposed to chemicals that cause random gene mutations to uncover mutations that can cause congenital heart disease. Through conducting ultrasound scans on mouse fetuses, the study revealed more than 3,000 independent cases of congenital heart defects. Researchers then sequenced the genes of the mice with the defects and compared them to the unaffected fetuses to identify 145 recessive mutations in 94 genes. This study yielded findings that point to the hair-like cellular organelle known as cilia as playing a central role in disrupting developmental processes that can contribute to structural heart defects. "We were surprised to learn many of the genes recovered from the screen were related to the cilia, or cilia-transduced cell signaling," Lo said. "These findings suggest that cilia play a central role in heart development, including regulating patterning left-right asymmetry in the cardiovascular system critical for efficient oxygenation of blood from air in the lungs."

VACCINE MAY PREVENT MERS SPREAD

In the Middle East, camels are used for transportation and as a food source. Yet they’re also believed to be the source of Middle East respiratory syndrome (MERS). The deadly disease, which does not always show symptoms, can spread to humans. The virus has proliferated to the United States and other countries through passenger air travel. However, an international team of scientists led by Pitt researchers has developed a vaccine that protects mice against the virus and is a promising candidate for immunizing camels. "If we can protect camels against MERS, we may make it so difficult for MERS to infect people that its threat to the human population is significantly diminished," said senior author Andrea Gambotto, MD, associate professor of surgery and of medicine.

STORAGE TECHNIQUE IMPROVES LIFESPAN OF LIVERS WAITING FOR TRANSPLANT

The discard rate of livers recovered for transplantation stands between 20 and 40 percent. Livers for transplant are currently preserved by cold static preservation (CSP), a method that cools tissue to four degrees Celsius to slow metabolism while reducing oxygen demand from cells. However, most of the organs considered as expanded criteria donors are worsened by CSP, according to senior investigator Paulo Fontes, MD, associate professor of surgery and deputy director, McGowan Institute for Regenerative Medicine. In preclinical studies aimed at prolonging organ lifespan, researchers used a machine-perfusion (MP) device to pump a newly developed, oxygen-rich fluid into livers to support adequate function during organ preservation. With this system, the liver cells’ integrity and vital metabolic activities are preserved, Fontes said. Donor livers were immersed in a chilled fluid at 21 degrees Celsius with a hemoglobin-based oxygen carrier component. The fluid was actively perfused through the blood vessels to promote effective oxygenation of the tissues ex vivo. After nine hours of organ preservation, researchers transplanted six pigs with the livers preserved with MP and compared them to six pigs transplanted with livers stored conventionally by CSP. All the pigs transplanted with livers after MP survived, had excellent liver function postoperatively, and produced more bile compared to the pigs with conventionally stored livers, of which only 33 percent survived. "It was immediately obvious to us that the pigs that received MP livers looked much healthier and easily moved around their pens just hours after they woke up from the surgery," Fontes said. Analyses of various clinical and laboratorial features, including transcriptomics, inflammatory mediators, and metabolomics, revealed that the MP livers were better preserved. Researchers hope the new preservation technique will lead to more livers being available for transplant and shorten wait times for those needing transplants. They hope to conduct clinical trials soon.
of the Richard King Mellon Foundation Institute for Pediatric Science and director of the University of Pittsburgh Asthma Institute; professor of medicine, of immunology, and of clinical and translational science for clinical use.” The research team also included Sally Wenzel, MD, professor of medicine and of immunology; Stephen O’Keefe, MD, visiting professor of medicine, Division of Gastroenterology, Hepatology, and Nutrition. To study diet’s effect on colon cancer risk, Pitt researchers had a group of 20 African Americans and 20 Africans from rural South Africa swap typical diets for two weeks. To ensure compliance, all participants were studied in-house, where food was cooked and given under strict supervision. After analyzing alterations of gut bacteria in both groups, the study found that each group took on the other’s risk of colon cancer as shown by biomarkers. In each group, the turnover rate of cells in the intestinal lining, levels of fiber fermentation, and markers of bacterial metabolic activity were characteristic of the other group’s typical patterns. The study may be indicative of diet’s significant impact on colon cancer occurrence. “These findings are really very good news,” O’Keefe said. “In just two weeks, a change in diet from a Westernized composition to a traditional African high-fiber, low-fat diet reduced these biomarkers of cancer risk, indicating that it is likely never too late to modify the risk of colon cancer.”

**JOURNAL OF CLINICAL INVESTIGATION**

**BOOSTING INHIBITOR PROTEIN LEVELS COULD HELP SEVERE ASTHMA PATIENTS**

About 10 percent of asthma patients have severe asthma, in which the airways become inflamed and constricted. According to Pitt researchers, these patients exhibit markedly different immune responses than those with milder forms of the lung condition; even with high doses of corticosteroids, they do not get better. Researchers observed that, in severe asthmatics, immune cells called CD4 T-cells with high doses of corticosteroids, they do not get better. Researchers created a mouse model comparable to human severe asthma patients and observed that mice lacking the interferon gamma. Researchers created a mouse model comparable to human severe asthma patients and observed that mice lacking the interferon gamma gene could not be induced to develop severe asthma. The study used computer modeling to learn that, as interferon gamma levels rise, levels of the protein secretory leukocyte protease inhibitor (SLPI) drop. Follow-up experiments showed that boosting SLPI levels reduced airway hyper-reactivity in animal models. “We’d like to better understand why severe asthma occurs in most people right from the start,” said Anuradha Ray, PhD, professor of medicine and of immunology. “We also want to find agents that can raise SLPI levels for clinical use.” The research team also included Sally Wenzel, MD, professor of medicine, of immunology, and of clinical and translational science and director of the University of Pittsburgh Asthma Institute; Prabir Ray, PhD, professor of medicine and of immunology; Jay Kolls, MD, professor of pediatrics and of medicine and director of the Richard King Mellon Foundation Institute for Pediatric Research; and others.

**NEW ENGLAND JOURNAL OF MEDICINE**

**BOOSTING QUALITY OF CARE ALSO IMPROVES RACIAL EQUITY OF CARE**

When U.S. hospitals strive to improve quality of care, they can also improve equity of care across racial and ethnic lines. Disparities in quality of care for black and Hispanic patients with heart attack, heart failure, and pneumonia lessened considerably between 2005 and 2010, according to a study in the *New England Journal of Medicine*. The study compared more than 12 million acute care admissions to U.S. hospitals for these conditions and found that, as hospitals improved quality of care, more equal care resulted for minorities at institutions that deliver both large and small amounts of medical care to these potentially vulnerable patients. Actions such as providing aspirin to and quickly clearing blood clots in heart attack patients were examined. “In the future, it will be critically important to demonstrate that these improvements in health care delivery are accompanied by better patient outcomes,” said senior author Michael Fine, MD, MSc, professor of medicine.

**SCIENCE TRANSLATIONAL MEDICINE**

**COMPUTER SIMULATION EFFECTIVE FOR REPLICATING TRAUMA OUTCOMES**

Most patients who require trauma care are likely to survive, thanks to surgery and proper care. During treatment, however, some may experience complications from inflammation such as multiple organ failure, which can be difficult to predict. Pitt researchers recently devised a computer simulation, or *in silico* model, of the body’s inflammatory response to traumatic injury that replicated known outcomes to predict results for individuals and populations. By using blood samples from 33 survivors of traumatic injury and data from nearly 150 other trauma patients, researchers generated a computer model of 10,000 virtual patients with similar injuries to replicate outcomes. The model successfully replicated results such as length of hospital stay and degree of multi-organ dysfunction. By looking at interleukin-6 (IL-6), a marker of inflammation, the model predicted that individuals who made more IL-6 were less likely to survive, yet predicted otherwise at the population level. In actuality, IL-6 levels did not significantly affect survival rates, indicating the importance of analyzing multiple factors in simulation. “Dynamic computational models like ours that simulate multiple factors that interact with each other in complex diseases could be a more efficient and accurate way of predicting outcomes for both individuals and populations,” said Yoram Vodovotz, PhD, professor of surgery, of immunology, of computational and systems biology, and of clinical and translational science; professor of bioengineering, Swanson School of Engineering; and professor of communication science and disorders, School of Health and Rehabilitation Sciences. “Then we can pursue those avenues that have the greatest likelihood of success in clinical trials.”
Use of PET/CT scans on tuberculosis-infected humans and macaques has shown certain drugs’ effectiveness at treating drug-resistant tuberculosis, or XDR TB, which typically involves taking as many as six drugs for two years to clear. While the drug linezolid was previously shown to be effective for XDR TB, researchers further examined linezolid and another similar drug by performing PET/CT scans on TB-infected humans and macaques. The lung imaging revealed that both subject types have similar disease profiles and that drug treatment improved the conditions. The findings show that a macaque model and PET scanning can be effective in determining which drugs are more likely to be successful in clinical trials. “Our challenge is to find more effective treatments that work in a shorter time period,” said senior investigator JoAnne L. Flynn, PhD, professor of microbiology and molecular genetics and of medicine.

Pressure ulcers, which cause discomfort and functional limitations, are a common secondary complication after spinal cord injuries. They impair movement and can lead to infection and even death. When immobility disrupts oxygenation in a patient lying down, the sudden and repeated resumption of blood flow after turning the patient in bed may cause pressure sores, a process that is further stimulated by the lack of innervation to the tissue in spinal-cord-injury patients. Immobility and decreased or absent sensation increase a patient’s risk of developing a pressure sore, but often detection of the sore is delayed, complicating treatment. To study the biologic pathways surrounding ulcer development following spinal cord injury, Pitt researchers created an in silico model to simulate ulcer development. By using photos taken at various stages of ulcer development, researchers were able to create a computational model in which they could alter factors like inflammatory mediators and tissue oxygenation to accurately portray and manipulate realistic-looking “virtual ulcers.” Researchers then simulated anti-inflammatory interventions and found them effective only if applied very early during ulcer development. It’s hoped that the model could eventually be used to analyze a photograph of a patient’s reddened skin to determine whether an ulcer is likely to develop. “Computational models like this one might one day be able to predict the clinical course of a disease or injury, as well as make it possible to do less expensive testing of experimental drugs and interventions,” said senior investigator Yoram Vodovotz, PhD, professor of surgery, of immunology, of computational and systems biology, and of clinical and translational science; professor of bioengineering, Swanson School of Engineering; and professor of communication science and disorders, School of Health and Rehabilitation Sciences. The research team also included Gwendolyn A. Sowa, MD, PhD, associate professor of physical medicine and rehabilitation and assistant dean for medical student research, and others.

About 20 percent of infertile men have azoospermia, meaning they don’t produce sperm. Conventional genetic testing usually doesn’t reveal a chromosomal problem, however, leaving the cause unknown. Researchers at Pitt and Magee-Womens Research Institute (MWRI) conducted a study showing that mutations in the maternal X chromosome prevent development of viable sperm in some infertile men. The team scanned the genomes of 15 men with azoospermia and found that part of the DNA coding of the TEX11 gene on the X-chromosome was missing. The missing component results in meiotic arrest, disrupting cell division and causing infertility. The Pittsburgh research team, in collaboration with centers in Poland and Germany, also found the TEX11 gene mutation in six other men with azoospermia. Up to 15 percent of mutations are shown in patients with azoospermia and meiotic arrest. This protein study confirmed the relationship of TEX11 mutations and protein defects. A likely explanation is that an older father, whose precursor sperm cells are more likely to acquire a mutation, could pass the defect to a daughter, whose son would likely be incapable of producing viable sperm, said coprincipal investigator Alexander Yatsenko, MD, PhD, visiting assistant professor of obstetrics, gynecology, and reproductive sciences, visiting assistant professor of pathology, and MWRI investigator. “This research suggests that screening for TEX11 gene mutations might be useful in cases of otherwise unexplained azoospermia,” Yatsenko said. “It might be possible to one day correct these problems with gene therapy and other interventions.”

Treating ischemic stroke typically calls for the “clot-busting drug” tPA to dissolve the blood clot. However, researchers from Pitt and other institutions have shown that endovascular treatment (ET), a clot-retrieval procedure, can dramatically improve patient outcomes after acute ischemic stroke. Clinicians insert a tube through an artery in the groin and thread it up to the brain vessels. Then, a retrievable stent opens the blocked vessel and pulls the clot out as it’s retracted. With ET, mortality was reduced from two in 10 to one in 10 patients, and overall positive outcomes for stroke patients increased from 30 to 55 percent. Endovascular treatments were first developed in the 1990s, but the procedure is possible today only because of technological and systems-of-care advances allowing faster and more effective flow restoration, as well as better imaging studies, said Tudor Jovin, MD, associate professor of neurology and of neurological surgery and director, UPMC Stroke Institute. The findings reported by a trial (ESCAPE) conducted at 22 sites across the U.S., U.K., South Korea, and Canada, confirmed positive results previously reported by a study conducted in the Netherlands. Pitt helped lead three of the five recent major trials on endovascular treatment and stroke worldwide, Jovin said.
Sisterly Love Forges New Scientific Path To Save Jon
Lisa Boyette, MD, PhD, needs to beat primary sclerosing cholangitis (PSC) before the disease destroys the liver of her brother, Jonathan. With help from mentors at Pitt and across the country, Boyette has sidestepped the traditional framework of biomedical scientific inquiry to find a more agile way.

“I didn’t want to take 10 years to get to a place where I was starting to help him,” Boyette says of her decision to found a nonprofit organization after completing postdoctoral training at the University of Pittsburgh’s Thomas E. Starzl Transplantation Institute (with which she remains affiliated) in 2014.

Called SAVE JON, the organization aims to concentrate the widest possible range of expertise on new treatments to halt or slow the progression of PSC, an autoimmune disease that typically leads to liver failure within 10 years of diagnosis. Jon Boyette was diagnosed with PSC five years ago at age 21.

Other than liver transplant, no therapies that can stop PSC exist today, and patients are at risk of developing cancer before a donor organ is available. SAVE JON, however, is quickly gathering high-level support.

“These types of diseases are usually underrepresented with respect to research focus. Very few have even heard of PSC, let alone developed programs, because the market’s so small. But those lives are no less valuable.”

—STEPHAN

“These types of diseases are usually underrepresented with respect to research focus,” says SAVE JON cofounder Dietrich Stephan, PhD, professor and chair of human genetics in Pitt’s Graduate School of Public Health. “Very few have even heard of PSC, let alone developed programs, because the market’s so small. But those lives are no less valuable.”

Boyette’s drive appeals to Stephan, who founded a number of biotech companies before joining Pitt’s faculty. With Jeremy Berg, PhD, Pittsburgh Foundation Professor of Personalized Medicine in the Department of Computational and Systems Biology and Pitt’s associate senior vice chancellor for science strategy and planning, health sciences, Stephan urged Boyette to forge a path to discovery that matched the boldness of her vision.

In addition to Stephan, SAVE JON’s board includes Boyette’s postdoctoral mentor, Fadi Lakkis, MD, Frank and Athena Sarris Professor of Transplantation Biology in Pitt’s Department of Surgery.

Also on board is retired NFL head coach and Pitt football legend “Iron Mike” Ditka, whose Chicago Bears roster included running back Walter Payton. Known as “Sweetness” for his effortless grace, Payton died in 1999 from PSC-related liver cancer.

The innovative and extensive “collaboration, partnership, and engagement” for which SAVE JON’s backers strive are exactly the kinds of activities being advocated by Pitt Chancellor Patrick Gallagher, who announced a renewed University-wide focus on research-based entrepreneurship in early 2015.

SAVE JON has established a base within the offices of the Pittsburgh Technology Council. More information is available at https://save-jon.org.
Pittsburgh is a city on the rise. 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.
In 2000, Maria Luisa Escolar, MD, MS, met a family whose young daughter had been given a terminal diagnosis and a heartbreaking recommendation. “A doctor had told them their baby had Krabbe disease and to just take her home to die,” says Escolar, associate professor of pediatrics in the School of Medicine.

Like many physicians, Escolar had never seen a patient with the disease (only one in 100,000 people in the U.S. are affected by Krabbe), so she researched it exhaustively. Krabbe—the common name for globoid cell leukodystrophy—is caused partly by a deficiency of the galactosylceramidase enzyme, which interferes with the growth and maintenance of myelin in the brain's nerve cells and throughout the nervous system. Symptoms usually appear before the child's first year but can be confused with colic and other common infant problems, which makes diagnosis difficult for physicians unfamiliar with the disease. The children's muscles progressively weaken, affecting their ability to move, chew, swallow, and breathe, among other effects. Without early diagnosis, children with Krabbe often die by age 2.

Escolar immediately felt a calling to help these children and their families. Because of a dearth of physicians with knowledge in the field, Escolar quickly found herself becoming an expert in rare neurodegenerative diseases, including Krabbe, Hurler syndrome, metachromatic leukodystrophy, and many others. She developed a multidisciplinary program to treat the children and enable clinical research and training in their diseases while she was at the University of North Carolina, Chapel Hill. In 2011, Escolar joined the faculty of Pitt’s School of Medicine and moved her work to Children’s Hospital of Pittsburgh of UPMC, where she is founding director of the Program for the Study of Neurodevelopment in Rare Disorders (NDRD)—the only program of its kind in the world. The only physician in the program, Escolar is sought after because her expertise is rare. She cares for more patients with Krabbe and other leukodystrophies than any other physician in the world; and she trains medical students, residents, and physicians in different specialties to recognize and treat these disorders.

“NDRD has a training element because we realized that the more physicians who have experience with rare diseases, the better they can recognize symptoms and save critical time in diagnosing and getting help for children,” says Escolar.

At Children’s, Escolar’s patients often meet with multiple specialists over several days, including physical therapists, neurologists, and psychologists. She calls it her “snapshot approach”—information from all of the appointments provides her with
a full portrait of the disease’s effect on the child at that point in its progression, which she then summarizes in her recommendations to the family. Her office coordinates everything, including specialist appointments, finding out-of-town families a place to stay, and helping with insurance approvals.

“We meet with families and help translate all the tests and appointments their children have had, and we try to predict what their lives will be like in the next six months,” says Escolar. “The families appreciate knowing. The diseases change as they progress, so it can be like having a new disease every two weeks. Parents will say, ‘Today my child is talking to and smiling at me, but what will happen tomorrow?’ It’s extremely difficult.”

“People sometimes wonder how we can go through a child’s deterioration,” says Escolar, “but families need help so badly during that process. It’s very rewarding to help a child not suffer.”

A large, flat-screen monitor hangs just opposite Escolar’s desk. She uses UPMC’s telemedicine program and NDRD’s Virtual Medical Home to help diagnose and coordinate care for patients around the world—anyone who has access to a computer hooked up to a camera can speak to her.

Escolar is committed to translating her research into knowledge for her patients and their families. She says she noticed that families, clinicians, and basic science researchers didn’t interact much, so she started two groups—the Krabbe
Translational Research Network, to provide that interaction between basic and clinical researchers, and the Family-Centered Krabbe Translational Research Network, to help families understand the research process and learn how to advocate for improving treatments in a useful, informed way.

Research is just as important to NDRD’s mission as are its clinical services and training. Escolar has been studying the progression of several rare neurodegenerative diseases and therapy outcomes since she started this work and has been having success with neuroimaging, behavioral outcomes, and umbilical cord blood transplantation following early detection.

“We make the patient the center of everything. It’s all about improving their quality of life—families can’t find this anywhere else, and that’s what makes this program unique.”

One muggy day in June, nearly 60 rising high school seniors gathered at Hillman Cancer Center to begin their summer break. Their “break” involved participating in the University of Pittsburgh Cancer Institute (UPCI) Academy, a cancer research-focused didactic and learning experience. Over the next eight weeks, the students, almost half of whom are from minority or disadvantaged backgrounds (and thus are underrepresented in the biological sciences), pursued their interest in cancer-related careers by learning about cancer biology, clinical care, and research. Each student completed an independent research project in a mentor’s lab. At the conclusion of the program, they displayed their communication skills by presenting their research orally and in a poster session. They also visited Carnegie Mellon University to present their research and tour the campus.

The program, now in its seventh year, was a finalist for Coro’s 2015 Martin Luther King Jr. Leadership Award in the Distinguished Organizational Leadership category. (Coro Pittsburgh is a program designed to revitalize communities by providing training, mentoring, coaching, and other support for leaders.) In 2014, Michael T. Lotze, MD, program director, won a Carnegie Science Award for Leadership in STEM Education for his work on the academy and other efforts.

UPCI’s scholars are selected for the competitive program based on academic prowess and status as an underrepresented minority or disadvantaged student. The program also admits some scholars based on the strategic partnerships of UPCI—for example, from the Center for Integrated Oncology in Cologne, Germany, which now has a parallel program.

“Doing such research is an incredibly beneficial experience for the high school students,” says Lotze, who is a Pitt professor of surgery, of bioengineering, and of immunology; vice chair for research in the Department of Surgery; and assistant vice chancellor for sponsored training grants, health sciences. “We’ve had students go on to academic programs in fields ranging from biomedical informatics to pathology.”

An academy scholar in 2013, Paula Lee-Oesterreich, now resident advisor for the 2015 summer, says that her experience was a once-in-a-lifetime opportunity. She worked in the labs of Yuan Chang, MD, Distinguished Professor of Pathology and UPMC Professor of Cancer Virology Research, and Patrick S. Moore, MD, MPH, Distinguished Professor of Microbiology and Molecular Genetics, Pittsburgh Foundation Professor of Innovative Cancer Research, and director of the Cancer Virology Program at UPCI.

“You just usually can’t get this kind of experience before college otherwise,” says Lee-Oesterreich. “I mean, it’s unbelievable to be working with researchers who discovered two viruses that cause cancer,” referring to Chang and Moore’s codiscovery of Merkel cell polyomavirus and Kaposi’s sarcoma-associated herpesvirus. Lee-Oesterreich, now a Pitt undergrad planning to major in either biology or mathematical biology, continued to work in the Chang-Moore lab after her experience in the academy.

“After doing this, I saw that you can really take what you learn in class and apply it to medicine, which is really cool,” she continues. “I always wanted to go to medical school, but this experience definitely solidified my decision to become a physician-scientist.”
PITCH PERFECT

Pitt med students’ talents have always transcended academics. The School of Medicine intentionally seeks creative students with a wide range of experiences, skills, and interests. For singers, the a cappella group PalPITTations is a creative outlet for students from all six health sciences schools.

Some of the group’s concerts serve as fundraisers for the Birmingham Free Clinic, a no-cost clinic in Pittsburgh’s South Side that provides health care for uninsured and medically vulnerable individuals. At a recent performance, the group swayed and grooved through a lively rendition of James Brown’s “I Feel Good.” Their beat-keeping movements and rhythmic bass vocals were a testament to the title of the concert, “Shockable Rhythm.” For “Seasons of Love” from the musical Rent, the group gathered around an overhead mic, providing harmonies and percussive notes while med student Terry Kho sang, How do you measure the life of a woman or man?

It’s an inspiring question for aspiring physicians. After witnessing a display of their artistic abilities—cultivated while holding demanding “day jobs” as medical students—it’s easy to conclude that these students are ready to contribute something special to the world, in the medical realm and beyond.
PalPITTations
With opiate use and overdoses steadily increasing in Pennsylvania, local health care providers, including School of Medicine faculty, are working together to help an especially vulnerable population—women who are pregnant and use opiates. One of the first programs of its kind in the country, the Pregnancy Recovery Center (PRC) was created by Magee-Womens Hospital of UPMC, the Allegheny County Office of Behavioral Health, and four managed-care organizations—Community Care Behavioral Health Organization, UPMC for You, Gateway Health, and United Healthcare for Families and Communities—to provide consistent treatment for opiate dependence and prenatal care and delivery. Operating as a medical home, PRC arranges for women to receive behavioral counseling and offers treatment with buprenorphine, a drug used to treat opiate addiction, on a weekly outpatient basis. Buprenorphine is similar to methadone but has fewer side effects, doesn’t require hospitalization to administer (which reduces costs significantly), and has a much shorter weaning time for infants. The treatment is integrated with the women’s routine obstetrical care, and women continue to receive care four to six weeks after delivery.

“Pregnancy can be an opportune time to help women struggling with addiction,” says Dennis H. English, MD, recently retired clinical professor and vice chair for clinical operations in the Department of Obstetrics, Gynecology, and Reproductive Sciences and vice president of medical affairs at Magee-Womens. “The instinct to care for a newborn baby can be a powerful motivating factor.”

Currently in its first year, PRC has had nearly 70 women go through the program so far. English says all of the women in the program have shown much better outcomes and lower costs compared with women receiving methadone treatment or a similar withdrawal drug from their health care providers. The majority of infants delivered in the program have not required treatment for neonatal abstinence syndrome, which occurs when a fetus has been exposed to opiates in the womb and needs treatment for substance withdrawal after birth.

“We try to take a supportive, nonjudgmental approach, and I think that’s why we’re finding more moms wanting to be in the program,” says English.

On a stage in Scaife Hall that typically hosts top-tier scientific talks, one blustery February night saw a presentation more typical of, say, Saturday Night Live. The chiseled bodies of several Pitt med students were on display dancing, gyrating, and vying for the title of “Mr. Pitt Med.”

In its ninth year, the 2015 Mr. Pitt Med contest featured a superhero theme. The annual fundraiser mixes male beauty pageant and talent show rakishness to support the International Health Initiative, a Pitt-based student group that partners with global health charities. The contestants’ flex poses drew the loudest swoons, applause, and cheers from a raucous audience of mostly fellow students, and the swimsuit competition prompted more than a few suggestive jokes from the Pitt med faculty judges.

The talent show portion comprised breakdown routines, pop-song lip syncing, and one particularly macho Superman med student hefting female students over his head like barbells. First-year med student Adel Mahjoub’s Aqua Man skit saw him fighting off a man-eating dolphin, a hilarious highlight that helped him win the show’s Mr. Congeniality award, given to the contestant who raised the most money from the audience.

A black silhouette of Pittsburgh’s skyline provided the perfect backdrop as fourth-year student Jordan Knox slinked around the stage in a Batman-theme bathrobe that gave way to, yes, Batman underwear and Batman knee-high socks. During the Q and A, Knox stated that, if declared the winner, he’d reinstate the school’s honors/pass/fail grading system—and eliminate the fail option. After prolonged deliberation, judges declared Knox the victor.

In the spirit of a hero, Knox was off to pick up his girlfriend from the airport after the show, just in time for Valentine’s Day. This year, the show donated proceeds of more than $1,600 to Shoulder to Shoulder, a group that brings volunteer physicians, medical residents, and students to San José del Negrito, Honduras, to make house calls, provide checkups for children, and administer other health care services in this poor, rural area with limited access to health care.

Before the crowd dispersed, Knox, who had himself volunteered in Honduras with Shoulder to Shoulder, reminded all that their attendance and ticket purchases would help bring vital services to an underserved Honduran population.
With grateful appreciation for their generosity, we acknowledge the following individual, corporate, and foundation donors whose contributions of $500 or more to the University of Pittsburgh School of Medicine, University of Pittsburgh Cancer Institute, and Western Psychiatric Institute and Clinic of UPMC between July 1, 2013, and June 30, 2014, have supported us in our academic, research, and clinical missions.

Thank you.
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After finding out he had ALS, Mr. Alexander remembered feeling “shoved around” by the diagnosis for about two weeks, but then he and his wife found the strength and inspiration to take charge of their new lives. They created Live Like Lou, a donor-advised fund with The Pittsburgh Foundation, and kicked it off with their 20th wedding anniversary celebration. Live Like Lou, a name Mrs. Alexander created, has a three-part mission—to raise awareness of ALS, funds for patient care, and funds for research. The Alexanders wanted to strengthen the ALS research already happening in Western Pennsylvania. They began collaborating with Peter L. Strick, PhD, Thomas Detre Professor of Neuroscience, Distinguished Professor, and chair of neurobiology, on the creation of the Live Like Lou Center for ALS Research within Pitt’s Brain Institute, of which Strick is founding director. They committed to raising $2.5 million over five years, with Pitt matching that amount and hoping to raise $10 million for the center. They consider the partnership with Pitt the capstone achievement of their efforts.

“We’ve been able to do a lot of good with Live Like Lou because of The Pittsburgh Foundation, Pitt, and our incredible circle of friends,” said Mrs. Alexander. “It’s a brick-and-mortar indication of how we’ve persevered.”

The good the Alexanders have done with their organization includes raising more than $1.25 million so far. They have standing fundraising events, like a 52-mile bike ride and annual golf outings, but they’re quick to mention community support that comes in smaller increments, like donations through bat/bar mitzvahs, a child who rang their doorbell with a sandwich baggie of change from her lemonade stand, and their swim club’s swim-a-thon benefiting Live Like Lou.

“We live among some generous, high-energy, supportive people,” said Mrs. Alexander. “We’re the luckiest family. This is a mixed bag of blessings and devastating losses. But, we’ve had the privilege of seeing the strength and courage of our friends and having complete strangers become like family to us.

“The underlying goal was to get our kids through this in a way that doesn’t ruin them and in a way that teaches them that, when something bad happens, you have to find a path through it. They’ve observed their dad deal with incredible losses, and they’ve seen him be so strong.”

Mr. Alexander said, “If someone asks my kids what it was like to have a dad with ALS, they’ll be able to say I ran an organization and that I was the same old guy who told bad jokes and sang really off-key.”

Mr. Alexander died from complications of ALS in spring 2015. Pitt awarded him the Bill Baierl Distinguished Alumni Service Award a few months later.

“There’s a quote Neil said that I love,” said Mrs. Alexander. “He said, ‘I’ve never been hungry, I’ve never been lonely, and I’ve never lived in fear. I’ve been lucky.’ It references Lou Gehrig and is so elegant. It’s a glimpse into his character and why he’s willing to put himself forth to do all this. He’s taking the rest of us along, and I feel pretty lucky, too.”

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**NEIL AND SUZANNE ALEXANDER AND THE LIVE LIKE LOU ORGANIZATION**

On June 29, 2011, at the age of 46, Neil Alexander was diagnosed with amyotrophic lateral sclerosis (ALS) — a disease with a two- to three-year life expectancy, with no helpful therapy or cure. Mr. Alexander remembered breathing through the next 30 seconds of shock before asking his doctor what he should do. The reply? “Do what you love.” So, the devoted husband, father of two, and self-described “do-er” did just that. He continued to work as a financial planner, spent time and took vacations with friends and family, and was guided by three powerful motivators for how to live his remaining years — his two children and Lou Gehrig.

In the weeks following the diagnosis, “A good friend reminded us that our children were watching how we dealt with this and that we were modeling for them how to act when life gets tough,” said Mr. Alexander. “Suzanne always says, ‘Our kids are watching us.’ ”

Mr. Alexander was also inspired by a biography of Lou Gehrig, the famed baseball player who developed ALS and for whom the disease is commonly known. A baseball fan, Mr. Alexander was struck by Gehrig’s dignity and famous speech as he bowed out of the game.

“Gehrig said he had gotten a bad break but that he considered himself the luckiest man on the face of the earth,” said Mr. Alexander. “Suzanne and I related to that. We have a strong marriage, two healthy kids, wonderful family and friends, and many reasons to be grateful. We became concerned about other families facing the same situation that didn’t have the resources we did.”
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*BEFORE AN INDIVIDUAL’S NAME INDICATES THE PERSON IS DECEASED
In the summer of 2011, Gertrude and Homer Chisholm were headed to a baseball game when they received a phone call no parent wants to get. A hospital in Narvik, Norway, had admitted their 20-year-old son, Reid. He had just completed an outdoor leadership program in the Arctic Circle and was due to return home soon. The doctors said they weren't sure what was wrong with Reid. They thought he had had an allergic reaction and possibly an infection but that he would probably leave the hospital soon. When the Chisholms spoke to their son, his voice was barely audible. After a few frustrating days of changing diagnoses, Mrs. Chisholm flew to Norway.

“Reid couldn’t speak very well, had lost a considerable amount of weight, and was having great difficulty swallowing,” said Mrs. Chisholm. “I was running around Narvik, trying to find Gatorade or Jell-O because he couldn’t even attempt to eat the coffee, tea, toast, and other foods the hospital was giving him. The doctors said he had a severe case of strep and an oral virus, for which they were treating him, but that there was nothing else they could do except wait for him to get better.”

Reid would appear to be getting better, but sometimes, especially overnight, he became very ill. After several days of rest, the doctors felt Reid was stable enough to fly home. At a hotel at the Oslo airport, Mrs. Chisholm became alarmed when she witnessed Reid becoming violently ill during the night. By morning, he had improved enough that they felt he could make the trip home—something they were both desperate to do. One hour before departure, Reid’s condition worsened. He was rushed to Oslo University Hospital and stabilized.

“They reassured me Reid wasn’t going to die, but he was in significant pain, and his emotional state had greatly deteriorated,” Mrs. Chisholm said. “Although the quality of care appeared more competent in Oslo, Homer and I decided enough was enough, and he chartered an ambulance plane that flew us directly home to Cleveland.”

At University Hospitals of Cleveland, an ear-nose-and-throat doctor took one look at Reid’s throat and gave them shocking news: Reid’s injuries were the result of a caustic burn that had damaged his mouth, throat, and esophagus. The doctor said he looked like a cancer patient after months of radiation.

While the Chisholms say they will never know for certain how Reid ingested a toxic substance, they believe he was poisoned by an alkaline substance that was put into his drink at a bar in Narvik. They and Reid’s doctors suspect it was lye, which is used in Scandinavia to cure fish. When ingested, lye causes immediate burns, but it has no odor or taste and can be taken accidentally in dangerous quantities.

Although Reid finally had a diagnosis and tentative treatment plan, the Chisholms grew frustrated with his care. He hadn’t swallowed in six months—not even his saliva—and was fed through tubes in his small intestine and stomach. They searched for an expert in esophageal injury and found James D. Luketich, MD, Henry T. Bahnson Professor and chair of cardiothoracic surgery at the University of Pittsburgh. Dr. Luketich treats thoracic and esophageal injuries, diseases, and cancers and is world-renowned for successfully completing complex operations using minimally invasive techniques. Within days, they had their first meeting with Dr. Luketich, who spent two hours reviewing Reid’s injury with them.

“Once we saw Dr. Luketich, there was no looking back,” said Mr. Chisholm.

Reid underwent dozens of procedures to prepare for a planned esophagectomy and gastric reconstruction. About nine months after his injury, Reid was finally able to swallow. Following the final procedure before his planned surgery, Reid developed endocarditis. Dr. Luketich told the Chisholms that the infection was too widespread, and he strongly recommended an emergency esophagectomy. “It was a shock but necessary,” said Mrs. Chisholm. “Dr. Luketich removed Reid’s esophagus and said it looked like a dried-up piece of wood.”

After six weeks of recovery from the surgery, Dr. Luketich performed a 15-hour gastric reconstruction, even removing part of Reid’s collarbone to fashion a new esophagus out of two-thirds of his stomach.

The Chisholms were so thankful for Dr. Luketich’s expert care of their son that they established the Reid H. Chisholm Esophageal Research Fund in the Department of Cardiothoracic Surgery to support life-changing research on esophageal disorders.

“I would walk to the end of the earth for Dr. Luketich. It’s as simple as that,” said Mrs. Chisholm. “He saved my son. We feared Reid would never be able to eat or drink again, to live a normal life, but he has recovered so much, so quickly. You’d never know what happened to him by looking at him. Reid being so steadfast and strong throughout made it easy for us to be strong.”

After the gastric reconstruction, Reid began a gradual eating program. Eventually, on his 22nd birthday, he was able to eat a piece of apple pie. His parents treasure the memory of the big grin on his face.
A medical student, Richard Pan turned down what some might have considered a golden opportunity with the National Institutes of Health (NIH). He had applied for and was offered a virology research fellowship for the summer between his second and third years at the University of Pittsburgh School of Medicine. But he had a competing offer from the U.S. Public Health Service’s National Health Service Corps.

“Everyone said, ‘Well, of course you choose NIH,’” says Dr. Pan. “It looks great on a résumé, and virology was a hot topic then because of the HIV/AIDS crisis.”

But the med school’s dean of student affairs at the time didn’t think NIH was the obvious choice. Knowing that he already had research experience and an undergraduate degree in biophysics, the dean suggested that Dr. Pan, as a “big-picture guy,” might be well-suited to the service corps position.

“So, I turned down NIH to work at a clinic in York, Pennsylvania,” says Dr. Pan. “The clinic director had a broad view of health and talked about the social determinants of health before people were talking about social determinants. It was one of the turning points of my career.”

That noteworthy career has included a degree in public health from Harvard University and many hours in community clinics as a pediatrician, in addition to directing the pediatric residency program at the University of California, Davis. He’s the founder of Communities and Health Professionals Together, which connects resident physicians with disadvantaged communities, and cofounder of Healthy Kids Healthy Future, which has provided health, dental, and vision coverage to more than 65,000 California children. During the 2009 economic recession, when California government was mired in gridlock and clinics were closing because the state couldn’t pass a budget or pay employees, he decided to run for election to the California State Assembly. In 2010, he won a seat as a Democrat that had been held by Republicans for the previous 28 years. After two terms, he was elected to the state senate in 2014.

Even as a medical student, Dr. Pan wanted to be engaged in policy and planning. He wrote articles for the Allegheny County Medical Society, some of which criticized the medical school’s curriculum. Impressed with this med student’s ideas, faculty members invited him to be involved in curriculum development. He was elected class president. Feeling that his time at Pitt significantly influenced him and his perspective on medicine, Dr. Pan, who earned his MD here in 1991, has encouraged classmates to make gifts to the School of Medicine, and he supports the Medical Student Scholarship Fund. “I was concerned about the cost of medical education and the level of medical student debt being so high—nothing like when I was there,” says Dr. Pan. “Pitt’s trying to attract the best medical students, and some of those students have need. I was fortunate myself and got a little financial aid, so I want to help create opportunities for other students.”

In December 2014, a large measles outbreak began in Disneyland, causing 127 cases. It spurred Dr. Pan to coauthor Senate Bill 277, eliminating loopholes that allowed California parents to opt out of immunizations because of personal beliefs and permitting only medical exemptions. Though the bill was signed into law and has many supporters, not everyone welcomes Dr. Pan’s public health efforts. Some people have protested the law, and Dr. Pan has received death threats. But he remains steadfast in his conviction and knowledge that vaccinations are important for public health.

“In 1991, when I was a fourth-year medical student, I worked at a community health center in Philadelphia during a measles outbreak,” Dr. Pan says. “More than 900 people got infected, and nine children died. They told us in medical school that we probably wouldn’t see measles in our practices unless we went overseas. When I’m asked why I’m doing this bill, I say that I’ve seen measles, and it’s awful. Children and adults die because of measles; it’s not just a rash. People say that no one died in the measles outbreak in Disneyland, but more than 20 people were hospitalized. We’re fortunate that no one died. The roots of all of this started at Pitt. Immunizations were a big deal in our education, with Pitt being the home of the polio vaccine. My interest in community health is partly driven by the values instilled in me in my medical education. I want to help provide more opportunities to students who can then go and do the same things with their careers,” says Dr. Pan.
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n 2007, David Levidow opened The New York Times and read an article about Alzheimer’s disease (AD) research that impressed him and spurred him to action. Mr. Levidow was intrigued by the article’s frequent mention of University of Pittsburgh researchers and their development of Pittsburgh Compound B (PiB), a radioactive dye used with positron emission tomography to see the location and distribution of the beta-amyloid plaque deposits associated with Alzheimer’s in the brains of living humans. Before PiB, the plaque could not be seen until after death when an autopsy was performed.

Mr. Levidow knew only too well the effects of Alzheimer’s, after having nursed his mother, Lulu, for three years until she died from complications of the disease. After reading the article, he immediately called the University of Pittsburgh’s Alzheimer Disease Research Center (ADRC) to speak with the codiscoverer of PiB, William E. Klunk, MD, PhD, Distinguished Professor of Psychiatry, professor of neurology, and codirector of the center, about a planned gift. The center put him in touch with James Olsen, MBA, and Gary Dubin, major gift officers with Pitt’s Medical and Health Sciences Foundation.

Mr. Levidow was the son of Russian immigrants and cofounded a successful law firm specializing in worker’s compensation rights. After Mr. Levidow’s mother’s death and in his retirement, he became increasingly focused on preparing his own estate, most of which he had decided to earmark for AD research support. Mr. Olsen cultivated Pitt’s relationship with Mr. Levidow for several years until Mr. Levidow’s unexpected death in 2013.

“He was a warm, generous man,” said Mr. Olsen. “He expressed some interest in endowing a chair in Alzheimer’s research to honor his parents but worried whether his gift amount would meet the endowed chair minimum. He gave more than enough.” At the time of Mr. Levidow’s bequest to establish the Lulu P. and David J. Levidow Fund, The Pittsburgh Foundation had been exploring ways its donors could support AD research at Pitt. The Pittsburgh Foundation is a community foundation with more than 2,000 funds, each set up by different donors for different purposes.

“We’re particularly interested in helping to endow chairs,” said Jeanne Pearlman, PhD, senior vice president for program and policy at The Pittsburgh Foundation. “They allow Pitt to attract and retain the finest talent in the world. The generosity of Mr. Levidow and of our donors all came together at the same time.”

Pitt pooled Mr. Levidow’s gift and funds from The Pittsburgh Foundation to create two endowed chairs—one each for Dr. Klunk and Oscar L. Lopez, MD, who is a professor of neurology and of clinical and translational science, as well as being director of ADRC, one of the first centers funded by the National Institute on Aging to advance and coordinate study of Alzheimer’s disease.

“Technically, we could give the money anywhere,” said Dr. Pearlman. “But the fact that we have one of the leading research institutions in the world five blocks away is extraordinary.

“The generosity of spirit people like Mr. Levidow have—people who simply want to leave a legacy to make life better for others without seeking recognition in their lifetimes—is remarkable.”
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