UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE

NEXT

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WHAT'S NEXT?

Good question. The simple answer is that *NEXT* is the annual report of the University of Pittsburgh School of Medicine.

At Pitt, "What's next?" is a question we ask ourselves all the time. *What's next in medical education? What's next in biomedical research? What's next in clinical care? What's next in community engagement and health care innovation?* Like all scientists worth their salt, we strive to provide the answers.

Global collaborations are next. The marriage of basic and clinical science is next. What's next is a biomedical research institution with a commitment to turning scientific discoveries into healthier people. It's the academic medical center of the future and the next generation of physician-scientists in the same place. *Pittsburgh* is next.

A VIEW FROM HERE

WHERE THE FUTURE IS NOW

A Message from the Dean

Out of the blue, someone recently asked me, "What do you see from your office?"

There are multiple ways to answer that question. In the literal sense, I look out my window here in Scaife Hall and see a street informally known as "Cardiac Hill" for both its proximity to UPMC Presbyterian Hospital and the cardiovascular challenge it presents daily to pedestrians, runners, and bicyclists. Across the street I see the University's Petersen Events Center, where one of the top NCAA basketball programs in the country plays to sell-out crowds.

It's a fine view, but I much prefer the figurative response to the question. In that sense, the view from my office is like none other. It is informed by the 13 years I have spent in this singular place as senior vice chancellor for the health sciences and dean of the School of Medicine. From this vantage, I see the outlines, as well as some very particular details, of what I believe is the academic medical enterprise of the future—one that is global, nimble, translational, and engaged on every level with the society it serves.

Pittsburgh is a unique place in so many ways, as anyone who has spent time here knows. Geographically and culturally, it is neither East Coast nor Midwest. It has elements of both regions, while drawing an Appalachian flavor from the hills and hollows of Western Pennsylvania. Pittsburgh is a city that remembers the recent trauma of de-urbanization and the loss of industry, even as it embraces the current reversal of these trends. The city bears its history like a coat of arms. And the people who call Pittsburgh home—even "transplants" such as myself who are transformed by living here—are justifiably proud that its resurgence is envied and emulated across the country and around the globe.

I remember my early days here as a time of discovery and serendipity. Here was one of the top public research universities, and one that was on a decidedly upward trend. The School of Medicine was in a particularly good position, with a long track record of biomedical research and innovation; a vigorous academic community that included leaders in psychiatry, organ transplantation, pediatrics, and endocrinology, among other fields; and a thriving clinical partner in UPMC.

As I put down roots and inevitably became a Pittsburgher, those of us at the University carried on the daily work of developing this academic jewel in its Appalachian setting. For the School of Medicine, this meant expansion on several fronts. We added state-of-the-art facilities for biomedical research and teaching, and we recruited extraordinary faculty members to occupy them. We anticipated and kept pace with critical shifts in science by creating new academic departments in emerging scientific disciplines like biomedical informatics,

cardiothoracic surgery, computational and systems biology, critical care medicine, developmental biology, immunology, and structural biology. All the while, we accelerated the University of Pittsburgh's rapid climb in the ranks of research institutions. Having cracked the top 10 list of recipients of National Institutes of Health funding in 1997, the University of Pittsburgh cemented its position within this enviable echelon by climbing as high as fifth in recent years.

Which brings us to today's question: "What's next?" The School of Medicine at the University of Pittsburgh has emerged as a national leader in education and research, with highly accomplished students and graduates who go on to train at many of the top programs in the country. We are known for our commitment to rigorous training programs for physician-scientists and as the home of curricular innovations such as the scholarly project (see page 39). As a research institution, we have exploited our traditional strengths and added a broad base of basic science expertise that is focused on translational science.

What's next, then, is the academic medical center of the future, where the research portfolio embraces both basic science and clinical trials of new therapies, supported by an institutional commitment to translating discoveries into healthier patients in the community. It is a place where investigators arrive knowing that they are expected to do imaginative, boldly creative work with colleagues from many different disciplines—the sort of collaborations that lead to unexpected ideas and great leaps forward.

While firmly anchored in and responsive to its community, this academic medical center is one that is global and agile, with a dramatic and expanding vision of the diverse collaborations and partnerships that will strengthen its position and improve the human condition.

> I invite you to explore the pages of this report and discover for yourself that the University of Pittsburgh School of Medicine is among those rare places where the physicians and scientists of the future are now.
>
> **ARTHUR S. LEVINE, MD**
> Senior Vice Chancellor for the Health Sciences and Dean, School of Medicine

OFFICIALS FROM THE UNIVERSITY OF PITTSBURGH AND TSINGHUA UNIVERSITY MET IN BEIJING IN APRIL 2011 TO RATIFY AN AGREEMENT THAT MAKES TWO YEARS IN PITTSBURGH PART OF THE BIOMEDICAL RESEARCH TRAINING OF TSINGHUA STUDENTS.

A HISTORIC UNIVERSITY COLLABORATION

Beijing in Pittsburgh

A few months ago, Yigong Shi felt that his university was missing something. As dean of Beijing's prestigious Tsinghua University School of Life Sciences, Shi, a PhD, was searching for a U.S. school to send Tsinghua medical students to for biomedical research experience. Meanwhile, the University of Pittsburgh's Arthur S. Levine, MD, senior vice chancellor for the health sciences and dean, School of Medicine, had been traveling to China in an effort to build relationships with universities there. This was unfolding while Jeremy Berg, PhD, was about to step down as director of the National Institute of General Medical Sciences to accept a senior position at Pitt. Berg knew both men and, sensing an extraordinary opportunity, introduced them.

Levine and Shi met in Beijing, and, though he had a couple of other high-profile U.S. universities interested, Shi chose the University of Pittsburgh for the unique collaboration. Beginning in the summer of 2012, 25 to 45 Tsinghua medical and graduate students each year will travel to the University of Pittsburgh to enter a two-year biomedical research training program at the medical school. The two years the students spend at Pitt will complement the six years of training they'll receive in China. In addition, the two universities will take turns hosting an annual symposium featuring researchers from both institutions.

A big deal? Simply put, yes. Here's why: Tsinghua is highly regarded for its top science and engineering programs. It has produced one-fourth of the members of the Chinese Academy of Sciences and many prominent leaders in China, including Hu Jintao, China's current president. Shi, himself, is a celebrated structural biologist, renowned for discovering a novel path in cancer treatment. He is also what the Chinese call a "sea turtle"—part of a wave of Chinese professionals who gave up prominent positions abroad to return home. In 2008, while he was professor of molecular biology at Princeton University and after an 18-year residence in the United States, Shi surprised the science community when he turned down a $10 million Howard Hughes Medical Institute investigatorship and resigned from Princeton to return to Tsinghua, his alma mater. (Shi earned his undergraduate degrees in biology and mathematics there.) After careful consideration, Shi chose to partner with Pitt. Levine considers it a win-win, noting, "Our medical school is almost unique among U.S. medical schools for the extraordinary growth and visibility we've had in a short period of time. The advantage for Tsinghua students coming to Pitt is that they will become immersed in a peer-reviewed research culture to complement their medical studies. And, we're adding to our lab workforce medical students who are the best-of-the-best from a country of almost 1.4 billion people and who will, undoubtedly, become leaders of medicine and biomedical research in China. They, presumably, will have a good experience in Pittsburgh, and that will create a durable and important relationship."

Shi knew Berg (who is now Pitt's associate senior vice chancellor for science strategy and planning) from his grad school days. He received his PhD in molecular biophysics from Johns Hopkins University, where Berg was his thesis advisor; and he was eager for Tsinghua students to share the experience and opportunities he had with a U.S. education. Now, in a sense, Tsinghua students will share Shi's mentor, as well—Berg will oversee the program at Pitt.

Recently Dean Shi shared his perspective on the partnership and on medicine and science education in both countries.

PITT MED: The United States faces a dearth of physician-scientists. Can you talk a bit about the importance of graduating more physician-scientists in China?

YIGONG SHI: China has 7 million physicians, of whom 2 million have received reasonable training and are providing quality health care to the majority of China's 1.35 billion people. However, China has a severe shortage of physician-scientists. Compared to the U.S., the situation is much direr.

Why this partnership? Why Pitt?

The medical school at the University of Pittsburgh is exceedingly strong in basic biomedical and translational research. The affiliated hospitals are first rate in the U.S. and perhaps in the world. In addition, the size of the medical community at Pitt is large enough to accommodate our students. Last, but not least, I have been favorably impressed by the vision and leadership of Dr. Levine.

You've spoken of modernizing Tsinghua's teaching philosophy. What did you mean?

The traditional teaching method in China emphasizes passive listening and memorization. Students seldom raise critical questions and comments. I have been advocating for active learning in the classroom (engagement between teachers and students, small class size, active discussion groups, student presentations, research-based learning, etc.) ever since I returned to China.

You are a product of both the American and Chinese educational systems. What do you see as the strengths and weaknesses of each?

The strength of the Chinese educational system is clear: Students receive comprehensive and sound knowledge in mathematics and natural sciences. The weakness is also evident: The system does not encourage innovation! In the United States, it is quite the opposite: Innovation is encouraged by the educational system, but students are only exposed to shallow training in mathematics and natural sciences.

Faculty members here are excited to work with students from Tsinghua. What might they learn from them?

They will be impressed by the overall "raw" quality of the students. But these students need to be carefully crafted before they can be truly "useful" to our society.

As one of China's "sea turtles," how has the experience been for you and your family?

So far, so good. I am physically and mentally exhausted in China, much more so than in the U.S. But I am happy and enormously enjoy what I am doing for my home country.

GLOBAL REACH

Med students at Pitt enjoy opportunities to experience clinical rotations in hospitals located in Ireland and Sicily. With both the School of Medicine and UPMC increasingly engaged with partners around the globe, such opportunities will only become more common. Pictured (right) is the Mediterranean Institute for Transplantation and Advanced Specialized Therapies. This hospital in Palermo, Sicily, is a joint project of UPMC, Pitt, and the Italian government. In nearby Carini, the same public-private partnership is generating another game-changing facility—the Ri.MED Biomedical Research and Biotechnology Center, which is scheduled for completion in 2015. Phase II of the project will include a 300-bed hospital directly linked to the biomedical research facility.

CLINICAL COLLABORATION

Partnering Is a Plus

Through its affiliation with UPMC (University of Pittsburgh Medical Center), the School of Medicine offers students opportunities for clinical training, educational experiences, and research in virtually any medical specialty. Although legally separate and distinct entities, the School of Medicine and UPMC share mutual interdependence and a synergy that is reflected in a common commitment to excellence in education, research, clinical care, and entrepreneurship.

As an integrated global health enterprise and one of the nation's leading academic health care systems, UPMC has nearly 5,000 affiliated physicians, including more than 2,700 employed by the health system and nearly 1,400 who are also full-time faculty of the School of Medicine; more than 20 tertiary care, specialty, and community hospitals serving 29 counties throughout Pennsylvania; as well as specialized outpatient facilities, cancer centers, rehabilitation facilities, retirement and long-term care facilities, imaging services, doctors' offices, and a health insurance plan covering 1.58 million members. As of August 1, 2011, the UPMC Medical Education Program has 1,091 medical residents and 322 clinical fellows in programs approved by the Accreditation Council for Graduate Medical Education, plus 62 clinical fellows in other programs. What this means for medical students is near limitless opportunity for engaging their interests and for finding mentors in a wide variety of clinical and scientific specialties.

The core of the health system is located in the Oakland, Shadyside, and Lawrenceville neighborhoods of Pittsburgh, where the following health care facilities are interwoven with University of Pittsburgh facilities: UPMC Presbyterian, UPMC Montefiore, Eye and Ear Institute, Magee-Womens Hospital of UPMC, Western Psychiatric Institute and Clinic of UPMC, Hillman Cancer Center, UPMC Shadyside, and Children's Hospital of Pittsburgh of UPMC.

UPMC's clinical programs have earned international recognition, drawing patients from around the world. In addition, the medical center is now transporting its expertise to other countries, including Italy (where it manages the 70-bed Mediterranean Institute for Transplantation and Advanced Specialized Therapies in Palermo) and Ireland (where it manages UPMC Beacon Hospital near Dublin) as well as ventures in Japan and China.

Something there is that doesn't love a wall,
That sends the frozen-ground-swell under it,
And spills the upper boulders in the sun,
And makes gaps even two can pass abreast.
–Robert Frost

TEAR DOWN THESE WALLS

Multidisciplinary Approach

Students and faculty who come to the University of Pittsburgh learn quickly that around here, we don't like walls.

As Robert Frost would say, "Before I built a wall I'd ask to know what I was walling in or walling out, and to whom I was like to give offence." Indeed.

A key element in Pitt's dramatic growth over the past several decades was the establishment of multidisciplinary collaborations and centers that knock down the artificial barriers that separate schools, departments, and even universities. In our view, it's this approach that often leads to unexpected, creative ideas and big discoveries.

Take one example of a successful experiment that entered the scientific literature in 2011. A team of Pitt researchers reproduced the brain's complex electrical impulses using *in vitro* models made of living brain cells that provide an unprecedented view of the neuron activity behind memory formation.

Research suggests that working memories are formed when the cortex, or outer layer of the brain, launches into extended electrical activity after the initial stimulus. However, observing this activity in real time is nearly impossible.

The Pitt team fashioned ring-shaped networks of brain cells that could transmit an electrical impulse and remain in a state of persistent activity associated with memory formation. They disabled the cells' inhibitory response, excited the neurons with an electrical pulse, and were able to observe cells in the excited state for up to 12 seconds.

The work, published in the Royal Society of Chemistry journal *Lab on a Chip*, is a fine example of the multidisciplinary approach, involving faculty from the School of Engineering (Henry Zeringue, PhD, assistant professor of bioengineering) and the School of Medicine (Guo-Qiang Bi, PhD, associate professor of neurobiology) and carried out by a graduate student in bioengineering (Ashwin Vishwanathan, now a PhD graduate).

PITT & CMU LEVERAGE STRENGTHS

Two-Campus Collaboration

The research described above was conducted through a truly extraordinary collaboration between the University of Pittsburgh and Carnegie Mellon University (CMU) called the Center for the Neural Basis of Cognition. CNBC, as it is known, has been described as a veritable "Who's Who" of neuroscience.

Led by Peter Strick, PhD, distinguished professor of neurobiology at Pitt, and Michael Tarr, PhD, CMU professor of psychology, CNBC leverages Pitt's strengths in basic and clinical neuroscience and those of Carnegie Mellon in cognitive and computational science to support a coordinated cross-university research and educational program of international stature. The center boasts more than 200 world-class faculty and trainees investigating the cognitive and neural mechanisms that give rise to biological intelligence and behavior. Research topics include affective, cognitive, linguistic, perceptual, motor, and social systems in both normal and disordered populations. The center also promotes the translation of findings from basic research into applications for medicine, education, robotics, and artificial intelligence.

The linked campuses of Pitt and CMU are home to many such collaborations and joint efforts. Another of particular note is the NIH-supported Medical Scientist Training Program, one of the premier MD/PhD programs in the country (see story on page 40).

A MIGHTY MODEL ORGANISM

The Fish that Saved Kidneys

The School of Medicine's extensive research facilities house more than hives of busy biomedical researchers. Of unique value are the colonies of model organisms that swim and squirm and make so many areas of research possible, including drug discovery and design, vaccine development, and basic science research into developmental biology, vascular biology, and more. The University faculty harbors considerable expertise in the biology of a traditional laboratory workhorse, the microscopic worm *C. elegans*. Even more noteworthy, the recently constructed Biomedical Science Tower 3 includes one of the world's largest colonies (more than 10,000 tanks) of an increasingly important model organism, the zebrafish.

Though you may not feel much kinship with fish, human biology is fundamentally very similar to that of *Danio rerio*. Scientists share a fondness for its facile genetics and transparent embryos. Take, for example, a few Pitt scientists working on the science of recovering from kidney injury. Kidneys subjected to acute injury can heal themselves, but do so slowly and often with scarring. In 2008, with the help of Billy Day, PhD, a University of Pittsburgh professor of pharmaceutical sciences, Neil Hukriede, PhD, associate professor of developmental biology in the School of Medicine, found and tested a compound that may hold promise for patients experiencing renal injury. The compound, of a class called histone deacetylase inhibitors (HDACi), reversed the effects of acute kidney injury in zebrafish and did so without scarring. Hukriede, in collaboration with investigators at Vanderbilt University, won a three-year, $2.8 million federal stimulus funding grant to pursue this line of inquiry further, this time in mice. "It's very exciting," Hukriede says. "So far, we've seen a 30 to 40 percent increase in the rates of renal recovery in zebrafish and mice. We're hoping to find molecules that are more effective and show no toxicity at lower doses." Hukriede and Pittsburgh colleagues, many of whom are members of the University's Drug Discovery Institute, will identify the compounds that may spur kidney regeneration. Vanderbilt collaborators will use the mouse model to see whether the compounds are hitting their targets and to test their toxicity.

NOT YOUR AVERAGE MED STUDENTS

The Next Generation of Physician-Scientists

(LEFT) AMAR MEHTA
(MIDDLE) KEERAT SINGH
(BELOW) CYNTHIA GRADY

Going just by the numbers, students at Pitt's School of Medicine are a formidable group. Their MCAT scores are among the highest in the nation; and there is broad diversity in race, ethnicity, and sex. Delve a bit deeper into the well of people behind the numbers, and one will find even more reasons to be intrigued and impressed.

Take medical students Amar Mehta, Ajeet Mehta, and Keerat Singh. In addition to their studies, the three started the Sikh Medical Society to address the health concerns and disparities of people in Sikh communities in the U.S. The trio's plan, which Amar calls a "marriage between activism and education," is to publish a magazine about common health care issues within the Sikh community and to provide health fairs in gurdwaras across the country. Topics would include nutrition, how to reduce barriers to health care, and how to get the most out of a visit to the doctor, to name a few. Ajeet says, "We hope the health fairs are one day in the year people mark on their calendars to set aside and assess where their health is and what they can do to better the health of their families." The goals are lofty; but the health fairs they envision are already happening, and the Mehtas (identical twins who were accepted into the School of Medicine's Guaranteed Admit Program out of high school) and Singh have always been hard workers. "The Sikh Medical Society was something I've wanted to do for a long time," says Singh, whose father is a mechanic and who grew up working alongside him. (He hopes to transfer his mechanical skills to the field of orthopaedic surgery.) "I've seen chronic disease take more of a toll on people in my community because they don't have the early access to or knowledge about health care."

"The Sikh Medical Society was something I've wanted to do for a long time, says Singh. "I've seen chronic disease take more of a toll on people in my community because they don't have the early access to or knowledge about health care."

The Mehtas and Singh aren't the only compelling medical students. Cynthia Grady grew up in an extended family that included up to six foster "cousins" at any given time. Her family established a human services organization that spawned a group home and other programs for adolescents. Jeremy Kauffman planned on entering the ministry until he worked in Peru with homeless children and realized that being a doctor was both a calling and a powerful way to help people. Ben Meza completed an internship in Ecuador with pediatric surgeons, which awakened in him a sense of social justice and the desire for a career that would help even the most underserved populations achieve the kind of health they deserve.

Pick a student and ask, "Why medicine? Why Pitt?" The stories behind the numbers reveal individuals who are as fascinating as they are inspiring.

VIROLOGIST RECOGNIZED WITH "GENIUS" GRANT

New MacArthur Fellow

Elodie Ghedin, PhD, a University of Pittsburgh assistant professor of computational and systems biology, is one of 22 high achievers to win a prestigious 2011 MacArthur Fellowship. The $500,000 grant over five years can be spent as she sees fit.

The fellowship program recognizes talented individuals who have shown extraordinary originality and dedication in their creative pursuits and a marked capacity for self-direction. The John D. and Catherine T. MacArthur Foundation's three criteria for selection of fellows are exceptional creativity, promise for important future advances based on a track record of significant accomplishment, and potential for the fellowship to facilitate subsequent creative work.

As a master's student from the University of Quebec at Montreal doing field work in West Africa in the early 1990s, Ghedin found a passion for studying parasites causing serious or fatal diseases like sleeping sickness and river blindness in millions of people across the developing world. She honed her DNA-sequencing skills at The Institute for Genomic Research, which is now part of the J. Craig Venter Institute.

Now at the University of Pittsburgh School of Medicine, she leads collaborative projects to map the genes of those parasites — as well as more common sickness-causing viruses like influenza — to learn how they adapt and evolve so they can be targeted by new vaccines and drugs.

You call many of the pathogens you study "neglected." Why?

They're categorized as neglected tropical diseases, and that's because they affect mostly people in developing countries. ... The worm I work on, *Brugia malayi* [which can cause elephantiasis], is really not something that's funded regularly. But it affects a huge number of people in the world, mainly in Africa and Southeast Asia.

How could your work help fight disease?

We try to use genomic information to develop functional assays that would allow us to better understand how the parasite functions. When you think about it, parasites are incredible machines because they've learned to adapt to their host, and they're able to secrete things into their environment to modulate and change the immune system of their host. So one aspect I'd like to really look at is what do parasites put out in their environment that is controlling the immune system? When you look at the genome of any of these parasites we've ever decoded, you can see about 20 to 40 percent of the genes are complete unknowns, and we call them "orphans." They don't match anything we've found before, we don't know what they do, so there's a huge potential for discovery.

What plans do you have for the money?

The timing was unbelievable because funding was becoming very difficult in the U.S., and I think everywhere else. The research I do — working on neglected parasitic diseases — is, of course, not very high up on the priority list of what gets funded. I have a grant ending on this parasite I work on, *Brugia malayi* , and no follow-up funding, and I thought, "I'm going to have to just stop this kind of research." This really allows me to continue and even go into riskier research because nowadays you really have to have a sure thing when you submit grant proposals — money is so tight reviewers want to make sure you won't be wasting the money that you'll be given. I think that really feeds into the MacArthur, because they want you to be creative. ... I think I'll use it very well. I'm not going to buy a boat with it (laughs).

The MacArthur Foundation is famously secretive about its fellowships. How did you learn you'd won one?

I was at a seminar and I got this cryptic e-mail that had a subject line, "Confidential," and then it simply said: "Dear Dr. Ghedin, I would appreciate if you would call me back at work or at home," signed Bob Gallucci. All week, I had been getting these weird Nigerian-type e-mails saying they had millions of dollars they would give me, so I was really annoyed. And I turned to my colleague and I said [sarcastically], "Unless this guy is giving me a boatload of money, I'm not calling back." But I Googled Bob Gallucci and I said, "Wait a minute, it's the MacArthur Foundation's president. They probably want to talk to me about somebody they want to give the award to. There's no way they would call me." So I reached the president, and he says, "Are you alone?" I thought I was going to faint.

FUTURISTIC TECHNOLOGY TODAY

Skin Gun Saves Both Superheroes and Everyday Heroes

In an instant, a summer bonfire went horribly wrong for an off-duty police officer named Matthew Uram. As he stood next to the fire, a partygoer tossed gasoline onto the flames. Parts of Uram's face and neck, plus his entire right arm from shoulder to wrist, sustained serious first- and second-degree flash burns. "I was in so much pain," he says, describing his arm as "charred like a hot dog left too long on the grill." Ten days later, Uram underwent a revolutionary experimental treatment that had been used only a handful of times in Europe before his 2009 visit to the burn unit at UPMC Mercy.

To get started, Uram had to sacrifice a bit more healthy skin. Working with burn surgeon Alain Corcos, MD, Jörg Gerlach, MD, PhD, professor of surgery and of bioengineering, removed a thin, two-centimeter by two-centimeter square of skin from his right hip. The skin was cut into smaller pieces and put into a solution with enzymes that help to isolate epidermal stem cells called basal keratinocytes. The solution was run through a sieve and set spinning in a centrifuge for several minutes. The process yielded three 2-milliliter syringes filled with a solution rich in Matthew Uram's own skin cells.

Corcos loaded the syringes onto an instrument known as the skin gun. He sprayed the solution in a gentle mist over Uram's burned skin. The whole process took about 90 minutes to prepare and apply. "It's like a paint sprayer, but it's more sophisticated and computer-controlled," says Gerlach, whose case report was published in the June 2011 issue of the journal *Burns*.

Within four days of treatment, Uram's burn wounds had closed and he was sent home. "He did not need a wound dressing anymore, which is amazing," says Gerlach, adding that there were no complications, inflammation, or infection. As healing progressed, the functionality and appearance of the new skin improved. After a year, only minor skin discoloration remained.

"We hope to address third-degree burns in the future," says Gerlach.

That future is now in the comic book world of Marvel's *Avengers Academy*, where Hank "Giant-Man" Pym taps the latest burn-treatment technology to help his friends "Reptil" and "Tigra" to recover from their injuries. Superheroes may save the world, but first the University of Pittsburgh saves them. And just *how cool is that?*

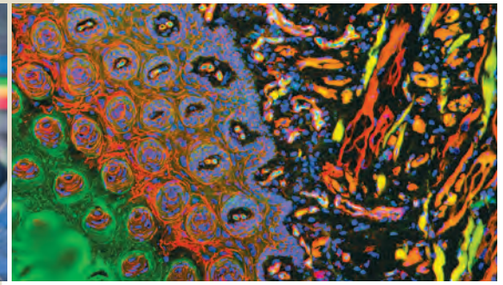
REAL-WORLD BURN RESEARCH AT PITT SEEMS SO FUTURISTIC TO MARVEL THAT IT WAS INCLUDED IN AN ISSUE OF THE COMIC BOOK *AVENGERS ACADEMY*.

Giant-Man
SIZE-CHANGING
SCIENTIST SUPREME

Jocasta
SYNTHETIC BEING.
LOYAL TO GIANT-MAN OF ULTRON?

Jörg Gerlach, MD, PhD
PROFESSOR OF SURGERY AND OF BIOENGINEERING

"WITHIN FOUR DAYS OF TREATMENT HE DID NOT NEED A WOUND DRESSING ANYMORE, WHICH IS AMAZING," SAYS GERLACH. "WE HOPE TO ADDRESS THIRD-DEGREE BURNS IN THE FUTURE."



SIMON WATKINS, PHD

When Simon Watkins was a graduate student, he spilled a cup of coffee on an electron microscope that probably cost more than all his years of education to that point. Quick: What to do? "I slammed the off switch—Bam! I let it dry out, took the microscope apart, and washed it," Watkins says in his lilting English accent. "This happened Saturday morning. I put it back together again, and it worked fine! Five years later, they were scrapping this microscope. Someone called me and said, 'They blamed you for it.'"

Apparently, a few telltale java stains were found when the microscope was dismantled. By then, Watkins was long gone (not to mention a bit more careful with his coffee and rather skilled with a microscope). After departing the University of Newcastle upon Tyne with his PhD at age 25, Watkins held postdoctoral positions at the Pasteur Institute in Paris and Harvard's Dana-Farber Cancer Institute. While involved with seminal studies of muscle structure and muscular dystrophy, he learned to use the most advanced optical microscopes and to exploit computer-aided image analysis.

In 1991, he arrived at the University of Pittsburgh, where he founded the Center for Biologic Imaging (CBI). Over the past two decades, he and associate director Donna Beer Stolz, PhD, have painstakingly built it into a unique, world-renowned facility.

Every top-tier research institution has at least a handful of sophisticated microscopes scattered about its campus. Typically, they are proprietary—dedicated to particular research groups, departments, or divisions, each with its own protocols, permissions, and restrictions. Researchers can pool these resources and declare that they have an imaging center, but that makes for a somewhat "virtual" center.

CBI is different. Its microscopy suites, computer labs, and wet and dry bench space occupy 5,500 square feet of prime real estate in the Thomas E. Starzl Biomedical Science Tower. A staggering 20 state-of-the-art confocal and electron microscopes are housed here. There is dedicated space for CBI's leadership and 14 full-time research specialists, plus postdoctoral fellows and graduate students. In addition, bench space is available for the scores of collaborators who rely on this unparalleled imaging center.

CBI

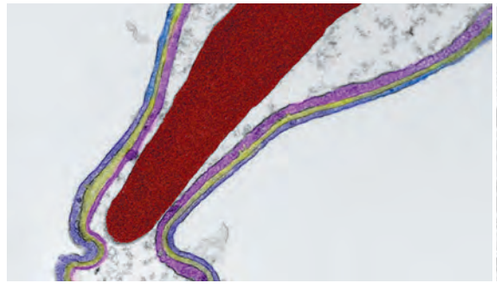
The first time Watkins imaged a cell as a student, he manually pushed the button that controlled the shutter. Click. Click. Click. Nowadays, he says, the microscopes are robots with unbelievably fast and fine controls. Live-cell imaging underway at CBI now involves ultra-high-resolution digital pictures taken every two milliseconds. The data appear as rainbows of color and are analyzed by computers, freeing scientists up for more creative thinking.

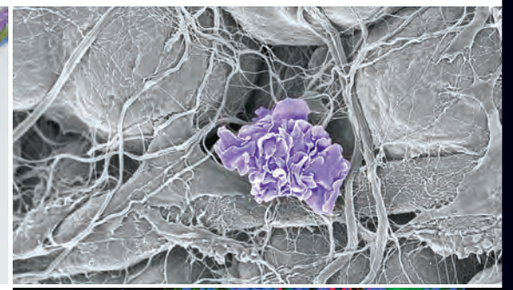
CBI doesn't charge investigators to walk in the door and use this futuristic equipment. "We take a very high road. An academic high road," says Watkins. "We work with people to get funding, and then we share the funding. It means that we all grow together."

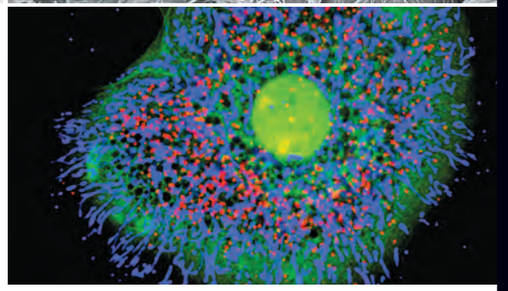
Forget departmental boundaries or even those of the med school or geographic region. Some 260 research groups from this University and others make use of CBI. The only paying customers are those from industry, who are studying, for example, the rheology of ketchup. (It is Pittsburgh, home of Heinz, after all.)

The equipment comes from NIH grants written and submitted by Watkins, Stolz, and colleagues. They seem to have hit on a winning formula—an open-door policy combined with a track record of productive collaborations and critical support for NIH-funded investigators.

The latest purchase is a $1.2 million confocal microscope and related equipment boxed up in CBI's hallway. It is destined for Pitt's regional biocontainment laboratory,







where it will be available for live-cell imaging of preparations containing pathogens such as tuberculosis, HIV, and anthrax. Once this robot rolls into those infectious environs, it will never leave. It will provide rare capabilities for infectious disease researchers, who typically can't transport a live sample to a state-of-the-art microscopy lab.

With such incredible machines and so many collaborators, you might think CBI would adopt a rather strict coffee-and-microscope policy. You'd be wrong.

"One of the problems with a lot of shared facilities is that people treat them like they would a rental car," says Watkins. "You leave Coke cans in the back. You don't look after it. But because we don't charge, people look after our toys like they would their own. You know, if you borrow your friend's car, you bring it back full of gas. That's how people deal with our toys. They show them a lot of respect."

NEWS & ACHIEVEMENTS

(TOP) LEVINE, MALLAMPALLI, DAVIDSON, GRANDIS

Four Added to Elite Society

Among the newest members of the Association of American Physicians (AAP) are **Arthur S. Levine, MD**, **Rama K. Mallampalli, MD**, **Nancy E. Davidson, MD**, and **Jennifer R. Grandis, MD**. Levine and Mallampalli were elected to AAP in 2011; Davidson and Grandis in 2010. Levine has served as senior vice chancellor for the health sciences and dean of the School of Medicine since 1998. Mallampalli is professor of medicine, director of the Acute Lung Injury Center of Excellence, and chief of the pulmonary division of the VA Pittsburgh Healthcare System.

Davidson is director of the University of Pittsburgh Cancer Institute (UPCI) and UPMC Cancer Centers. Also a recipient of the prestigious 2010 Gianni Bonadonna Breast Cancer Award from the American Society of Clinical Oncology, Davidson is associate vice chancellor for cancer research, Hillman Professor of Oncology, and professor of medicine and of pharmacology and chemical biology. Grandis is professor of otolaryngology, UPMC Professor of Head and Neck Cancer Surgical Research, and director of the UPCI Head and Neck Cancer Program. Holder of a prestigious American Cancer Society Clinical Research Professorship, she was recently appointed assistant vice chancellor for research program integration in the health 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. There are now close to 1,200 active members and approximately 550 emeritus and honorary members from the United States, Canada, and throughout the world. Each year, 60 people are nominated for membership in recognition of excellence in their fields. Members include Nobel laureates, members of the National Academy of Sciences, and members of the Institute of Medicine. Today, the association represents the best medical minds and provides a forum to promote friendship, create and disseminate knowledge, and provide role models for generations of upcoming physicians and scientists.

Distinguished Professors Named

Five School of Medicine faculty members have been honored as Distinguished Professors, another as a Distinguished University Professor, and one as a Distinguished Service Professor by Pitt Chancellor Mark A. Nordenberg. The rank of Distinguished Professor recognizes extraordinary, internationally recognized scholarly attainment in an individual discipline or field; that of Distinguished University Professor recognizes eminence in several fields of study, transcending accomplishments in and contributions to a single discipline; that of Distinguished Service Professor recognizes distinctive contribution and outstanding service to the University community in support of its multifaceted teaching, research, and service mission.

Timothy R. Billiar, MD, the George Vance Foster Professor and chair of the Department of Surgery, has been named Distinguished Professor of Surgery. Billiar's research focuses on immune response to injury and shock, gene therapy, inflammation, and liver disease. His lab led the effort to identify the human inducible nitric oxide synthase gene, a discovery that has resulted in seven U.S. patents and generated interest by pharmaceutical companies pursuing a wide range of therapeutic applications from wound healing to tumor inhibition. Billiar has been honored with the Flance-Karl Award from the American Surgical Association and is a member of the Institute of Medicine and National Academy of Sciences.

Donald S. Burke, MD, the UPMC Jonas Salk Professor of Global Health and dean of the Graduate School of Public Health, has been named Distinguished University Professor of Health Science and Policy. Burke is one of the world's foremost experts on the prevention, diagnosis, and control of infectious diseases of global concern, including HIV/AIDS, hepatitis A, and avian influenza. A former United States Army colonel who led infectious disease research at the Walter Reed Army Institute of Research in Washington, D.C., and at the Armed Forces Research Institute of Medical Sciences in Bangkok, Thailand, Burke conducts research that ranges from "bench to bush" and has included development of new diagnostics, population-based field studies, clinical vaccine trials, computational modeling of epidemic control strategies, and policy analysis. At Pitt, Burke is director of the Center for Vaccine Research and associate vice chancellor for global health, health sciences. He has published more than 200 research reports and, in 2009, was elected to the Institute of Medicine.

Freddie H. Fu, MD, the David Silver Professor and chair of the Department of Orthopaedic Surgery, has been named Distinguished Service Professor of Orthopaedic Surgery. Fu, a Pitt med graduate, is known internationally as a pioneer in anatomic double-bundle anterior cruciate ligament (ACL) reconstruction surgery, and he and his research team were recently awarded a $2.9 million National Institute of Arthritis, Musculoskeletal, and Skin Diseases grant to compare anatomic double- and single-bundle ACL reconstruction procedures. He is the founding medical director of the UPMC Center for Sports Medicine and has served as the head team physician for Pitt's Department of Athletics for more than 25 years. In addition to having held numerous offices with professional and academic organizations, Fu has received more than 190 professional awards and honors, given nearly 950 national and international presentations, authored more than 400 peer-reviewed journal articles, and edited 29 major orthopaedic textbooks.

Angela M. Gronenborn, PhD, the UPMC Rosalind Franklin Professor and chair of the Department of Structural Biology, has been named Distinguished Professor of Structural Biology. She has made key contributions to the field in solving the structures of a large number of medically and biologically important proteins, including cytokines and chemokines, tumor-suppressor proteins, transcription factors and their complexes, and HIV-encoded proteins. She is also an expert in the application of NMR technology to solving complex biomedical problems. Former chief of structural biology for the National Institute of Diabetes and Digestive and Kidney Diseases, Gronenborn has published more than 400 articles and numerous book chapters.

William E. Klunk, MD, PhD, professor of psychiatry and of neurology, has been named Distinguished Professor of Psychiatry. One of the nation's leading experts in the early detection of Alzheimer's disease, Klunk was part of the Pitt team that developed the groundbreaking Pittsburgh Compound B, a radioactive compound that, when coupled with PET imaging, can be used to localize the beta-amyloid plaques associated with Alzheimer's disease in the brains of living patients. He is codirector of Pitt's Alzheimer's Disease Research Center. Klunk shares the 2004 MetLife Foundation Award, the 2008 Potamkin Prize, and the 2009 Ronald and Nancy Reagan Research Institute Award for research in Alzheimer's disease with Pitt colleague Chester A. Mathis, PhD, Radiology PET Research Professor, professor of radiology and of pharmacology and chemical biology.

Maria Kovacs, PhD, professor of psychiatry, has been named Distinguished Professor of Psychiatry. An internationally renowned expert in child and adolescent depression, Kovacs has conducted extensive research on the presentation, outcome, and public health implications of early onset affective disorders and developed a novel psychotherapy for the treatment of childhood depression. The Institute for Scientific Information lists Kovacs in the top 1.5 percent of most-cited researchers in psychology and psychiatry from 1981 to 1999, and she served on the advisory committees for the third and fourth editions of the *Diagnostic and Statistical Manual of Mental Disorders* standard reference. She is a fellow of the American Psychological Society.

Peter L. Strick, PhD, professor of neurobiology, has been named Distinguished Professor of Neurobiology. Strick is internationally recognized for his work on the neural basis of movement and cognition. His research identified the multiple cortical areas in the frontal lobe that are responsible for the generation and control of volitional movement. He has pioneered the use of neurotropic viruses as transneuronal tracers to unravel the complex circuitry of the central nervous system. This novel approach enabled him to revolutionize our understanding of the basal ganglia and cerebellum to include their role in cognitive as well as motor function. Strick is director of the Systems Neuroscience Institute and codirector of the Center for the Neural Basis of Cognition (see story page 9). He is a member of the American Academy of Arts and Sciences and a fellow of the American Association for the Advancement of Science.

Bioengineering Award Is a Pitt Tradition

David Vorp, PhD, bridges two worlds as a professor of bioengineering and of surgery. His research focuses on use of experimental and computational techniques to predict abdominal aortic aneurysm rupture and the design of tissue-engineered vascular grafts. This year, he was awarded the 2011 Van C. Mow Medal from the American Society of Mechanical Engineers for his contributions to bioengineering through research, education, professional development, mentorship, and service. Vorp received his BS and PhD degrees in mechanical engineering with an emphasis on vascular biomechanics from the University of Pittsburgh, and he currently serves as director of the Center for Vascular Remodeling and Regeneration.

Vorp is the second Pitt faculty member to win the award in the past three years. McGowan Institute for Regenerative Medicine faculty member Michael Sacks, PhD, who occupies the John A. Swanson Chair in Bioengineering, was honored in 2009 for his work on stress test modeling of native and bioprosthetic heart valve tissues.

Improving the Care of Patients Every Day

As director of the VA Center for Health Equity Research and Promotion and professor of medicine in the Division of General Internal Medicine at Pitt, **Michael J. Fine, MD, MSc,** has spent the last 24 years conducting groundbreaking research on the clinical management of community-acquired pneumonia. In 2011, he was awarded the John M. Eisenberg Award for Career Achievement in Research by the Society of General Internal Medicine. This prestigious honor recognizes the career achievement of a senior member of the society whose innovative research has changed the way generalists care for patients, conduct research, or educate students.

Fine is also involved in the field of health disparities research and developed a widely used conceptual framework to detect, understand, and eliminate disparities in health care among vulnerable patient populations. Fine's most recent work includes studies to identify low-risk patients with pulmonary embolus and reduce the hospitalization of these patients.

Leader of Pitt's Asthma Institute Lauded

Sally E. Wenzel, MD, professor of medicine and director of the University of Pittsburgh Asthma Institute, received the 2010 Recognition Award for Scientific Accomplishment from the American Thoracic Society (ATS).

The award is given each year to ATS members who demonstrate outstanding scientific contributions in basic or clinical research that further the understanding, prevention, and treatment of respiratory disease or critical illness.

Wenzel has a longstanding interest in severe asthma and is one of four National Heart, Lung, and Blood Institute–funded investigators in Pitt's Severe Asthma Research Program. A translational physician-scientist, Wenzel conducts bench research on epithelial changes in severe asthma that contribute to different clinical and inflammatory phenotypes. In addition to treating patients with asthma, she conducts clinical trials that explore response to therapy based on those phenotypic differences.

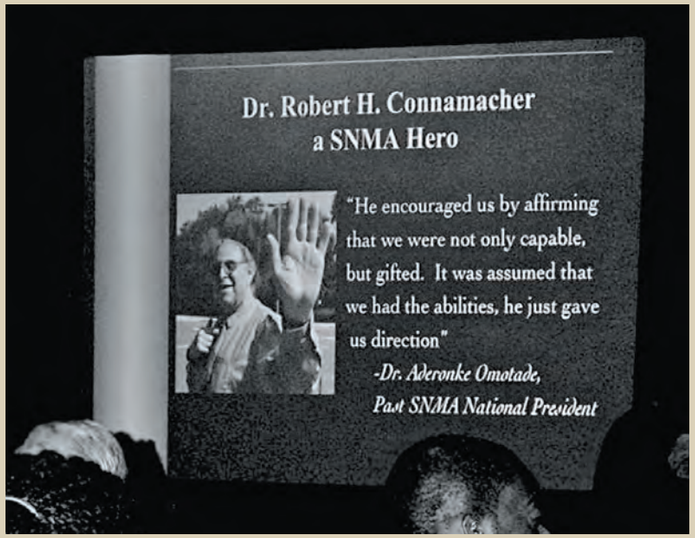
As a junior researcher with her inaugural NIH grant in the early 1980s, Wenzel was among the first pulmonologists to study the lungs of asthma patients using a bronchoscope and also one of the first to biopsy the distal lung in severe asthmatics. Through years of painstaking work, she has amassed a unique, valuable clinical database of nearly 500 research participants with and without asthma; for most of these individuals, there are specimens of tissue, cells, and sputum/lavage. This repository has enabled Wenzel to publish widely on differing inflammatory phenotypes in asthma and their correlation to clinical characteristics. She has achieved national prominence through organizing workshops for severe asthma at the American Thoracic Society and has received recognition from NIH for her efforts to expand knowledge about lung architecture and the changes that occur with asthma progression.

"Despite significant advances in diagnosis and treatment, asthma remains a major public health problem in the United States, affecting approximately 15 million people and contributing to approximately 5,000 asthma-related deaths each year," Wenzel said. "To be recognized for my contribution to a body of work in asthma, and severe asthma in particular, is a tremendous but humbling experience."

Surgical History

For more than four decades, **David K.C. Cooper, MD, PhD**, professor of surgery and director of the xenotransplantation research group at the Thomas E. Starzl Transplantation Institute, has been at the leading edge of the field of cardiothoracic and transplantation surgery. He was part of the team that performed the U.K.'s first series of successful heart transplants in the 1970s and worked with Christiaan Barnard, MBChB, who performed the world's first heart transplant in 1967. In 2010, Cooper was honored with the TTS-Roche Award for Excellence in Translational Science, which is presented annually at the International Congress of the Transplantation Society to a recipient who has made outstanding contributions in transplantation.

For the past 25 years, Cooper has focused his attention on xenotransplantation research, transplanting corneas, hearts, and islet cells from genetically engineered pigs into nonhuman primate models. His latest book is *Open Heart: The Radical Surgeons Who Revolutionized Medicine* (Kaplan Publishing, 2010), a history of cardiac surgery and the lives of its surgeons.



Connamacher Enters Hall of Heroes

Robert H. Connamacher, PhD, associate professor of family medicine, has been selected for induction into the Student National Medical Association (SNMA) Hall of Heroes in recognition of his work "supporting current and future underrepresented minority medical students, addressing the needs of underserved communities, and increasing the number of clinically excellent, culturally competent and socially conscious physicians."

Connamacher, outreach coordinator for diversity programs in the Office of Student Affairs, directs Medical Explorers, an enrichment program for minority and disadvantaged middle and high school students in Pittsburgh. The program provides lectures, lab experience, physician shadowing, and mentorship by minority faculty. He is also a faculty advisor for Pitt's Premedical Organization for Minority Students and the American Medical Student Association.

Paula K. Davis, MA, assistant vice chancellor for health sciences diversity, says, "There is no individual more passionate about students' growth and development than Bob Connamacher. This statement is as true today as when I first met him almost 20 years ago. He is never off-the-clock, does whatever it takes to engage a student, and never, ever, gives up on anyone. He's a teacher in every sense of the word, recruiting students for Medical Explorers from wherever he is—from the halls of local high schools to the grocery store checkout line. One of my fondest memories is riding with Bob and a van full of medical and premed students to Philadelphia for an SNMA regional conference. I know he was exhausted, but he insisted on personally making sure that the students got there—he drove the whole way out and back."

Pathologically Successful

Charleen T. Chu, MD, PhD, associate professor of pathology, has been recognized with the prestigious American Society for Investigative Pathology Outstanding Investigator Award in 2010. The honor recognizes mid-career investigators with demonstrated excellence in research in experimental pathology.

Chu's work focuses on the cellular and molecular mechanisms underlying neurodegeneration in Parkinson's disease. By integrating molecular and biochemical studies in cell culture and mouse models with pathologic studies of diseased human brain tissues, Chu has demonstrated that unbalanced macroautophagy and biosynthetic responses to mitochondrial dysfunction contribute to failure of adaptive pathways, neurite injury, and neuronal cell death. Her discovery of a novel phosphorylation site on the autophagy mediator LC3, which prevents neurite shortening, offers a potential mechanism for kinases to exert a neuroprotective effect in age-related neurodegenerative diseases.

An Inaugural Appointment

Edward P. Mulvey, PhD, professor of psychiatry and director of law and psychiatry research, has published widely in the medical literature about mental illness, juvenile delinquency, and community violence. This year, he was one of 18 experts named by U.S. Attorney General Eric Holder to the newly created Science Advisory Board for the Department of Justice's Office of Justice Programs.

In fiscal year 2010, the office awarded nearly 5,000 grants totaling $2.6 billion to support criminal and juvenile justice policymakers and practitioners working at federal, state, local, and tribal law enforcement agencies and community organizations.

Grandis Targets Research Program Integration

With Pitt investigators receiving more than 1,000 individual grants and bringing in a combined total of more than $443 million in NIH funding each year, the task of developing and administering the Pitt research enterprise continues to grow. Thus, in October 2010, Arthur S. Levine, MD, senior vice chancellor for the health sciences, appointed **Jennifer R. Grandis, MD**, to the newly created position of assistant vice chancellor for research program integration, health sciences. In this capacity, Grandis is responsible for aiding the development of research-related programs throughout the Schools of the Health Sciences, with a focus on integrating this effort with those of the several research support offices at the University of Pittsburgh.

Grandis is also professor and vice chair for research in the Department of Otolaryngology, with a secondary appointment in the Department of Pharmacology and Chemical Biology, director of the Head and Neck Cancer Program in the University of Pittsburgh Cancer Institute, and UPMC Professor of Head and Neck Cancer Surgical Research. A native Pittsburgher and 1987 graduate of the University of Pittsburgh School of Medicine, she has spent her entire professional career at Pitt. Her research focuses on signaling pathways in squamous cell carcinoma of the head and neck, including studies of the mechanisms and efficacy of selective molecules and gene therapy to suppress tumor growth, and she was awarded a five-year American Cancer Society Clinical Research Professorship in 2008. She recently received an $800,000 grant from the National Cancer Institute to develop inhibitory agents for STAT3, a cellular signaling protein that, when activated and present in excess levels, can drive the transformation of healthy cells into cancer.

Of her new position, Grandis remarks, "I've been fortunate to have had really good mentors and know that the day-to-day interaction is critical. I hope to bring that experience to this role, facilitating the lines of communication between faculty in the Schools of the Health Sciences and the research administrative offices at the University of Pittsburgh. Ultimately, this will reduce the administrative burden for faculty and allow them to focus on achieving their research objectives."

Leading the Way

Katherine L. Wisner, MD, MS, is the recipient of the 2011 Women in Science award from the American Medical Women's Association, an honor given to a female physician who has made exceptional contributions to medical science, especially in women's health, through basic and/or clinical research, publications, and leadership.

Wisner is professor of psychiatry; of obstetrics, gynecology and reproductive sciences; and of epidemiology and director of the Women's Behavioral HealthCARE program at Western Psychiatric Institute and Clinic of UPMC. Her research focuses on the psychiatric treatment of women of childbearing age.

Wisner receives funding from the National Institute of Mental Health to study the effect of selective serotonin reuptake inhibitor (SSRI) treatment for major depression during pregnancy on maternal and infant outcomes. She is also conducting a clinical trial that includes treatment with an estradiol skin patch, the SSRI sertraline, or placebo for women with postpartum depression.

"I was delighted to hear about the award," noted Wisner. "I am honored to have contributed to research in perinatal mental health over the last 25 years, as it has gone from being essentially unknown in the U.S. to a field of great interest among investigators and clinicians."

Stem Cell Expert Is New Plastic Surgery Chief

J. Peter Rubin, MD, a noted expert on clinical applications for adipose-derived stem cells, has been named chief of Pitt's Division of Plastic and Reconstructive Surgery. The recipient of several multimillion dollar grants from NIH and the U.S. Department of Defense, Rubin directs active laboratory research and clinical trials programs testing innovative strategies for the use of adult fat stem cells to restore soft tissues after trauma and cancer therapy.

"As many as 26 percent of wounded soldiers suffer some kind of facial injury, which can have a huge impact on quality of life. While we can reconstruct bony structures very well, it is the surrounding soft tissues that give people a recognizable face," he said. Using specially designed tools and surgical technologies, Rubin harvests fat tissue and grafts it onto scarred areas.

Rubin has published extensively and received numerous awards for his work, including a 2007 Presidential Early Career Award for Scientists and Engineers and the Peter J. Gingrass Award from the Plastic Surgery Research Council. He is codirector of the Adipose Stem Cell Center at the University of Pittsburgh and the UPMC Aesthetic Plastic Surgery Center.

New Faces

JEREMY BERG

As the University of Pittsburgh's first associate senior vice chancellor for science strategy and planning, health sciences, Jeremy M. Berg, PhD, faces formidable challenges ranging from economic, political, and regulatory uncertainties to shifting research priorities. Luckily for Pitt, the former director of the National Institute of General Medical Sciences (NIGMS) is an old hand at formidable challenges.

"Dr. Berg is a leader who asks incisive questions and applies a range of analytical approaches to guide policy and initiative development," says Arthur S. Levine, MD, senior vice chancellor for the health sciences and dean, School of Medicine. Recognizing opportunity's knock, Levine was quick to nab an impressive "two-fer" while recruiting Berg's wife, noted breast imaging researcher Wendie A. Berg, MD, PhD (see page 23).

At NIGMS, Berg managed a nearly $2 billion budget. He organized the institute's first formal strategic plan, supported research training and workforce development initiatives, conducted reviews of major programs, increased funding for innovative research, and encouraged dialogue through interactive outreach to the scientific community. He also led efforts, both within NIGMS and throughout the National Institutes of Health, to increase diversity in the biomedical workforce. Berg was honored with the 2011 Public Service Award by the American Chemical Society for his stellar record of leadership and advocacy for basic research while at NIH. Also in 2011, he was elected president of the American Society for Biochemistry and Molecular Biology for a term beginning in 2012.

The "can-do attitude" of Pitt faculty members captivated Berg from his very first visit to the city, he says. "Pitt has been on a great trajectory for a long time now, but it's clear that there's a lot of hunger and ambition to do new things and find the great scientific opportunities that are out there," Berg adds, saying he believes he can "contribute in a significant way" to the University's future success.

In the lab, Berg's research focuses on molecular recognition processes and the structural and functional roles that metal ions, especially zinc, have in proteins. He has advanced understanding of how zinc-containing proteins bind to DNA and RNA and regulate gene activity, and he is continuing this research as a professor in the Department of Computational and Systems Biology.

EVERETTE JAMES

Good luck trying to catch Everette James, JD, MBA, in his Scaife Hall office. Pennsylvania's former secretary of health hasn't spent much time getting acquainted with his chair since October 1, 2010, when he was appointed to the newly created position of associate vice chancellor for health policy and planning in the Schools of the Health Sciences. He's meeting people and learning his way around all the small, interconnected parts that make up the University and its clinical partner, the global health care enterprise called UPMC.

Among James's duties in health policy are teaching, taking part in collaborative research, and advising on legal issues related to new care delivery models driven by health care reform.

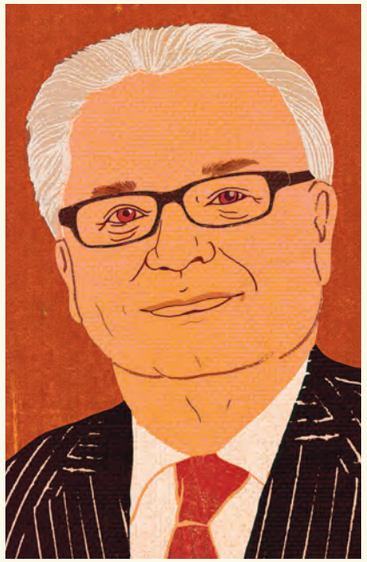
"I think the biggest challenge is to continue building our institution, and by that I mean all the Schools of the Health Sciences, the University, and UPMC in the context of a changing regulatory and reimbursement environment," says James, who is also director of Pitt's Health Policy Institute and professor of health policy and management at the Graduate School of Public Health. "We need to harness all of that incredible talent, expertise, and the best practices that exist here to help make Pittsburgh a laboratory for improving health care delivery."

James is no stranger to large undertakings. As Pennsylvania's 25th secretary of health, he supervised the regulation of all hospitals, nursing homes, and managed care plans in the Commonwealth. In addition, he was responsible for managing the Pennsylvania Department of Health's 1,700 employees and nearly $1 billion annual budget, and for administration of the state's disease surveillance and prevention program. In Harrisburg, he successfully implemented a statewide smoking ban and the most comprehensive law in the U.S. targeting the elimination of hospital-acquired infections. New regulations to ensure independent, timely hearing of insurance claims and appeals also were enacted under his leadership.

James's government service has given him invaluable experience, particularly in terms of the fluidity of legislation and the critical relationship between regulatory requirements and the business of health care and education. For example, passage of the Patient Protection and Affordable Care Act of 2010 has been described as among the most comprehensive legislative efforts in health care reform since the 1965 introduction of Medicare and Medicaid. Congressional debate on the matter, however, is far from over.

"There is opportunity in the chaos of health reform," James says with a smile. "I don't agree with all the components of the law, but it has started to drive system change—especially in the area of better integration and coordination of care, and looking seriously at the cost effectiveness of care delivery."

Prior to joining Pennsylvania government, James was a partner in the Washington, D.C., law office of LeBoeuf, Lamb, Greene, and MacRae, with a practice focused on health, safety, and insurance regulatory and compliance matters. He also served as senior advisor and deputy assistant secretary of the U.S. Department of Commerce.



LANS TAYLOR

With his silvery, coiffed hair and stylish clothes, D. Lansing "Lans" Taylor doesn't exactly fit the scientist stereotype, yet he is an NIH MERIT awardee who has authored more than 150 peer-reviewed publications. Taylor's warm, engaging demeanor may better fit his history as a CEO and successful entrepreneur who has founded multiple biotechnology companies and chaired the board of the Pittsburgh Life Sciences Greenhouse. In discussion, he effortlessly skips back and forth over the boundary of science and business, making it even more difficult to put a label on him.

Taylor, who has a PhD in cell biology from the State University of New York at Albany, is the new director of Pitt's Drug Discovery Institute and the Allegheny Foundation Professor of Computational and Systems Biology. The department feels like home to him, he says, because he has been using a biological systems approach since his days as a Harvard professor: "Living organisms are integrated networks of genes, cells, and proteins. It is essential to understand the biological systems and address this complexity early in the drug discovery process."

Taylor pioneered fluorescence imaging techniques at Harvard and later moved to Carnegie Mellon University (CMU) to build the Center for Fluorescence Research, a multidisciplinary center that combined his love of biology with CMU's strengths — engineering and computer science. Soon after, he cofounded his first company and caught the entrepreneurial "bug." And so began his venture into the world of pharmaceutical and biotech industries. He pioneered high content screening (HCS) methods, and his first-generation technologies were the basis of his first Pittsburgh-based company, Cellomics. He later founded Cellumen, combining HCS methods with systems biology to evaluate the efficacy and toxicity of new drug candidates.

Although Taylor has plenty of industry know-how, he insists that he will not run the Drug Discovery Institute like a mini-pharma company. He does, however, see tremendous value in cultivating industry partnerships, particularly in today's bleak funding climate. He explains, "Our academic prowess will attract pharma; and together we'll develop new technologies, offering mutual value and helping our institution and the world." Taylor's excitement is palpable. He points out that Harvard and Washington University in St. Louis have already formed high-profile industry partnerships—but he's hot on their tails. He warns, "If we don't get in the queue, we're going to miss the wave." In other words, wax up the boards and hang on for the ride!

WENDIE BERG

In the 19th century, Pittsburgh was the civilized edge of the Western frontier. Today, Wendie A. Berg, MD, PhD, considers the University of Pittsburgh School of Medicine to be on the leading edge of pioneering research. An internationally noted clinician scientist, she joined the University in March 2011 as professor of radiology.

"I've been in the clinical practice of breast imaging my whole career, doing research on using screening technologies like ultrasound and MRI in women with dense breasts," says Berg, former professor and director of breast imaging at the University of Maryland School of Medicine and co-author of a leading diagnostic imaging text. Among her important studies are findings that cancer-detection rates increase when ultrasound is combined with mammography for high-risk women. Cancers identified were also more likely to be invasive.

Doing research was not always encouraged throughout her academic career, notes Berg, who was recruited by a number of institutions. "But Pittsburgh has a long history in women's health research—with NSABP [National Surgical Adjuvant Breast and Bowel Project] and other work—and that made this a very attractive move."

Joining Berg on faculty is her husband, Jeremy M. Berg, PhD, former director of the National Institute of General Medical Sciences (see page 21). The couple finds the University's "culture of trying to test new things," especially inviting, Berg says.

In breast cancer screening, for example, Pitt is moving to add molecular breast imaging, or MBI, to an array of diagnostic tools that includes MRI, ultrasound, helical cone beam computed tomography, and tomosynthesis. MBI combines funtional imaging and a high-resolution camera to sharpen imaging capabilities. Also on the horizon is new shearwave elastography ultrasound to evaluate the stiffness of breast lesions—a potential indicator of malignancy.

"Mammography saves lives," says Berg. "But for women with dense breast tissue—more than half of women younger than 50 and at least a third of those over 50—mammography detects cancer less than half the time when it is present." Berg's research mission, she says, is to keep improving the odds.

EDWARD CHU

A key ingredient in Edward Chu's recipe for conducting innovative research is collaboration. As professor of medicine and chief of the Division of Hematology/Oncology since September 2010, Chu says he has found an embarrassment of riches and a scientific home at Pitt.

"Pittsburgh has a tremendous reputation as a center of clinical excellence, and there's no question that the research programs are outstanding," adds Chu, an MD who came to Pitt after 18 years at the Yale University School of Medicine, where he was professor and chief of medical oncology. "So for me, as both a basic research and clinical, translational scientist, to be able to bring those two worlds together, the opportunities here are really second to none."

Particularly appealing to Chu are opportunities to connect with scientific colleagues throughout the University of Pittsburgh Cancer Institute and its affiliated network of UPMC Cancer Centers and community partners. "This is a very rare situation," he says. "I think the opportunities for really making an impact on cancer care are just amazing."

Chu's investigations focus on the potential for using Chinese herbal medicines to temper the debilitating diarrhea and other gastrointestinal symptoms caused by standard chemotherapy treatments for colorectal cancers, which destroy not only tumor cells but also fast-dividing normal cells in the gut.

"We're about to conduct clinical studies here in Pittsburgh," he says, explaining that an herbal medicine that scientists call PHY906 has been used for 2,000 years in Asia to treat diarrhea. Compounded from Chinese varieties of peonies, date tree fruit, licorice, and a plant called skullcap, the mixture is typically administered as a brewed tea, says Chu. "Within these four herbs, we've now identified up to 65 individual components plus individual molecules that function like targeted therapies."

Another investigation involves combining PHY906 with the anti-cancer agent irinotecan in patients with metastatic colorectal cancer. "We're quite hopeful because our very first study with PHY906 and a chemo cocktail that included irinotecan found that, in fact, the herb did reduce the side effects of nausea, vomiting, and diarrhea, as well as improve the overall quality of life for patients," Chu says.

DNA replication is the foundation of life on Earth. Every cell division, though, offers opportunities for mistakes as DNA strands unwind and their basic structural units, called nucleotides, join to form new base pairs during DNA synthesis. Damage can also arise from radiation, normal metabolic processes, and certain chemical and environmental exposures, amounting to as many as 10,000–100,000 molecular lesions per cell daily. Fortunately, our cells incorporate multiple strategies to repair DNA. Enzymes patrol the genome for strand breaks and altered nucleotides. They employ excision-repair and other mechanisms to fix DNA damage, which, if not repaired, can lead to mutations, cell death, or cellular dysfunction.

DNA repair is critical because faulty DNA repair is among the most fundamental causes of cancer, neurodegeneration, and aging. Much about the process remains unknown, but University of Pittsburgh faculty members are on the forefront of its scientific investigation.

"We have a really strong genome stability group," says Bennett Van Houten, PhD, Richard M. Cyert Professor of Molecular Oncology in the Department of Pharmacology and Chemical Biology, and head of the Molecular and Cellular Cancer Biology Program at the University of Pittsburgh Cancer Institute. "All of us work on different things."

"It's been a wonderful group to watch mature," says Van Houten, who was recruited to Pitt in 2008 from the National Institute of Environmental Health Sciences, where he ran a productive research laboratory and was chief of the Program Analysis Branch in the Division of Extramural Research and Training.

BENNETT VAN HOUTEN, PHD

Van Houten investigates the structure and function of repair proteins and mitochondrial physiology. Other group members include:

Christopher Bakkenist, PhD, assistant professor of radiation oncology and of pharmacology and chemical biology, investigates ataxia telangiectasia-mutated gene signaling and double-strand break repair.

Laura Niedernhofer, MD, PhD, associate professor of microbiology and molecular genetics, studies the excision-repair protein ERCC1 and cross-link repair using a remarkable mouse model of accelerated aging.

Vesna Rapic-Otrin, PhD, assistant professor of microbiology and molecular genetics, studies DNA damage binding proteins and histone ubiquitination in chromatin, in collaboration with assistant professors of microbiology and molecular genetics Li Lan, PhD, and Satoshi Nakajima, PhD, and Arthur S. Levine, MD, senior vice chancellor for the health sciences and dean of the School of Medicine.

Kara Bernstein, PhD, assistant professor of microbiology and molecular genetics, studies mechanisms of error-free DNA recombination, particularly as related to the proteins Sgs1 and the Shu complex.

Robert Sobol, PhD, assistant professor of pharmacology and chemical biology, studies base excision repair, poly (ADP-ribose) polymerase, and chemotherapeutic approaches in brain cancer.

Yong Wan, PhD, associate professor of cell biology and physiology, investigates ubiquitin-dependent proteolysis, cell-cycle control, and DNA damage responses.

BAKKENIST (TOP), NIEDERNHOFER, RAPIC-OTRIN, BERNSTEIN, SOBOL, WAN

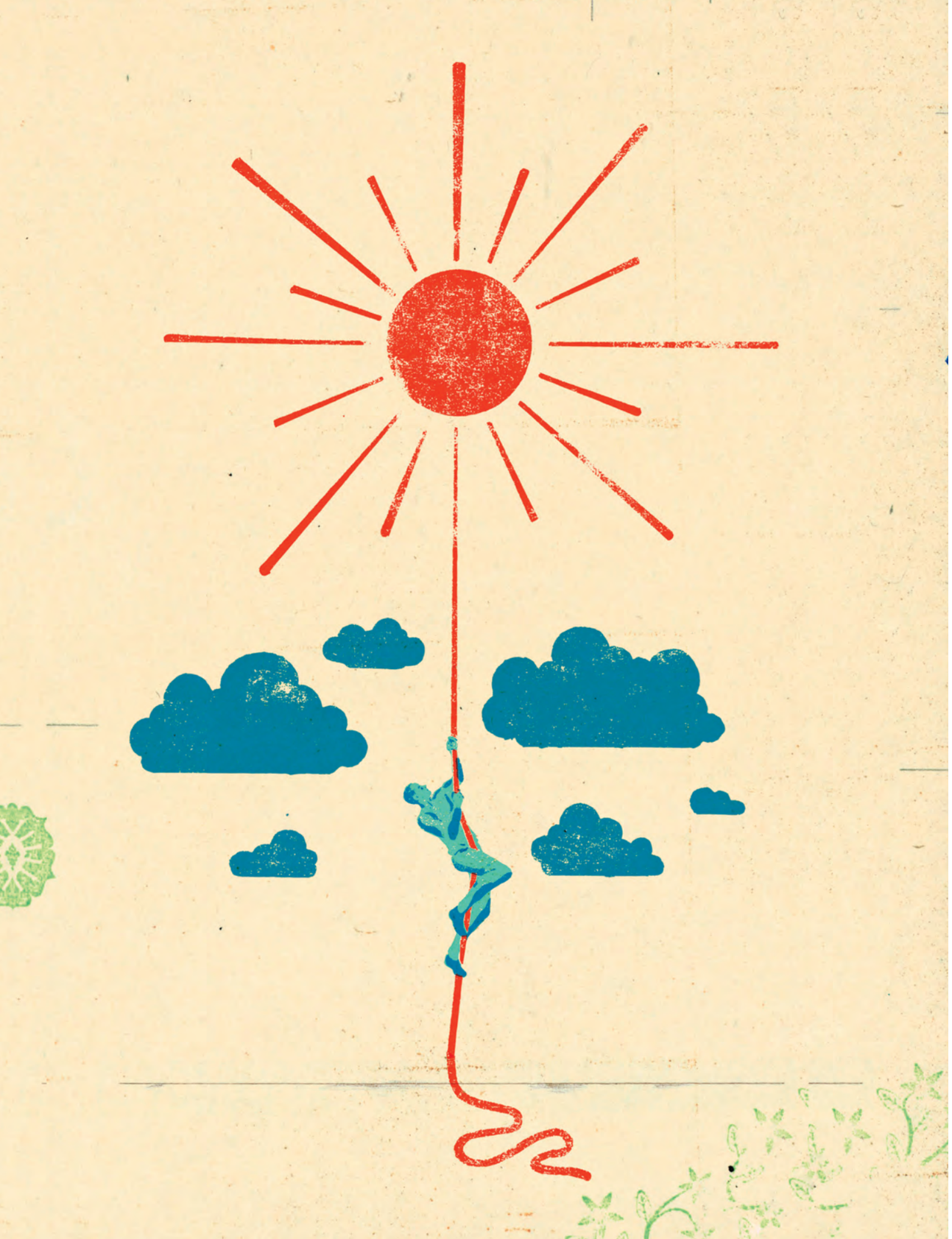
A five-time recipient of NIH's Award of Merit, Van Houten uses quantum dot technology and atomic force microscopy to observe DNA repair proteins at work in bacteria. As described in a 2010 issue of the prestigious journal *Molecular Cell*, quantum dots are highly fluorescent nanocrystals that Van Houten and colleagues use to tag infinitesimal DNA repair proteins. These crystals retain color and brilliance while marking protein movement along the genome.

"Imagine you have something like a record-player needle, and you're scanning back and forth, and the probe 'sees' the protein by bumping over it," says Van Houten, pointing to a computer screen image that resembles a series of glowing mountain peaks. "These quantum dots are 20 nanometers, compared to a protein that's maybe three or four nanometers."

DNA, by contrast, is about half the size of the repair protein, he says, adding that the base pairs upon which these tiny proteins toil are themselves an atomic fraction of DNA. "What we're talking about are amazing small machines—indispensable parts of the biochemistry of life that we are," says Van Houten.

It's when the chemistry goes awry that accumulating mutations can lead to tumorigenesis. "Our long-term goal is to translate findings in basic research into the clinic," says Van Houten. "A major area of research that has huge potential is the understanding of which DNA repair pathways have been altered in tumor cells so that specific therapeutic approaches can be tailored to specific tumors."

Before this happens, however, Van Houten and colleagues continue to stir the pot of DNA repair mechanisms, seeking clues. "We want to be able to watch DNA repair one molecule at a time, in real time, in a living cell," he says, confessing another goal—one he admits may be audacious. "I want to build the best DNA repair group in the country—so that if you want to do genome stability, you have to be in Pittsburgh," says Van Houten. "We're not there yet, but we're on our way."



THE STRUCTURE OF SUPPORT

BENCHMARKING

Research the Bottom Line

The University of Pittsburgh spent over $800 million for research of all kinds in fiscal year 2011. More than 80 percent of this amount was for research in the health sciences. University research spending from all sources grew 8 percent over the fiscal year 2010 level.

Funding from the National Institutes of Health (NIH) is considered the benchmark of overall stature among research-intensive academic health centers. Since 1997, the University of Pittsburgh, led mainly by School of Medicine faculty, has ranked among the top 10 recipients of NIH funding. In fact, in the past three years, the University has risen as high as fifth in NIH research funding and in the number of individual grants received.

As of June 30, 2011, the University of Pittsburgh had received nearly $210 million through the American Recovery and Reinvestment Act (ARRA). The vast majority of Pitt's 524 individual awards—nearly 85 percent—went to the Schools of the Health Sciences, with the School of Medicine receiving the lion's share of those. A total of 377 "stimulus" awards were granted to the School of Medicine.

Stimulus funding has been a great boon to the University, particularly in light of the decline of the NIH budget in inflation-adjusted dollars. But ARRA is a short-term proposition. That is why, even as we continue to attract significant NIH funding, we are moving aggressively to put ourselves in the best position to gain future support from diverse sources, including private industry, philanthropic organizations, international collaborations, and other federal agencies such as the Department of Defense.

NIH FUNDING

1,093

INDIVIDUAL GRANTS

RANKED #5

IN NUMBER OF AWARDS OUT OF MORE THAN 2,500 INSTITUTIONS

$443

MILLION

RECEIVED IN RESEARCH SUPPORT

SUPERCOMPUTER HUNTS MOLECULAR DYNAMICS

Revealing Science at "Anton-ic" Speed

Transporter proteins move neurotransmitters across cell membranes in the marvelous *pas de deux* of nerve cell communication that powers the human brain. Like members of the *corps de ballet*, these neurotransmitters flow across the nerve synapse to join with their partners, called receptors, to move the nerve impulse, or "action potential" to the neighboring nerve cell. This pattern repeats cell-to-cell, often at speeds equivalent to nearly 400 feet per second. Now Anton, a lightning-fast supercomputer on loan to the Pittsburgh Supercomputing Center (PSC) from New York–based D.E. Shaw Research, is helping University of Pittsburgh scientists to chart the mystery of this protein choreography.

"The longer we can run simulations, the better chance we have to see something physiologically meaningful," says Ivet Bahar, PhD, John K. Vries Professor and chair of the Department of Computational and Systems Biology, one of two Pitt faculty members whose projects received computational allocations as part of a highly competitive review process undertaken by the National Research Council of the National Academy of Sciences. The other is Michael Grabe, PhD, an assistant professor of biological sciences with a secondary appointment in the School of Medicine's Department of Computational and Systems Biology. His project evaluates the structure of sodium-galactose transporter proteins. Bahar and Grabe are among 47 investigators across the country using Anton.

Anton's 512 nodes can parse nanoseconds (a billionth of a second) down to milliseconds (a thousandth of a second), explains Elia Zomot, PhD, a postdoctoral associate in the Bahar lab. Previously, even the most powerful computers could track only about a millionth of a second of protein movement—still insufficient to capture the elaborate rippling of cellular proteins at work. Imagine trying to understand Tchaikovsky's Swan Princess based on her first step onstage, a glimpse of knee, and the final fluttering fingertips of her death scene.

"Time scales of biologically interesting things typically start in the millisecond range and longer," says Markus Dittrich, PhD, a senior scientific specialist at PSC.

Anton's hardware runs molecular dynamics exclusively and at a speed Zomot says surpasses other available equipment "by three or four orders of magnitude." This capacity allows Bahar's group to scan protein patterns for the decision points at which targeted therapies could conceivably influence the course of microphysical events. "We're generating tons of data," he says. "Half the task is just describing the trajectories." After all, the best partner can not only see the curving peak of a ballerina's leap but correctly plot the intersecting path he must take to catch her.

Imagine trying to understand Tchaikovsky's Swan Princess based on her first step onstage, a glimpse of knee, and the final fluttering fingertips of her death scene. That's what it's like trying to track some biological processes without a supercomputer.

PORTABLE PREVENTION

NIH Backs Microbicide Research against HIV

More than 30 million people are living with HIV/AIDS today, and women comprise more than half of that population. For many women worldwide, practicing abstinence or using condoms is simply not an option. Sharon Hillier, PhD, professor of obstetrics, gynecology, and reproductive sciences, and Lisa Rohan, PhD, associate professor of pharmaceutical sciences, School of Pharmacy, are focusing on microbicides women could discreetly apply topically to reduce HIV acquisition.

Hillier and Rohan recently received an $11.8 million, five-year grant from the National Institute of Allergy and Infectious Diseases to develop new microbicides in the form of dissolvable vaginal films. The films, which are similar to breath freshener strips, will contain the antiretroviral drugs tenofovir and dapivirine. In gel form, tenofovir has been shown to dramatically reduce HIV infection in women. If effective, film-based microbicides could offer women a new method of HIV prevention that may be more portable, cost effective, and convenient than gels.

Hillier is principal investigator of the NIH-funded Microbicide Trials Network, where she leads a collaboration of international researchers who perform clinical trials of various HIV prevention strategies.

HARM REDUCTION

Therapy Protects against Radiation

Cancer may be debilitating and deadly, but the treatment is no picnic either. Radiation therapy improves the likelihood of survival in many cancer patients, but radiation toxicity can limit their ability to complete treatment and lead to complications like tissue scarring and organ failure. Joel S. Greenberger, MD, professor and chair of radiation oncology and codirector of UPCI's lung and esophageal cancer program, is searching for ways to limit this damage. With $13.9 million from the National Institute of Allergy and Infectious Diseases, he aims to reduce the harmful effects of frequent radiation exposure from cancer therapy or widespread exposure because of a radiological accident or attack.

High levels of ionizing radiation can badly damage cellular DNA, leading to apoptosis and widespread tissue death. Greenberger develops drugs that target and stimulate the mitochondria, the cell's energy generators, to enhance cellular repair. He explains, "We hope to develop strategies to deliver drugs quickly and intelligently to block mitochondria 'wrongdoings' that could lead to massive cell death after a nuclear event." In collaboration with Peter Wipf, PhD, Distinguished Professor of Chemistry in the School of Arts and Sciences and associate director of Pitt's Drug Discovery Institute, Greenberger developed JP4-039, a small molecule derived from the antioxidant 4-amino-tempo. Greenberger's team at Pitt's federally funded Center for Medical Countermeasures against Radiation found that JP4-039 significantly reduced esophageal cell death associated with irradiation—a finding that could lead to improved outcomes in lung and esophageal cancer treatment and have important implications in biodefense research. This five-year grant renewal will allow Greenberger to design gene-targeting strategies and explore new methods of drug discovery and delivery to mitigate radiation's harmful effects.

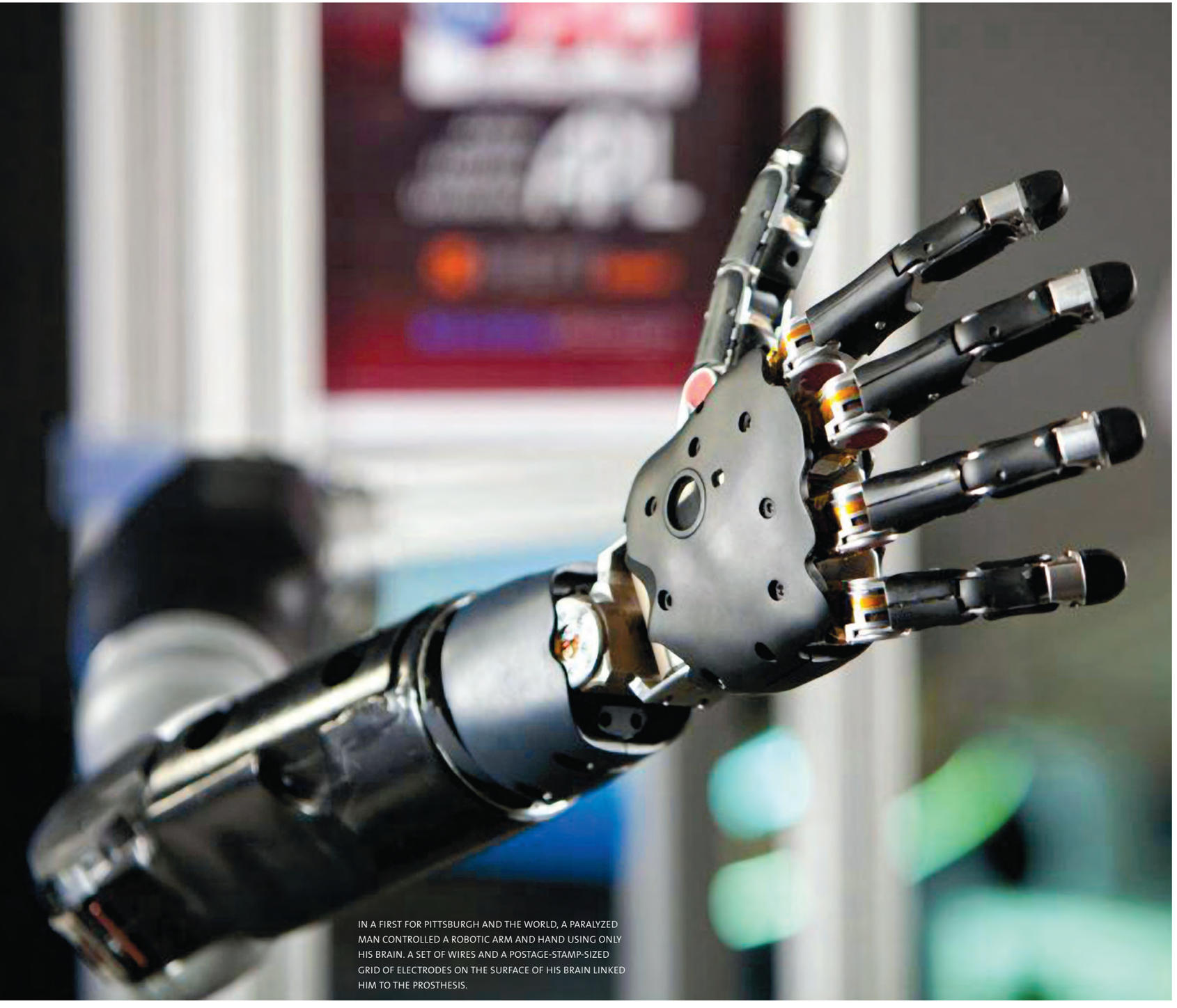
GETTING GOOD ZZZs

Pitt Receives $9.8 Million to Study Insomnia in the Elderly

People seem to need less sleep as they age. Ever notice that your grandparents have finished breakfast and the newspaper by 7:30 a.m.? If not, it's probably because you're still asleep. True insomnia, however is a very serious problem that effects nearly 25 percent of senior citizens. It isn't known precisely why the elderly have so much trouble staying asleep, but some biological causes might include genetics, biological clock problems, stress reactivity, and aspects of functional brain anatomy. Older adults also often face life hurdles such as illness and pain, which can present sleep challenges.

Timothy H. Monk, PhD, DSc, professor of psychiatry and director of the Human Chronobiology Research Program at Western Psychiatric Institute and Clinic of UPMC, believes reducing sleep disruptions in the elderly is vitally important to their well-being and that a full understanding of the biological underpinnings of insomnia in seniors is sorely needed. He and his colleagues recently received $9.8 million from the National Institute on Aging to investigate the neurobiology of insomnia and its treatment in those 60 and older. Their study will focus on sleep intensity and biological clock issues, stress reactivity, genetics, and aspects of functional brain anatomy.

On average, 10,000 baby boomers a day will turn 65 in 2011, making it even more essential to understand the health concerns of the elderly and to promote good health into the golden years. After reaching this milestone, they deserve a good night's sleep.



IN A FIRST FOR PITTSBURGH AND THE WORLD, A PARALYZED MAN CONTROLLED A ROBOTIC ARM AND HAND USING ONLY HIS BRAIN. A SET OF WIRES AND A POSTAGE-STAMP-SIZED GRID OF ELECTRODES ON THE SURFACE OF HIS BRAIN LINKED HIM TO THE PROSTHESIS.

THINK IT, DO IT

Brain, Meet Robot

Pitt researchers have been awarded funding for two projects that will place brain-computer interfaces (BCI) in patients with spinal cord injuries to test whether it is possible for them to control external devices, such as a computer cursor or a prosthetic limb, with their thoughts.

The projects build upon ongoing research conducted in epilepsy patients who had the interfaces temporarily placed on their brains and were able to move cursors and play computer games, as well as in monkeys that, through interfaces, guided a robotic arm to feed themselves marshmallows and turn a doorknob.

"We are now testing BCI technology in the patients who might benefit from it the most, namely those who have lost the ability to move their upper limbs due to a spinal cord injury," says Michael L. Boninger, MD, professor and chair of physical medicine and rehabilitation. "It's particularly exciting for us to be able to test two types of interfaces within the brain."

"By expanding our research from the laboratory to clinical settings, we hope to gain a better understanding of how to train and motivate patients who will benefit from BCI technology," says Elizabeth Tyler-Kabara, MD, PhD, assistant professor of neurological surgery and of bioengineering and the lead surgeon on both projects.

In one project, funded by an $800,000 NIH grant, a BCI based on electrocorticography was placed on the motor cortex surface of a spinal cord injury patient's brain for about four weeks. The neural activity picked up by the BCI was translated through a computer processor, allowing the patient to learn to control computer cursors, virtual hands, computer games, and, finally, a robotic arm and hand. In an emotional session at the culmination of the four-week period, the patient was able to use his mind to raise the robotic hand and "high-five" a researcher. He then extended the hand to touch his girlfriend's hand—for "the first time in seven years," he said through tears.

The second project, funded by the Defense Advanced Research Projects Agency for up to $6 million over three years, is part of a program led by the Johns Hopkins University Applied Physics Laboratory. It will further develop technology tested in monkeys by Andrew Schwartz, PhD, Pitt professor of neurobiology.

The interface is a tiny, 10-by-10 array of electrodes that is implanted on the brain's surface to read activity from individual neurons. Those signals are processed and relayed to maneuver a sophisticated prosthetic arm.

"Our animal studies have shown that we can interpret the messages the brain sends to make a simple robotic arm reach for an object and turn a mechanical wrist," Schwartz says. "The next step is to see not only if we can make these techniques work for people but also if we can make the movements more complex."

In the study, participants will get two separate electrodes. In future research efforts, the technology may be enhanced with an innovative telemetry system that would allow wireless control of a prosthetic arm, as well as a sensory component.

"Our ultimate aim is to develop technologies that can give patients with physical disabilities control of assistive devices that will help restore their independence," Boninger says.

ENGAGEMENT AND OUTREACH

CTSI Fuels Translational Science

In 2006, the National Institutes of Health (NIH) named the University of Pittsburgh to a prestigious inaugural class of 12 institutions receiving a Clinical and Translational Science Award (CTSA), an ambitious program conceived to spur scientific innovation and speed new treatments to people who need them. The plan called for nothing less than a complete transformation in research practice. Since then, Pitt's Clinical and Translational Science Institute (CTSI) has demonstrated that the University is worthy of NIH's $83.5 million trust—a conviction renewed in 2011 with an additional $67.3 million over the next five years.

"The institute has more than exceeded my expectations," says Steven E. Reis, MD, CTSI director and associate vice chancellor for clinical research for the health sciences. CTSI collaborations include investigators from Pitt's Schools of Medicine, Nursing, Pharmacy, Dental Medicine, Health and Rehabilitation Sciences, and the Graduate School of Public Health. The institute reaches beyond the University and its clinical counterpart, UPMC, to involve Carnegie Mellon University, RAND Corporation, and a community partner, the Urban League of Greater Pittsburgh. Among its accomplishments, CTSI has:

- Distributed $2.5 million in pilot investments for investigators with novel ideas to gather preliminary data that can help secure more funding to advance research
- Supported nearly 3,000 studies and 1,500 individual investigators
- Established a network of 11 facilities equipped for researchers to conduct exams or evaluate treatments and interventions as part of research studies
- Used the CTSI Mobile Lab, a specially outfitted 18-wheel rig, to engage nearly 9,000 middle and high school students in hands-on experiments that build enthusiasm for science
- Sponsored more than 130 outreach activities in partnership with nearly 100 community groups to share clinical research and health promotion information with more than 400,000 people
- Created an Internet-based research participant registry that contains the names of more than 20,000 people interested in taking part in clinical studies

In addition, CTSI has supported research studies that have been awarded hundreds of millions of dollars in NIH funding to advance clinical and translational science, and CTSI investigators' research has been cited in more than 10,000 journal articles, a substantial portion of which have appeared in influential publications like the *New England Journal of Medicine*, *Journal of Clinical Oncology*, and *Archives of General Psychiatry*. Career development programs organized by CTSI have also benefited more than 800 trainees, from nondegree students to medical students, residents, predoctoral fellows, and PhD candidates.

"Most importantly, CTSI is accessible," says Kyle Orwig, PhD, assistant professor of obstetrics, gynecology, and reproductive sciences, who depended on CTSI's research facilitators for regulatory guidance while organizing a fertility preservation program for children undergoing cancer treatment. "They were great in terms of putting together institutional review board (IRB) applications and fiscal reviews," he says. "CTSI reserved rooms, got everyone together, and were real advocates for what we were trying to do."

In coordination with patient care and counseling, Orwig's group freezes testicular tissue taken from boys, with the hope that stem cells can be obtained from an immature sperm cell line and later infused to promote resumed sperm production after cancer treatment. For girls, the program offers storage of frozen ovarian tissue. Meanwhile, research continues on experimental fertility preservation technologies. About half a dozen boys have taken part to date. CTSI expertise and service throughout "have been absolutely fantastic," Orwig says.

Michael Boninger, MD, professor and chair of the Department of Physical Medicine and Rehabilitation, credits CTSI with making crucial contributions to the pioneering work for which he and Andrew Schwartz, PhD, professor of neurobiology, are coprincipal investigators.

With funding from CTSI's Translational Tool Pilot and Clinical Research Scholars programs, Boninger and Schwartz recently received U.S. Food and Drug Administration and IRB approval to study the use of revolutionary brain-computer interfaces in individuals with paralysis. Trial participants are being recruited now (see story page 31).

"CTSI is an amazingly valuable resource to the University," notes Boninger.

CTSI-supported projects, training, and infrastructure innovations have begun a University-level transformation by forging unprecedented connections among research scientists, clinicians, and the community. In coming years, CTSI resources for research and education will continue to coalesce into a new and distinct clinical and translational research enterprise to accelerate scientific progress and benefit public health in Pittsburgh and around the world.

CAPITAL GAINS

UPCI Turns 25, Wraps up Campaign

As the University of Pittsburgh Cancer Institute turns 25, it—and the UPMC Cancer Centers—celebrates another milestone: the conclusion of a five-year, $100 million capital campaign to support research, faculty recruitment, and infrastructure projects.

The campaign began with a $20 million contribution from the Henry L. Hillman Foundation and the Hillman Foundation. That gift created the Hillman Fellows Program for Innovative Cancer Research. The fundraising effort has also resulted in the establishment of the Arnold Palmer Chair in Cancer Prevention, the Thomas and Sandra Usher Chair in Melanoma, the Jane and Carl Citron Chair in Colon Cancer, and the Stanley M. Marks, MD, Research Fund. Other money generated by the capital campaign has funded research into nutritional and dietary methods of combating cancer, new treatments for melanoma and mesothelioma, and the identification of blood proteins responsible for the development and recurrence of cancer.

A STUDY IN MODERATION

Homanics Wins Prestigious MERIT Award

Step into a bar on Friday at 5 p.m., and you'll be lucky to find a seat. As any social drinker will tell you, few things take the edge off like a glass of chardonnay or a pint of IPA. How exactly does alcohol soothe the nerves? Scientists don't know for sure; but, as it turns out, our brains have a natural mechanism for managing stress and nervous tension. The GABA (gamma-aminobutyric acid) neurotransmitter pathway acts to quiet electrical activity in certain parts of the brain. When GABA binds to its receptor, neuronal activity slows down. Ethanol binds to these same receptors, enhancing the relaxation effect.

Gregg E. Homanics, PhD, professor of anesthesiology and of pharmacology and chemical biology, studies the mechanisms by which alcohol exerts its effects on the central nervous system. He was recently selected by the National Institute on Alcohol Abuse and Alcoholism to receive a coveted NIH MERIT (Method to Extend Research in Time) award. Homanics strategically mutates the genes encoding GABA receptors and observes the effect of subsequent alcohol exposure at the cellular, molecular, and organismal levels. Shedding light on these processes might lead to advancements in the treatment of alcoholism, as GABA receptors are also implicated in alcohol addiction, tolerance, and withdrawal. The studies could also provide valuable clues into the mechanisms of anesthesia, epilepsy, learning, memory, and developmental abnormalities.

MERIT awards provide stable, long-term funding to outstanding investigators who have made significant advancements in their fields. (The University of Pittsburgh counts 17 current MERIT awards among its faculty members.) Less than 5 percent of NIH-supported researchers receive this award, which affords the opportunity to obtain up to 10 years of funding. The award will provide Homanics with approximately $4.7 million until 2020.

YOUNG SCIENTISTS AT PITT GET A BIG BOUNCE

NEXT GEN

Five years ago, the National Institutes of Health introduced a new way to identify promising young scientists and shepherd them along a career path to becoming independent investigators. The goal is to overcome a problem that has gestated for years: In 1970, the average age for a scientist receiving a first independent investigator award (R01-equivalent, in NIH parlance) was 34. Today, it's over 42—and that's just PhDs; MDs and MD/PhDs tend to be even older. Good scientists are getting hung up in the pipeline, so NIH introduced an award that begins as a mentored training grant (K99), then transitions to an independent investigator award (R00). It's called the Pathway to Independence, but the nickname "kangaroo grant" has stuck.

The University of Pittsburgh is in the top tier of universities receiving coveted Pathway to Independence awards, with some 16 active in the School of Medicine as of July 1, 2011.

Tanja Bekhuis, PhD, Department of Biomedical Informatics
→ *Screening Nonrandomized Studies for Inclusion in Systemic Reviews of Evidence*

Michael Butterworth, PhD, Department of Cell Biology and Physiology → *ENAC Regulation in the Kidney by Vesicle Trafficking and Recycling*

Jason Cannon, PhD, Department of Neurology
→ *New Approaches to Gene-Environment Interaction Modeling in Parkinson's Disease*

Marsha Cole, PhD, Department of Pharmacology and Chemical Biology → *Metabolic Street-Induced Fatty Acid Nitration and Cardiovascular Function*

Indrani Halder, PhD, Department of Medicine, Division of Cardiology → *Biobehavioral Genetics of CVD Risk*

Jacqueline Ho, PhD, Department of Pediatrics, Division of Pediatric Nephrology → *MicroRNAs in Kidney Progenitor Cells*

Youko Ikeda, PhD, Department of Medicine
→ *The Role of Urothelial-Interstitial Cell Communication in Detrusor Overactivity*

Xia Jiang, PhD, Department of Biomedical Informatics
→ *Detecting Genome-Wide Epistasis with Efficient Bayesian Network Learning*

Shabaana Khader, PhD, Department of Pediatrics, Division of Pediatric Infectious Diseases → *Novel IL-17 Producing Memory Cells Are Key to Vaccine-Based Immunity in the Lung*

Hongjun Liu, PhD, Department of Microbiology and Molecular Genetics → *Mechanisms of WNT Signaling in Regulating Metabolism and Mammalian Aging*

Michele Okun, PhD, Department of Psychiatry
→ *Pregnancy-Related Sleep Disturbances May Increase Pregnancy Complications*

Monica Perez, PhD, Department of Physical Medicine and Rehabilitation → *Intermanual Transfer of Learning in Healthy and Spinal Cord Injured Individuals*

Matthew Smith, PhD, Department of Ophthalmology
→ *Influences of Attention and Eye Movement Signals of Population Coding in Area V4*

Alejandro Soto-Gutiérrez, MD, PhD, Department of Surgery, Division of Experimental Pathology → *Engineering of Hepatic Grafts with Decellularized Native Matrices*

Heth Turnquist, PhD, Department of Pathology, Division of Transplantation → *Influence of ST2 and IL-33 on Cardiac Allograft Vasculopathy and Outcome*

Hong Wang, PhD, Department of Pharmacology and Chemical Biology → *DNA Damage–Induced Structural and Dynamic Changes at Telomeres*

As a postdoctoral fellow in surgical research at Harvard University, **Alejandro Soto-Gutiérrez, MD, PhD**, completed preliminary experiments suggesting that ischemic livers unsuitable for transplantation might be engineered to make them usable. In a rodent model, he used a detergent solution to strip the liver of its cells, leaving a pale, rubbery ghost of an organ, mainly consisting of collagen and other structural proteins. He seeded this liver-shaped scaffolding with cultured rodent liver cells, which seemed to make themselves at home, propagate, and eventually form a functional liver.

When he was awarded a K99/R00 to further this research, Soto-Gutiérrez began to cast about his institution for collaborators but came up short. What he proposed to do was something of a *tour de force* involving advanced tissue engineering, fundamental liver biology at every level from cell to organ, and cultivation of engineered livers in bioreactors, plus the complex surgical aspects of liver transplantation.

"Pittsburgh really started to look like heaven," he says. "There are groups in all these different areas. I really came to believe that to advance this project, I needed to be here."

It's very unusual to transfer to another institution right off the bat, while still in the mentored training phase of the award. But Soto-Gutiérrez had a strong case. Even his mentor at the time, who wanted him to stay in Boston, came to agree that Pittsburgh was a better place for him. In July 2010, Soto-Gutiérrez and several colleagues published their report on this novel means of producing liver grafts in *Nature Medicine*. Currently, the group is working to extend the survival of these grafts beyond just a few days, in part by improving the function of the graft's bile duct. Stay tuned.

"Pittsburgh really started to look like heaven…I really came to believe that to advance this project, I needed to be here."

"People know we're here."

Monica Perez, PhD, is asking fundamental questions about how the brain and spinal cord control voluntary movements such as reaching and grasping. Answers to these questions could reveal a wealth of information about how people recover and regain function after spinal cord injury. Perez earned her PhD at the University of Miami School of Medicine, and she received a Pathway to Independence award during her postdoctoral fellowship at the National Institute of Neurological Disorders and Stroke. In 2009, she transitioned to the independent phase of the award and joined the faculty of the University of Pittsburgh School of Medicine's Department of Physical Medicine and Rehabilitation, becoming one of several investigators in Pitt's Systems Neuroscience Institute.

Perez adds a vital new dimension to this group. She uses a noninvasive method called transcranial magnetic stimulation (TMS) to map activity in the cortex as research participants move their limbs and respond to peripheral nerve stimulation. Her volunteers include healthy adults as well as those with spinal cord injuries. Her lab may be the only one in the country using TMS in patients in this way.

"Presently, this is the best way to stimulate the brain noninvasively and without pain to look at these connections," says Perez. And though she points out that her group is interested in learning basic information about how the brain and spinal cord function, there are important potential applications for this information. For this reason, a large number of patients have found their way to her lab.

"We have a large database of patients now," she says. "People know we're here. We try to provide them with information. For example, we may be able to find remaining connections to muscles that cannot exert visible voluntary activity. This insight may suggest ways to improve motor function working with their physicians and therapists. Recovery is limited, so interventions are typically attempts to maximize functional improvements."

It's the dawn of a new day atop Biomedical Science Tower 3, where leaders of the University of Pittsburgh's Drug Discovery Institute are positioning the University to take advantage of a unique moment in history.

The fact is that the process of drug discovery and development in this country simply doesn't work as well as it should. It takes too long. It costs too much. The odds of success are low. As a result, big pharmaceutical companies are rethinking how they engage in research and development. Increasingly, they are looking to partner with academia to help them turn the corner and produce the next major therapeutic advance.

Academics can't teach industry much about manufacturing and marketing—those will always be industry's areas of expertise. But the University of Pittsburgh has much to offer pharmaceutical companies as a potential partner. In addition to its traditional strength in multidisciplinary research and its growing capabilities in structural biology, computational and systems biology, and combinatorial chemistry, the University has a retooled, refocused Drug Discovery Institute (DDI) that combines scientific excellence with business savvy. The institute has entered an exciting transition period under the leadership of D. Lansing Taylor, PhD, a cell biologist with extensive background as an entrepreneur, having founded multiple biotechnology companies.

"We have tremendous talent, world-class facilities, and the drive to push discovery into the future," says Taylor, DDI director and Allegheny Foundation Professor of Computational and Systems Biology in the School of Medicine. "By combining our intellectual power and expertise in the early phases of the discovery process with the pharmaceutical industry's knowledge about preclinical and clinical trials, we will gain mutual value that will help our institution and the world. It's all here."

DDI opened its doors in 2006, one of the first tenants of Pitt's new, $205-million Biomedical Science Tower 3. The institute has rapidly expanded to become a high-production facility, capable of holding as many as 5 million chemical compounds and equipped with more than 10 robots for automated assay plating, giving researchers virtually infinite drug-screening opportunities. Its faculty members hail primarily from three Pitt schools—the School of Medicine, the School of Arts and Sciences, and the School of Pharmacy—and create a unique mosaic of scientists working along the continuum of drug discovery. One of Taylor's innovations was to grow the institute by bringing on board those scientists already working in these critical areas at Pitt and adding key investigators recruited from industry. The institute is adding to its strengths in chemistry, computational chemistry, and computational and systems biology. Taylor and his colleagues aim to tackle the complexity of the human system to help create a new generation of drugs.

D. LANSING TAYLOR, PHD

We have tremendous talent, world-class facilities, and the drive to push discovery into the future.

It's all here.

DDI

The institute has four associate directors, including Barry Gold, PhD, professor and chair of pharmaceutical sciences, School of Pharmacy; Edward Chu, MD, professor of medicine and of pharmacology and chemical biology as well as chief of the Division of Hematology/Oncology and deputy director of the University of Pittsburgh Cancer Institute; Peter Wipf, PhD, Distinguished University Professor of Chemistry and director of Pitt's Combinatorial Chemistry Center; and Ivet Bahar, PhD, John K. Vries Professor and chair of computational and systems biology.

Partnerships with pharmaceutical companies have already begun and more are on the way, particularly in cancer and neurological diseases, areas with long track records of success at Pitt. In 2011, Johnson & Johnson began working with the University on potential cancer therapeutics. A project exploring personalized genomic approaches to treating cancer is under discussion.

Among the mountains of discoveries made in Pitt labs in recent years, nearly three dozen small molecules are in various stages of the patent process because of their significant promise for treating diseases like cancer, pulmonary hypertension, diabetes, and HIV/AIDS. Opportunities to commercialize these molecules are being aggressively pursued through a partnership between DDI and the University's Office of Technology Management.

With all of the promising science produced at Pitt, backed by a rejuvenated, retooled DDI, Taylor feels the window of opportunity is now to secure comprehensive, long-term pharmaceutical collaborations that will help drive the discovery process at Pitt and lead to big gains in global health.

GENERATION NEXT

MATTHEW TAYLOR, MD

EDUCATIONAL INNOVATION

Pitt's Baby, the Scholarly Project, All Grown Up

The School of Medicine's scholarly project, once considered a revolutionary idea to engage medical students in biomedical research, is now a fully integrated and widely celebrated part of the medical school curriculum. Now in its sixth year, the program requires medical students to formulate and complete a scholarly project through preparatory course work, longitudinal self-directed learning, and faculty mentorship. The payoff has been impressive; for the class of 2010, scholarly project endeavors netted 38 fellowships, grants, or other national awards, 28 School of Medicine awards, co-authorship of 104 peer-reviewed papers, and more than 120 national presentations and abstracts.

"The biggest benefit of the scholarly project for the students is that they learn how to do science," says David Hackam, MD, PhD, Watson Family Professor of Surgery and associate dean for medical student research. "Graduate schools teach you how to do science. Medical schools teach you how to be a clinician. Very few medical schools teach both, and that's the void that the program aims to fill. As a result, our medical students have a nontraditional, open-minded approach to their educational experience. They're constantly questioning, critiquing, and challenging what they're taught, and this mindset is the outcome of immersion in a curriculum that teaches the scientific method through direct learning."

For Matthew Taylor, MD '11, the opportunity to conduct research was crucial to choosing Pitt for medical school. "I knew when I was applying to medical school that I was interested in exploring academic medicine as a career. I'd had some lab experience as an undergraduate chemistry major, and I wanted a place that would allow me the time and space to try health-related research. The scholarly project was a big draw for me, as was Pitt's reputation as a strong research institution."

Taylor quickly found opportunity in the lab of Yatin Vyas, MBBS, MD, assistant professor of pediatrics and of immunology. Between his second and third years, he took a year off to devote his efforts to full-time research. Vyas guided Taylor toward a project investigating the role of deficient Wiskott-Aldrich syndrome protein (WASp) in the pathogenesis of Wiskott-Aldrich syndrome, an X-linked disease associated with severe autoimmunity and immunodeficiency. Through a series of elegantly designed *in vitro* experiments, Taylor demonstrated a previously unappreciated role for WASp as a transcription factor involved in aberrant histone modification and dysregulated adaptive immunity, a paradigm-shifting find for WASp investigators. Taylor received a Dean's Research Scholarship Award for his work and was first author of an article published in the high-profile journal *Science Translational Medicine* in June 2010.

"Mentoring Matthew through his scholarly project and watching him grow from medical student to physician-scientist has been a fantastic experience," Vyas enthusiastically reports. "I've had fellows, postdocs, and graduate students in my lab; but Matthew was my first medical student, and he brought with him a completely different perspective on biomedical research. He sees the big picture and is able to think beyond the level of the cell to see the more global implications and clinical applications for the diseases we study."

After graduation, Taylor embarked on a residency in pediatrics at Children's Hospital of Pittsburgh of UPMC. He plans to build upon the work started through his scholarly project and is already considering a research fellowship in hematology/oncology or critical care medicine. His advice to

incoming medical students: "It's important to choose a good mentor—someone who is invested in you, knows what level you're coming in at, and has reasonable expectations. Working with a mentor like Dr. Vyas was pivotal to my having a great experience. He gave me a lot of freedom and understood my obligations as a medical student while still making sure the experiments were going in the right direction. He was a great role model for me of a clinician scientist—a physician who does science and does it well."

With the scholarly project program now firmly established in the curriculum, Hackam is looking to improve and augment the experience for students and faculty. Efforts to identify and train skilled mentors, facilitate student-mentor relationships, build an interactive Web site, and enhance the quality and scientific rigor of the projects are all under way. Says Hackam, "Our long-term goal is to make this the premier medical student research experience in the country."

RICH CULTURE MEDIUM

Incubating the Biomedical Scientist

In addition to those in the MD/PhD program, more than 200 students are pursuing PhDs in the School of Medicine. Most are in the Interdisciplinary Biomedical Graduate Program, which offers six research tracks to choose from: cell biology and molecular physiology, cellular and molecular pathology, molecular genetics and developmental biology, molecular virology and microbiology, molecular pharmacology, and immunology. In addition, new programs have been created to embrace emerging fields of science. They include clinical and translational science, biomedical informatics, neuroscience, integrative molecular biology, molecular biophysics and structural biology, and a novel program in computational biology run jointly by the University of Pittsburgh and Carnegie Mellon University.

"I was really impressed with the translational aspect of Pitt's PhD program," says Kelly Quesnelle, a student in the molecular pharmacology track. Her thesis explores mechanisms by which cancer patients become resistant to drug therapy over time and ways of overcoming that resistance with drug combinations. "There's this great interface between physicians and scientists here. It's important to me, because I do cancer research, finding reasons why drugs work and don't work. I have a paper under review now with my advisor that supports phase I trials going on around the country, coming up with a scientific rationale for why this might work for patients with head and neck cancer."

CAMARADERIE

The Few, the Proud, and the Karaoke Machine

Even in the rarefied atmosphere of a top medical school, where diligence and excellence are the norm, there's no denying that MD/PhD students are hardcore. They're like the Marines, except these comrades are armed with stethoscopes, pipettes, and well-worn lab notebooks.

Accounting for roughly 11 percent of students in the school, those in the MSTP (Medical Scientist Training Program) are intent on careers that combine biomedical research and clinical medicine in equal measure. They are considered key to the nation's continued advancement in science and medicine, particularly the translation of science from the laboratory to the clinic, and this is why NIH supports 42 such programs across the country. With more than 90 students, Pitt boasts one of the largest. The program is known for blurring the line between its two halves—the PhD and the MD—creating a seamless training program for physician-scientists. As a joint program with Carnegie Mellon University, the MSTP gives students the option of pursuing their PhD studies at this university known for its expertise in robotics, engineering, and computation.

"We recreated the MSTP in 1997 and thought way out of the box," says MSTP director and professor of pathology Clayton Wiley, MD, PhD. "The PhD and clinical work are integrated in a comprehensive way. An enrichment program runs throughout. The end result is that you're in basic and clinical science at all times. That's critical, because when these students are done, they have to bring the two together to make a career. At Pitt, they've already lived it."

"You never felt like you were just in grad school or just in med school," says Judson Englert, MD, PhD, who graduated in 2011. "That's what an MSTP is supposed to be; and in Pittsburgh, they hit the nail on the head."

A critical measure of success for a scientist is the ability to garner funding. To that end, MSTP students take a grant-writing class during their third year, with Wiley as the primary instructor. The students write a mock F30 grant (technically, a Ruth L. Kirschstein National Research Service Award), which is NIH's individual training grant for MD/PhD candidates. Students critique one another's proposals as though they were on the review committee. Among the many lessons MSTP grad Corrine Kliment, MD, PhD, learned in the course was the importance of scope in a successful proposal. "If the project's too broad, somebody will read it and say, 'There's no way you're going to get all that done,'" she says.

Kliment used the class to write a grant to study the antioxidant properties of a protein in the lung.

"None of the other students studied oxidative stress or the lung," she says. "The class forced me to be able to communicate my work to people who weren't in my field."

Wiley likens the class to a highly specific writing workshop. It used to be that MD/PhDs like Wiley were trained in "the school of hard knocks." You write a grant application, "then somebody trashes it because you don't know how to write it," Wiley says. "It's like somebody asked you to write a sonnet, and you didn't know what the structure of a sonnet was. We teach them to write the sonnet."

Pitt's MSTP students now lead the country in F30s. (Pitt had 25 at last count, ahead of Washington University's 20 and the University of North Carolina's 18.) The program also trains students in the art of poster presentation, reading research papers critically (and quickly!), and medical ethics.

According to recent graduates and current students, *esprit de corps* is a less tangible quality that nevertheless sets Pitt's program apart from its peers.

"The people in the program are like family, through good and bad," says MSTP student David Wheeler. "When someone stumbles and is going through a bad patch, we chip in and we help out. And when something great happens—engagement, wedding, birth, scientific publication—we show up to celebrate."

Leading this uncommon family is the guy everyone calls "Clayton." (A student might get away with calling him "Dr. Wiley" once, but usually not a second time.) He is known for enthusiastically joining the activities at the MSTP annual retreat—volleyball, poker, and even karaoke. Wiley, who is rumored to have a fine singing voice, admits to performing a forgettable rendition of Madonna's "Die Another Day" at the most recent retreat. But he claims it was the result of a misunderstanding, saying, "I was set up for Perry Como."

"I think the program director makes the program," says Kliment. "Clayton invests in the students, and you sense that when you talk with him. He helps you think through where you want to go career-wise, what you can do now to get there, and how to choose the residency program you want. He pushes us to know ourselves."

For Kliment and Englert, who wed this summer within weeks of graduation, this seven-year mentorship culminated on Match Day with the announcement that they had both been selected for the internal medicine residency program at Harvard's Brigham and Women's Hospital. (All 11 members of the MSTP Class of 2011 did themselves proud on Match Day, landing coveted residency spots at Duke, Harvard, Michigan, Penn, UCLA, UCSF, and Pittsburgh.)

OPTIONS FOR STUDENTS

What's Next? A Generation of Physician-Scientists

For a handful of elite medical students intent on developing their abilities as physician-scientists, the four-year MD is not quite enough. Fortunately for them, Pitt offers two five-year programs that immerse students in biomedical research.

Physician-Scientist Training Program

After graduating from Harvard in 2004, Mamie Thant entered a PhD program in surface/materials science but soon realized that she was more interested in medicine. "I felt that medicine was more applicable to everyday life," she says. She joined Pitt's Physician-Scientist Training Program (PSTP). The program admits up to six exceptionally talented students each year who, in addition to the rigorous med school curriculum, undertake two summers and a year of basic science research training to prepare them for careers in academic medicine. PSTP students receive partial tuition assistance for the four years of medical school plus a stipend during the research summers and the research year.

Thant works in the lab of cancer virologists Patrick Moore, MD, MPH, professor of microbiology and molecular genetics, and Yuan Chang, MD, professor of pathology. In 2010, she was one of 74 students in the nation to win a Howard Hughes Medical Institute medical research fellowship, which provides financial support for one year of research. Thant works on two related but independent research projects: She studies the mechanisms of how a particular viral protein transforms cells in Merkel cell carcinoma, and she is developing a "best practices" protocol for separating and preserving the blood of patients with Merkel cell carcinoma. When asked which project she enjoys more, Thant jokes, "Whichever one is giving me results." She elaborates, "I like that basic science is a bit more straightforward. In translational research, you're dealing with the heterogeneity of a large group of patients, making it more difficult to draw conclusions. But, that's how it is in real life."

Another PSTP student, Kristy Shine, started medical school within weeks of successfully defending her PhD thesis in medical engineering/medical physics at the Health Sciences and Technology program of Harvard-MIT. She was accepted to several medical schools but chose Pitt for its emphasis on research and its PSTP. Shine joined the lab of Rocky Tuan, PhD, professor of orthopaedic surgery and director of Pitt's Center for Cellular and Molecular Engineering, where she studies the relationship between the age of donor stem cells and their migration in wound

healing. Shine feels that the PSTP helps to bridge the gap between traditional PhD and MD programs and produces well-rounded physician-scientists. "We understand not only the basic science behind new discoveries but also the challenges involved in translating such laboratory findings into practical, clinical applications. If a technology isn't designed for health care providers to use efficiently, it isn't going to work clinically," she explains.

The Clinical Scientist Training Program & Doris Duke Clinical Research Fellowship

When Constantinos "Taki" Michaelidis applied to Pitt's medical school, he was told that the Clinical Scientist Training Program (CSTP) was designed for students with a "fire in the belly" for research. The program is designed to encourage exceptional medical students to pursue careers in clinical research by giving them a one-year opportunity to learn and practice clinical and translational research skills. Interested students apply to the University of Pittsburgh Doris Duke Clinical Research Fellowship Program 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 Doris Duke Clinical Research Fellows for the research year, during which they receive a living stipend, health insurance, and tuition toward a graduate certificate in clinical research. After successful completion of the fellowship year, they receive a CSTP scholarship toward the final year of medical school.

After being accepted, Michaelidis joined the lab of Kenneth Smith, MD, MS, associate professor of medicine. He felt that his previous experience as a health care financial modeler would mesh well with Smith's vaccine modeling research. His hunch was correct. After only one summer of research, he was first author on a publication in *Vaccine* that examined the cost effectiveness of a national influenza vaccination program. After graduation, Michaelidis hopes to combine his clinical research and business skills to improve health care quality.

Former CSTP student Annie Silk (MD '08) says that her clinical science training helps her to critically examine and address problems in the clinic. A member of Pitt's very first CSTP class, Silk once struggled to perform physical exams on obese patients because their organs are more difficult to palpate. She knew that an incomplete exam could lead to missed diagnoses and unnecessary tests, and she wrestled with how to overcome this problem. "We deal with obese patients every single day," she says, "but no one really talks about it."

Silk began to review the literature and interview clinicians to learn how they handle obese patients in the examination room. She compiled a list of practical suggestions for physicians, such as asking an obese patient to lift his head to expose the thyroid gland. Her findings were published in the *Journal of the American Medical Association* in 2011. Having completed her internal medicine residency in Pittsburgh this year, Silk now applies her clinical research training as a research fellow in hematology/oncology at the University of Michigan.

IN THE ZONE

Med-Ed Goes High-Tech

Every Pitt medical student benefits daily from innovative programs and services provided by a small but dedicated group of people in the School of Medicine's Laboratory for Educational Technology (LET). The Zone, a Web portal that serves as the centralized area for medical student online activity, and Learning Log, a clinical log that allows medical students to record their educational and clinical experiences from patient encounters, are just two of the more widely recognized and heavily used applications created here. LET is a research and development group engaged in the discovery, development, and validation of new technologies that support the educational mission of the School of Medicine.

Led by James B. McGee, MD, assistant dean for medical education technology and associate professor of medicine in the Division of Gastroenterology, Hepatology, and Nutrition, LET has created custom learning management systems, online collaborative learning Web sites, independent learning modules, and virtual patient simulation for use by medical students and faculty here and across the country. For example, vpSim is an easy-to-use, standards-based virtual patient simulator for education and assessment that was conceived, designed, developed, and tested by LET. For this invention, LET received the 2010 Pitt Innovator Award from the Office of Technology Management and the "best implementation of the virtual patient standard" award at the 2009 MedBiquitous annual conference.

Says McGee, "vpSim has made developing Web-based clinical simulations for teaching and assessment as easy as using PowerPoint. Faculty at the medical, dental, and pharmacy schools now use vpSim interactive cases in the classroom, in workshops, and for independent learning. It's also used by a dozen medical schools around the world and throughout the Veterans Affairs health system."

WHAT MATTERS MOST

One-on-One with a Master Educator

Generations of Pitt physicians have learned the art and science of medicine under the tutelage of Basil J. Zitelli, MD, professor of pediatrics and holder of the Edmund R. McClusky Chair in Pediatric Education. A 1971 graduate of the School of Medicine and a founding member of its Academy of Master Educators, Zitelli reflects on what matters most in medical education.

As a faculty member since 1978, you've seen dramatic changes in the use of technology in the practice of medicine. How has technology changed education?

Technology can be a valuable adjunct to basic clinical skills and decision making. The computers we carry with us on daily rounds, for example, allow us to have immediate access to the patient's medical record and the Internet. The downside is that we spend more time in front of computers and less time at the bedside. So, I constantly remind students to address the patient and not the computer because the doctor-patient relationship is the foundation for all that we do. As William Osler said, medicine is learned at the bedside, not in the classroom.

The history and physical examination remain the most efficient and cost-effective means of making a diagnosis. They establish the needed contact between physician and patient, particularly with the laying on of hands. I think we should use the history and physical exam to formulate the diagnosis, then use technology to verify it.

How does your philosophy manifest itself in the way you teach?

I challenge students to find something in their examination that the resident or attending physician hasn't documented. When we're doing a physical examination of a baby, I'll sometimes ask students to tell me what they see without touching the patient. When they are challenged in that way, students are able to do an excellent physical examination, just by observation. My aim is to improve their powers of observation so that when they walk into the room, their powers of observation are tuned up. I also tell them, as Osler said, "Listening is a form of respect." He also reminds us that, "to educate the eye to see, the ear to hear, and the finger to feel takes time;" and to start a student on the right path is all that we can do.

How do patients benefit from a low-tech approach?

Several years ago, a 12-year-old boy was referred to our practice for headache and a possible brain tumor. His primary care physician had referred him to an optometrist, who noted a mild refractive error. He then was referred for skull X-rays, which were normal. A CT scan of the head showed some abnormality, and the question of a tumor was raised, further heightening anxiety and fear. He then was referred to our clinic. My partner, through careful history, learned that the boy had had a two-week history of headaches without visual changes or nausea, generally relieved by simple non-steroidal medication. The physical examination, including a detailed neurological examination, was entirely normal. A review of the records and films revealed that the abnormality seen on CT and MRI was a benign arachnoid cyst. By the time all the studies were completed, the patient's headaches had spontaneously resolved.

This story was an important lesson for us in a risk associated with technology known as the "cascade effect" — a chain of events initiated by an unnecessary test, unexpected result, or patient or physician anxiety, which results in ill-advised tests or treatments that may themselves cause avoidable adverse effects and/or morbidity. In this particular case, had a thorough history and physical exam been done earlier, this boy and his family could have been saved a very expensive and time-consuming workup, as well as a great deal of unnecessary fear and anxiety.

What makes for a successful educator?

Three things: understanding that learning is a continuous lifelong process, knowing your audience, and recognizing teachable moments. You don't stop learning after your residency, chief residency, or fellowship. Just as I am still learning myself how to do a better history and physical exam, I challenge my students to continue honing their skills throughout their careers. It's also important to understand who your audience is. When I teach medical students, it's very different from when I teach residents or postgraduate physicians. I start with the basics and explain how basic pathophysiology leads to certain physical findings, which in turn explains what we see clinically, which then determines how we approach the patient therapeutically. Learning becomes a common thread that extends throughout the entire educational experience. The third part of being a good teacher is recognizing teachable moments — even in the middle of resident work rounds, I will stop to explain a concept to medical students and bring them up to a higher level of understanding. That's all part of being a good teacher.

What's next for you?

Well, mentoring junior faculty and developing programs that benefit patient care and the educational mission of the Department of Pediatrics are always high priorities. I also plan to continue working [with associate professor of pediatrics Holly Davis, MD] on the *Atlas of Pediatric Physical Diagnosis*, which is now in its fifth edition. I've been humbled and pleased by how well it's been received and how much it has helped students and residents over the years.

If you could give one piece of advice to future physicians, what would it be?

Be passionate about your career. From that springs everything else. The love of learning, the importance of taking care of patients, the keeping of the humanity of patients and families with you, the excitement of teaching — all of that stems from being passionate.

THE ENVELOPES, PLEASE

Meet Your Match

The lecture room in Scaife Hall is buzzing like a nightclub and bumping with bass as the Black Eyed Peas croon *I gotta feeling that tonight's gonna be a good night*. Snapshots of the Class of 2011 flash across the screen, bringing laughter, shouts, and cheers from the actual members of the class, who swarm the aisles. They are glowing, as if lit from within. They embrace, slap hands. Handshakes are firmer than usual. Quiet, knowing nods and pats on the back are pregnant with meaning. It's Match Day. Time to meet the oracle.

The hands of the clock meet at 12, and spontaneous applause builds to a crescendo. Associate dean for student affairs Joan Harvey, MD, steps to the podium and proudly smiles at the class, her academic children of the past several years. Similar scenes are playing out all over the United States, as more than 22,000 new medical professionals are poised to learn where they will begin their residency training. Prolonging the drama, Harvey reports that a record 150 individuals from the University of Pittsburgh School of Medicine have secured residency positions for next year. Two-thirds of you, she says to applause, matched at top-tier programs (per *U.S. News & World Report*).

"Along with many placements at our own most prestigious institution, UPMC, your programs include Johns Hopkins, Brigham and Women's, Mass General, Beth Israel Deaconess, Yale, Stanford, the University of Chicago, Columbia, Cornell, UCSF, Michigan, Barnes-Jewish, Penn, Rochester, UCLA, the University of Washington, and Children's Hospital of Philadelphia—to name a few—virtually all the top programs in the country," Harvey says with a smile. "The Harvard programs, the University of Washington, Vanderbilt, and Michigan head up the list of other institutions that will be most populated by our students next year, with Duke, Brown, and Yale close behind."

Encouraging news, no doubt. But it's an impatient, expectant crowd; and it's all they can do to keep from shouting, "The envelopes, please!" There are babes in arms, couples gripping one another's forearms, and med students anxiously perched between their parents. Finally, one by one, members of the Class of 2011 are summoned by Harvey, by Arthur S. Levine, MD, dean of the School of Medicine, and by Chenits Pettigrew, PhD, assistant dean for student affairs.

Cameras flash as students make their way to the front. Attire ranges from nightclub chic to sports-fan casual. There is at least one Pittsburgh Penguins jersey, along with glittering green top hats for St. Patrick's Day. Upon hearing her name called, the owner of one spectacular pair of spike-heeled boots takes approximately one half of her med school career to descend 36 steps from the back of the auditorium. (What's the point of learning your future if you can't look stunning while doing it?)

Most open the envelope on the spot. Many borrow a mike to share their news. There are bursts of emotion and celebration.

"I'm staying in Pittsburgh!" someone shouts, commencing a vigorous touchdown dance.

One student reads her letter and nearly pitches forward as she clutches something invisible at her throat. She looks at the paper in her hand again, takes a mike, says "Anesthesiology, Massachusetts General Hospital," and returns to the front row to cry and collapse into the arms of her loved ones. Another student discharges a can of spray confetti indiscriminately as his classmates climb the stairs clutching their letters.

Faculty and staff soak up the atmosphere. In the back of the hall, a salt-and-pepper-haired doc stands with his hands in the pockets of his white coat, surveys the scene, and smiles. He applauds vigorously each time another fourth-year says "Pittsburgh!"

Some approach the stage like boxers entering the ring. Another quietly sneaks up the stairs with her still-sealed envelope in hand. A questioning look from a friend causes her to shake her head and whisper, "Not yet." She exits the auditorium. Five minutes later, she's back with a grin and a thumbs-up. Meanwhile, a man in African garb quietly says "Yale" into a mike, then takes the steps two at a time through a raucous ovation and a smattering of high fives.

Displaying a measure of composure that only the young can manage (and makes parents blink back tears), a young woman looks up from her letter and says, "Mom and Dad, I'm coming home." And that's all you need to know about what's happening here. Classmates are embraced, supported, and caught as they stumble in their emotion. Nobody falls down here. Some will swear their feet never touched the ground.

A woman says "Radiology at UCSF" into a microphone, then seems to bite her finger in some inexplicable attempt to hold it together long enough to make it up the stairs to row 14. She runs a gauntlet of hands—guiding, lifting, reaching out to say *we're here with you*—all the way to the middle of row 14, where she finally reaches the husband and child she is looking for and dissolves into tears as she is wrapped in the crushing embrace of her future.

DONALD S. BURKE, MD

RONALD C. MONTELARO, PHD

Pitt's Center for Vaccine Research (CVR) is home to some heavy hitters in the fight against infectious disease. Since the CVR opened in 2006, the staff has grown from a skeleton crew to 17 faculty, 10 affiliate faculty, five graduate students, 14 postdocs, and 28 research technicians. The growth comes in large part from the creative leadership of Donald S. Burke, MD, and Ronald C. Montelaro, PhD.

Burke, in addition to his role as CVR director, serves as dean of the Graduate School of Public Health and associate vice chancellor for global health. He is a former U.S. Army colonel who worked extensively in Thailand and in the rainforests of Cameroon studying emerging infectious diseases. He is a world leader in "bench to bush science," which includes the development of new diagnostics, field studies, clinical vaccine trials, policy analysis, and computational modeling of disease.

Montelaro, professor of microbiology and molecular genetics and a pioneer in the study of HIV, is CVR codirector. His virology expertise was critical in early HIV studies, when researchers were struggling to understand the nuances of the tricky retrovirus. He has since dedicated his career to deciphering how lentiviruses (the family to which HIV belongs) so persistently and efficiently dodge the immune system.

"Lentiviruses enter the body waving a red flag," he explains. "The immune system attacks that red flag, and the virus quickly switches to a yellow flag, confusing the system. We want to know how many different colored flags the virus has and how to stop it."

CVR researchers are up against some formidable pathogens: HIV, influenza, and tuberculosis, to name a few. By applying innovative methods and a team science approach, they have made big strides in a few short years in the effort to develop new vaccines against epidemic diseases. The CVR is home to Pitt's regional biocontainment laboratory, one of 13 federally-funded labs in the country designated for biosafety level 3 (BSL-3) containment.

ELODIE GHEDIN, PHD, assistant professor of computational and systems biology, pioneered methods to explore the genomes of RNA viruses, such as influenza, and uses that information to predict future outbreaks. Ghedin, who was awarded a prestigious, five-year fellowship from the John D. and Catherine T. MacArthur Foundation in 2011, uses revolutionary, next-generation sequencing techniques to uncover the sequences of these rapidly evolving viruses and predict which regions of the genome are more prone to mutations. This information helps scientists predict which emerging viral strains can survive inhospitable environments and are likely to cause widespread disease.

TED ROSS, PHD, associate professor of microbiology and molecular genetics, uses animal models to understand pathogen-host interactions and focuses on creating newer, better vaccines against bugs like influenza, dengue, and Rift Valley fever virus. His latest endeavors have centered on the development of virus-like particle vaccines (VLPs), which contain the outer proteins, or "shell," of a virus but lack the genetic information needed for the virus to replicate and cause illness. The idea is that the viral proteins will trigger an immune response from the host, thereby creating a "memory" of the virus and instilling lasting immunity. Ross has developed several VLPs with computationally optimized broadly reactive antigen (COBRA) technology that enhances the breadth of protection in animals. His flu VLP has gained the most attention for the speed with which it could be mass-produced, making flu vaccines more widely available to a larger population in a shorter amount of time.

JOANNE FLYNN, PHD, professor of microbiology and molecular genetics, is an internationally recognized expert in tuberculosis (TB). With ingenuity and a strategic collaboration, she overcame a nagging obstacle in her research and landed significant support—$12 million to be exact—from the Bill and Melinda Gates Foundation. Teaming up with Pitt radiologists, Flynn developed one of the world's first hybrid positron emission tomography/computed tomography (PET/CT) scanners located in a BSL-3 lab. The scanner allows Flynn to watch, in real time, as TB takes its toll on the lungs over the course of the disease rather than simply examining static postmortem tissues. Her team can see how lung lesions respond to drugs over time. So far, she has had promising results with drugs that are known to be effective; the next step is to initiate studies with newer drugs and, eventually, vaccines. "We want to see what vaccine protection looks like," Flynn says.

INVESTIGATIONS & REVELATIONS

This just in

As one of the top NIH-funded med schools in the country, and one with more than 2,000 faculty members, the School of Medicine is the source of an impressive array of biomedical research—from the most basic biological science to the translational and clinical research that helps us all lead healthier lives. Here is a sampling of the most interesting and promising research publications by Pitt investigators over the past year.

THE LANCET
JULY 2011 VOL. 378 | ISSUE 9785

Pulmonary embolism (PE) is a life-threatening blockage of the main artery of the lung, but it may not always warrant hospitalization. An international research team led by **Donald M. Yealy, MD**, professor and chair of emergency medicine, randomly assigned 344 low-risk PE patients to outpatient and inpatient treatment groups and determined that the groups received equally safe and effective care. The findings, published in *The Lancet*, could have important quality-of-care implications for PE patients and help reduce unnecessary hospital costs. "Patients with PE prefer outpatient treatment, and these reassuring trial results should prompt physicians to consider such care more often for low-risk patients," Yealy explains.

NATURE
JULY 2010 VOL. 466 | ISSUE 7306

Reporting in *Nature*, **Bino John, PhD**, assistant professor of computational and systems biology, and colleagues described novel small RNAs that correspond to an entirely new mechanism of RNA synthesis in human cells. Their work confirms that human cells have the capability to copy RNA as well as DNA—a process that had previously been documented only in plants and simple organisms like yeast. Further research could identify new diagnostic and therapeutic fronts.

JAMA
JUNE 2010 VOL. 303 | ISSUE 24

More than 750,000 Americans suffer from severe sepsis each year, and African Americans are disproportionately affected. In a retrospective cohort study, assistant professor of critical care medicine **Sachin Yende, MD**, and colleagues analyzed data from 2,261,857 infection-related hospitalizations and found that Black patients had significantly higher infection rates and higher risk of acute organ dysfunction than Caucasian patients. It is not known why, but possibilities include differences in chronic disease burden, socioeconomic factors, genetic predisposition, or quality of health care facilities. The findings have important implications for health disparity research and suggest the need for community- and hospital-based interventions to prevent severe sepsis in African Americans. Yende's study was published in the June 2010 issue of the *Journal of the American Medical Association*.

PNAS
MAY 2011 VOL. 108 | NO. 18

In May 2011, **Thanos Tzounopoulos, PhD**, assistant professor of otolaryngology and of neurobiology, reported important findings on tinnitus in *Proceedings of the National Academy of Sciences*. Tinnitus, a relentless and often life-changing ringing in the ears known to disable soldiers exposed to blasts, unwary listeners of too-loud music, and millions of others, is the result of under-inhibition of key neural pathways in the brain's auditory center. The discovery, which used a new technique to image auditory circuits using slices of brain tissue in the lab, points the way to drug development and effective treatment for a condition that currently has no cure.

CELL
NOVEMBER 2010 VOL. 143 | ISSUE 4

Acute and chronic pain affects as many as one in five adults worldwide, creating significant financial and emotional burdens. Yet the biological mechanisms of pain, to a large extent, remain a mystery. In a genome-wide screen in *Drosophila* described in the journal *Cell*, investigators representing more than a dozen institutions—including **Inna Belfer, MD, PhD**, and **Feng Dai, PhD**, of Pitt's Department of Anesthesiology—identified hundreds of genes that show signs of being involved in perception of pain. A large portion of these genes had no known function previously. Because many of these genes are found in a wide variety of organisms, including humans, the discoveries provide a starting point for human genomics studies aimed at finding novel pain genes and defining the molecular mechanisms of pain perception.

PNAS
NOVEMBER 2010 VOL. 107 | NO. 46

Some anti-cancer agents are as close as your medicine cabinet, but even these commonplace pharmaceuticals contain some mystery. For example, it had long been known that aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) could lower the risk of colon cancer, but nobody could explain why that was true. **Lin Zhang, PhD**, associate professor of pharmacology and chemical biology, has shed some light on the mystery. In a November 2010 issue of *Proceedings of the National Academy of Sciences*, Zhang and colleagues reported that NSAIDs interact with stem cells that have accumulated mutations, triggering a biochemical pathway that causes these potentially precancerous cells to self-destruct.

NEW ENGLAND JOURNAL OF MEDICINE
JANUARY 2011 VOL. 364 | NO. 2

Antibiotics are an effective treatment for young children with acute middle ear infections, according to a new study led by **Alejandro Hoberman, MD**, professor of pediatrics in the School of Medicine and vice chair for clinical research at Children's Hospital of Pittsburgh of UPMC. In an article published in January 2011 in the *New England Journal of Medicine*, Hoberman and colleagues reported that in children 6 to 23 months of age with acute otitis media, treatment with amoxicillin-clavulanate for 10 days tended to reduce the time to symptom resolution, overall symptom burden, and the rate of persistent signs of acute infection on otoscopic examination.

"Based on these findings, there is strong evidence in favor of treating children younger than 2 years of age with antibiotics, irrespective of the severity of the ear infection," said Hoberman. "We expect our study to have an impact on treatment guidelines for the United States that currently are being revised."

SCIENCE
JULY 2010 VOL. 329 | NO. 5988

Carbamazepine, an anti-seizure medication used for decades to treat epilepsy, is now a promising candidate to reverse liver scarring in patients with alpha-1 antitrypsin deficiency, according to a study published in *Science* by **David H. Perlmutter, MD**; **Simon C. Watkins, PhD**; and **George Michalopoulos, MD, PhD**. The most common genetic cause for children needing liver transplantation, alpha-1 antitrypsin deficiency results from a gene mutation that leads to buildup of an abnormal protein, ATZ, in the liver, causing fibrosis and scarring. In a mouse model of alpha-1 antitrypsin deficiency–associated disease, treatment with carbamazepine markedly decreased ATZ.

"The most amazing finding was that the drug reversed the fibrosis in the livers of the mice, and after two weeks of treatment, the liver tissue resembled that of a healthy mouse," Perlmutter remarked.

AMERICAN JOURNAL OF MEDICAL GENETICS, PART B

JULY 2011 VOL. 156 | ISSUE 5

Researchers in Pitt's Department of Psychiatry have developed a mouse model of major depressive disorder based on a rare genetic mutation that appears to cause the disease in the majority of people who inherit it. The findings could help to clarify brain events that lead to major depressive disorder and contribute to the development of new and better means of treatment and prevention. This report, driven by lead author **George S. Zubenko, MD, PhD**, professor of psychiatry, also illustrates an advance in the design of recombinant mouse models that should be applicable to many human diseases.

NATURE

OCTOBER 2010 VOL. 467 | ISSUE 7317

A protein called X nondisjunction factor (XND-1) has critical influence on the rearrangement of genetic material between maternal and paternal chromosomes during the genesis of sperm and egg cells, **Judith Yanowitz, PhD**, assistant professor of obstetrics, gynecology, and reproductive sciences, and colleagues reported in *Nature*. While such recombination produces greater genetic diversity, defects in the process can lead to offspring with improper numbers of chromosomes. In humans, such defects are known to be a leading cause of infertility. Using a worm model, the Yanowitz investigation found that XND-1 mutation affects chromosome packaging in the nuclear portion of a cell known as chromatin, which is directly responsible for genetic crossover formation.

PNAS

DECEMBER 2010 VOL. 107 | NO. 50

Chemotherapy drugs that target DNA in later-stage cancers could also be effective treatments for the earliest of breast tumors—those that likely originate from DNA repair defects that allow mutations to accumulate, **Jean J. Latimer, PhD**, assistant professor of obstetrics, gynecology, and reproductive sciences, reported in *Proceedings of the National Academy of Sciences*. Latimer and colleagues grew stage I breast cancer cells in culture to assess the excision repair protein pathways of 19 sporadic (not caused by genetic inheritance) tumors. In every case, there was a deficiency in repair capacity compared to disease-free breast tissue. "We rarely see a universal rule when it comes to breast cancer," said Latimer.

SCIENCE SIGNALING

JUNE 2010 VOL. 3 | ISSUE 124

Inhibiting a key molecule in a DNA repair pathway could increase cancer cells' sensitivity to radiation therapy while protecting healthy cells, according to an investigation led by **Christopher Bakkenist, PhD**, assistant professor of radiation oncology and of pharmacology and chemical biology. The findings, published in *Science Signaling*, describe DNA repair mechanisms associated with the neurological disorder ataxia-telangiectasia. Patients with the disease lack the protein ATM kinase, which promotes cell division. Heightened susceptibility to ionizing radiation is a characteristic symptom, and the Bakkenist team is now exploring ways to exploit this pathway and make cancer cells more sensitive to radiation therapy.

AMERICAN JOURNAL OF PSYCHIATRY

NOVEMBER 2010 VOL. 167 | ISSUE 11

The majority of postpartum depression research is focused on hormonal factors, but **Eydie L. Moses-Kolko, MD**, assistant professor of psychiatry, examined brain activity in depressed and nondepressed mothers. She reported in the *American Journal of Psychiatry* that negative emotional cues activated the left dorsomedial prefrontal cortex, a social cognition region of the brain, significantly less in depressed mothers than in healthy mothers. Moses-Kolko also found that, while negative images were viewed, communication between the left dorsomedial prefrontal cortex and the left amygdala was present in healthy moms but not in the depressed ones, suggesting that this neural circuit might be important in regulating emotional response to unpleasant stimuli, such as a crying baby.

SLEEP

DECEMBER 2010 VOL. 33 | NO. 12

People who rattle the windows with their snores have more to fear than the ire of a sleepy spouse. According to a study published in the journal *SLEEP* and led by **Wendy M. Troxel, PhD**, assistant professor of psychiatry and of psychology, loud snoring and two common insomnia symptoms—difficulty falling asleep and unrefreshing sleep—each significantly predict the development of metabolic syndrome, a group of obesity-related risk factors that increase an individual's risk of heart disease, diabetes, and stroke. The study provides the first prospective evidence to support a link between common sleep complaints and metabolic syndrome.

PLOS ONE

DECEMBER 2010 VOL. 5 | ISSUE 12

With colleagues from the National Cancer Institute, **Jeffrey S. Isenberg, MD, MPH**, associate professor of medicine, published findings on nitric oxide (NO) in *Public Library of Science One* that could lead to new therapeutic approaches for Alzheimer's disease. Reasons for reduced levels of NO—a signaling molecule that helps to regulate blood flow as well as immunological and neurological processes—in the brains of people with Alzheimer's are unclear. However, Isenberg's investigation implicates a cell-surface protein, CD47, in the accumulation of the disease's signature amyloid plaques. Moreover, the team has identified CD47 blocking agents that maximize the beneficial effects of NO and may one day prevent or ameliorate Alzheimer's disease.

NATURE MEDICINE

OCTOBER 2010 VOL. 16 | ISSUE 10

Pneumonia is the leading cause of death from infection in the United States, yet little is known about the biological mechanisms that influence its severity. In the October 2010 issue of *Nature Medicine*, **Rama Mallampalli, MD**, professor of medicine and director of the Acute Lung Injury Center of Excellence, described a key role played by cardiolipin, a rare, mitochondria-specific phospholipid, and its binding carrier protein, Atp8b1. By altering the protein in mice and treating them with an engineered cardiolipin-binding peptide fragment, Mallampalli and colleagues were able to alter the severity of the pneumonia infection. "Our study reveals some of the molecular steps that can lead to lung injury after infection and shows us new avenues for pneumonia therapy that don't have to target bacteria, as antibiotics do," Mallampalli said.

ARCHIVES OF GENERAL PSYCHIATRY

JANUARY 2011 VOL. 68 | NO. 1

Cognitive impairment is known to contribute to late-life depression, making it a tempting target for treatment. **Charles F. Reynolds III, MD**, UPMC Professor of Geriatric Psychiatry, recently published results from a clinical study of 130 senior citizens recently diagnosed with major depression. In *Archives of General Psychiatry*, he reported that a combination of antidepressants and donepezil, a medication used to treat dementia in Alzheimer's patients, enhanced the participants' language, memory, and executive functioning more than antidepressants alone. The results suggest that a cholinesterase inhibitor, such as donepezil, might be a plausible option to enhance treatment of depression in older individuals suffering from mild cognitive impairment.

ARCHIVES OF SURGERY

MARCH 2011 VOL. 146 | NO. 3

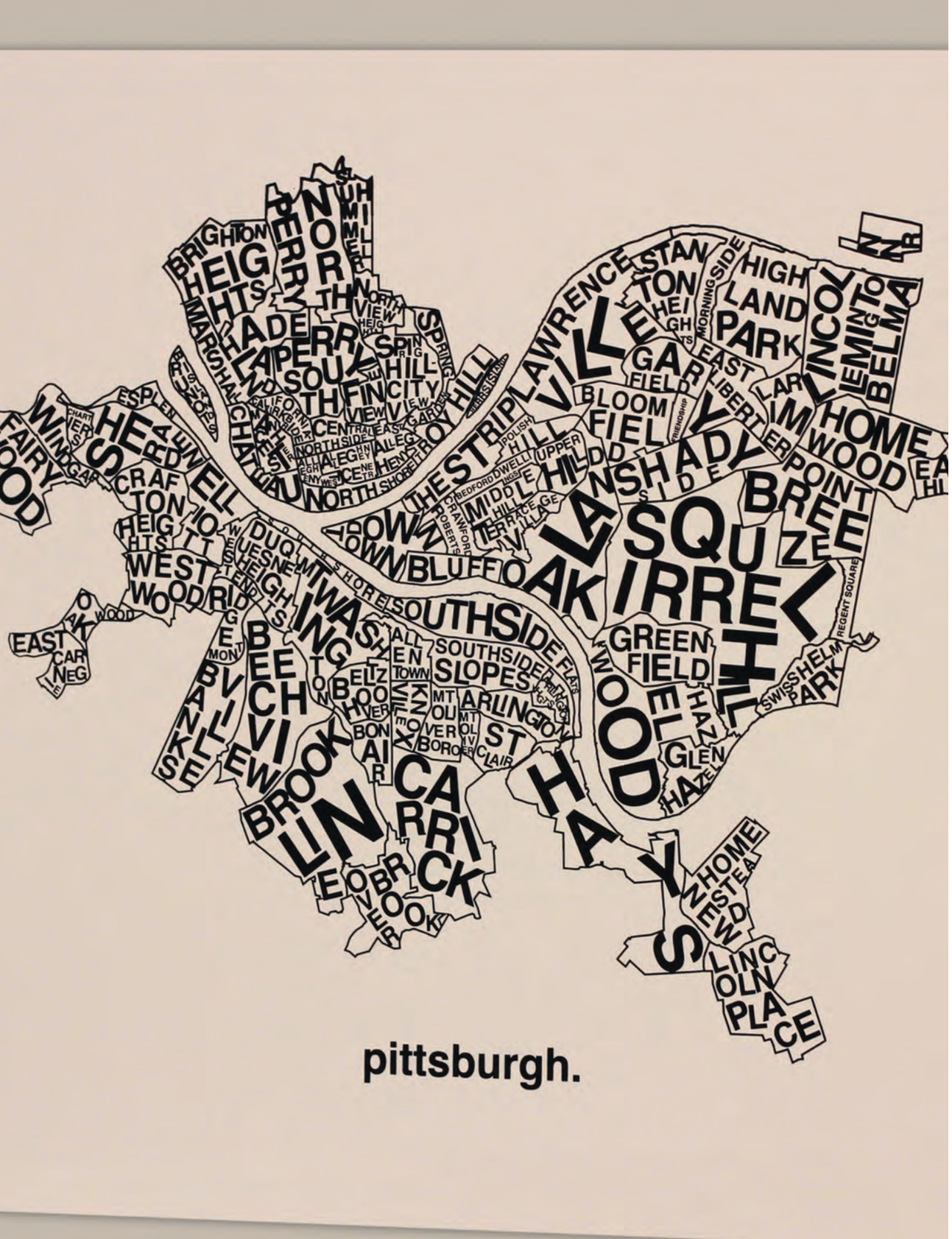
The Whipple operation—one of the longest, most dangerous, and most complex surgical procedures in medicine and the stuff of nightmares for every retractor-wielding medical student—is being revolutionized through new, state-of-the-art, minimally invasive techniques being performed by **James Moser, MD**, and **Herbert Zeh, MD**, codirectors of the UPMC Pancreatic Cancer Center. In *Archives of Surgery*, they described 30 patients who underwent robotic-assisted pancreatic resection in Pittsburgh. Key outcomes from the "robotic Whipple" were the same as traditional open surgery in terms of length of surgery, duration of hospital stay, and complications. "As robotic-assisted pancreatic surgery continues to evolve, we may be able to reduce operative times," said Zeh. "Ideally, we believe robotic-assisted pancreatic surgeries could lead to shorter hospital stays, fewer wound- and lung-related complications, and decreased recovery time for patients."

DIABETES

AUGUST 2010 VOL. 59 | NO. 8

Scientists have known for decades that diabetes results from the loss of insulin-producing beta cells in the pancreas, but little progress has been made in correcting this underlying deficiency until recently. **Andrew F. Stewart, MD**, professor of medicine and chief of the Division of Endocrinology and Metabolism, and **Nathalie Fiaschi-Taesch, PhD,** research assistant professor of medicine, identified a single key regulatory molecule, cdk-6, that induces human beta cell division. In a novel experiment, they transplanted cadaveric human islet cells transfected with cdk-6 into diabetic mice. The results were astounding: In two papers published in 2010 in *Diabetes,* the investigators reported that cdk-6-treated human islets were at least three times as effective in reversing diabetes as normal human islets. Furthermore, within three days, the beta cells replicated. "Our work provided the first proof-of-principle that the proliferation of human beta cells can be stimulated and that they function effectively both *in vitro* and *in vivo*," Stewart noted.

IN SITU



CTSI SERVING THE PITTSBURGH COMMUNITY

A Win-Win Situation

Ask colleagues Michael Yonas, DrPH, and Jessica Burke, PhD, to talk about an important moment in their research and they pause. Yonas, assistant professor of family medicine, and Burke, assistant professor of behavioral and community health sciences, Graduate School of Public Health, have worked together for close to 10 years and certainly have memorable experiences—so many that it's hard to choose just one. They've worked with children expressing themselves through art in town hall meetings, schools, and neighborhoods. As deputy directors of the Community PARTners (Partnering to Assist in Research Translation) Core of Pitt's Clinical and Translational Science Institute (CTSI), Yonas and Burke conduct research that involves a lot of hands-on community interaction and an approach called community-based participatory research (CBPR). Their goal is to engage community members, academic researchers, and other stakeholders in the research process. All partners share in the decision making and ownership, and all contribute expertise to the projects.

"The value of CBPR is that it's informed by the lived experiences of the participants. Research findings can be put into practice that much sooner because everyone needed to do so is already at the table," says Burke.

Burke and Yonas have cultivated several partnerships through Community PARTners, including those with Pittsburgh's Community Health Services Corporation, a community support and intervention agency; Johns Hopkins University; and Baltimore's House of Ruth, a nationally known domestic violence center. They've organized workshops to create awareness of CBPR in Pittsburgh and Baltimore and seen their efforts lead to successful outcomes.

"We've worked with people in organizations that really had an aversion to research in the beginning," Burke says. "But now those same people are doing the research and enjoy being a part of the process."

One example of a successful project is Visual Voices, an arts-based program started by Yonas in 1993. It is designed to bring children from a community together at a fun, creative venue to explore issues concerning their lives, communities, and their futures. (An artist himself, Yonas has replicated the program in nine cities around the country.) Children use familiar tools and materials—such as paint and markers—to visually represent what's important in their lives, and their efforts result in a collaged, public, "visual voices" exhibit.

In collaboration with Burke, the Visual Voices process has evolved into a qualitative participatory data collection method designed to integrate youth expertise into the research process and lead to public health improvement strategies.

"The children paint, write, talk, and we build relationships with them and their parents," says Yonas. "They help us and community organizations that work with them to identify possible interventions. That's why Jessie and I have a lot of meaningful experiences in our research; we listen to what they need, and we work with the whole community to make it happen. It's satisfying for everyone."

LISTENING IS A FORM OF RESPECT

SALUD!

Imagine a sharp pain in your chest. You have no health insurance. English isn't your first language, and you're not sure if you could communicate with a doctor at the emergency room. What would you do? Having a serious health problem is scary enough without adding the fear of not being able to communicate into the scenario. For the growing Spanish-speaking community in Pittsburgh, the Birmingham Free Clinic (BFC) is a place where they know they'll be understood and treated, regardless of their health insurance status.

BFC offers a weekly, completely free clinic to Spanish speakers; and, thanks to the University of Pittsburgh School of Medicine student group SALUD (Students and Latinos United against Disparities), the clinic is staffed with Spanish interpreters/translators. Formed in 2002 by then-medical students Julian Escobar and Melisha Krejci with the help of a Schweitzer Fellowship, SALUD helps the local population of uninsured Spanish speakers access medical services and health information through outreach in churches and the SALUD clinic, which draws approximately 400 patients per year.

That's 400 fewer people who, despite other barriers to services, now know where to find health care help should they need it.

MEETING PATIENTS WHERE THEY ARE

The Problem Solvers — Birmingham Free Clinic

"I know you've got something else to say, so go ahead and say it," Don* says, chuckling and pointing a finger at the woman facing him.

His chuckle trails off into wheezing, and erupts into a gasping, shoulder-hunching cough. The people in the room at the Birmingham Free Clinic (BFC) seem to take it in stride. They listen and laugh along with his jokes. They reminisce about when they all met. One comments on the change in his cough since he first came to the clinic three months ago.

"Don, you do sound better, and I'm glad your medication is working," says the woman, a volunteer pharmacist at BFC. "You'd feel a whole lot better if you stopped smoking. You know you can come to the smoking cessation clinic."

"Yeah, I know," Don says with a smile. "See you next month!"

Don would have to pay approximately $600 a month for the medications he receives for free from BFC. But $600 is rent for the apartment he shares with his ailing mother, and he has been too ill to hold a job that supports them.

Roughly 3,000 patient visits occur annually at BFC, which is run by the Program for Health Care to Underserved Populations, a program administratively housed within the Division of General Internal Medicine, and the Salvation Army of Pittsburgh. The only free, walk-in health clinic in Pittsburgh, BFC provides acute and primary care, diagnostics, specialty care, medications, health education, and (as Don has been told) smoking cessation programs to uninsured and vulnerable people.

All clinical services at BFC are provided by a volunteer staff of University of Pittsburgh faculty, UPMC staff and residents, and students in the Schools of Medicine and Pharmacy — all told, almost 2,000 volunteer hours a year. Coordinating all the clinical services is Mary Herbert, MS, MPH, a former scientist who found her calling in public and community health after serving in AmeriCorps.

Herbert remembers many patients with fondness, including a man who had severe pain but came to the clinic instead of the hospital. "He didn't go to the emergency room because he had no insurance, wasn't in the country legally, and spoke almost no English," she says. "He knew something was wrong and just needed help. After an exam, we were worried that he may have something really serious going on, like cancer. We helped him fill out paperwork for emergency medical assistance. He went to a hospital for treatment and found out he did have kidney cancer. That's all we heard for a long time. Eventually, he stopped

back in the clinic, and he looked great. His cancer was in remission, and he was so grateful. We were so happy."

"But, we don't want to sugar coat it," Herbert says. "The work is hard. I got hooked because the people who come in here just need help, and I get to work in several of my interests — public health, community advocacy, social work — you name it. We're really a team of problem solvers here."

The clinic devotes days each month to specific health concerns. Under the guidance of medical director Thuy Bui, MD, an associate professor of medicine, BFC holds clinics for cardiovascular health, women's health, dermatology, vision, and medication therapy management.

"All our volunteers are busy people, but once they come in, they get hooked. It's great to see people who have no time make the time to volunteer," Herbert says.

Students find working at the clinic a unique experience in their studies. Fourth-year medical student Jaime Moore has been a volunteer throughout medical school (she completed her scholarly project here, an analysis of the financial burden of clinic patients and barriers to their financial assistance).

"I don't think I could get this experience in any other setting," says Moore. "I have tremendous confidence from working at the clinic, and the diversity of the population — from people who are street homeless to people just out of prison to people who are working two to three jobs but have no health insurance — has given me a very practical skill set and prepared me for many medical situations."

Since BFC opened in 1994, Herbert has seen a change in the kind of patient who comes to the clinic. Patients used to be people who were homeless or otherwise on society's outskirts. "We still see all kinds of people," Herbert says. "But now, we most frequently see people who work but have no access to insurance. We regularly see an uninsured woman in her mid-20s who works in a grocery store. She is diabetic, and her medicine alone costs $1,800 a month. We're getting to know people a lot more because they come in monthly for chronic conditions. They're employed, but they have no other access to affordable health care. We can help keep them from using the emergency room as primary care."

Coming to the clinic has helped Don to get back on his feet, despite the wicked cough. Now that he's healthier, he's well enough to look for work. He doesn't worry quite as much about how he will support himself and his mother. Herbert hopes to continue seeing Don in the clinic, though.

"We'll keep working to get him to a smoking cessation clinic," she says. "Somehow we'll convince him."

At Birmingham Free Clinic, a problem is just the thing that precedes a solution.

**not his real name*

BIRMINGHAM FREE CLINIC HAS BECOME A TREASURED INSTITUTION IN THE LIVES OF MED STUDENTS, STAFF, FACULTY, AND PATIENTS.

DIPESH PATEL

HOSPITAL STAFF AT KAMUZU CENTRAL HOSPITAL IN LILONGWE, MALAWI

GLOBAL citizens

It happened quickly, as accidents usually do. Pitt medical student Dipesh Patel was in a Malawian hospital, observing doctors grouped around the bed of a young woman with pain and stiffness in her neck. The doctors needed to do a lumbar puncture. As they began, the woman yelled and twisted. Her movements became more and more frantic. Nurses held her still and comforted her, because moving around while a long needle is pushed into your spinal column can have devastating consequences. Eventually, the procedure was completed, but the woman continued to wail. Patel asked a nurse what had happened. One of the doctors had accidentally broken the strings of beads around the woman's waist, she said. The beads symbolized her purity.

"They're her lifeline," the nurse said. "Without them, her dowry price will go up, and she'll have a harder time getting married."

The memory of the woman's grief has stuck with Patel, all the way to Pittsburgh and back to Africa again, as a reminder of the need to be culturally sensitive in any health care situation. Patel had internalized a great deal of cultural sensitivity before medical school even began. As a teenager, he volunteered in poverty-stricken communities in Kenya. Now that he's a medical student, he wants to delve more deeply into the nuts and bolts of global health.

At Pitt, all medical students engage in independent, scholarly research, so Patel pursued a global health topic. When he learned that pneumonia is the leading cause of death in children worldwide, he knew he had his project. With the help of faculty mentors Thuy Bui, MD, associate professor of medicine and director of the global health residency track, he went to Malawi, where one in five children die before age 5 and only a handful of pediatricians practice. The Malawian government had developed initiatives to improve diagnosis, standardize treatment, and supply adequate antibiotics for pneumonia. Patel's project measured outcomes and explored whether the program could transfer successfully to other developing countries.

The experience changed the kind of doctor Patel hopes to be. "Working there gave me real confidence," he says. "I resolved that global health will always be a part of my life."

Patel's mentor, Bui, also was a Peace Corps volunteer in Malawi. She returns there regularly as a volunteer physician, and she cofounded Baobab Health, which uses technological innovation to improve health care in Malawi. In her first year in the Peace Corps, she was placed in a government hospital where she saw around 75 patients a day. As she dealt with a sometimes-empty pharmacy, power outages, and water shortages, she sometimes felt that she wasn't accomplishing anything. "So, I spent the second year creating teaching sessions, journal clubs, organizing learning rounds, and making sure the pharmacy was stocked," she says. "I learned that teamwork is essential in medicine."

Bui sees faculty and medical student global health pursuits as nothing but enriching. "I'm a refugee, and I consider myself a global citizen. If I can help students to see the world in a broader perspective, then they will be better physicians. I see that as my contribution to the world. That's my joy," she says.

"It's very important for students to see themselves as part of a bigger world and learn from other countries' health care systems," Peter Veldkamp, MD, MSc, associate professor of medicine and director of the area of concentration (AOC) in global health, says in agreement. "For instance, their physical exam skills get better if their access to diagnostic tools (such as X-ray or extensive lab tests) is limited. They learn to think creatively. They face different ethical questions and see diseases they wouldn't normally see in the U.S."

Veldkamp works on several projects in Mozambique. He helped to build an HIV treatment and research center on the grounds of the Catholic University of Mozambique, one of the country's two medical schools. The treatment center is a clinical rotation site for Mozambican medical students.

In a country with fewer than 1,000 doctors for 20 million citizens, 1.5 million of whom may be HIV-positive, doctors trained in HIV treatment and research are a vital resource.

Medical student Chris Berger spent one year working in the Mozambican clinic and says that the experience cemented his desire to do research. Working with Peter Millard, MD, MPH, Pitt's on-site faculty member at the clinic, Berger is comparing disease patterns and treatment of human papillomavirus in women who test positive versus negative for HIV. Berger wants to eventually study malaria and other parasitic infections, and he believes international locations will provide the best training grounds. "It's challenging to think of solutions to really complex problems that aren't only medically complex but are intrinsically tied to socioeconomic, geopolitical, climatological, geographical problems. It's an opportunity to do a lot of good for people," he says.

With 15 students in the global health AOC, 10 residents in the global health track, and countless faculty members engaged in global health research University-wide, Bui reports that Pitt's global presence is well established and growing. "We're building new sites internationally for service and scholarship," she says. "In a lot of ways, this big world is getting smaller."

ALUMNI OF NOTE

"I am thrilled to be back at Pitt and in my hometown. I am proud to be a part of the Regional Biocontainment Laboratory—a world-class facility designed to help protect the country from emerging diseases and bioterrorism threats. The lab complements Pitt's existing expertise in infectious disease research and puts us on the leading edge of this increasingly important area of research." – AMY HARTMAN, PHD

"Science is a field where most things just don't work. You have to be a gambler. You have to not mind losing and go for the big win." – BERT O'MALLEY, MD

"To this day, I regard the physicians and the teachers at Pitt as the best in their field because they instilled in us an incredible love for the profession and a dedication to our patients." – HARRY E. RUBASH, MD

INFECTIOUS ENTHUSIASM

Amy Hartman

Category A pathogens are potential bioterror agents that, if released into the population, could lead to high mortality, public panic, and social disruption. Some of the most widely recognized Category A pathogens sound like characters in a scary movie—Ebola, anthrax, and plague to name a few. Another member of the group, the mosquito-borne Rift Valley fever virus (RVFV), might not get as much airplay, but it is a major global health concern and is of particular danger to our military personnel stationed overseas. Outbreaks have occurred recently in Africa and the Middle East, and the virus is easily transmitted from animals to humans. It ravages farming communities, causing spontaneous abortion in pregnant livestock and killing up to 90 percent of infected lambs. People who work in close contact with animals (like farmers and slaughterhouse workers) are at particular risk for contracting the virus, which can lead to hemorrhagic fever, encephalitis, permanent vision loss, or death.

While these pathogens might cause some people to run in the opposite direction, for Pitt alumna Amy Hartman, PhD, research assistant professor in infectious diseases and microbiology in the Graduate School of Public Health and research manager of Pitt's NIH-funded regional biocontainment laboratory (RBL), working with deadly bugs like RVFV is just another day at the office. After receiving her PhD from the School of Medicine in 2003, Hartman studied Ebola Zaire virus as a postdoc in the Special Pathogens Branch of the Centers for Disease Control and Prevention and was a member of the Marburg virus outbreak response team in Luanda, Angola, in 2005. She returned to Pittsburgh in 2007 to manage Pitt's RBL, one of 13 such labs in the nation.

Hartman recently secured a $1.9 million contract with the U.S. Department of Defense to develop animal models that mimic the effects of RVFV on humans. She will partner with Doug Reed, PhD, RBL aerobiology manager, to test vaccines and drugs in these models, which may one day protect soldiers and civilians against bioterror attacks or natural RVFV infection.

FATHER OF MOLECULAR ENDOCRINOLOGY

Bert O'Malley

Pitt med school alum and Pittsburgh native Bert O'Malley, MD, has been awarded the 2011 Ernst Schering Prize in recognition of his pioneering work on the actions of steroid hormones and nuclear receptors. The prize is one of the most prestigious German science honors, bestowing an unrestricted cash award of €50,000 for outstanding work in medicine, biology, and chemistry.

This is a significant and much deserved honor," said Arthur S. Levine, MD, Pitt's senior vice chancellor for the health sciences and dean, School of Medicine. "Dr. O'Malley has made outstanding contributions to our understanding of how hormones work and how their expression is regulated, which is critical to many areas of medicine, including endocrinology and cancer."

Often called the "father of molecular endocrinology," O'Malley was a champion for the establishment of the first professional journal in the field, *Molecular Endocrinology*. Early in his career, he focused on elucidating the mechanisms by which steroid hormones such as estrogen and progesterone initiate gene transcription in the nucleus. O'Malley's subsequent discovery of steroid receptor coactivators, genes that regulate the activity of other genes and influence the growth of hormone-producing tissues, was a seminal finding that later spurred the development of multiple cancer treatments, like tamoxifen, that block this pathway.

O'Malley earned his medical degree from the University of Pittsburgh in 1963 and completed his residency at Duke University Medical Center. He then spent time at the National Institute of Child Health and Human Development and Vanderbilt University before moving to Baylor College of Medicine, where he is chair and Tom Thompson Distinguished Service Professor of Molecular and Cellular Biology. In addition to numerous honorary degrees and awards, he received the nation's highest scientific honor, the National Medal of Science, in 2007.

AN ORTHOPAEDIC LEGACY

Harry Rubash

Harry E. Rubash, MD, is part of a distinguished thread running through the School of Medicine's history. Like many leaders of orthopaedics around the world, Rubash trained under Albert Ferguson, MD, who chaired Pitt's Department of Orthopaedic Surgery from 1953 to 1986. On average, Ferguson turned out a future department chair or division chief nearly every year for 33 years. In addition to Rubash, now the Edith M. Ashley Professor of Orthopaedic Surgery, Harvard Medical School, and chief of the Department of Orthopaedic Surgery at Massachusetts General Hospital, this dynasty includes Henry J. Mankin, MD, former chair of orthopaedic surgery at Harvard and the emeritus holder of the Ashley chair.

Rubash was born in a humble town outside of Pittsburgh called Turtle Creek. He worked as a mechanic to pay for college. As a Pitt medical student in the late 1970s, Rubash scrubbed in with Ferguson one day and knew immediately that orthopaedics was the field where his mechanical skills would find a medical outlet.

In his distinguished career, Rubash has made significant contributions to major joint replacement surgery, including the development of innovative reconstructive techniques, landmark research that has reduced complications and improved outcomes for patients, and the advancement of the study of biomechanics and failure mechanisms of joint arthroplasty in the hip and knee, leading to enhanced implant designs.

Of his years in Pittsburgh, as a student, resident, and young faculty member, Rubash says, "To this day, I regard the physicians and the teachers at Pitt as the best in their field because they instilled in us an incredible love for the profession and a dedication to our patients." Shortly after leaving Pittsburgh for Boston many years ago, Rubash created a full medical scholarship at Pitt in his late father's name. In 2010, he was named one of 13 new Legacy Laureates of the University of Pittsburgh.

THANK YOU

Our generous alumni and friends move mountains. As we continue our pursuit of the University of Pittsburgh's $2 billion capital campaign goal—nearly half of which is for the Schools of the Health Sciences—I am pleased to report that the School of Medicine alone has raised an astounding $606 million to date. We are on track to meet our campaign goals and raise the funds needed to support the research and academic enterprise that is Pitt medicine today. For this, we have our donors to thank. We couldn't do it without your partnership and confidence in our ability to deliver.

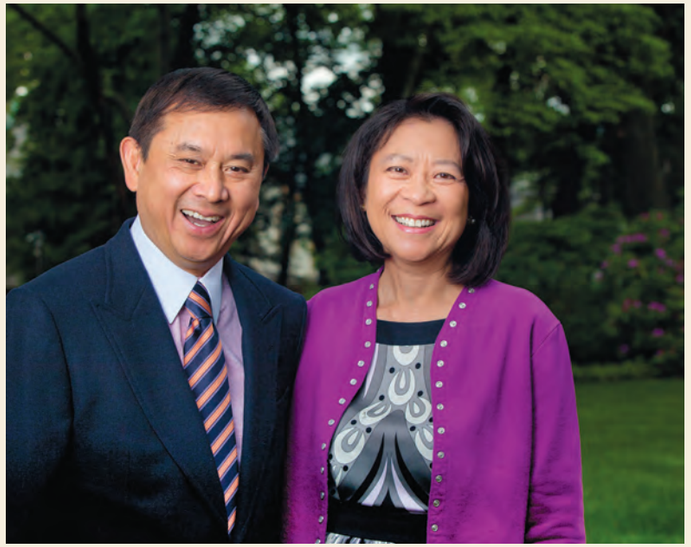
Individuals, foundations, and corporations choose to support Pitt because our University is a global leader in the science that shapes health care. Our reputation for excellence in ever-expanding fields of endeavor precedes us. Whether at the Winter Academy—our eagerly anticipated annual event in Naples, Florida—or through our outreach to alumni around the world, we are spreading the good news about our growth as an organization.

Even in this tempestuous economic environment, we remain nimble, poised to explore new opportunities, and optimistic about the future. Our supporters know that giving to the University of Pittsburgh School of Medicine is a wise investment and one that pays dividends in public health and scientific advancement far beyond the Pittsburgh region.

We are in the vanguard of academic medical institutions. Our facilities are state-of-the-art. Our faculty and physicians are at the top of their professions. Our exceptional students have chosen Pitt over some of the most highly regarded programs in the nation. All of this is possible because of the many donors who give generously to Pitt med, providing us the ability to recruit and retain the best and to make sure they have the resources to think big. On behalf of the University, you have my thanks for, indeed, moving mountains to get us to where we are today. Working with you to raise funds for the School of Medicine is my distinct privilege.

CLYDE B. JONES III

Vice Chancellor for Health Sciences Development
President, University of Pittsburgh/UPMC Medical and Health Sciences Foundation



Hilda and Freddie Fu's Hometown Philosophy

The Fus are widely recognized as an accomplished couple. Freddie H.K. Fu, MD, Distinguished Service Professor of Orthopaedic Surgery and David Silver Professor and Chair of Pitt's Department of Orthopaedic Surgery, is internationally known for his pioneering surgical techniques to treat sports-related injuries and his extensive scientific and clinical research in the biomechanics of such injuries. Hilda P. Fu, MLS, MPM, is a founder and leader in regional development, an advocate for gender equity, works to promote the vibrancy of Pittsburgh and the improvement of the city's image, and currently is most focused on developing mind-broadening activities for the people who live in the region. She has built academic and programmatic partnerships locally and worldwide.

But what about her future husband caught her attention when they first met at a party in Hong Kong? Not that he was obviously bright and leaving to study at Dartmouth—it was that he had a driver's license.

"It's true! As 18-year-olds, we all wanted to pass our driving exams, which in Hong Kong was extremely difficult to do because they limited the number of drivers on the already-congested roads," says Mrs. Fu. "Getting a license involved three separate exams, and only 10 percent of people passed. People who got accepted into the very competitive University of Hong Kong would still flunk the driving tests repeatedly. But Freddie passed all three exams on the first try. It was impressive."

Mrs. Fu impressed in her own right by getting accepted into the prestigious University of Hong Kong. "Then I took her out bowling, which was the hot sport in Hong Kong at the time," Dr. Fu says.

"Yes, and he beat me, too, and that also impressed me," says Mrs. Fu with a laugh.

Their courtship continued via airmailed letters until they married and Mrs. Fu joined her husband in the United States. They both earned graduate degrees from Pitt and, since 1975, have lived together in Pittsburgh (where Dr. Fu is an avid cyclist and often bikes around the city).

"We fell in love with the people in Pittsburgh," says Mrs. Fu. "We've made a conscious decision to stay here because we love it, and it's home."

Home is important to the Fus, as they travel extensively; so when they contribute to the School of Medicine through different gifts, it is personally very satisfying to them.

"Everything good comes from home—your kids, your family," says Dr. Fu. "I've worked at Pitt, a great institution, for a long, long time. Anything we can do to support our own faculty and the development of the region is important to us."

And support they have. Their most recent gift to the School of Medicine established the Freddie and Hilda Fu Endowed Fund in Orthopaedic Surgery, income from which will support education and training in the department. Because of this fund and numerous other gifts, the couple was recently honored with induction into the inaugural class of the Brackenridge Circle, comprising people who have contributed $1 million or more to Pitt in planned gifts, pledges, or other contributions. The Fus want to show by example that faculty members can support their own institution and see the effects of their contributions. Philanthropy also fits into the couple's philosophy of life in general.

"You come into the world with nothing; and when you pass away, you can only take so much," Dr. Fu says. "You give wealth away because you don't really own it in the first place. And, if you can provide an opportunity for someone else to move forward, everyone gains in the process."

The Fus are motivated by a passion for Pitt and Pittsburgh, which they call their "second hometown." Mrs. Fu says, "We don't do philanthropy out of responsibility. It energizes us to see its positive effects. Plus, it's fun to learn about the amazing scientists Pitt has and to support their great projects."

Dr. Fu agrees, saying, "You have to take joy in life."

Pitt is lucky that the Fus find their joy here, at home in Pittsburgh.

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 between July 1, 2009, and June 30, 2010, have supported us in our academic, research, and clinical missions.

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CHENITS PETTIGREW, PHD, AND MARGARET LARKINS-PETTIGREW, MD

Meet the Champion's Champions

As assistant dean for student affairs and director of diversity programs for the University of Pittsburgh School of Medicine, Chenits Pettigrew, PhD, loves Match Day. On the day when medical students learn where they will spend the next several years of their lives in residency, he revels in watching those he recruited and supported through years of medical school. "Match Day is a culmination of all their work," he explains. "And it's the moment when their dreams turn into reality. It's their launching point, and it's very satisfying to have made a contribution to it."

Dr. Pettigrew has been the champion of many Pitt medical students from diverse backgrounds. He's the coach in the corner, encouraging them to keep fighting. For some, getting into and through medical school has been just that—a fight. Dr. Pettigrew helps students to meet any challenge that could possibly hinder their studies, from finances to child care and everything in between. Many are first-generation medical students, and Dr. Pettigrew talks to the students and their families about what medical school will be like. Others come from underrepresented groups, and they may just need someone to talk to about their experiences in medical school. Dr. Pettigrew supports them unconditionally.

Dr. Pettigrew is himself a Pitt alumnus, having earned his Master of Education degree here in 1976. (He received his PhD from Pepperdine University in 1984.) Since 1969, he has been a part of outreach efforts to recruit, admit, develop, and graduate students from groups that are underrepresented at Pitt. Joan Harvey, MD, associate dean for student affairs, describes Dr. Pettigrew's devotion to students: "He sends personalized e-mails to hundreds of potential students and then will answer them when they reply with what he calls 'the promise.' He promises to be personally committed to their academic, career, and personal success. And, he keeps his promises; students who have long-since graduated from the School of Medicine still return to him for guidance."

Dr. Pettigrew's devotion inspired two alumni to create a fund in his honor. Margaret Larkins-Pettigrew, MD, assistant professor of medicine and director of global health, Case Western Reserve University (who also happens to be married to Dr. Pettigrew), and their long-time friend Vaughn S. Clagette, MD, founder, clinical codirector, and practicing hospitalist of Tanner Intensive Medical Services in Georgia, established an endowment that supplies the Office of Diversity Affairs in the School of Medicine with need-based scholarships and program support. The gift put the $3 million African American Alumni Council student financial assistance fundraising campaign beyond the $2 million mark just one year after the campaign's public phase began.

Dr. Clagette, an active member of the School of Medicine's alumni community who is involved in the School's summer programs to support and develop the medical school aspirations of students from diverse backgrounds, always wanted to create a fund; and he found a perfect model in Dr. Pettigrew. "There's no better person than Chenits to create an endowment in honor of," says Dr. Clagette. "He's cerebral, has a high moral standard, never loses sight of the humanity in any situation, and has helped transform hundreds of students into leaders."

VAUGHN S. CLAGETTE, MD

And, no matter how many Match Days and graduations Dr. Pettigrew witnesses, he will see each as a success because he knows firsthand how hard students have worked to get that residency placement, that degree.

"Chenits has dedicated his career to changing the world, one life at a time," says Dr. Larkins-Pettigrew. "He has stood watch and guided many students who have realized their dreams. This gift is a testament to Chenits and a guarantee that someone will always be there to stand watch."

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Sandy Gerson Snyder: Families First

"People tell me I could never write a memoir because I had such a happy childhood," says Sandy Gerson Snyder.

Throughout her childhood, Mrs. Snyder's parents taught her that family comes first, and they lived happily by that rule. Mrs. Snyder remembers eating dinner as a family every day at 6 p.m. and how close they were. Her parents were, as she calls them, "real love birds who did everything together—even the grocery shopping. If they fought, I never saw it."

When Mrs. Snyder's mother was diagnosed with colon cancer and died two years later at age 51, it was nothing short of devastating to the family. "It was a difficult time," says Mrs. Snyder.

Helping her mother through those two challenging years spurred Mrs. Snyder to take action in two ways. The first was that she began getting colonoscopies in her 40s, earlier than is recommended for the general population, because colon cancer can have a genetic component. One such exam revealed precancerous polyps, and Mrs. Snyder's doctors were able to halt their progress. Mrs. Snyder feels that she owes her life to the research and clinical progress made in prevention and early detection.

"I was saved by all the research that's been done," Mrs. Snyder says. "By the time my mother exhibited symptoms and was diagnosed, it was too late. That doesn't have to be the case anymore."

Mrs. Snyder's second call to action was to help researchers fighting disease. To do this, she created the Sadie Gerson Distinguished Scholar Award in the University of Pittsburgh School of Medicine to support scientists and physicians working to fight colon cancer. She also endowed the Leonard Gerson Distinguished Visiting Scholar Program to honor her father, who passed away from problems associated with amyotrophic lateral sclerosis (more commonly known as ALS or Lou Gehrig's disease) a mere three months after diagnosis. The disease, she explains, "hit him out of nowhere, and we were told there was nothing—nothing, zero—that could be done for him."

In addition to creating these endowments and supporting vital research, Mrs. Snyder hopes to spread the word about the caliber of care she has received at UPMC. "We're so lucky to live in this city," she says. "We have wonderful doctors and researchers who are really caring and smart individuals, great clinicians, and passionate about finding cures."

It is Mrs. Snyder's desire to help other families protect loved ones that inspires her philanthropy; in fact, she and her husband, Edgar, are well known for working to improve the lives of others locally and internationally. And Mrs. Snyder regularly volunteers in elderly and other communities because she, as she puts it, "is not just a check writer."

"I feel that if you're lucky enough to be successful in life, then you should give back. It's very important to me. They always say, 'You get more than you give,' and that's how I feel," she says.

Mrs. Snyder is happy if her efforts help keep families healthy, intact, and first in each other's lives. It's what her parents taught her.

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A Most Valuable Donor

In 1993, hockey legend Mario Lemieux was having a fantastic season playing for the Pittsburgh Penguins when he was diagnosed with Hodgkin's lymphoma. After Mr. Lemieux beat the cancer, he could've retired and been happy with a celebrated, award-winning career. Instead, he boarded a plane to get to the next game. He finished the season by leading the Penguins on a record-breaking, 17-game-winning streak and then hoisting the Hart Memorial Trophy, the National Hockey League's award for most valuable player (an honor he received three times in his career). He considered himself so fortunate to survive the disease that, in the same year, he created the Mario Lemieux Foundation to raise funds for cancer research and help patients and their families cope with cancer. Since then, Pittsburgh medical and scientific communities have benefited from several major gifts from the foundation, including a $5 million gift to UPMC to establish the Mario Lemieux Centers for Patient Care and Research; a $1 million gift to establish an endowed chair in pediatric oncology research at Children's Hospital of Pittsburgh of UPMC; and a $2 million gift to create the Lemieux Family Center at the Children's Home of Pittsburgh, an initiative that supports and nurtures families during the difficult process of transitioning from hospital care to life back at home.

Because Mario Lemieux and his wife, Nathalie, know what it's like to battle cancer, they strive through their foundation to help those who are in the fight of their lives. The Lemieux Foundation recently gave $3 million to establish the Mario Lemieux Center for Blood Cancers at the University of Pittsburgh Cancer Institute's (UPCI) Hillman Cancer Center. The Center will be used for the diagnosis and treatment of people with blood cancers, such as leukemia, myeloma, and lymphoma, and for people receiving blood and marrow transplants, but it will be unique in its focus on patient- and family-centered care.

"This is the best project I've ever been a part of," says Clayton A. Smith, MD, professor of medicine, director of the hematological malignancies program and of leukemia and stem cell clinical transplant services at UPMC Cancer Centers and UPCI, and one of the principal planners of the project. "We're planning the center as a combination of patient- and family-centered care, cutting-edge science and treatments, and information technology in service to people. We haven't seen a place that has these elements as integrated in one place as what we're hoping to do here."

The center's core is its focus on the patients, their families, and their comfort. To achieve this, the project planners—who include Nancy Davidson, MD, UPCI director and associate vice chancellor for cancer research, and Stanley Marks, MD, professor of medicine and director of clinical services and chief medical officer for UPMC Cancer Centers—are mapping out a place that will best serve the purpose. The environment will be focused on what patient feedback says helps them the most—lots of light, outdoor views, privacy, space for families to congregate, work areas, and strategies to minimize waiting. It is being designed as an outpatient center so that patients can spend evenings with their families outside the hospital; a long-term care facility, where patients will be able to schedule all their follow-up appointments on one floor; a place to facilitate clinical research trials, with access to research investigators and information on site; and an information technology hub where patients and their families have access to tablet-based technology, the Internet, disease information, and teaching modules.

"This planning process has been a wonderful team effort," says Dr. Smith. "We're trying to think outside the box to bring care to people that is both cutting-edge and compassionate; those things no longer have to be mutually exclusive. We've done a lot of listening to patients and given a lot of thought to what we would want if we or our families were in the same situation. It's exciting to work with the Lemieuxs because they've walked the walk. They're incredibly committed and inspirational."

The Lemieuxs envision the 24,000-square-foot center as a place where Mr. Lemieux himself would've gone for treatments. "Mario has not forgotten what cancer treatment was like," says Nancy Angus, executive director of the Lemieux Foundation. "People battling cancer can benefit from his experience. This project is all about patients and their families and making their experiences as easy as possible in a very difficult situation."

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