

Devoted to noteworthy happenings

at the medical school

DNA Repair How-to

DNA undergoes a lot of wear—so much that it occasionally breaks. Previous studies suggested cells fixed this with a dab of molecular glue, taking two separate, but seemingly compatible, DNA strands and rejoining them. But such a sloppy process could upset minute segments of DNA and lead to harmful coding errors.

Yuri Nikiforov, MD/PhD professor of pathology, thinks cells are a little more precise. "Our new study dramatically changes our understanding of how these breaks are fixed," Nikiforov says. "This kind of damage is actually repaired by using the complementary parental gene as a blueprint for rebuilding." Instead of gluing strands back together, cells repair the original genes using the matching chromosome as a guide. The researchers believe that contact between the two chromosomes gets the DNA repair pathway started, at the same time offering a template for repair of the broken section.

The study, published in the *Proceedings of the National Academy of Sciences*, used fluorescent probes to monitor the interactions between homologous chromosomes. —*Em Maier*

FOOTNOTE

Medicine is a noble calling. Medicine and economics, for Alvin Roth, are a Nobel calling. Roth, Pitt's Andrew W. Mellon Professor of Economics from 1982 to 1998, is cowinner of the 2012 Nobel for economic sciences for his work on market design. One market Roth influenced was that of med students searching for residencies. As more women entered medicine, more medical couples sought residencies near one another and outside of the system. In 1995, Roth was asked to redesign the match algorithm; his was adopted three years later. Another Roth algorithm is used to match organ donors and recipients.



PHOTO ILLUSTRATION BY JESSE LENZ, BASED ON PHOTO BY ELLEN JAFFE

Lasker Chair Alfred Sommer with Thomas Starzl at the Lasker Awards.

STARZL WINS LASKER

In the 1950s, Thomas Starzl, an MD/PhD, was looking for a "lifetime project"—something with no easy solution or foreseeable timeline, he says. This September, he received the 2012 Lasker–DeBakey Clinical Medical Research Award, which he shares with Sir Roy Calne of the University of Cambridge, for the development of liver transplantation. For decades, the two worked collaboratively at separate institutions, developing a friendship that Starzl says spurred progress more than competition ever could have.

When Starzl's work began in 1958, many doctors scoffed at the notion of organ transplantation. They didn't know whether donor organs could be preserved, let alone how to prevent rejection. "There was no doubt this was going to require a lot of swimming against the current," says Starzl, now Distinguished Service Professor of Surgery at Pitt.

Starzl calls the work a "University-wide project" and is donating his half of the $250,000 prize to the Joy Starzl Scholarship Fund, which is named for his wife and provides need-based aid to students in the School of Social Work. —*Jenelle Pifer*



CAMI MESA

The Latest on Concussions

With Michael Collins and Anthony Kontos

In 2000, UPMC founded its Sports Medicine Concussion Program—which was little more than a handful of docs and one room on the South Side. Today, the program's staff of 24 sees 15,000 patients annually in a 3,500-square-foot facility, which opened in early 2012. Pitt's Michael "Micky" Collins (shown right), a PhD associate professor of orthopaedic surgery and program director, has been there since the early days; Anthony Kontos (shown left), also a PhD associate professor of orthopaedic surgery, was recruited in 2010 to beef up the program's research arm. Lately, the profs have been partnering with the military and delving into how concussion affects the youngest athletes.

Linking mild TBI and PTSD in soldiers.

Kontos: We were able to do a very large study with over 22,000 U.S. Army Special Operations Forces. . . . We found that 13 percent of that population has been diagnosed with at least one mTBI (mild traumatic brain injury). And among that 13 percent, 28 percent were reporting clinical levels of PTSD (post-traumatic stress disorder). So nearly one-third with a history of mTBI are reporting clinical levels of PTSD, which is pretty high. Six percent without a history of diagnosed mTBI had clinical levels of PTSD symptoms.

Surprising findings in youth football leagues.

Kontos: These are 8- to 12-year-olds. What we found is that concussion risk or incidence was much higher in games than it was for practices. That's quite interesting, because some youth leagues, such as Pop Warner, have reduced the number of practices in which you can have contact [in an attempt to limit concussions]. And practice is where kids are learning the [proper tackling] technique. They're still going to be exposed in the games, but with less practice of proper technique.

The future of concussion treatment.

Collins: There's a lot of morbidity with this injury, but it's treatable—and we really don't think concussion is the boogeyman anymore. I saw about 25 to 35 cases today, and there were some people who are . . . having a hard time. But there are not that many people who walk out of here and aren't getting better from this, if you treat it the right way.

What about other repercussions, like the apparent link to PTSD?

Collins: A lot of the time, [experiencing] concussion and PTSD together is like throwing gas on a fire. Each makes the other worse. At the end of the day, concussion is an energy problem, and anxiety is one of the biggest energy-users in the brain. So when we treat the injury, we see improvement in PTSD and vice versa. *—Interview by Joe Miksch*

Next Generation

No longer students, but perhaps not yet independent researchers, postdocs are dipping their toes into the waters of academic medicine. But being something of a neophyte doesn't mean you can't be a roaring success. Witness these award winners.

Lisa Boyette, a PhD working under the guidance of MDs Fadi Lakkis and Diana Metes in the Thomas E. Starzl Transplantation Institute since last October, won the American Society of Nephrology Research Fellowship for examining how different classes of white blood cells function after renal transplant.

Xueqin Gao, an MD/PhD, won the Orthopaedic Research Society's 2012 New Investigator Recognition Award for her project studying the interactions between donor and host cells after stem cell–mediated bone regenerations. Gao, who works in the lab of PhD Johnny Huard (professor of orthopaedic surgery, molecular genetics, biochemistry, bioengineering, and pathology, as well as director of Pitt's Stem Cell Research Center), found stem cells contribute and attract a significant number of inflammatory and vascular cells and inhibit a host's initial immune response at the defect site to promote bone repair. She also demonstrated the importance of an inflammatory enzyme for stem cell–mediated bone healing.

David Boone, in addition to receiving the Susan G. Komen for the Cure Postdoctoral Fellowship Grant to examine how insulinlike growth factor 1 affects breast cancer, landed a fellowship to reach out to the community in Nashville, where he attended graduate school. He taught a science program in a local high school for three years, and last year his students won second place in the Tennessee Junior Academy of Science. Boone, a PhD, is mentored by Adrian Lee, PhD professor of pharmacology and chemical biology.

Matthew Sikora also studies breast cancer, particularly how one gene, HDAC7, influences resistance to endocrine therapy. Sikora, a PhD who works with Steffi Oesterreich, PhD professor of pharmacology and chemical biology, investigates an understudied type of breast cancer called invasive lobular carcinoma. Sikora has received funding from the Department of Defense Breast Cancer Research Program to continue his work. *—EM*

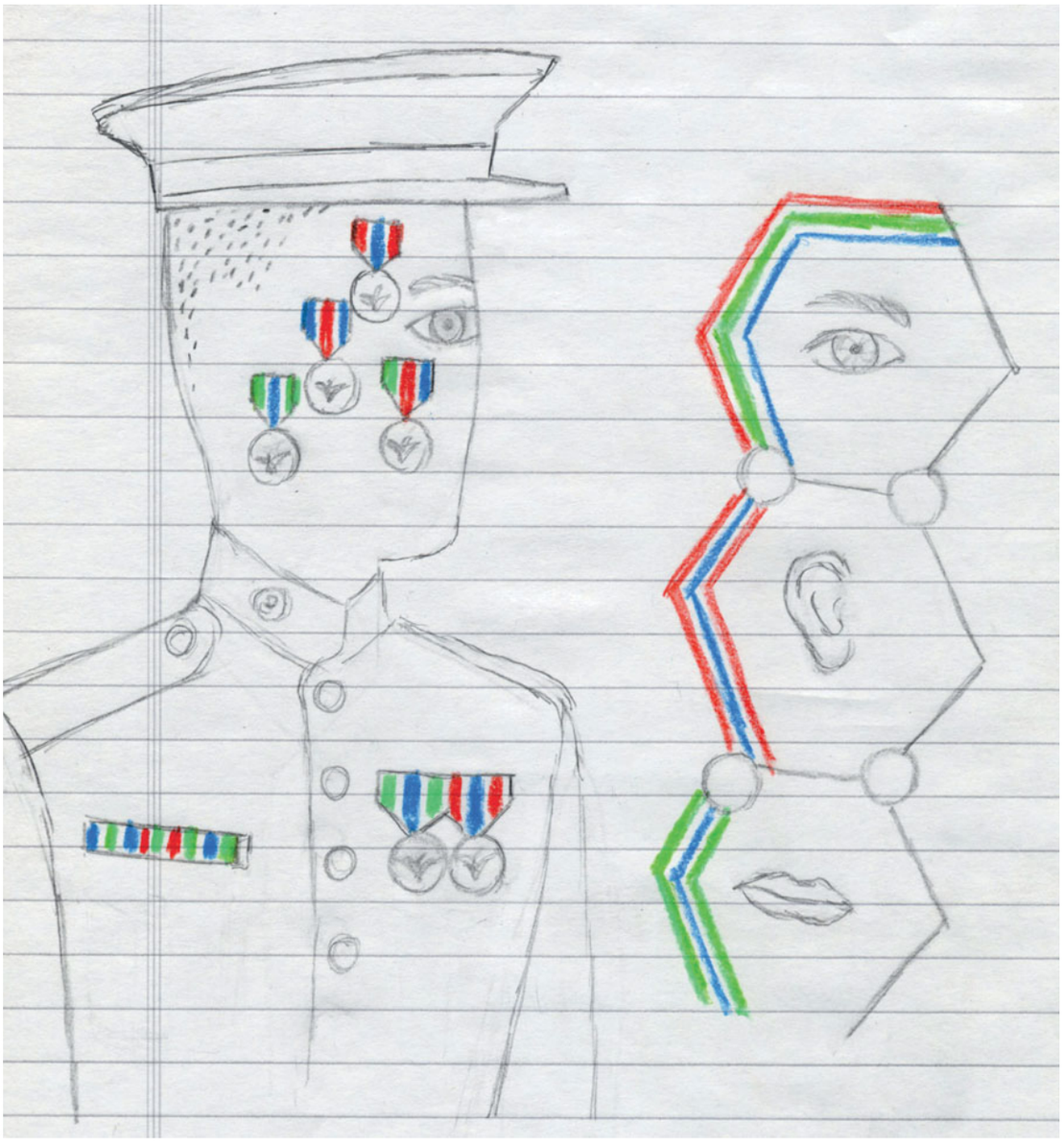
Military Targets

The armed forces and scientific advancement aren't strangers. Since World War II, military-funded and related research has led to Bob Beamon-esque leaps forward in physics, computing, engineering, and electronics. It's medicine's turn.

The new Center for Military Medicine Research here will "serve as a catalytic infrastructure to advance the fields of regenerative medicine, reconstructive surgery, transplant immunology, tissue engineering, neuroscience, and neuroprosthetics," organizers say. With funding from the U.S. Department of Defense, Pitt scientists are already attempting to grow skin, nerves, bone, and cartilage in the lab. And they are experimenting with ways to regrow lost muscle and restore craniofacial tissue.

Founding director Rocky Tuan (a PhD, Arthur J. Rooney Sr. Professor of Sports Medicine, professor and executive vice chair for orthopaedics research, and director of the Center for Cellular and Molecular Engineering) says the military medicine research hub will also promote investigations into numerous therapies and courses for rehabilitation, with plans to accelerate their transition from lab to clinic.

Tuan works closely with Distinguished Professor of Neurobiology and Neurobiology Chair Peter Strick, a PhD who also codirects the Pitt–Carnegie Mellon Center for the Neural Basis of Cognition. "What we're doing now is trying to make the community and federal agencies aware of the science that's going on in Pittsburgh—and at the same time, trying to make the scientists who are making discoveries aware of opportunities to help wounded warriors and veterans," says Strick. "We're making a match between the two, to raise funds for the remarkable work that's already ongoing." *—EM*



CATHERINE LAZURE

A MODEL GRANT

Wet bench work is central to scientific discovery, but it's not the only path available. With a five-year, $9.3 million grant from the National Institutes of Health, the University of Pittsburgh School of Medicine, Carnegie Mellon University, and the Pittsburgh Supercomputing Center will be delving into the realm of the cyber for insight into the central nervous system.

The grant establishes the Biomedical Technology Research Center (BTRC), which will develop computational tools for modeling and simulating biological systems from the big (tissue) to the tiny (the molecule). Pitt's Ivet Bahar, a PhD and John K. Vries Professor and chair of the Department of Computational and Systems Biology, is the principal investigator.

"With these tools, our goal is to better understand and appreciate the impact of defective proteins and interactions at the cellular level, and their effects on the central nervous system behavior," she says. "We hope to bridge the gaps between molecular-, cellular-, and tissue-level information to build integrated models of cell signaling and regulation."

Bahar adds that the BTRC will collaborate with renowned researchers in neuronal- and T-cell-signaling and regulation at Pitt—including Alexander (Sasha) Sorkin, a PhD and Richard Beatty Mellon Professor and chair of the Department of Cell Biology, and Susan G. Amara, the PhD former chair of neurobiology who is now scientific director of the National Institute of Mental Health—as well as with labs at the Allen Institute for Brain Science in Seattle, the California Institute of Technology, and the University of Bristol in England. *—JM*

FOOTNOTE

According to new numbers from the National Science Foundation, in terms of federal funding, the University receives the third-largest sum among public universities and fifth largest among all schools. That's almost $600 million for fiscal year 2010, the time period covered in the report, and an increase of 30 percent from 2009.



WELCOME TO REALITY

Lift your tail, shift yo' body. If you need some help, ask somebody. **It sounds like rap duo 4 Wheel City is enumerating the next dance craze. But Namel "Tapwaterz" Norris and Ricardo "Rickfire" Velasquez, who both ended up in wheelchairs, perform motivational "rap therapy." Their September concert, cosponsored by Pitt's Office of Health Sciences Diversity and the School of Health and Rehabilitation Sciences (SHRS), was held at the August Wilson Center for African American Culture. (Velasquez and Norris are shown here, to the left and right, respectively, of their "hype man," Elsun Gunter.) Jonathan Duvall, an SHRS student who helped organize the event, recalls how Norris grew serious when telling the audience his story. Norris was injured when a gun went off accidentally. That happened three years after Velasquez, a neighbor in the Bronx, was caught in crossfire while walking home. "I remember [Norris] saying, 'How do you tie your shoes in a wheelchair?' The other guy walked him through it." Now the artists are hoping to show how much more people with disabilities can do. They're also sounding a wakeup call to young people. "The lyrics are really powerful," says Duvall.** ***—JP***

COURTESY MICHAEL LAIN/HUMAN ENGINEERING RESEARCH LABORATORIES



Strick

Appointments

Peter Strick, a PhD and Distinguished Professor of Neurobiology, is now chair of the Department of Neurobiology and, he says, thrilled to be in a position where he can facilitate young scientists' careers and enable cutting-edge research.

A member of the National Academy of Sciences (NAS), Strick is codirector of the Pitt/CMU Center for the Neural Basis of Cognition, coleader of the Center for Military Medicine Research (see p. 5), and a senior research career scientist at the VA Pittsburgh Healthcare System. He succeeds Susan Amara as neurobiology chair. Amara is also an NAS member; she recently joined the Maryland-based National Institute of Mental Health as scientific director.



Michalopoulos

This fall, four Pitt med faculty members became Distinguished Professors, a rank acknowledging extraordinary scholarly attainment in a particular field.

George Michalopoulos has been named Distinguished Professor of Pathology. In 1989 his lab was one of three to independently discover hepatocyte growth factor (HGF), a major driver of regeneration in a variety of tissues and cell types. He is the Maud L. Menten Professor and chair of Pitt's Department of Pathology, the biggest academic clinical organization of its kind.



Peitzman

Pitt's Mark M. Ravitch Professor of Surgery, vice chair for clinical services, and chief of general surgery, Andrew Peitzman (MD '76, Res '84), is now Distinguished Professor of Surgery. Peitzman has traveled extensively, particularly in Latin America, to improve trauma care abroad and at home. He opened the trauma center at UPMC Presbyterian in 1984 and maintains clinical interests in complex abdominal surgery, critical care medicine, and hernia repair.



Shroff

Newly named Distinguished Professor in Bioengineering, Sanjeev Shroff is interested in the cardiovascular system. Specifically, he investigates the relationship between contractile and regulatory proteins and heart function, as well as how vascular stiffness affects cardiovascular function. He is also Gerald E. McGinnis Professor of Bioengineering, a professor of medicine, and a member of the Pitt-UPMC McGowan Institute for Regenerative Medicine.



Grandis

Jennifer Grandis (MD '87, Fel '92, Res '93), named Distinguished Professor of Otolaryngology, was also elected to the Institute of Medicine (IOM) this year. She studies the genetic alterations resulting in head and neck cancers and is working towards novel therapies targeting the signaling pathways involved. She is director of the head and neck cancer program at the University of Pittsburgh Cancer Institute, a UPMC Endowed Professor, and assistant vice chancellor for research integration, health sciences.

Joining Grandis in the IOM is Michael Boninger, an MD who serves as chair of the Department of Physical Medicine and Rehabilitation and director of the UPMC Rehabilitation Institute. Boninger's research focuses on technologies to improve the lives of people with spinal cord injury and other disabilities. His team's wheelchair work, primarily conducted at Pitt's Human Engineering Research Laboratories, where he is the medical director, has led to patents for devices used throughout the world. He also helps lead the Pitt neuroprosthetics team. ***—JP***