

Devoted to noteworthy happenings at the medical school ... To stay abreast of school news day by day, see www.health.pitt.edu.



VEER

Breakthrough in Arthritis Gene Therapy

At a time when the medical community was beginning to wonder about the promise of gene therapy, a Pitt/Harvard team has restored the confidence of many. The team administered experimental rheumatoid arthritis gene therapy to nine women between 1996 and 1999 at UPMC Presbyterian. Chris Evans (former Henry J. Mankin Professor of Orthopaedic Surgery at Pitt, now at Harvard Medical School) and Paul Robbins (professor of molecular genetics and biochemistry and of orthopaedic surgery as well as director of Pitt's Viral Vector Core Facility) led the trial. The investigators removed cells from the knuckles of the women and grew them in culture using gene therapy to stimulate production of a protein that inhibits joint tissue inflammation. They then reinserted the cells into the patients.

The study offers evidence for gene therapy proponents that the technique can be a safe alternative. Evans and Robbins safely used a viral vector that was also administered in a recent French study in which patients developed leukemia as a result of gene therapy. The Evans/Robbins study was designed to test the safety and feasibility of the gene therapy, but not its efficacy. It's not clear whether the therapy would have helped the severe cases of arthritis in the women, because they all went ahead with previously scheduled joint replacement surgery. In future studies, the researchers plan to intervene at an earlier stage of the illness (with a different vector) and measure the therapy's effectiveness in treating arthritis. ***—Nita Chawla***

FLASHBACK

"Although the propriety of establishing a medical school here has been sharply questioned by some, we will not attempt to argue the question. Results will determine whether or not the promoters of the enterprise were mistaken in their judgment and action. This city, we think, offers ample opportunity for all that is desirable in a first-class medical school."

—John Milton Duff's comments to the first class of the Western Pennsylvania Medical College, 1886

READ ALL ABOUT PITT

If you think you've noticed University of Pittsburgh School of Medicine faculty in the news more recently, you're not imagining it. Last year, UPMC, whose doctors and researchers are often School of Medicine faculty, ranked sixth among the top academic medical centers mentioned in major national publications. In April, it was tied with the University of California, San Francisco for third. (Harvard's and UCLA's hospitals placed first and second, respectively.)

Jane Duffield, director of the UPMC News Bureau, started keeping track more closely a few years ago, "when we shifted our emphasis from local to national visibility," she says. Her staff checks how often the medical center is cited in stories compared to other top medical research centers. Bureau staff monitor seven publications: *The Wall Street Journal*, *The New York Times*, *USA Today*, *The Washington Post*, *Time*, *Newsweek*, and *U.S. News & World Report*.

The favorable visibility "promises to increase," says Duffield, "because of the caliber of the research going on in the University." The competition to get noticed by these publications is fierce, she notes. ***—Erica Lloyd***



CAMI MESA

A&Q

With Lifelong Neighbors Vonzell Williams and Kevin Vilsaint

After attending the same small high school in Brooklyn, N.Y., and then graduating together from St. Joseph's College, also in New York, Vonzell Williams (left) and Kevin Vilsaint (right) didn't plan to go to the same medical school, yet each decided that Pitt was the place for him. Vilsaint will graduate in 2006 and plans to go into anesthesiology. Williams, who took time off to do research and is considering family medicine, will finish a year later. They are next-door neighbors.

On moving away from home for the first time, only to live next door to each other:

Williams: This is our first real experience moving away and having to deal with a whole bunch of new personalities ... and making new friends. The fact that we have so many similarities—we're both first-generation Americans (Kevin's parents are Haitian and my parents are from St. Vincent), we're both really Brooklyn kids, we both talk about going back to New York—means that we do go out and explore, but at the same time, because of our relationship, we get to remain ourselves. We don't get lost. If I see him doing something that I know is out of character for him, I can call him on it, and vice versa.

On providing support for each other during med school:

Vilsaint: I definitely feel like the majority of our classmates give us opportunities, but to see a big, tall dude with dreads is unusual for some people. It's good to have someone who can relate to me so I can go home and have my comfort zone, where I can talk about New York or whatever.

Why medicine?

Vilsaint: I volunteered at a hospital during high school and college, and I was struck by a discrepancy—that minority people were patients but often didn't necessarily have the resources to become doctors. ... [Medicine] is very results oriented: You see who's sick, you diagnose it, and, hopefully, you fix it. And even though I sort of keep to myself, I do appreciate the interaction with people. ... You can't make a deep connection with every single person, but once in a while, there are people you really can help and make a connection with.

On the future—together again?

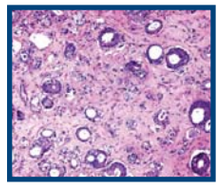
Williams: We'll definitely meet back up, because he [plans to go] to New York for residency, and I want to go back and work, if not in the community I was raised in, very close to that community.

Their question for the world:

Where do you want your life to take you, and what will you have to do to get there?

—Interview by Hattie Fletcher

Faculty Snapshots



Lung cancer cells die with a new treatment.

Estrogen is linked to lung cancer. Oncologists have long known that targeting estrogen receptors yields effective treatments for breast cancer. More recently, researchers have shown that estrogen-receptor levels in cases of lung cancer—in both men and women—rival those in breast cancer. Pitt pharmacologists Pamela Hershberger, Mark Nichols, Jill Siegfried, and Laura Stabile tested how breast cancer treatments might be parlayed in the lung. In two reports in the February issue of *Cancer Research,* they described the synergistic effects of a treatment that targets both estrogen and epidermal growth factor receptors on lung cancer, documented how estrogen affects gene expression in lung cancer cells, and confirmed the ability of an estrogen inhibitor called fulvestrant to block that effect.



Chang



Moore

How a virus manufactures tumors has been laid bare by Yuan Chang, a Pitt professor of pathology, and Patrick Moore, an epidemiologist and professor of molecular genetics and biochemistry. The husband-and-wife MD pair has found the mechanism by which KSHV—the herpes virus that causes Kaposi's sarcoma, the leading malignancy in AIDS patients—creates tumors. "It targets the tumor suppressor pathways that keep the cell from running amok," says Moore. "If a cell recognizes that it is infected, it will try to commit suicide—apoptosis—to prevent itself from acting as a source of infection," he says. The virus has evolved mechanisms to try to dampen that response. In the process, it pushes the cell toward an "immortalized phenotype," as Moore puts it, enhancing its likelihood of becoming a cancer cell. "If a person has immunodeficiency from AIDS and can't control the virus, the cell could then be free to grow under the influence of the virus, which is trying to promote its own survival."

The American Society for Clinical Investigation again gave the big nod to researchers in the School of Medicine: This year, Steven Reis, associate vice chancellor for clinical research, and Ian Pollack, the Walter E. Dandy Professor of Neurosurgery, were asked to become members of the society, an invitation considered a weighty recognition for physician-scientists early in their careers. (Doctors must be invited by the age of 45.) Reis, 42, studies gender- and race-related differences in cardiovascular disease. Pollack, 44, one of the few surgeons elected to the society, researches novel approaches to diagnosing and treating brain tumors. *—Sharon Tregaskis*

Advanced Age and Cunning v. Youth and Skill



ILLUSTRATION JOHN RITTER/PHOTO NITA CHAWLA

"Where's the ball control?" fourth-year Neil Bhayani asks his opponents, Vice Dean Steven Kanter and Associate Dean of Students Joan Harvey. As Bhayani chides, he carefully maneuvers the foosball, preparing it for a shot. He wears royal-blue scrubs, sneakers, and a gold chain with the letter N hanging from his neck. It was Bhayani's idea to break in the new foosball table—an addition to the student lounge funded by the Medical Alumni Association (MAA)—with this inaugural student/faculty foosball tournament.

Today, the lounge is full of cheers, jeers, and pep talks—sometimes self-inflicted: "Come on Bill, put the little guys up!" Bill McIvor (Res '94), assistant professor of anesthesiology, demanded of himself as the brown ball slipped away from his armless players in the match he lost to second-year Kristen Scopaz. Students and faculty have squished themselves into the tiny area around the table to watch as a ball meanders into the reach of players. Occasionally, they're rewarded with a sharp snap of the axle for a cross-table goal. Those moves are likely to be followed by a high-five.

A new game is starting, and expectations run high about Samuel Tisherman's (MD '85, Res '93, Fel '91 & '94) prowess.

"He's a surgeon. His coordination at baseline beats most people's here," Bhayani says of the associate professor. To everyone's surprise, the student team shreds him and his wife, Susan Dunmire (MD '85, Res '88), emergency medicine prof and MAA executive director. Youthful response time beats seasoned agility, 5 to 0.

But the professors still hold the upper edge. Bhayani playfully teases Dunmire about losing; her reply: "You still have a test to take on Monday, baby!" *—NC*

PREVENTING SCHIAVO-LIKE CASES

This spring, the nation watched as Terri Schiavo's family struggled over her medical care. Although few families grapple publicly, physicians report that conflict erupts in nearly 80 percent of cases involving a decision to limit life-sustaining care. Most doctors would rather avoid open disagreement, be it with colleagues or family members. But according to palliative care expert Robert Arnold, effectively dealing with such situations has the potential to greatly improve patient care and reduce physician stress. "If you ignore conflicts, they fester," says the physician. "To a certain extent, this isn't about medicine; it's about life. If you don't say anything, the conflict just gets worse."

In its March 16 issue, *The Journal of the American Medical Association* published "Dealing with Conflict in Caring for the Seriously Ill," by Arnold, the Leo H. Criep Professor of Patient Care at Pitt, and Anthony Back, a professor of medicine at the University of Washington, Seattle. The article is a case study of the course of treatment for an 84-year-old woman suffering from dementia. It discusses how conflicts tend to arise; details the pitfalls that often beset clinicians, patients, and families; and suggests strategies for working through disagreements. "For doctors, who are problem solvers, the hardest initial thing is to be curious and realize that stepping back, going slow, and really understanding the other person's story may be the most helpful way to move the conversation forward," says Arnold.

"Communication about conflict, about issues that you have strong emotions about, is hard work," says Arnold. "This is something you have to be intentional about." *—ST*

FISHER HONORED

On a rare warm, sunny day in March, surgeon Bernard Fisher joined Nobel laureate Philip S. Hench (MD '20) and other Pitt med greats in the portrait gallery of the Biomedical Science Tower lobby. Fisher (MD '43) is best known for his studies of breast cancer that led surgeons, in some cases, to replace radical mastectomy with more conservative local surgeries combined with chemotherapy.

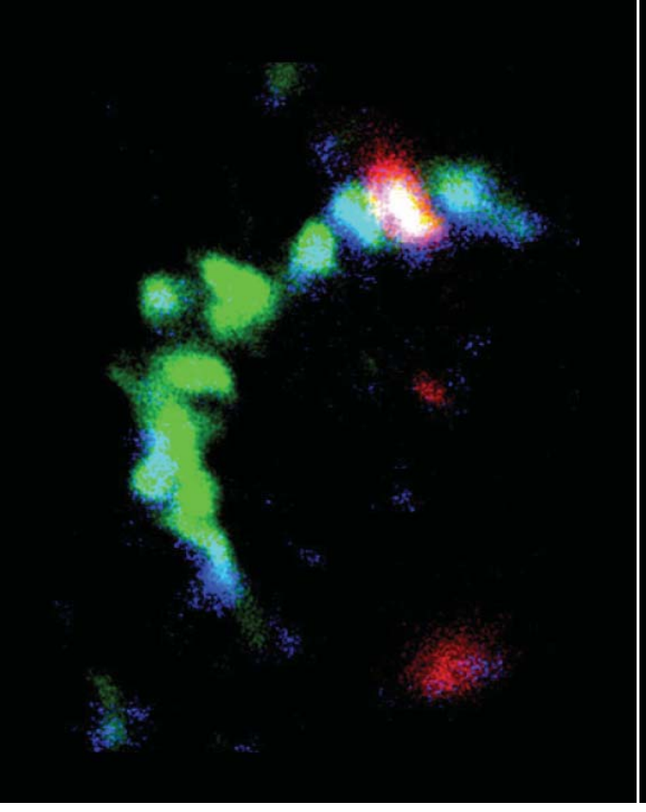
"It was an honor to give Bernard Fisher the acknowledgment he truly deserves," says Arthur S. Levine, dean of the School of Medicine and senior vice chancellor for the health sciences. "His work changed the course of treatment, the rate of survival, and the quality of life for women with breast cancer."

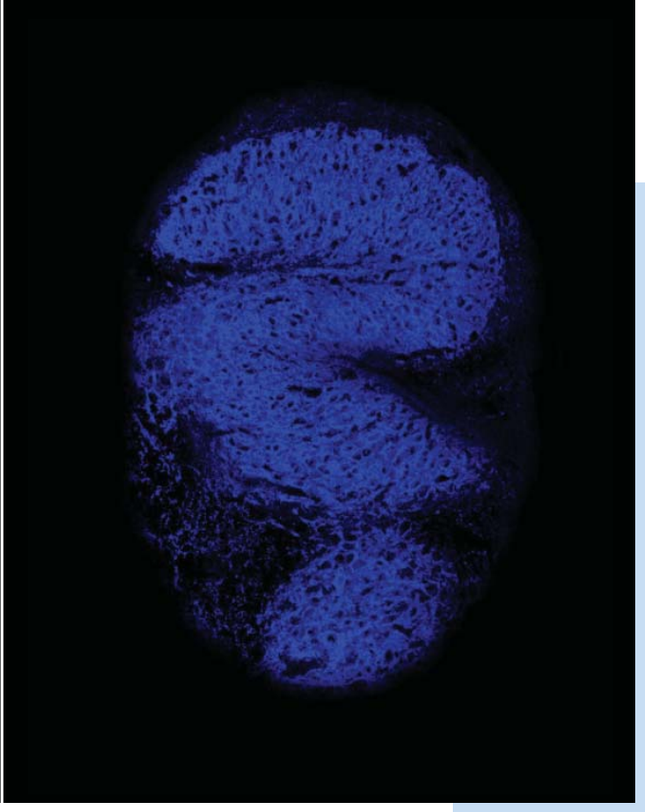
Painted by artist Greg Kavalec, the portrait in oils was unveiled during a celebration attended by more than 200 faculty and students. Prominent University of Washington breast cancer researcher Mary-Claire King, who collaborated with Fisher on a study of the gene BRCA1, implicated in the development of hereditary breast cancer, gave a talk on her genomic analyses of inherited breast cancer.

"For anyone else, it was probably just another day at the office," says Fisher, a Distinguished Service Professor of Surgery at the University. "For me, it was momentous." *—ST*



PORTRAITS PITTSBURGH/ GREG KAVALEC





LEFT: Close-up of a synaptic contact where you might find both stimulating and calming neurotransmitters. RIGHT: Glutamate runs rampant where no one thought it would, in the part of the brain called the LSO. (Blue here labels a protein that enables glutamate release.)

Calm Down Hurry Up

Sure the brain is mysterious, but scientists thought they had at least this much figured out: Some neurons release neurotransmitters that are considered excitatory—they help neurons propagate impulses. And some release inhibitory neurotransmitters—which dampen impulses. No neuron that helped dampen impulses would also excite them. Straightforward, right? Wrong. The latest finding by Deda Gillespie, a research assistant professor, and Karl Kandler, an associate professor of neurobiology, is getting a lot of attention. Gillespie was running an experiment on the part of the brain known as the LSO, until a few months ago considered a "pure inhibitory pathway," says Kandler. Neurons in the LSO produce calming transmitters like GABA, which is key to how barbiturates and alcohol quell brain activity. But the pathway isn't so pure. The LSO is where Gillespie came across neurons able to release not only the inhibitory transmitters GABA and glycine, but also glutamate, the classic excitatory transmitter. Glutamate is involved in learning and memory; it also plays a role in addiction (which some scientists now think is another kind of learning), chronic pain, epilepsy, and other conditions.

At first Kandler thought no one would believe their finding. But since the discovery was the cover story in March's *Nature Neuroscience,* colleagues have said to him, *I thought I saw clues to something like that happening, too.* "It wasn't supposed to be there," says Kandler of the glutamate. "So they'd discussed it away." *—EL*



The new Biomedical Science Tower on Fifth Avenue

CAMI MESA

PA. INVESTS TOBACCO MONEY AT PITT

"Now, close your eyes and imagine this room filled with robots," says John S. Lazo, Allegheny Foundation Professor of Pharmacology, to a small group of state legislators wearing white hard hats and goggles. On this May morning, the legislators are on hand to tour the University's still-under-construction Biomedical Science Tower 3, and Lazo is trying to give them a sense of the research facilities that state funds support, including a coming robot crew that will help organize the new building's chemical library for drug discovery. His is one of several five-minute presentations. The combination of real researchers describing their labs-to-be and a little imagination seems to work. "I see [the building] as a cauldron of activity," says State Senator Mary Jo White.

In a historic legal settlement in the late '90s, tobacco companies agreed to pay $206 billion to 46 states between 2000 and 2025. Many states have used the money for a range of purposes, but the Pennsylvania legislature decided to narrow the allocation of its share to health programs and medical research. The new Biomedical Science Tower is one beneficiary; about $4.5 million from the settlement has gone toward design and construction. Tobacco settlement funds also support a number of research programs at the University, and Pitt researchers have done well securing competitive grants funded out of the settlement, bringing in support for programs on cardiovascular disease, neurodegenerative and mental disorders, cancer, and early warning systems for disease outbreaks.

As the state now faces budget challenges, some have argued for revisiting the funding formula, a move that University officials oppose. "Pennsylvania is one of the only states that is investing all of its tobacco money in health-related initiatives," says Margaret McDonald, associate vice chancellor for academic affairs, health sciences. "It's also a time when other states are pumping money into research. It makes no sense to stop just when the competition is heating up, and we have just the tiniest of head starts."

—Nita Chawla and Robin Mejia