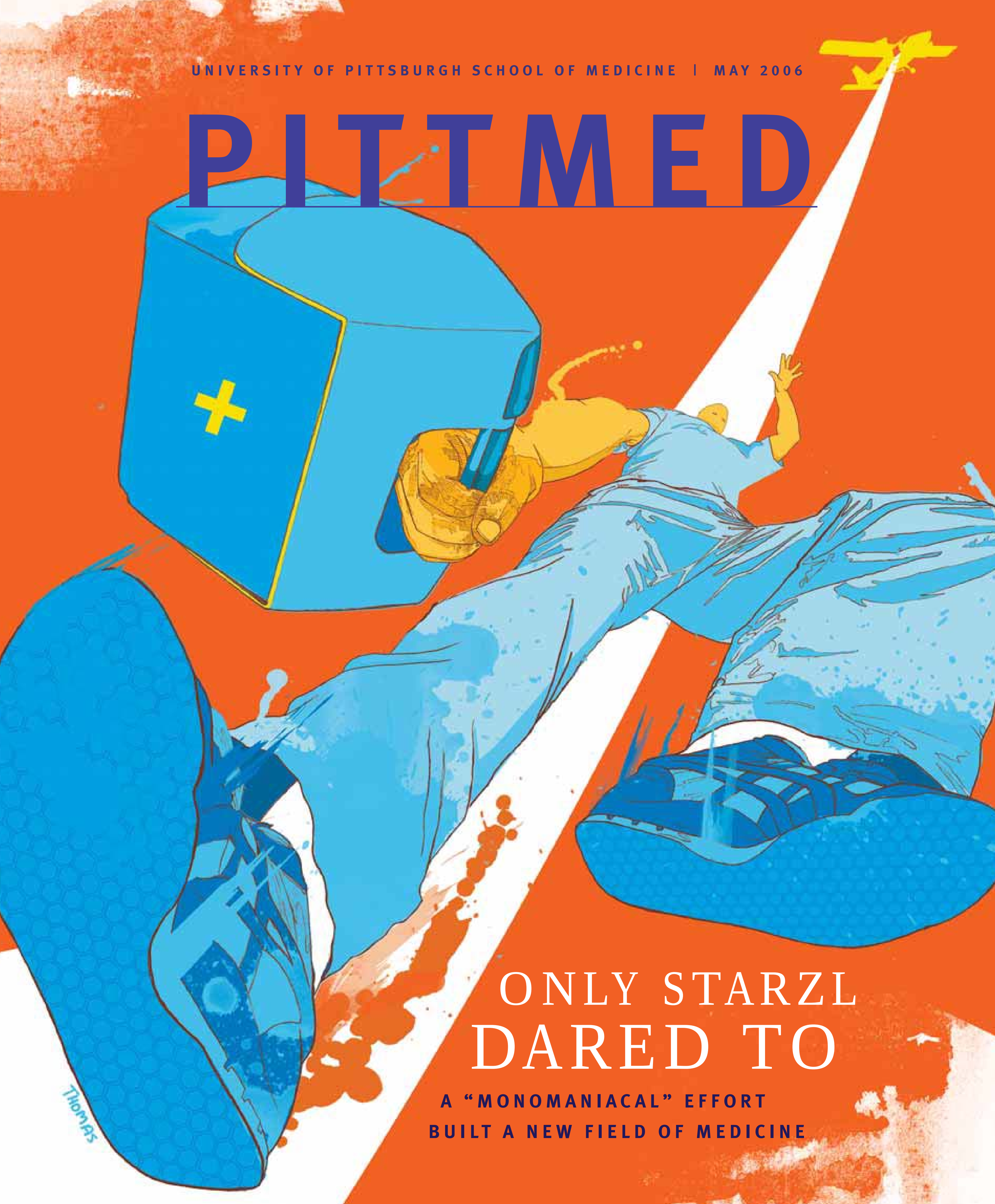
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | MAY 2006

PITTMED

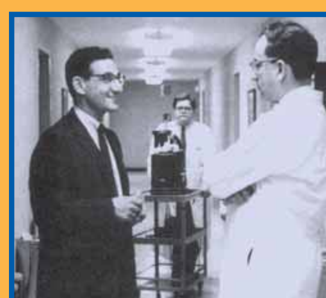


ONLY STARZL DARED TO

A “MONOMANIACAL” EFFORT BUILT A NEW FIELD OF MEDICINE

PLUMBING AND PATHOLOGY

I was tickled to read your story about Dr. Bernard Klionsky. I was intrigued enough with the field of pathology to accept Dr. Klionsky's offer to spend a year as a post-sophomore fellow. During that year, I was bombarded with all types of "Klionsky-isms," e.g., "If you know the plumbing of the body, you know a helluva lot of pathology." I am not alone. Every medical student he knew remembers them because Dr. Klionsky was passionate not only about teaching us the details of pathology but about how to critically solve problems. Those were some of the most important lessons we learned.



Klionsky (left) is known for his evangelical stance on pathology.

Bruce Gomberg (MD '96)
Augusta, Maine

HOW TO TREAT PEOPLE

I wanted to pass along my thanks for the article "What Matters Most" that appeared in the February issue. It was a terrific portrait of what being a healthcare provider is all about. It is critical that we, as students, learn early the lessons of empathy and compassion that our colleagues and mentors can show us. May we never forget what it is like to be a patient and that our every word and action makes a difference.

Alexander C. Krach
Pittsburgh, Pa.

PEKRUHN REMEMBERED

It was with great sadness that I read my classmate William "Trey" Pekruhn (MD '75) died last year. I had both the privilege and misfortune to spend a lot of clinical clerkships with Trey. I say it was a privilege because Trey was always a personable guy, easy to talk to, always wanting to be helpful to his fellow students. On the other side of the coin, it was difficult being in clerkships with him because he was so good. He was such a smart guy that he always made the rest of us look bad. I remember a time when he and I were at St. Margaret's Hospital. We were third-year medical students, and he was debating a case with another former Pitt stalwart, Dr. James Ferrante, who was a formidable, brilliant, and intimidating professor. Trey held his own. He had a phenomenal memory, too. We would take turns at Scaife Hall during lunch, coming up with obscure medical problems, and he would quote the page and text of where each problem could be found in Robbins' textbook of pathology. The faculty and administration were aghast when he told them he was not planning to go into academics, which is what everyone assumed. He wanted to go into family practice because he wanted to use his skills to help people. Although I had not seen Trey since we graduated, I know that his passing is a great loss to mankind, and I am sure he is sorely missed.

George M. Orr (MD '75)
Greensboro, N.C.

READABLE

The February issue of the magazine is just spectacular, from the obituary by our dean for Dr. Katherine Detre to the article on the summer enrichment program for the medical students. Thanks for doing such a superb job.

Beth Piraino, MD
Professor of Medicine
Associate Dean of Admissions
University of Pittsburgh

COULDN'T CARE LESS

I don't have time for your magazine. I couldn't care less about *Pitt Med*. I read the sucker cover to cover.

Heck of a magazine.

Brian Doyle
Portland, Ore.

Brian Doyle edits Portland, *the University of Portland's magazine.*

We gladly receive letters (which we may edit for length, style, and clarity).

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RECENT MAGAZINE HONORS

AAMC Robert G. Fenley Writing Award of Distinction
(for Chuck Staresinic's "Why Do We Age?")

AAMC Robert G. Fenley Writing Award of Distinction
(for Erica Lloyd's "Cyborg Medicine")

IABC Best of Show

IABC Golden Triangle Award of Excellence
Magazine Design

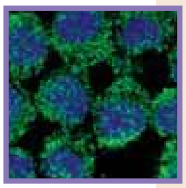
CASE District II Accolades
Silver, Visual Design in Print, Covers

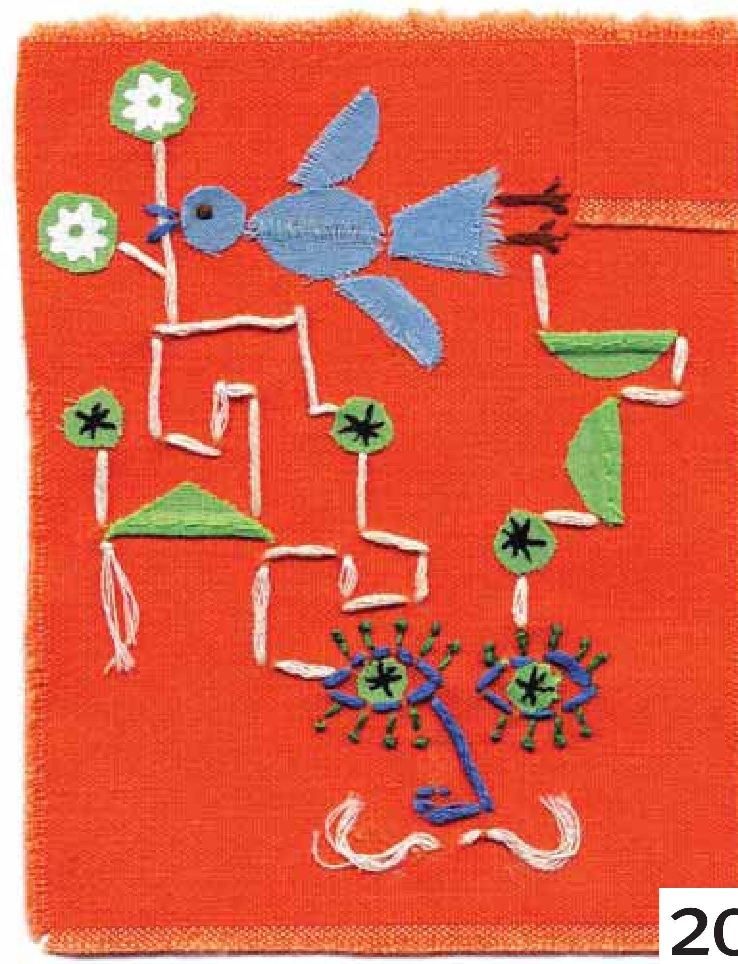
CASE District II Accolades
Bronze, Best Article

PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE | MAY 2006, VOL. 8, ISSUE 2

DEPARTMENTS





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FEATURES

CONTRIBUTORS

There was a time when you could find illustrator JACOB THOMAS ["Only Starzl Dared To"] discussing oil spills with eighth graders. The Coast-Guard-environmental-inspector-and-educator-turned-artist attended the Art Institute of Pittsburgh after his time in the service.

He was recently recognized in the *HOW International* and *Interactive Design Annual*. His illustrations for a graphic novel will appear in the art publication, *Semi-Permanent*. Like his chief influence, Andy Warhol—another Pittsburgher who became an artist—Thomas migrated to New York. He now works for Deco Zone, a design and production company.

On ELAINE VITONE'S ["Right Under Our Nodes"] first trip to Pittsburgh, she emerged from the Fort Pitt Tunnels so distracted by the skyline that she had to stop and check a map to get her bearings. After three years in "aloof" New England, she wasn't expecting any help. To her surprise, a stranger knocked on her car window and offered directions.

Three years later, this Dallas native feels at home here and plans to stick around for a while. A recent graduate of Pitt's creative nonfiction MFA program, she's at the beginning of her freelancing career, but has already been published in *Pittsburgh* magazine, *Access Texas Magazine*, *Creative Nonfiction*, and *Pitt Magazine*.

COVER

When Tom Starzl came to Pittsburgh, he put himself in the riskiest, bloodiest, and most difficult situations a surgeon could. He built a new field of medicine in the process. (Cover: Jacob Thomas of Deco Zone. © 2006)

PITTMED

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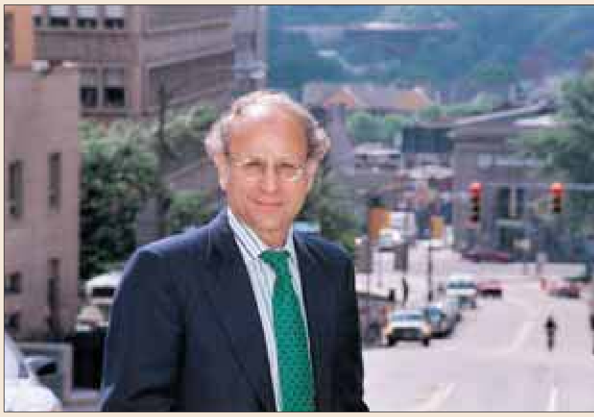
Know thyself? If knew myself I'd run away.
—Johann Wolfgang von Goethe



JULIA MAROUS STRAUT

Our lives are mostly a constant evasion of ourselves, T.S. Eliot suggested. Likewise, the study of medicine has evaded a fundamental science that promises to tell us much about ourselves and our health. But that's changing here at Pitt.

We're partnering with the Carnegie Museum of Natural History to infuse evolutionary biology into our way of thinking about medicine. Without the robust context the study of evolution adds, we risk missing critical way points leading to a fuller understanding of the origins of human illness and new avenues for prevention and treatment. Indeed, human health and illness can best be understood not only in a cultural, social, and economic context, but in an evolutionary one as well. Our med students are already immersing themselves in a paleobiology elective, and others are undertaking their required research project with Chris Beard (a museum curator and MacArthur Fellow).

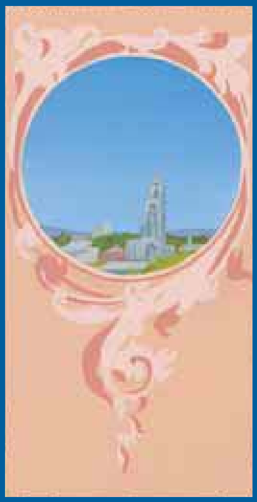
John Lazo, Pitt's Allegheny Foundation Professor of Pharmacology, is on the museum's board and fostered this partnership. John has been known to show audiences a slide of a tumor from a Jurassic dinosaur. It's a reminder that cancer has been around for a very long time—and is not just a byproduct of smoking or other contemporary pollutants. So how did creatures from 150 million years ago develop cancer? And what about the prehistoric animals that didn't?

Sharks very rarely get cancer. Investigators have revealed that the shark's immune response occurs much more rapidly than ours—preformed antitumor antibodies are at the ready in the bloodstream; the shark's immune system apparently needn't wait for the cascade of molecular events that gets ours churning. Why are our immune systems different from theirs? What can sharks tell us about cancer? Olivera Finn, chair of our immunology department, would probably like to know as she delves into how the human immune response might be honed to further detect and deter cancer. (Turn to page 28 for that story.)

We can expect the benefits of studying evolutionary biology to reach much more broadly than informing our understanding of oncogenesis. As the editors of *Science* noted in their Feb. 24 editorial, "the narrowness of the birth canal, the existence of wisdom teeth, and the persistence of genes that cause bipolar disease and senescence all have their origins in our evolutionary history." They make a plea to recognize evolution as a basic science of medicine.

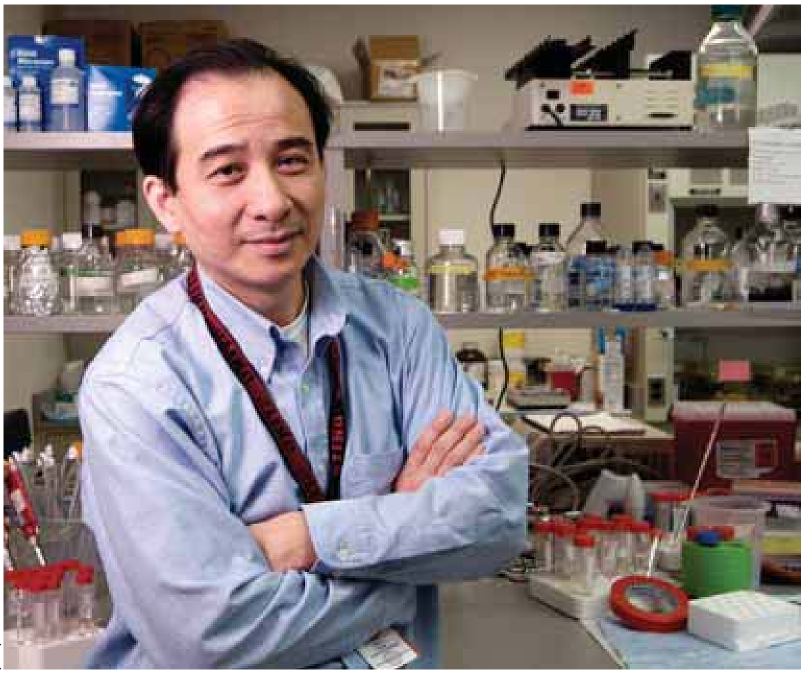
Although we might like to believe that "there is nothing new under the sun," evolution gives that the lie—at least with respect to our understanding of human biology. Indeed, our knowledge of human health and illness will profit greatly when we learn—starting presumably with the big bang—about the entire history of our molecules and cells.

Arthur S. Levine, MD
Senior Vice Chancellor for the Health Sciences
Dean, School of Medicine



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

GAINS IN WEIGHT RESEARCH



JIM JUDKIS

Zhao

In obesity research, a supposed panacea comes down the pike all the time, says Allan Zhao. Lots of people are hoping for a magic pill to control expanding waistlines.

So Zhao, a PhD and assistant professor of cell biology and physiology at the University of Pittsburgh, is cautious when he talks about his work with leptin, a hormone produced by fat cells. Leptin causes us to limit food intake, expend more energy, burn more fuel, and lose weight. It is found in high levels in the blood of the obese. But for some reason, it has trouble in that population getting to the hypothalamus, where it works. Zhao decided to pass human serum through a leptin column, suspecting that whatever bound to leptin could be retarding its progress. Five major protein bands stuck. Thus far, one—C-reactive protein (CRP)—has been fully explored by Zhao's lab. Zhao also found that CRP is more abundant in blood of the obese and can suppress leptin's functions. He wonders whether an agent can be developed that disrupts the CRP/leptin interaction. But he doesn't expect a panacea is around the corner: "Obesity is a complex problem." —*Joe Miksch*

FOOTNOTE

Some complain that the best acts bypass Pittsburgh. But in February, the Carnegie Science Center welcomed Super Colon. Pittsburgh was the first stop on a four-city tour. Super Colon? A punk band? Nope, a 20-foot-long, 8-foot-high replica of, well, a human colon. Super Colon—with warm-up acts by Pitt med experts—helped visitors identify risks, symptoms, and treatment options related to colorectal cancer.

No word yet on Galactic Gallbladder's tour schedule.

Tech Med

Two heads are better than one. How about four?

Recently the University of Pittsburgh, along with UPMC, signed a cooperative research agreement with Santa Clara, Calif.–based Intel, best known for manufacturing computer chips, and Carnegie Mellon University, where Intel Research Pittsburgh is based.

Here's a preview of a couple of the medically related collaborations: An interactive search system called Diamond will help physicians identify, for example, potentially cancerous skin lesions. The system will let users quickly mine terabytes of nonindexed data, such as large collections of medical images. Researchers plan to step up virtual reality by capturing and reproducing 3-D scenes so refined that the human senses would accept them as real. As the original moves, so would the 3-D model. Medical applications could include rendering active human organs to assist with diagnosis and treatment. —***JM***

CAMI MESA

A&Q

With the Chief of Pitt's Dirty Bomb Squad

Joel Greenberger (above), an MD professor, chair of the Department of Radiation Oncology in the School of Medicine, and codirector of the lung and esophageal cancer program in the University of Pittsburgh Cancer Institute, also directs Pitt's new Center for Medical Countermeasures Against Radiation. It's one of eight such entities nationwide funded by the National Institute of Allergy and Infectious Diseases and charged with developing ways to deal with radiation terrorism.

The urgency of the task

The government's concern is how you can handle hundreds or thousands of people who have had a moderate or low dose of radiation. We don't have anything in our national stockpile that we can dispense safely to hundreds and thousands of people that would be effective.

Promising development

We've got one home run with an agent called MnSOD, manganese superoxide dismutase, an enzyme the body naturally upregulates when it's exposed to ionizing radiation. We've found that if we give a plasmid, a little circle of DNA, in very high numbers and express it before radiation exposure, we get protection from total body radiation in mice.

What he worries about

Just in the scenarios I think of in my head—which are pretty scary things, [like] a dirty bomb with a plastic explosive or some equivalent surrounded by radioactive material that gets dispersed into the air—you're talking about a large number of people who will inhale this material, will have radioactivity that's detected in their lungs. There will be a lot of people coming to hospitals who want to be treated, and they're not going to want to be told there's nothing available for them.

His question for the world

Why aren't more people studying physics, chemistry, and radiation biology?

—Interview by Hattie Fletcher

Got to http://pittmed.health.pitt.edu for more interview excerpts.

Faculty Snapshots

Spend some time with the University of Pittsburgh's Linton Traub to learn about a little-known mechanism behind high cholesterol. And don't be surprised if you end up with the urge to belt out the Marvelettes' "Please Mr. Postman."

The reason? The associate professor of cell biology and physiology's research into how cells internalize what they need from the material in which they are bathed. As Traub would put it, individual "cargo" proteins have unique "zip codes" that tell the "postman" (an adaptor protein that sorts) which "mail truck" (intracellular clathrin-coated buds) to load the protein into.

Traub, a PhD, and his team uncovered the first protein of the clathrin coat machinery tied directly to human disease. That protein, ARH (autosomal recessive hypercholesterolemia), regulates the level of low-density lipoprotein (LDL) in the blood. When the postman is dysfunctional, Traub discovered, the zip code is ignored and LDL cannot be internalized by cells, accounting for high blood cholesterol levels.

Traub

A viral protein under investigation in Preet Chaudhary's lab is known to promote lymphoma. Recent work by the MD/PhD and visiting professor of medicine is changing the way people think about the mechanism that drives this bad actor.

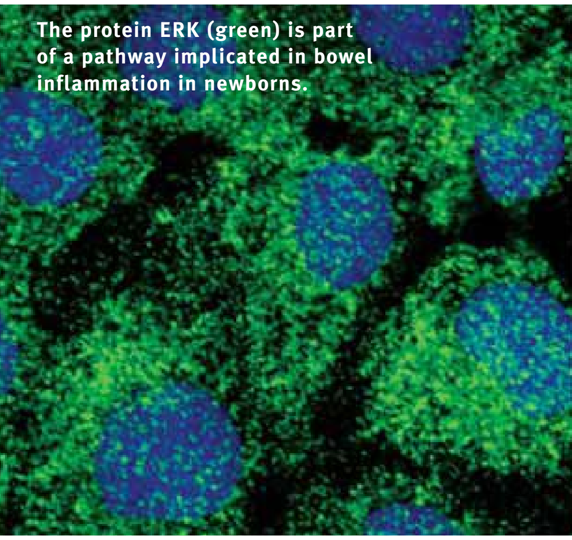
Chaudhary

Scientists believed the protein, which is associated with human herpesvirus 8 (vFLIP K13), promotes lymphoma by preventing cancer cells from dying through apoptosis, programmed cell death. Chaudhary's work indicates that rather than inhibiting an apoptosis-related cellular protein called caspase 8, vFLIP K13 activates a pathway involved in the promotion of lymphoma. If this pathway can be blocked, Chaudhary says, it may be possible to kill the lymphoma cells.

Barnes

Russell

What guarantees that the risks and rewards of the 4,000 or so clinical trials happening at Pitt's medical center are explained adequately to volunteers—that "informed consent" is truly that? Barbara Barnes, an MD and associate dean for continuing medical education, and Joanne Russell, registered nurse and administrator of research education, were part of a team that developed a program intended to protect research subjects by honing investigators' informed consent skills. The program was so successful that it won the Alliance for Continuing Medical Education's award for Most Outstanding Live CME Activity. *—JM*



The protein ERK (green) is part of a pathway implicated in bowel inflammation in newborns.

Another view of the same cells lining the intestines.

COURTESY J. CAVALLO

Student's Work May Help Newborns

Jaime Cavallo should be in her fourth year in Pitt's School of Medicine. Instead, she has taken a year off to work. Her decision has nothing to do with earning a few bucks to tamp down student debt or a desire to decompress. Rather, Cavallo is doing basic science research in pediatric surgeon David Hackam's lab.

Cavallo was named the inaugural fellow in Pitt's Surgical Translational Research Training Program, which Hackam, an MD/PhD, directs. In Hackam's lab, Cavallo has delved into necrotizing enterocolitis, an inflammatory disease of the bowel that affects one in 1,000 live births. It's the leading gastrointestinal cause of death among newborns.

She's not just tagging along in the lab. Cavallo determined that bacteria can cause a receptor in cells lining the intestines to switch on a signaling process that leads to the disease.

Hackam is pleased with Cavallo's work—"She's set a pretty high standard." He's not the only one. At an American Medical Association event last fall, Cavallo won the overall prize in the student research contest, besting 70 other students from throughout the country. —*JM*

PITT FOLKS WIN JEFFERSON AWARDS

As expected of a third-year medical student, Susan Wong is busy. When she's not in class, she's studying. If she's not studying, she's working. If she's not working she's—what? Sleeping? Nope, she's helping.

Since arriving at the University of Pittsburgh, Wong has developed and implemented a program at the Women's Center & Shelter of Greater Pittsburgh that teaches its residents about health, medical, and nutritional needs.

The American Institute for Public Service recognized Wong's efforts with one of eight Jefferson Awards given in the Pittsburgh area.

Another "Jeff" went to Edward J. Donnelly III (Res '78), an MD who has a private practice in Oakland and Aspinwall. Donnelly sees patients at an Uptown shelter for homeless women, Bethlehem Haven. Twenty-three years ago, he began volunteering; now he also raises money for the shelter and serves on its board.

Donnelly takes his hat off to his fellow Pitt med awardee. "[Wong] is really something. When I was in medical school, most students spent their Friday nights in a bar. She's at a shelter," he says. —*JM*

FLASHBACK

At the end of the 19th century, an unidentified Parisian girl jumped into the Seine and drowned. A death mask was made—perhaps someone could put a name to the face. In 1958, Peter Safar, the late founder of Pitt's anesthesiology department and "father" of CPR, met with Norwegian toymaker Asmund Laerdal, who would create a mannequin to teach CPR. The model for its face was the mystery girl's mask, then owned by Laerdal's father-in-law. She now has a name, "Resusci-Anne."

PAINTING, "GIRL FROM THE RIVER SEINE," BY LEILA WATHNE. PHOTO BY T.F. TOLHURST.

T.F. TOLHURST

HUG THIS BUILDING

In the end, the School of Medicine's efforts are about making people healthier. Now they're about making the Earth healthier, too. The U.S. Green Building Council bestowed its Leadership in Energy and Environmental Design Gold Award upon the McGowan Institute for Regenerative Medicine Laboratory Building on the South Side. It is the only academic building in Pennsylvania so honored.

The building stands on reclaimed industrial land; it has a 5,000-gallon holding tank for rain water (used for toilet flushing), has a heat-recovery system that reduces energy use, and is made chiefly of locally produced materials. —*JM*

Appointments

New Department of Medicine Chair **Steven Shapiro** has spent much of his career working with jittery mice. Mice in his lab develop cravings for tobacco—not surprising, since he exposes them to levels of cigarette smoke proportionate to what dedicated human smokers might inhale. Using gene knockout technology, his lab generates mice that don't get emphysema—even when they "smoke." The mice are no longer able to employ an enzyme that reacts to foreign invaders such as smoke by destroying lung tissue. Why not develop an emphysema therapy with this knowledge? Well, knocking out the enzyme also meant getting rid of its cancer-inhibiting actions. Having characterized this enzyme's role, Shapiro—who comes to Pitt after serving as the Parker B. Francis Professor of Medicine at Harvard—will study pathogenetic mechanisms of chronic obstructive pulmonary disease and lung cancer.

Shapiro

Shapiro speaks highly of the department's tradition of excellent care. As chair, Shapiro also will focus on career development and mentoring. In addition, he'll emphasize bringing interdisciplinary groups of researchers together to enhance the basic understanding of disease and translate that into new therapies.

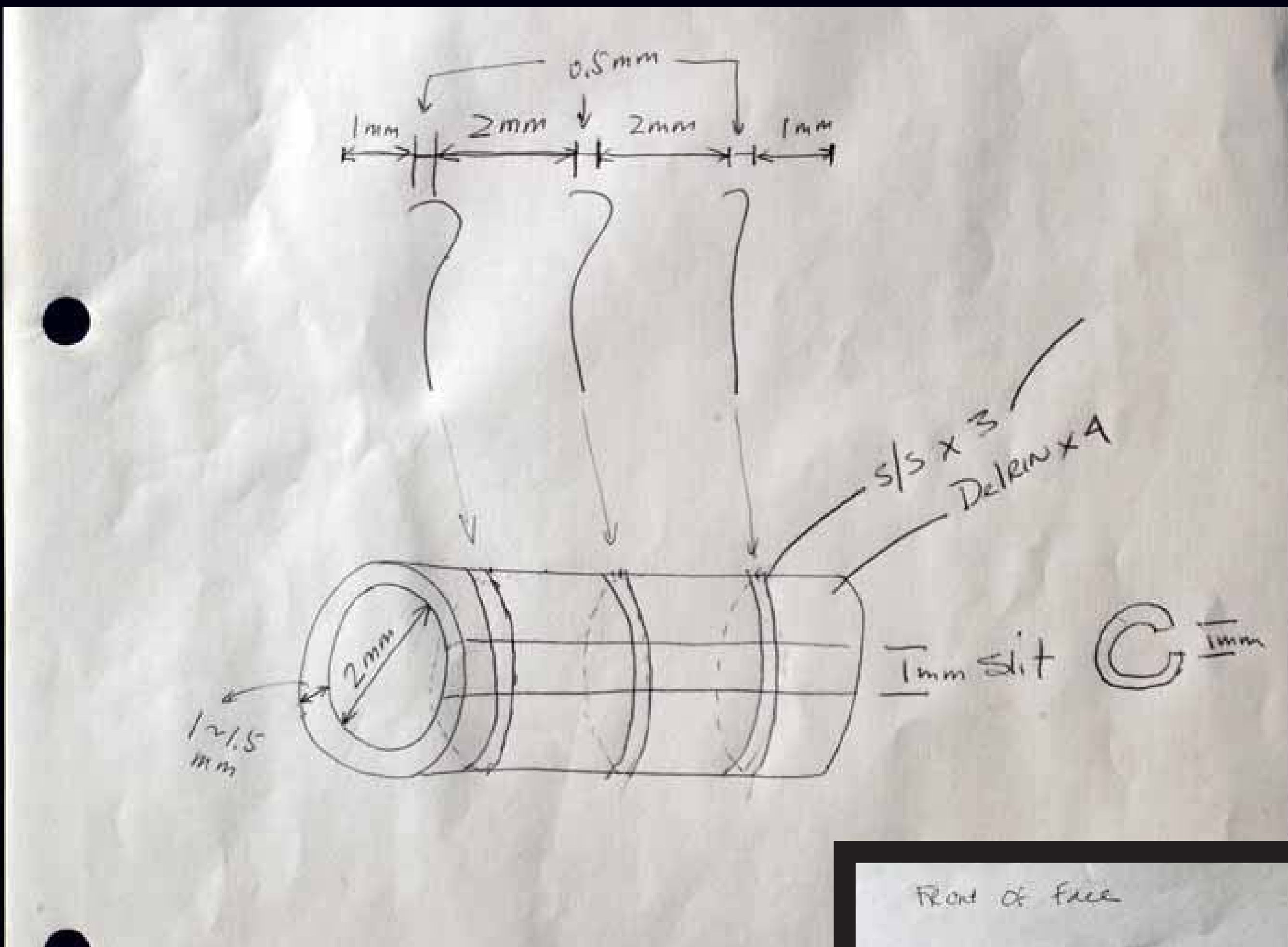
An ambulance delivers a patient with multiple traumas to an ER. Doctors must determine which injuries should be treated immediately and which can be operated on later. **Hans-Christoph Pape** teaches doctors how to make those snap decisions. Pitt has recruited the MD to be chief of orthopaedic trauma surgery from Germany's Hannover Medical School, where he was vice chair of trauma surgery.

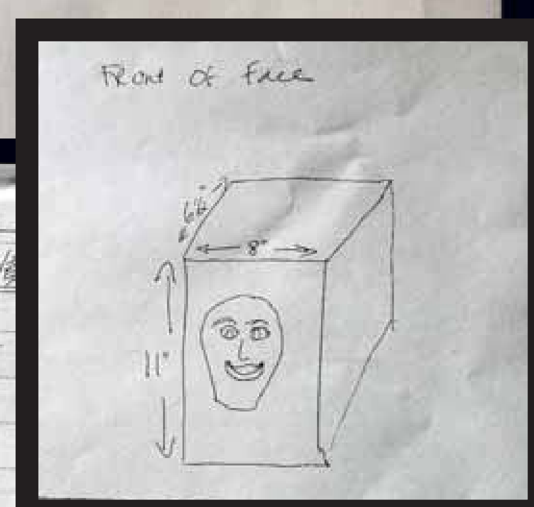
At Pitt, he hopes to pursue a study similar to one he conducted in Germany that involved tracking and reexamining multi-trauma patients a decade after they incurred injuries.

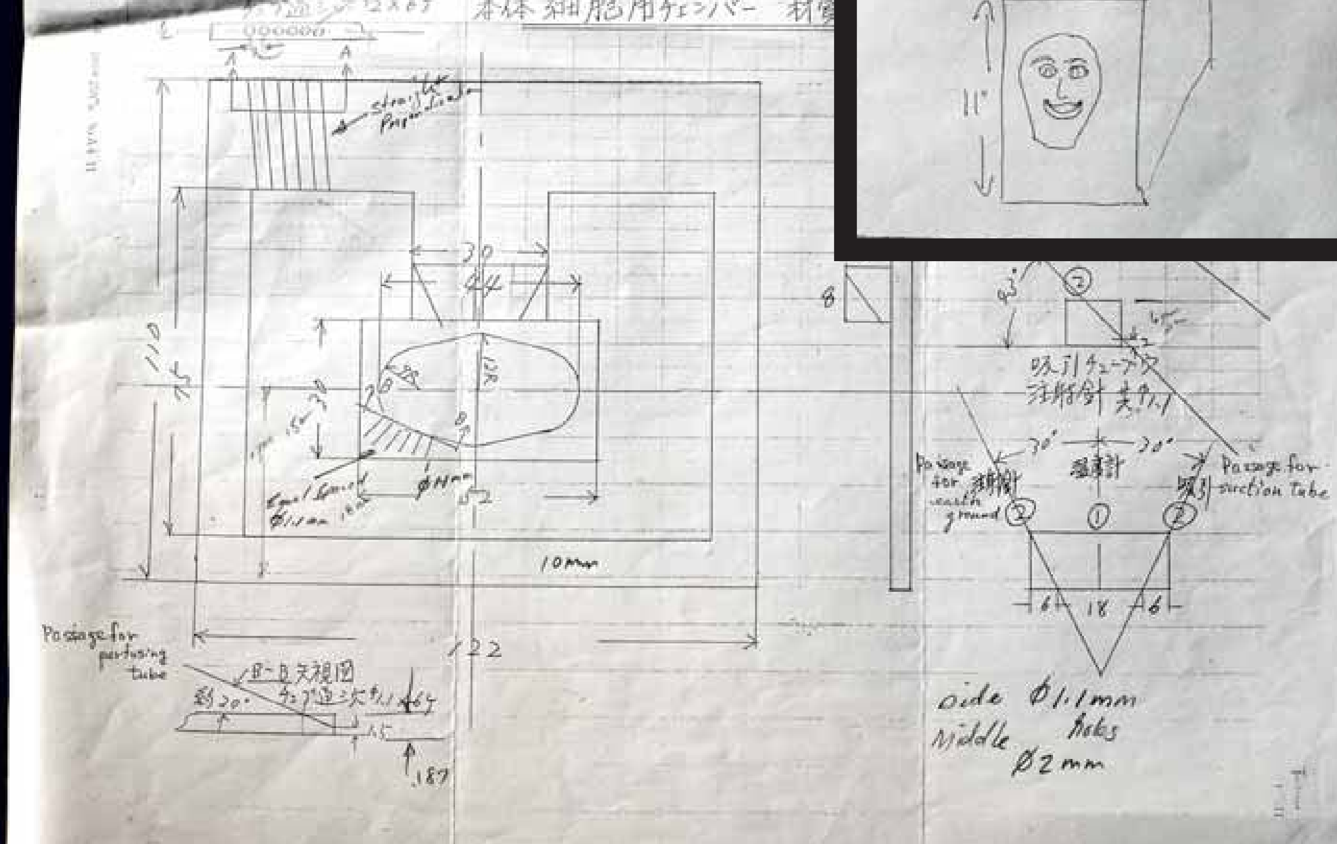
Pape

Many people have chronic pain that presents without an accompanying pathology. The insult is there but not the observable injury. Finding the mechanisms that cause such pain has been the holy grail of **Gerald Gebhart**'s work. Gebhart, a pharmacologist who specializes in organ-related pain, will head Pitt's new Center for Pain Research. The PhD hopes to elucidate these processes and determine better pain treatments. He arrives here from the University of Iowa, where he was the head of the Department of Pharmacology. At Pitt, he will continue to investigate how signals sent from injured nerves can produce chronic conditions like fibromyalgia and irritable bowel syndrome. —*Sydney Bergman*

Gebhart







COMING RIGHT UP

Imagine you're a scientist with 50 fruit flies. You're not satisfied to just sit around and count them all day. You want to poke around, find out what's going on with your little chums. First you need something to hold them so you can encase them in gel.

Where do you get one of those? Down you go into the bowels of Scaife Hall—past the laundry and medical equipment lining the corridors—to the Department of Cell Biology and Physiology/Pharmacology Machine Shop. There, you meet Bill Hughes.

You present him with a sketch. Some of the measurements are metric. Some are English. The drawing is not to scale. It's on a coffee-stained napkin. A few days later, Hughes presents you with a nifty fruit fly holder. It works perfectly.

For 42 years, Hughes has turned the vague sketches of School of Medicine researchers into devices that have pushed all manner of research forward. His shop, which now includes Travis Wheeler, has also built creations to help surgeons and disabled med students. Some recent favorites appear here.

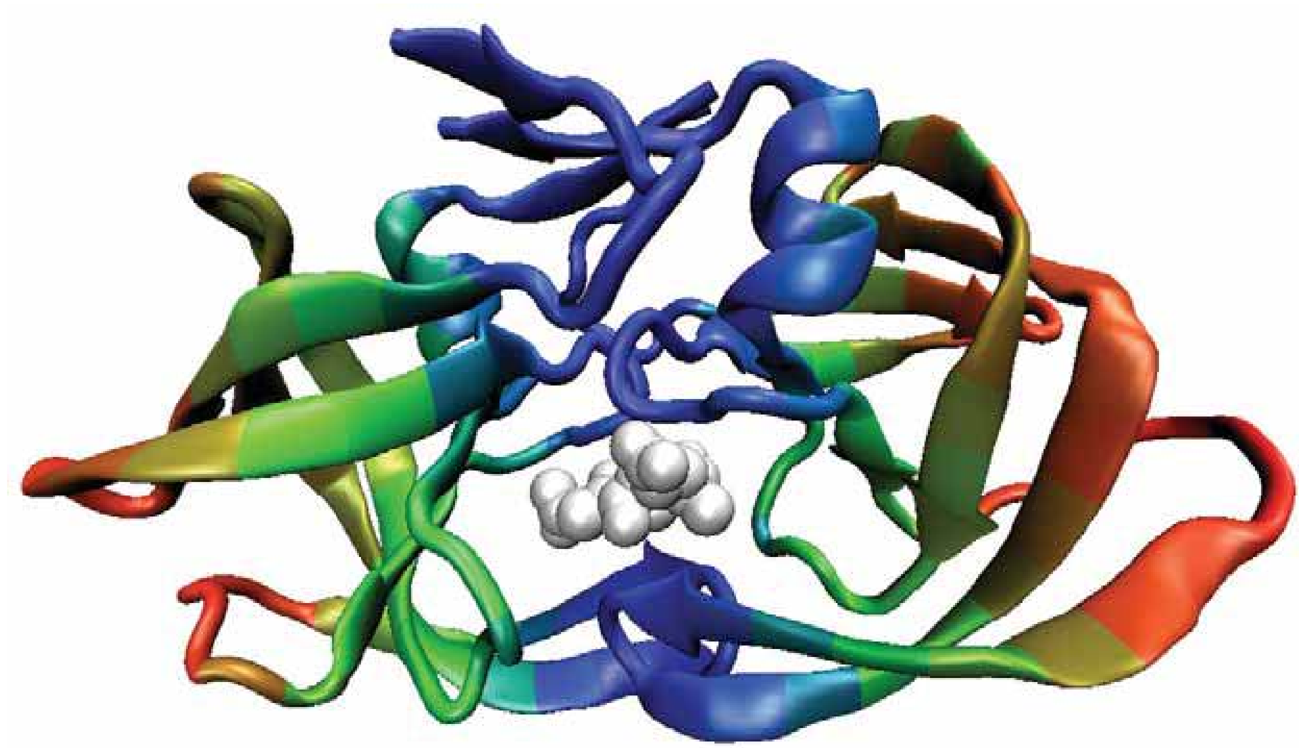
The ribbed sausage/barrel? A clamp to record electrical impulses through a nerve. The finished product is the size of a pencil tip. (See prototype below.)

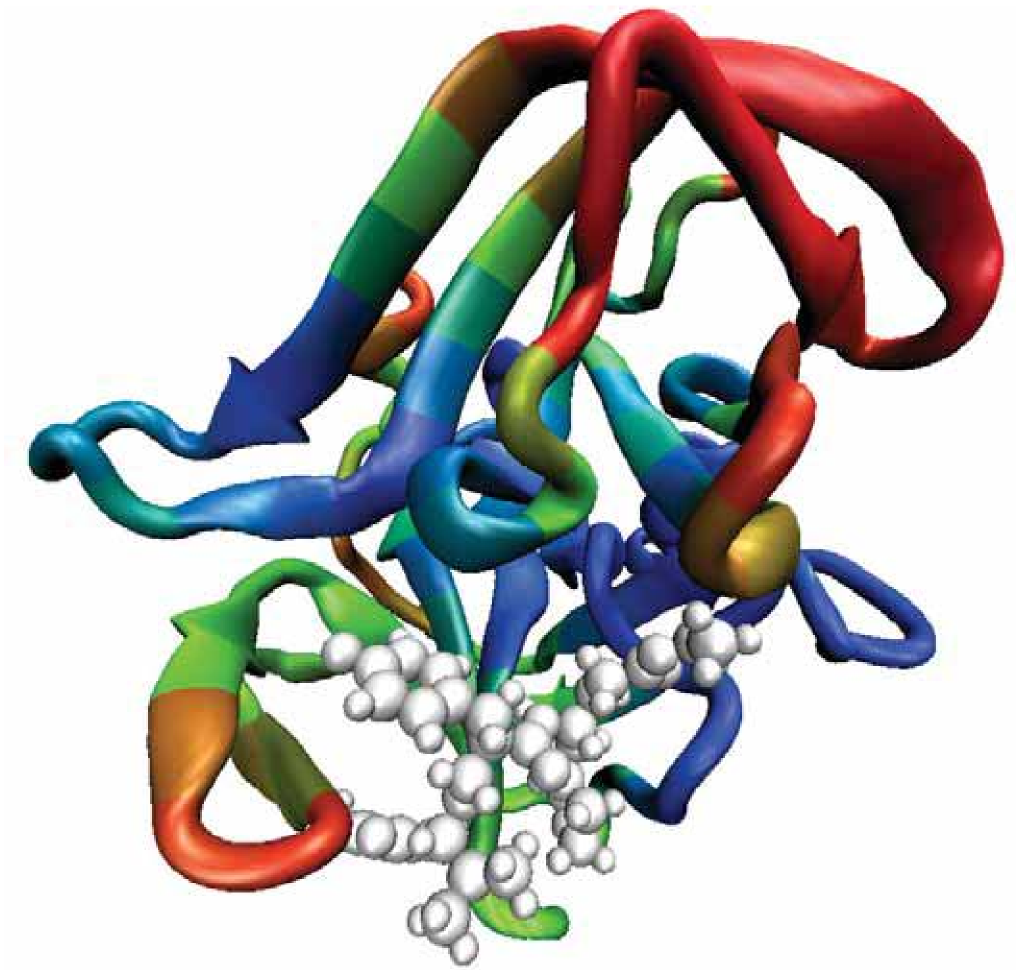
The box with the smiling face? Plexiglas case for an anatomy lab.

That thing at the bottom with the Japanese characters? Hughes figured it out—even though he cannot read, write, or speak Japanese. (It attaches electrodes to wafer-thin slices of spinal cord.) —*Joe Miksch*

PHOTOGRAPHY FRANK WALSH

Explorations and revelations taking place in the medical school





Ivet Bahar and Lee-Wei Yang made the connection between the architecture and stability of proteins and their function. Both figures here show the propensity of enzymes to bind ligands at highly stable regions. **TOP:** This HIV-1 protease is color coded by its ability to change structurally. Blue represents the most stable region. A binding molecule sits in the blue area at the bottom of the image—that's where the reaction that accounts for the protein activity occurs. **BOTTOM:** Similar features are illustrated for another enzyme (type 2 rhinovirus 3c protease) bound to an inhibitor (white).

COURTESY LEE-WEI YANG

IN SHAPE

RESEARCHERS SEEK LINK BETWEEN FORM AND FUNCTION | **BY SHARON TREGASKIS**

In 1913, biochemist Maud Menten—who would later spend four decades on the University of Pittsburgh School of Medicine faculty—copublished the Michaelis-Menten equation for predicting the rate of chemical reactions spurred by enzymes. Before the equation became standard, the pace at which any particular reaction might occur was a mystery. Even the most sophisticated scholars were stumped when it came to anticipating the speed at which the body's various biochemical feedback loops operated, and drug development was largely a game of chance.

In the intervening decades, the understanding of proteins and their functions has grown exponentially. Advanced imaging techniques reveal the molecular twists and turns of proteins, while the increasing speed and sophistication of computer processing allow for analysis of massive amounts of data. Yet, a clear conception of the relationship between a protein's chemical function and its shape has remained elusive. According to Pitt's Ivet Bahar, that means the basic science behind drug development really hasn't evolved much since Menten's day.

"Most drug discoveries are made through a kind of trial and error," says Bahar, the chair of the Department of Computational Biology, who is also a professor of molecular genetics and biochemistry.

"There are libraries of compounds that are screened against proteins to see which ones produce an effect."

A more rational—and effective—approach, she suggests, would allow researchers to identify optimal drug candidates in advance of experimentation, anticipating the molecular reactions they might initiate. Such capacity would save vast quantities of time and money.

But that means understanding both the rate at which any given reaction will proceed and how the structure of a particular enzyme influences its interactions.

Bahar, a PhD in chemistry, has dedicated her career to crafting sophisticated computer simulations that reveal the connection between form and function.

"Michaelis-Menten is useful and still widely used in experimental data," says Bahar, "but it doesn't provide a molecular understanding of what's happening."

In a June 2005 paper in the journal *Structure*, Bahar and postdoctoral research associate Lee-Wei Yang published their analyses of a set of two dozen proteins, examining both the chemical properties and physical dynamics of each.

"When we analyzed a whole bunch of proteins and identified their mechanical key regions—forget the chemistry, look at the mechanics—we identified key regions that act as a hinge," says Bahar.

Those hinge regions tended to be near the places where chemical reactions took place.

In the same issue of *Structure*, University of Wisconsin, Madison, biochemists Dimitry Kondrashov and George Phillips noted that the Pitt findings added a new dimension to the field of protein dynamics and would likely ease the job of solving protein structures.

The findings led Bahar and postdoctoral research associate Dror Tobi to investigate how chemical interactions between proteins relate to the shapes of increasingly complex macromolecules, such as immunoreceptors and muscle filaments.

Previously, scientists imagined proteins bound as interlocking rigid structures, much like a gate latch snapping down.

Bahar and Tobi's findings, published in the December *Proceedings of the National Academy of Sciences*, suggest that the architecture of a single protein—in its unbound state—provides clues as to where and how it will ultimately couple with other molecules.

Their studies suggest a more flexible coming together than the gate-latch model. Remember the popular Transformers toys from the '80s with multiple hinges and joints? They were two or three toys in one. (Like the "prehistoric pterodactyl" that became an "evil robot with snap-out attack blades.") Proteins also possess an "ensemble of conformations," says Bahar. One form best suits any given biological function, she explains, and binding stabilizes that particular shape.

As the name suggests, research in Bahar's department relies heavily on sophisticated algorithms and detailed computer coding. But the underlying conceptual framework takes precedence.

"First, we need to understand the fundamental phenomenon," she says. ■

DATA PLEASE

The Howard Hughes Medical Institute has honored the School of Medicine's new doctoral program in computational biology with a $1 million grant to develop a course to give students hands-on training in wet labs. More than 130 institutions across the country contended for the awards, intended to bolster interdisciplinary efforts. Ten programs received funding.

"There's a real necessity for closely coordinating experimental and computational approaches," says program codirector Ivet Bahar, who chairs Pitt's Department of Computational Biology.

She notes students can do *in silico* (her term for computational) studies to assess what might be eliminated from an experimental task. "That saves time and funds," she says. "On the other hand, computational biologists need data—all of our calculations are based on a repository of experimental results." ***—ST***

One student is writing a medical thriller for her scholarly research project.

BRIDGET LASCH

A RESEARCHER IS BORN

STUDENT PROJECTS OPEN DOORS TO ACADEMIC MEDICINE

BY HATTIE FLETCHER

The young doctor, fresh out of residency, suspects something fishy at the sports center where she just started a new job. Some athletes connected to the center's clinic are performing very well—almost too well. Their drug tests come back negative, but the young doctor is starting to wonder: What's going on in the lab late at night? And why do the mysterious men in military uniforms who visit the clinic have access to the athletes' medical records?

Intrigued? If you want to get to the bottom of things, you'll have to wait. The young doctor, the sports center, and the athletes currently exist only in the imagination of Giselle Aerni (Class of '08).

Aerni plans to have a draft of *Adrenaline Rush*, a mystery/thriller in the mold of a Robin Cook or Patricia Cornwell novel, completed by March 2008. That's when she, along with all of her Pitt med classmates, will hand in the final report for a scholarly project.

At first blush, writing a thriller might not seem like the most scholarly of projects, but it will require Aerni to learn a great deal, not only about chemistry and the development of undetectable and illegal supplements, but also about the daily practice of sports medicine.

Performing such independent and self-motivated research is exactly the point of the scholarly project, a new addition to the curriculum, beginning with the Class of '08.

The school asks each student to design and carry out a long-term, in-depth study requiring logical decision making and analyses, notes Nina Schor, who helped design and oversee the program. Schor, an MD/PhD, believes the project also will help students develop their verbal skills as they articulate the goals of their projects and explain the results to classmates, mentors, and an executive committee of faculty members and deans.

These are essential skills. But there's another motive behind the program. The requirement is one way the school has responded to the need for more academic physicians. Schor hopes it will inspire some students to consider careers in academic medicine.

The first set of project proposals reflects the diversity of Pitt student interests. For example, there's an interactive Web site for diabetic children and a short documentary about an uncommon genetic disorder. And many students have opted to work on more traditional projects, often diving into research the summer after the first year. The program requires students to stay involved throughout med school, analyzing data, building relationships with mentors, and putting their research into a larger context for a paper or presentation.

For Joan Striebel (Class of '08), a former elementary school teacher, the project offered a welcome opportunity to develop her lab skills. After she realized teaching children was not her calling, Striebel headed back to college. Then in medical school she felt at a slight disadvantage compared to students who had already done research.

"My idea was to find someone established in lab work and have [her] show me how to ask questions and analyze data," Striebel says.

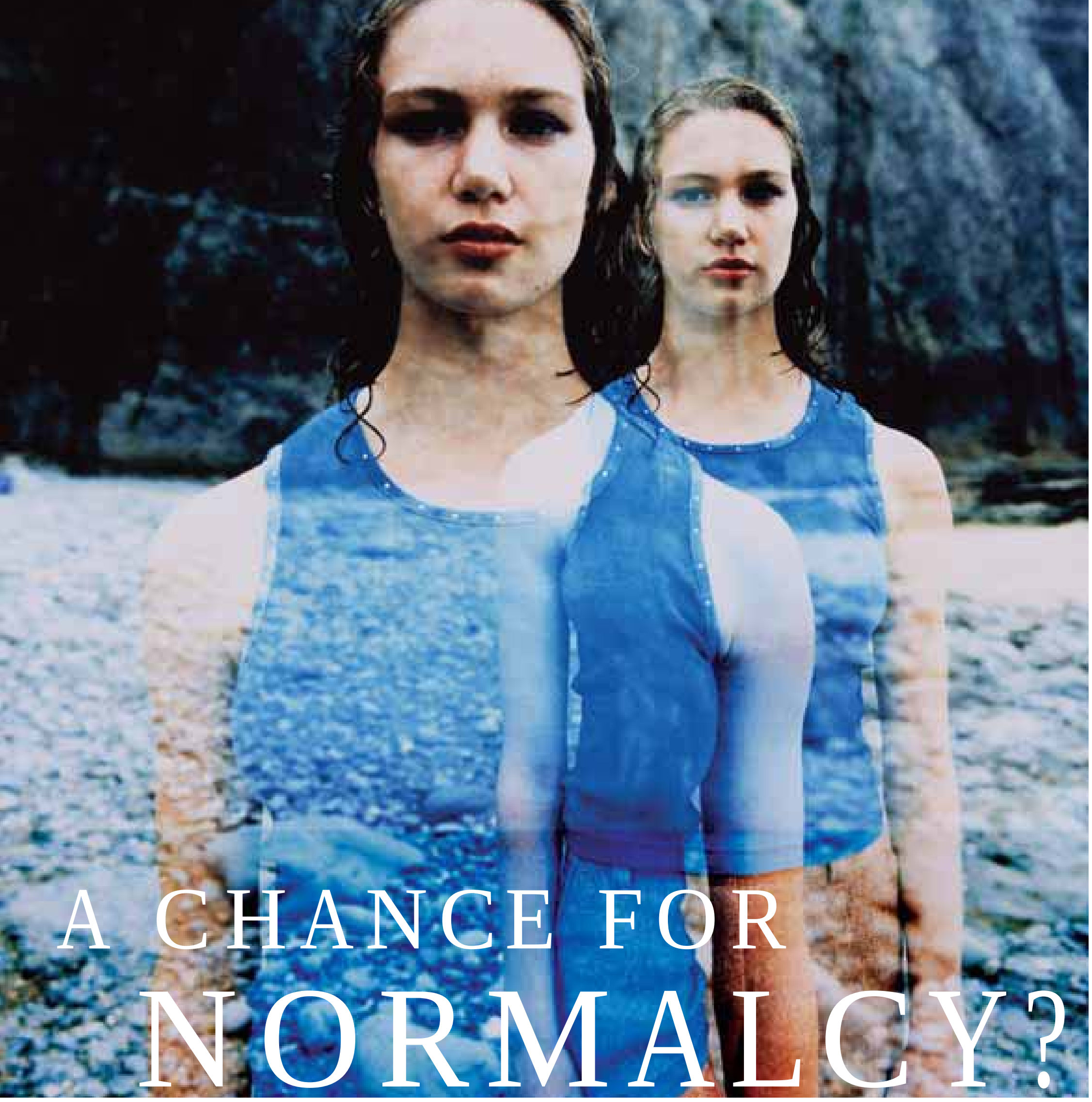
She found a willing mentor in Edith Tzeng, who suggested Striebel consider several projects relating to carbon monoxide and the vascular system. The student did preliminary work last summer; now she's seeking funding so she can take a leave during her third year to run the data again and continue the research.

Striebel is hooked. In part, she thinks it's because the project allowed her some independence at an otherwise very structured point in the curriculum. She's also grateful for the mentorship.

Perhaps the biggest thrill has been how much she enjoyed the lab work itself. On her return from a summer vacation, Striebel was surprised at her excitement to see "her" blood cell slides again. Now she's considering a career in pathology.

Schor says some students initially came to the project "kicking and screaming." But many of those students have stopped by Schor's office to offer sheepish apologies for being so resistant. *This has turned out to be the best thing I've done in medical school so far*, they tell her. ■

Watch future issues for more stories about how students shape their scholarly research projects.



A CHANCE FOR NORMALCY?

GETTY IMAGES

A NEW SCHIZOPHRENIA DRUG ON THE HORIZON | BY JOE MIKSCH

When David Lewis was growing up in Ohio, he had a favorite aunt. Both his mother and father were the youngest of seven. Lewis is the youngest of four. This meant, in Lewis' words, he was "the young cousin kind of left out" at densely populated family gatherings. This aunt took pity on the boy whose older cousins found better things to do than hang around with little David. She occupied his time and entertained him.

But, on occasion, his aunt wouldn't be around. No one talked about where she went or what she did when she was absent. She always came back; but when she did, Lewis perceived her to be out of sorts, different, not the same aunt he knew before. Gradually, she'd become her old self again, and the two would return to their usual relationship: kindly aunt and a young boy who otherwise would have been lonely.

As he got older, Lewis became aware that his aunt was mentally ill. Today, as director of the Translational Neuroscience Program and the Conte Center for the Neuroscience of Mental Disorders as well as professor of psychiatry and neuroscience at the University of Pittsburgh, it's his life's work to understand the mechanisms and costs associated with major psychiatric disorders.

"I really liked her," he says of his aunt. "I felt badly, though. I couldn't understand it at all. I didn't say, 'Okay, well, I'm going to go do research to try and solve this problem.' But it created within me a concern, a desire, compassion, and awareness."

Lewis, an MD who has been on the School of Medicine faculty since 1987, is in the midst of running a phase II clinical trial of a drug that may help subdue cognitive defects associated with schizophrenia, such as dysfunction of working memory.

The drug targets a class of GABA neurons (GABA is a kind of amino acid) that regulates working memory. Working memory is what healthy people draw on to briefly retain and use information. People with schizophrenia are likely to have certain neurons that don't produce enough GABA.

Yet, says Lewis, "If it were possible to just rev up the activity [of a GABA-producing cell] and make it kick out GABA more often, well, that would probably be worse than the situation is now. We want to preserve the timing but boost the signal."

He thinks he's found a way to do that.

In addition, he believes the drug will "boost GABA signaling just at the location where the signaling is deficient and not boost it at locations where things seem to be normal."

Lewis says that most schizophrenia drugs are directed toward controlling psychosis—the delusions and hallucinations commonly associated with the disease. Although these drugs help keep people with schizophrenia out of the hospital, they don't do anything to restore normal thought processes.

A combination of Lewis' yet-to-be-named experimental drug, antipsychotics, and cognitive and social rehabilitation training may ease a patient's reintegration into society.

It's also possible that the drug could be effective in treating teens and young adults at the onset of symptoms.

"There could be a treatment intervention," Lewis says.

"You could get involved early to enhance cognitive capacity. Could you delay or postpone or reduce the severity of the more evident clinical features of the illness? It's the grand target."

Lewis expects that trial results will be available toward the end of this year. If the trial volunteers don't show great improvement, the study still could be considered a success from Lewis' perspective.

"The hope is, even if we can't detect a clinical improvement, we will see a change in biology. That will at least let us know we're on the right track."

When Tom Starzl came to Pittsburgh, he put himself in the riskiest, bloodiest, and most difficult situations a surgeon could, and he trained others to do the same. Here we tell the first part of the story of how he built a new field of medicine.

A "MONOMANIACAL" EFFORT LED TO A CURE FOR LIVER DISEASE AND A NEW FIELD OF MEDICINE

BY CHUCK STARESINIC

ONLY STARZL DARED TO

John Sassano recalls what it was like to be an anesthesiologist watching the call schedule when Tom Starzl was performing the first liver transplants in Pittsburgh. Starzl was setting up the riskiest, bloodiest, most difficult situation a surgeon could get himself into—evidenced by the fact that he was the only one in the world to attempt it.

"It was like being up at bat," says Sassano (Res '80). "It's the bottom of the ninth, and are you going to be able to hit the ball? I mean you had to be the best. You had to be at the top of your game. This was not routine. This was doing things that had never been done before."

A professor of music had come to Pittsburgh from North Dakota in 1981, desperately ill, descending into a mental fog. Eventually, his hands began to move like a metronome—doctors call that the "liver flap." He staked out a hospital elevator where, sitting on a chair, he would grasp white coats and the hands of startled nurses as they passed and demand a liver.

ILLUSTRATION | JACOB THOMAS AT DECO ZONE

By the time an organ became available, it seemed like an exercise in futility. His kidneys had failed, and his liver had ceased to make clotting factors.

Sassano remembers the date and the experience like it was yesterday.

"It was a bloodbath," he says. In his critical care training, he had seen people bleed like this—people shot in the liver, for example—and back then, these were considered "acceptable deaths." Here, doctors were deliberately creating the same situation, and Starzl expected them to solve it. Sassano pumped close to 200 units of blood by hand.

"It was close to a 24-hour nonstop operation that was physically and emotionally the most demanding thing I've ever been through," he says.

"It was a marathon, and you couldn't stumble. You couldn't slow down or stop what you were doing, because we were just barely keeping up. There was a point where we were just doing it on faith, because we weren't sure whether his brain was dead or not because his blood pressure was so low. We just refused to let him die. That was it."

Without ever explicitly saying so, Starzl challenged those around him to work harder than they had ever worked and to do things that had never been done. That was the job description, and you could either keep up with him or get out of the way. If it was to be the latter, there was no shame in that, but you would not be long remembered around here. Starzl was busy creating a cure for liver disease.

Starzl describes Sassano the next day with his head in his hands, sobbing from the effort. Sassano doesn't know whether he was sobbing, but his arms and hands were cramped, and he still didn't believe the patient would live. He recalls telling Starzl that he was so frustrated he had to either fix the problem or leave the field.

By the next case, Sassano had devised a rapid infusion pump that he later patented. Today, rapid infusion is part of every emergency room setup; as a result, such massive bleeding presents a much more tenable situation.

The professor lay in the ICU for six weeks with an open incision—his liver and intestines remained exposed because of an infection. Ten years later, he wrote to Starzl describing his return to music, how he became the academic dean of his college, and how he thought of Starzl with gratitude every day.

To begin to locate Tom Starzl in the pantheon of great scientists and surgeons of the past century, one must first locate the Distinguished Service Professor of Surgery on the University of Pittsburgh's bustling Oakland campus. (Although his other title, director of the Thomas E. Starzl Transplantation Institute, includes the term "emeritus," you are excused if you start to think this Latin term means "eternal" based on Starzl's work habits. He turned 80 in March, and he is in his office today, as usual.) Don't bother looking for him at the transplantation institute, the headquarters of which are located in Pitt's Biomedical Science Tower (renamed for Starzl as an 80th birthday surprise). Nor should you attempt to navigate the maze of its clinical area, which sprawls over multiple levels of UPMC Montefiore. Though Starzl is largely responsible for the busiest and most important transplant center in the country, you won't find him there.

According to Pitt's directory, Starzl's campus address is PZHUT 3.

No joke. To meet the most-cited scientist in clinical medicine, author of some 2,400 publications, recipient of the National Medal of Science (in February), without whom the field of organ transplantation would be either unrecognizable or nonexistent today, you need to go to the third floor of the Pizza Hut Building. (Never mind that the pizza shop closed years ago—this is Pittsburgh, and we regularly give directions using landmarks that no longer exist.) You'll know you have the correct door—on Fifth Avenue, tucked between the Indian restaurant and the bookstore—when you see the torn piece of paper Scotch-taped to the window that reads, "Thomas E. Starzl Transplantation Institute." You'll take the stairs because there is no elevator. It helps if you're fond of dogs, by the way, because Starzl has five, any number of which are likely to be present. Don't trip over their dishes as you squeeze through the second-floor hall, and help yourself to a cookie from the torn package on the file cabinet on your way up. Don't worry about the crumbs.

This building, every room of which smelled like pizza when Starzl moved in nearly 20 years ago, says a lot about the man. He is unorthodox. He is not especially concerned with appearances. He is most comfortable residing outside the mainstream with his dogs nearby. Perhaps he is even shy. Years ago, the mother of a boy awaiting a liver transplant commented that Starzl seemed more comfortable with the children under his care than with adults.

Starzl's office is more thoughtfully furnished than the other rooms. He often works standing at a sloped drafting table with a view of a weathered wooden patio, empty but for an old picnic bench. He never goes out there, he says, unless visitors want to look at the rooftops of the neighborhood. At the opposite end of the room is a long sofa, large enough to serve as a daybed, and an open closet holding shirts, jackets, and clean white coats. These are vestiges of the days when Starzl worked around the clock, catching bits of sleep where and when he could, taking cross-country flights to procure organs, transplanting those organs in marathon procedures, checking on patients who awaited organs and others who battled rejection. Today, a patchwork mutt snoozes contentedly on the couch, and a golden retriever rests its muzzle on the floor. Starzl's daily excursion involves taking any dogs present—barking with excitement—down the back stairs to the alley just before lunch. They walk down the hill, cross Forbes Avenue, and circuit the block.

Starzl's appearance is somewhat in opposition to his larger-than-life reputation forged in the 1980s, when he made liver transplantation a reality with Pittsburgh as its crucible. He is of average height and trim. Today, he wears a dark, zippered sweater and a Giorgio Benelli tie dominated by an ornate crest that includes the initials "HB."

"I had someone put that on," says Starzl of the monogram.

It honors the late Henry Bahnson, legendary heart surgeon who had been Starzl's friend beginning in their residency days at Johns Hopkins University. Bahnson was chair of surgery at Pitt, and his unimpeachable character was the major reason that Starzl, who battled academic politics at the University of Colorado earlier in his career, decided that Pitt was a place he could work.

Starzl speaks in a reedy voice that is both friendly and, given his current age, grandfatherly.

"It was a nightmare," he says simply and honestly about how he built a new field of medicine, with the distance of a historian talking about a bygone war.

"That period was basically, for many of the people that were involved for a dozen years from 1980 until 1992, a life-ruining experience. … It was so monolithic—you could even call it monomaniacal. It required such intense focus."

This was the monumental struggle to make liver transplantation a viable, accepted therapy for liver disease. The patients who came to Pittsburgh from all over the world were facing death. They were gray. They were yellow. They swamped the halls of what was then Presbyterian University Hospital. Starzl was the court of last appeal. No one else could help them. No one else would try. It was more terminally ill people than should be in any one hospital, some thought—especially for a pie-in-the-sky experimental therapy like liver transplantation. Some said that the patients, wasting away as they awaited organs, deserved to die with more dignity than this. ("The liver was sort of a taboo organ then," says one Starzl colleague. "It was frightening, because operating on the liver itself was something that you just couldn't imagine. It was so bloody.") Following lengthy and sometimes multiple surgical procedures, patients and their doctors still faced gargantuan challenges. Even successful transplants threatened to drain the life out of those involved; the failures were almost too much to bear. This went on without pause for years, contributing to the ending of more than a few marriages, including Starzl's first.

Although Starzl had demonstrated as early as 1967 that liver transplantation was possible, that wasn't enough, he says.

"It was imagined that it was so difficult that only a single person in the world could do it. So how in the world were you going to train people—ever—to get this complex technology into the healthcare system? That was the problem. And that was a problem that was solved here in Pittsburgh, and it was made possible, I think, by the environment at the University of Pittsburgh."

Those who worked with Starzl in Pittsburgh can't imagine anyone else who could have made transplantation viable.

"He was the person that was necessary to do this," says Sassano. "He did what he had to do to accomplish it. And I don't mean that in a bad way. This was his mission, and if left in anyone else's hands, it wouldn't have been accomplished."

Starzl seems a bit embarrassed by the recent attention brought his way by honors such as the National Medal of Science. There are more television interviews and photo shoots than he cares to count. To hear Starzl talk about it, he is withdrawing from active engagement with the institute that bears his name, so the time for such indulgences is past.

"There's no reason to be fixated on a fossil when you've got these lively crustaceans coming up," he says.

The chief crustaceans Starzl jokingly refers to are the two men who recently assumed leadership of the institute—responsibilities that Starzl once handled by himself. (Incidentally, both insist that Starzl continues to provide valuable and regular input in their respective areas. Emeritus, indeed.) Amadeo Marcos is a transplant surgeon who heads up what is a very large and growing clinical transplant program. Fadi Lakkis is an MD and longtime lab researcher who left clinical nephrology and Yale University last year to devote himself entirely to research; now at Pitt, he is in charge of the institute's broad scientific research program.

Today, if you see Starzl on television accepting the congratulations of the president of the United States for his accomplishments, it's easy to forget that he built his career on the fringe. Less charitable observers and even some of his peers believed him to be on the *lunatic* fringe. Though Starzl never doubted that developing liver transplantation was the correct thing to do, there was a time when he was filled with doubts about his own abilities to simply make it as a surgeon.

"It was a marathon, and you couldn't stumble. You couldn't slow down or stop what you were doing, because we were just barely keeping up."

Starzl graduated from Northwestern University's medical school in Chicago with an MD and a PhD. He spent four years in surgical residency at Johns Hopkins and two more at the University of Miami. By the time he returned to Northwestern in 1958 for a final year of training—a fellowship in thoracic surgery—he felt like an eternal student and a highly skilled financial liability. He and his wife had two young children (soon they'd have three) and growing debts, yet he was a student again. His family wondered whether he was simply putting off the responsibilities of adulthood.

The truth was much worse, Starzl wrote in his 1992 memoir, *The Puzzle People*:

"I harbored anxieties which I was unable to discuss openly until more than three decades later, after I had stopped operating. I had an intense fear of failing the patients who had placed their health or life in my hands. Far from being relieved by each new layer of skill or experience, the anxieties grew worse. Even for simple operations, I would review books to be sure that no mistakes would be made or old lessons forgotten. Then, sick with apprehension, I would go to the operating room, almost unable to function until the case began."

Starzl was 32 years old. He believed himself ill-equipped to be a surgeon but too far along the path to turn back. To add to his consternation, he had committed to a year of training in thoracic surgery when he knew that his main interest was below the chest, in the liver.

As he describes it, he seemed perpetually on the edge of calamity. When it was time to take his general surgery board examinations at the University of Pennsylvania, he could not afford a hotel and slept in a movie theater until closing time at 3 a.m. He spent the rest of the night beneath his coat on a Philadelphia park bench. He had recently developed an ulcer that was eating away at his duodenum; abdominal pain and antacids were his constant companions. While weathering a bout of pain in a bathroom stall following his exam the next day, he overheard his examiners reveal that he had placed first in his group.

Starzl was still not the horse that everyone was betting on; his financial and directional struggles would continue. He became an associate professor of surgery at Northwestern, bringing some of his own funding with him, thanks to a scholarship for young physician-scientists. In the lab, he worked on animal models of liver transplantation at a time when the only successful organ transplants were of the kidney, a much simpler organ, between identical twins. With no clinical position, however, he was still living on a pittance. Just a few months out of training, he was visited by colleagues starting up a medical school at West Virginia University. Starzl smuggled a live rabbit out of his lab so that he and his wife could serve meat to their dinner guests. He told them that he would accept nothing less than the chair of surgery. They declined his offer.

In the lab, Starzl began to find his trajectory. In 1960, he attended the annual meeting of the prestigious American Surgical Association (ASA) as an invited guest. He was an unknown, but he went to offer discussion of his lab results following a presentation by Francis Moore, a superstar from Harvard University's Peter Bent Brigham Hospital. These were the only research programs in the country for liver transplantation, and as Starzl offered his own results, he realized that his animals were living longer. He was ahead of the Boston team. After that, he was no longer an unknown.

He was given hospital privileges at a suburban hospital to make ends meet. To allow time for travel and lab work, he began scheduling operations at 6 a.m. He learned to catch moments of sleep where he could, in hard office chairs and empty rooms. For a time, he left the house at 4 a.m. and returned around 2 a.m. He was 35 years old and wondered whether he would make 40.

One of the greatest surgeons and medical scientists of the last century can be found in the former Pizza Hut building.

At the end of 1961, Starzl achieved a measure of professional stability when he moved to the University of Colorado and became the chief of surgery at the Denver Veterans Administration Hospital. His express goal, which was supported by the department chair, was to make liver transplantation a reality. The first step was the kidney. Starzl had shown in the lab that the phenomenon of organ rejection was the same in kidneys, livers, and other organs. If rejection could be solved in the kidney, then transplanting the liver, a complex organ through which half the blood in the body can circulate in one minute, might be attempted.

The few examples worldwide of successful kidney transplants involved living related donors and required suppression of the immune system using drugs or radiation.

In his first few years at Colorado, Starzl could claim more kidney transplant survivors than anyone in the world. He prescribed a cocktail of immunosuppressive drugs and steroids to reverse rejection. At the time, it was believed that the immune system would always and forever reject a foreign organ—in other words, a transplant recipient would require suppression of the immune system for life. But in 1963, Starzl took the results of his Colorado kidney trials—the most successful series of organ transplants ever—and published a controversial and seminal paper.

The introduction stated the authors' belief that "the rejection process can almost never be entirely prevented, but that its effects can be reversed with a high degree of regularity and completeness. Furthermore, the subsequent behavior of patients who have been brought through a successfully treated rejection crisis suggests the early development of some degree of host-graft adaptation."

This was one of the first of Starzl's many contributions through which he changed our understanding of the immune system, eventually making it possible to conceive of and achieve acceptance of donor organs in transplant recipients.

While controversy raged over these conclusions, Starzl moved ahead with a liver transplantation trial in 1963. He made five attempts, all of which failed. He would not attempt another liver transplant until 1967.

"Most surgeons whom I know have been able to protect themselves, either by rationalizing errors which they had committed or by promptly erasing the bad memories. I could not do this," wrote Starzl.

"Instead of blotting out the failures, I remembered these forever. With growing concern, I came to believe that I was not emotionally equipped to be a surgeon or to deal with its brutality."

In the meantime, he became terribly ill with hepatitis contracted from one of his many infected patients. Yellow and feverish and clutching his newly released book, *Experience in Renal Transplantation*, he went to see his father in Iowa and wondered if his career was coming to an end.

In April of 1968, recovered from his bout with hepatitis, Starzl reported to the ASA on his second series of attempts at liver transplantation. In Colorado, the pediatric department had supported the liver trials while Starzl's own surgery department was against it. All seven patients were children. All had been dying from the diseases they suffered when they entered the hospital. Now three were still alive. Although four had lived only two to six months, their livers had functioned long enough to offer hope that liver transplantation could work if rejection could be controlled. Moore, still the leader of Harvard's liver program, remarked that "liver surgery as of this day has a new look."

To this day, Starzl's dearest possession is a painting of a child bathed in sunlight picking flowers; she lived 400 days postop. Another girl, a teenager with liver cancer, lived 14 months before the cancer recurred. A 2-year-old boy lived another 30 months. Before that boy died in 1970, Starzl transplanted a liver into a girl who would live another 20 years with her transplant.

Success required more failure than most people could stomach. For many years after, Starzl would get an occasional letter from a parent that began, "I know you won't remember…" this or that child who was your patient. "They were wrong about one thing," Starzl wrote. "That I would not remember."

Throughout the 1970s, Starzl's program made strong, steady advances in controlling rejection.

"One by one, my patients would save me by letting me help them," Starzl wrote of this period—the same period in which his marriage broke up—a fact he regretfully attributes to "Mistress Surgery" winning out.

By March of 1980, more than 20 of Starzl's kidney recipients had been treated with an experimental drug called cyclosporine. The results were favorable. Of the first 12 liver recipients treated with cyclosporine, 11 lived more than a year. Only a few other centers were licensed to use cyclosporine, and they were meeting with little success. Starzl's special alchemy was in the recipe and regimen of the cyclosporine-steroid cocktail. When the Colorado team published its results with cyclosporine in the *New England Journal of Medicine* in 1981, the genie leapt forth from the bottle, and hospitals scrambled to start liver programs.

Starzl's time in Colorado was coming to an end, however. Political wrangling in the surgery department suddenly made Starzl believe that an aggressive trial of cyclosporine was impossible there. Still, he might have stayed if not for one fact that he shared with almost no one: Amid the relentless pace and emotional exhaustion of transplantation and research, he had begun to fall in love. Her name was Joy. She had worked in his lab but had recently left Colorado for Texas and, for personal reasons, would never return. If they were to be together, it would not be in Colorado.

In the course of a year or more, Starzl worked out the details of moving to the University of California, Los Angeles (UCLA). The details of lab and clinical space and appointments for Starzl's collaborators had been worked out. As the point of no return approached, Starzl learned of a movement in the faculty to oppose his appointment. Then the space for the liver program became limited; UCLA might only want a kidney program. Kidney transplants were easier, safer, and accepted, not to mention profitable. With no backup plan in place, Starzl announced at a meeting in California that he couldn't come to UCLA.

While Starzl's colleagues in Denver tried to mend fences, Starzl called Bahnson in Pittsburgh and told him what had happened. The next day, he was on a plane to Pittsburgh.

Starzl can't recall whether they ever discussed salary, space, or anything like that. After his experiences elsewhere, the only thing that mattered to him was integrity and honesty, and after 25 years of friendship, Starzl did not need to ask Bahnson about those things.

"I came here for one reason only," Starzl said later, "and that was because Hank was here. I didn't know anything about this school other than the fact that if Hank Bahnson were here, and if I were in his department, then that would be the place to be."

There was a modest kidney transplant program in Pitt's urology department, started by Bernard Fisher and run by Thomas Hakala, who used Starzl's renal book as a bible, achieved good results with the drugs and steroids available then, and knew only rumors of cyclosporine.

Starzl was 32 years old. He believed himself ill-equipped to be a surgeon but too far along the path to turn back.

As Starzl recalls it, Hakala was unapologetic in wanting to protect his turf; he told Starzl to stay away from Pittsburgh. No one knew or cared what went on here, he said, and he preferred it that way.

"I liked him enormously," says Starzl.

He told Bahnson that Hakala was an honest man with whom he could work. Thus began the Starzl era in Pittsburgh. The experimental drug cyclosporine was only available in four places in the country: Harvard, the University of Minnesota, the University of Houston, and now Pittsburgh. Starzl's program would be the only one where liver transplantation was available, and the medical wards quickly filled with the sickest patients imaginable.

Three of the first four liver patients in Pittsburgh died, and some began to wonder whether the success with cyclosporine in Colorado was a statistical anomaly. Starzl, too busy to find a place to live, occupied a room in Bahnson's basement for six months. On the drive to work, Starzl heard a radio station conduct a poll on whether or not his liver transplant program should be shut down before more patients died. The result was too close to call. Then, just as suddenly, 19 of the next 22 survived and began to thrive.

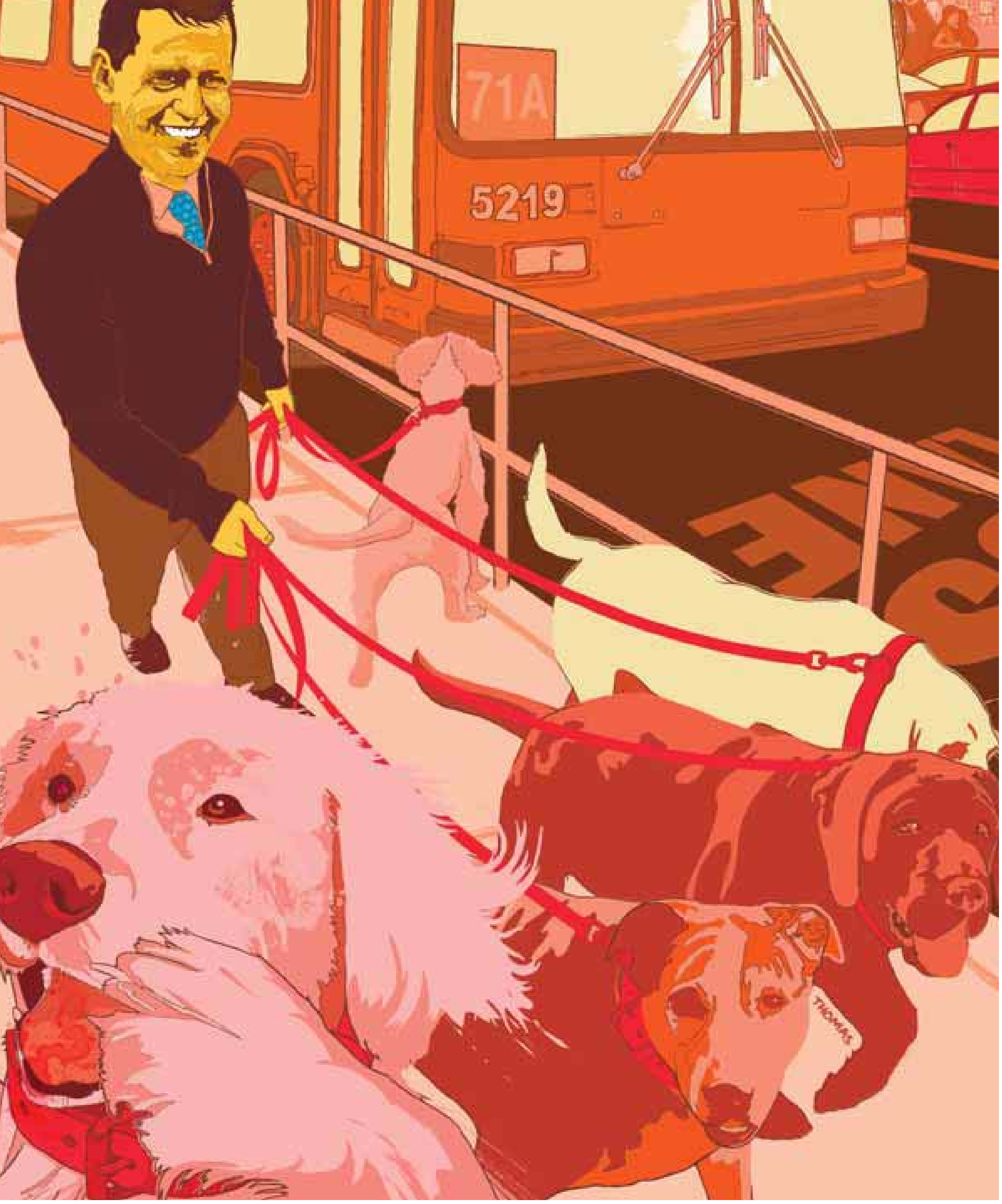
By the end of 1981, Starzl had been voted Pittsburgh's Man of the Year in science and medicine. Equally exciting for him, a huge sports fan, was the chance to meet the Pirates' Willie Stargell and the Steelers' Franco Harris at the awards gala. Starzl's wife, Joy, who had finally moved from Texas after their nuptials, was nervous about the event.

Pittsburghers have reason to be proud of Starzl's recollection of how Joy, who is African American, was received: "In a steel town, people are judged by what they do, not by the color of their skin. When she walked down the center aisle in an orange and yellow gown, there was silence, then thunderous applause. We were in the right city," he wrote.

There were still bumps in the road. All 54 residents and interns in the Department of Medicine signed a resolution denouncing liver transplantation as unrealistic and potentially unethical. Starzl and Bahnson evaded the potential deathblow by having transplant patients admitted to the surgery service and not to the general medical service, which had never been so swamped with deathly ill patients.

George Mazariegos, who was a transplantation fellow under Starzl in the early 1990s and is now a Pitt associate professor of surgery and director of pediatric transplantation at Children's Hospital of Pittsburgh, says that no one ever heard Starzl refer to a patient as "the liver I did yesterday." The patient was always remembered and referred to by name, even years afterward. Starzl can look at a slide of an organ and know the name of the child he removed it from a decade ago. Even in the most hectic and sleep-deprived stretches, he knew the family members, and he knew what they did for a living.

"He was the one person whom everyone would have forgiven if a name or other details



"Do you like dogs?" was the first question Starzl asked a recruit who would become clinical director of the Starzl Institute.

were forgotten," says Mazariegos, "but he was the one person who never forgot."

In August of 1981, a 12-year-old boy named David Yomtoob arrived at Children's Hospital with a rare genetic disease. Until a few months earlier, his parents had a seemingly healthy boy. Now, his liver was failing, and they were being sent to Pittsburgh by a physician who told them David had three months to live without a transplant.

David withered away to an unrecognizable shadow of a boy as he awaited a suitable liver. The child was perhaps hours away from death when Starzl brought another physician into David's room. There was a brain-dead child in the hospital, David's mother, Parichehr Yomtoob, later learned, and this doctor would be the one to talk to the parents about organ donation.

"Dr. Starzl took that other doctor over to the wall where I had placed photographs of David," Yomtoob wrote in her 1986 book, *The Gift of Life*.

"He showed the doctor David's soccer-team picture. He made the doctor study the life that had been David's, not the living corpse lying in the bed. 'He could play soccer again,' Dr. Starzl stressed to the doctor. 'He could be just as healthy as he used to be.' … It was the most gentle, loving, hope-filled act anyone could have done for us. Even if David had died, to this day I would love Dr. Starzl for that moment."

It appeared that the new liver had come too late. David's kidneys had failed, too. His skin was a deep yellow with purple blotches from hemorrhaging. He was paralyzed now. After transplant, he lay contorted and remained in that position for weeks. A camera was set up to monitor any progress he might make. Once, he somehow turned to face the camera, looking out from what Starzl described as "a mask of absolute hatred." Starzl wept when he saw it and privately wished that David had died before any of this had happened. If it had been a wounded animal, Starzl later said, he would have known what to do.

"He was the one person that never quit," says John Fung, a Pitt transplant fellow under Starzl and former Pitt professor of surgery and chief of the Division of Transplantation at the Starzl Institute.

"Almost everyone I know, including myself, would have given up a long time before he did. Even knowing that the idea was a rational one, people would have just gotten frustrated with all the failures he experienced in the beginning."

In November of 1982, Starzl showed the frightful video of David at a scientific conference following a rather dry talk filled with charts and graphs.

"This child is here today," he said. With that introduction, David Yomtoob, 13 months post-transplant, ran down the center aisle with a soccer ball tucked under one arm. He was the picture of health and vigor, and the audience rose to its feet to applaud him.

"Only those who know complete despair can understand the full meaning of jubilation," Starzl wrote. He leaves it to the reader to decide if he is speaking of himself, the boy, or both.

In the days when organ transplants were still largely experiments conducted at a few centers, Starzl and his team would travel almost anywhere in North America at a moment's notice to bring back organs for their patients. Prominent Pittsburgh companies made their corporate jets available for these organ runs—Starzl dubbed it the "University of Pittsburgh Air Force."

In 1982, a patient bled to death on the table during a transplant, and a pall settled over the program. Everything stopped. Starzl huddled with Bahnson and talked about what to do. At the time, liver transplants were performed in a crisis atmosphere as blood flowing to the liver was dammed up for 30 to 60 minutes while surgeons worked. It required incredible speed and skill. Few surgeons could pull it off. For the next procedure, the surgeons decided to attempt a venous bypass to keep the blood flowing but allow time to sew in the liver. It worked like a dream. Almost overnight, liver transplant became a much easier procedure. The technique, along with the documented success of cyclosporine in Pittsburgh, would spur the growth of liver transplant programs around the world. Those who trained in Pittsburgh would take a lead role in the expansion.

When Andreas Tzakis (Fel '85) first interviewed with Starzl, he waited for the transplant giant at the Falk Clinic, eagerly watching, he says, for a Mercedes or Cadillac to drop off the esteemed surgeon. Surely, Starzl will have a driver, he thought. (Starzl drove a Honda at the time, and he drove it himself.) When he did arrive, he was dressed casually, munching on some candy and wearing the same sneakers he wore while operating. The first question of the interview:

"Do you want some M&Ms?"

This story has a familiar ring for anyone who has come into Starzl's circle. Amadeo Marcos is one of the few transplant surgeons at Pitt not trained here. He was at the University of Rochester when an assistant told him Dr. Starzl was on the telephone for him. He thought it was a joke; he had never met Starzl. The next day he came to Pittsburgh to meet him. In his suit and tie at the institute's main office, Marcos was handed the telephone. Starzl was calling from above the old pizza shop. "Do you like dogs?" "Sure," Marcos replied. (Why not?) The interview began with the two of them walking Starzl's dogs.

Despite his casual introduction to Starzl, Tzakis says the atmosphere was tense in the 1980s; some surgeons were intimidated by Starzl, who exemplified and demanded perfection, and whose brain and body seemed always to work at maximum speed. After a year at Pitt, Tzakis received a dose of uncompromising criticism.

Starzl sat down with Tzakis and told him he would never be allowed to perform liver surgery. He wasn't fast enough or coordinated enough. After that, Tzakis was rarely seen without twirling and turning surgical instruments in his hands. He tied knots on every bedpost and table leg that he came near. Today, he is professor of surgery and codirector of the transplantation division in the University of Miami's medical school. Few surgeons have performed more liver transplants than Tzakis, and none holds Starzl in higher regard.

"[Starzl] basically never went home," says Fung, who now chairs the Department of General Surgery and directs the transplant center at the Cleveland Clinic.

"He carried around this beat-up, old orange sleeping bag. It was on the couch in his office, but if he had to travel somewhere, he'd take it with him. If we were on an airplane or at the donor hospital waiting to get going, he'd just roll out his orange sleeping bag and catch a few hours or minutes of sleep."

If you were Starzl's fellow, "he'd call you up at three, four, five o'clock in the morning and tell you to come down," says Fung. "He wanted you to work on a paper."

His fellows wanted to please him by working just as hard, or to make his life easier by doing more work. At the very least, they wanted to train with the only person in the world who could teach them about liver transplants, so they never refused.

Success required more failure than most people could stomach.

Starzl had been in surgery for 24 hours one day in 1981 when a doctor in Ohio called him and insisted he come help with a procedure. The doctor had his finger plugging a child's bleeding liver, and he needed Starzl's help to repair it. He sent a helicopter to Trees Hall. After they saved that child, Starzl lay on the floor of the helicopter for the return trip and wondered what was trying to eat its way out of his chest. As the hills of Western Pennsylvania passed by the window, he thought he might never see them again. He didn't have a scare like that again until nine years later. In 1990, while driving to the office, a volcano erupted in his chest. He dragged himself to the second floor landing and lay there panting and sweating. He made his way to the third floor and began going through the correspondence on his desk.

Later, in the emergency department, he declined the last rites offered by the priest. If there was a heaven, he wasn't going to get there on the strength of any last-minute rites. He'd rely on the whole record. His right coronary artery was 99 percent blocked. Angioplasty provided a temporary fix, and he had a bypass six weeks later.

Tzakis recalls the day in 1990 when he watched Starzl in surgery like so many times before.

"He was a supreme surgeon. A master surgeon. The best I've ever seen," says Tzakis. Where others took two or three moves to get from A to B, Starzl would make a simple acrobatic maneuver that only he could perform.

After surgery, they walked across Fifth Avenue and down to the Kunst Bakery on Forbes. ("That was a great, family-owned place," Starzl says of the now-closed cake shop. "They were down there baking at 4 a.m., and you could go knock on the window, and they'd let you in for a doughnut.")

On the walk back, sweets in hand, Starzl announced out of the blue that he was finished operating. Tzakis was stunned. He'd watched him work for seven years, but he didn't think it was long enough.

"We were all still learning from him, and we didn't think it was time for him to retire," he says. "But his mind was made up."

"It was an enormous relief," Starzl says now. "I was absolutely exhausted. I was wiped out." ■

To be continued in our August issue.

TRANSPLANTING MOZART

A sing-along of the ditty "Happy Birthday to You" would not do for Tom Starzl's 80th when colleagues, friends, and former patients gathered to honor the distinguished surgeon at a series of seminars and tributes. So at the suggestion of John Harvith (senior associate vice chancellor for University news and magazines), the surgery department and offices of the Chancellor and senior vice chancellor for health sciences commissioned Robert Lord Sutherland, Pitt professor emeritus of music, to "transplant" a theme from Mozart to the organ for the occasion. (Wink, wink.)

For "Mozart Transplantation for Organ," Lord recorded an improvisation on "La ci darem la mano" ("We will give to one another our hands") from *Don Giovanni* on the Heinz Memorial Chapel Organ. The recording was played as a surprise for Starzl at a March 10 celebration in Alumni Hall. (Those who didn't attend can still hear those chapel stones sing at www.pitt.edu/news/060313starzl.html.)

Mozart would have turned 250 this year. Starzl has been known to wonder out loud how much richer the world might have been if the composer had had a renal transplant, rather than dying of glomerulonephritis at age 35. —*Erica Lloyd*


A salon on choice,
volition, and apathy

WHY DO SOME PEOPLE SEEM TO HAVE CONTROL OVER THEIR ACTIONS WHILE OTHERS DON'T?

BY JOE MIKSCH

FREE-WILL HUNTING

Okay, there was this fellow. He worked down at the lower tip of Manhattan, on Wall Street. Essentially, he was your run-of-the-mill office drone. His primary task was to copy documents for a boss who was both an understanding gent and someone who avoided muddying the waters, rocking the boat, what have you. It wasn't a thrilling job, but our man was adept, reliable, and quiet. In short, he was a model employee—for a while, at least.

His friends, if he'd had them, would have called him Bart. Thin, sallow, and apparently shy, Bart wasn't one to chat around the water cooler, a trait that earned him some mistrust from his colleagues but pleased the head man. He spoke only when spoken to, and even then rarely responded with more than a word or two. Once this limited communication was complete, Bart went back to his desk and his work.

ILLUSTRATION | CATHERINE LAZURE

Then things began to change. In the small, cramped office in the middle of the world's financial hub, Bart stopped doing his job. Most people would have fired the guy, but the boss was concerned and tried to light a little fire under his odd copyist. He'd say something like, "Hey, Bart, how about you go mail these letters?" or, "Hey, big fella, whadd'ya say you run out and get some lunch? I'm buying." Each time Bart responded simply, "I would prefer not to," and got back to being busy doing nothing.

He seemed lethargic, almost incapable of moving. Bart's colleagues began to wonder whether there was something terribly wrong in the young man's brain that prevented him from acting, from behaving in a manner that was appropriate. Did he want to do what was asked but somehow just couldn't?

Or was he, as he said, expressing a preference to, well, to not do anything, to not move an inch, to stare at the wall all day long, and then putting that preference into action—or, rather—lack of action? Was that preference self-generated? Was Bart in the awkward position of mentally wishing to act but being unable to do so because of some malfunction in brain chemistry or brain circuitry? Was he predisposed to respond as he did under the circumstances that faced him? Did he have free will?

What ailed Herman Melville's Bartleby the Scrivener remains a mystery, but implications of free will arise in our daily lives, not just in classic literature. Why can some of us ignore the siren song of the bacon double cheeseburger, whereas others, also fully aware of the artery-clogging dangers, can't move ourselves to opt for the salad?

From dining choices to compulsiveness, movement disorders to Tourette's, doctors bump up against issues of will all the time. So with the University of Pittsburgh being home to some of the world's most prominent brain-focused brainiacs—at the Center for the Neural Basis of Cognition (CNBC), the Department of History and Philosophy of Science, and the Western Psychiatric Institute and Clinic—we couldn't resist posing a few really hard questions about why some people seem to be able to control their actions better than others. *Pitt Med* sat down with a philosopher, a neurobiologist, a psychologist, a psychiatrist, and a Parkinson's disease patient and hashed it out. Although these commentators haven't even attempted to solve the jigsaw puzzle of free will, their work and lives shed light on a few key pieces. ■

The Neurobiologist
How Do You Manufacture Volition?

Peter Strick talks over his omelet at the Holiday Inn Select in Oakland. Amid the clatter of plates and chatter of patrons, the soft-spoken and unfailingly pleasant man says, "Let me see that." Snatching a legal pad from a breakfast companion, he begins to sketch out the basal ganglia.

This set of structures, as one early observer put it, is set deep in the "dark basement of the brain" and tied to motor function, though Strick has convinced the neuroscience community that it's responsible for much more.

Strick is a member of the American Academy of Arts and Sciences, a PhD, and a professor of neurobiology and psychiatry at the University of Pittsburgh; he also codirects the CNBC. The joint venture between Pitt and Carnegie Mellon University looks to tease out the brain's secrets regarding awareness and judgment. With loops and lines, Strick illustrates components of the basal ganglia: globus pallidus, striatum, substantia nigra, subthalamic nucleus, and thalamus. (See p. 23 for more on the basal ganglia and Strick's contributions to understanding their function.) Complex interactions take the form of arrows and doodles. When he's done, the page is a mess. Thankfully, Strick is a better explainer than artist.

In the lab, Strick uses viruses as tracers to map the intricate circuitry and architecture of the nervous system. He has found that the basal ganglia play a part in the realms of vision, affect, sensation, higher executive processing, and, as long understood, motor control. If the ganglia aren't functioning properly, the result can be Tourette's syndrome, attention deficit hyperactivity disorder, obsessive-compulsive disorder, Huntington's disease, or Parkinson's disease.

The basal ganglia, Strick has made clear, have something to do with our behavior and our ability to control our actions.

Imagine a man with Parkinson's disease. One of his symptoms is akinesia, a disinclination to move. He knows that in order to place a phone call, he's got to get up from the easy chair, walk across the room, pick up the receiver, and dial. Yet, despite knowing all this, he can't. Not that he doesn't understand the situation. Not that he doesn't want to make the call. He's just unable to manufacture the internal drive that would propel him to do so.

Yet, Strick says, if someone were to, say, tape dance studio–style cut-out footprints to the floor, the man would be able to get to the phone without a problem.

"They will walk nearly normally," Strick says. "The thought is that when you provide the visual input to guide movement, the external stimulus will allow them to overcome the lack of internal generation of movement."

In this case, a loop (identified by Strick in 1986) involving elements of the basal ganglia isn't functioning properly. This, he says, is where you get into issues of free will.

"We can see consequences of when [the loop] is functioning abnormally," Strick says, "as in Parkinson's disease.

"People have argued if Parkinson's disease represents a disinclination to move, maybe this loop has something to do with volition." Strick won't commit as to whether he buys into that argument. His domain is figuring out the brain's circuitry.

What happens when circuitry goes haywire? We now know that the motor symptoms associated with Parkinson's—resting tremors, disinclination to move, and rigidity—are measurable consequences of the die-off of dopamine-producing cells integral to sensory motor function of the basal ganglia. What's less obvious to Strick and other neuroscientists is the basal ganglia's normal function. Is this collection of gray matter the will's home in the brain? Is it simply intended to inhibit tremors or make us more flexible?

Strick can't tell us—yet. "We know a tremendous amount about what happens when the basal ganglia [aren't] functioning normally, but we don't know quite as much about what happens when [they are] functioning normally," he says. "I think we're really at the beginning of that."

One of Strick's colleagues designed a study that let monkeys choose between treats that were equally appealing. A different section of the brain lit up when a monkey made a 50/50 choice compared to, say, what was active when making a choice involving a favorite juice.

When the results were presented at a recent Society for Neuroscience meeting, Strick was intrigued.

Certain parts of the cerebral cortex, which Strick believes are intertwined with the urge to move, were active only when the monkey determined that neither treat was preferable and was engaged in making a choice free from outside influence.

"When the values were judged to be equal, the neurons in the medial cortical areas were active. The urge-to-move area. Choice."

Strick looks at his pointer finger, holds it out in front of himself, and bends it.

"I became really interested in studying the nervous system by just being fascinated that I could move my finger whenever I wanted," Strick says.

"That still just amazes me. When you talk about internally initiating movement, how do you manufacture that? Those things get to the nature of consciousness, the nature of internal representations, and free will."

The conversation turns to addiction: How does someone, with finality, quit using drugs, smoking, or gambling? They probably can't, says Strick. Not cold turkey. The urge would stay with them.

After he's prodded for a solution, Strick adds, "You need to replace, substitute, the behavior." Carrots for cigarettes. The coffee shop for the bar. A new crowd as opposed to the old gang. Perhaps the circuitry, the loops and pathways that modulate behavior, becomes too strong to be broken. This isn't self-control, Strick says, it's "white-knuckling it through."

Is free will, then, just a question for philosophers to argue over, or is it hidden somewhere in the invaginations of the brain?

"I don't know," Strick says. "[Neurobiologists] may have some insights, but it is rather like asking a horse trainer which horse to bet on in a race. You get informed information, but by no means do you get a winner every time or perhaps even most of the time."

Strick keeps busy instead finding out what's answers are hidden in those deep dark basements of gray matter—what some might call the physical reality of the brain.

Answers to how we're able to control our actions seem to lie in circuits that travel the deep "dark basement of the brain."

CIRCUITOUS CIRCUITRY

In 1986, Peter Strick, then a researcher at the Veterans Administration Medical Center in Syracuse, N.Y., along with Garrett Alexander and Mahlon DeLong at Johns Hopkins University, published a paper in the *Annual Review of Neuroscience*. In layperson's terms, the paper was a very big deal. It more or less redefined the function of a portion of the brain.

At that time, the function of the basal ganglia—a collection of nerve cells deep inside the brain—was thought to lie exclusively in the realm of motor control.

The scientists identified four previously unknown loops involving the basal ganglia. It turned out circuits of the basal ganglia are not only involved in the control of limb and eye movement, they also play a role in decision making, affect, working memory, and behavior.

Strick, whose lab is still supported in part by the Veterans Administration, is now a Pitt professor of neurobiology and psychiatry, as well as codirector of the Center for the Neural Basis of Cognition, a University of Pittsburgh–Carnegie Mellon University collaboration. He points to two basal ganglia disorders—Parkinson's disease and Huntington's disease—as examples of the multifaceted nature of these loops. Parkinson's, he says, starts off with movement disorders and, as it progresses to different circuits, instigates behavioral disorders. Huntington's starts with behavioral problems, such as depression, and then creates motor problems. Strick believes basal ganglia loops are also factors in attention deficit hyperactivity disorder and obsessive-compulsive disorder.

He recently showed that premotor areas of the frontal cortex—once thought to influence motor function only through connection to the primary motor cortex—link with spinal motor neurons and may be responsible for some direct generation and control of voluntary movement. And he found that the cerebellum—formerly thought to be the seat of movement, coordination, and balance—is also a player in the thinking process. To top it off, he demonstrated that the cerebellum may control aspects of basal ganglia function.

As for the 1986 paper being a big deal—it has been cited 1,200 times and still averages between 120 and 150 citations a year two decades after publication. After 300 citations, a paper is considered a classic. —*JM*

The Philosopher
Can Science Make Room for Intention and Other Fuzzy Ideas?

The physical reality of the brain is genetic, chemical, and electrical. The feeling of having agency, of being in control of ourselves and our fate, is none of those things. It's a much more amorphous state, the notion that we are independent actors navigating life by making choices and having moral responsibility.

Neuroscientists like Strick who toil in labs have measurements, charts, and graphs; volumes of earlier measurements, charts, and graphs; and the gravitas that comes with all that. At the end of the day, if all goes well, these practitioners of the hard sciences come up with a generally accepted explanation of a physical phenomenon that is called "fact." Maybe, if a scientist is really good (and/or lucky) her work leads to a cure for, or maybe a better understanding of, some scourge.

Philosophy doesn't translate to the clinic and probably hasn't cured anything—even ennui. But, as a discipline, it has one thing going for it in the free will debate: It actually asks the question, "Is there free will, and what is its nature?"

In the extreme, consider that if free will is a mere construct, why should we have laws and courts? How can an individual who is nothing but a product of genetics and experience, who is predisposed to act in a certain manner under a particular set of circumstances, be held culpable for anything from jaywalking to homicide? The feeling of choice may have been there, yet crossing against that light or shooting that man was an event dictated by how the brain, constituted as it is, processed each and every event that led to that point in time.

"That's the philosophical problem of free will," says Jackie Sullivan, a PhD candidate studying the history and philosophy of science. Sullivan has an MS in neurobiology and is a member of the CNBC.

"On one hand, the question is whether agents act according to their intentions, beliefs, and desires, whether or not they're in control of those actions, whether or not they can act autonomously. Or is everything determined in advance?" Sullivan adds.

Ah, determinism. On one hand, it's a philosophical position that eliminates all the warm and fuzzy stuff like intentions and beliefs—the unverifiable—but on the other hand, well, on the other hand, who wants to feel like a rat in a Skinner box?

Sullivan has an answer to that question—no one.

"I think that if we were to throw out free will, it would have serious moral consequences in our society," she says. "And so I think that most people who want to reconcile free will and determinism say, 'Look, we have to believe that agents act autonomously in some cases because if we're to say, if we're to use environmental and genetic factors as a justification for why someone acted, then we lose the whole idea of moral responsibility.'"

Despite this stance, the philosopher/neurobiologist is unwilling to chuck science of the brain out of the equation.

"I think the story is ultimately a lot more complex than any particular individual area of science can possibly comprehend," she says. "And I think that's why nowadays you see a lot of areas of science becoming more integrative to deal with how complex the phenomena are."

Look, she says, at the myriad approaches that exist under the aegis of science. Some areas focus on the cognitive, others on strictly biological phenomena. But regardless of the scientific approach, Sullivan contends, many doing benchwork involving the brain are unwilling or unable to consider beliefs and feelings, things she believes are integral to making us human and making sense of the mind and all that stems from it. Maybe, she says, what we find out about how neural systems operate—such as Strick's work with the basal ganglia—can be integrated into how philosophers understand concepts such as free will. Maybe there can be some sort of synthesis.

"I'm not interested in debunking neuroscience. I think there is an approach in philosophy that's a lot different [from] the approach you find in science to certain kinds of questions. And I think there should be room for all different kinds of analysis," she says.

"I think somebody does need to keep science in check. Should it be the philosophers? I don't know."

All of which leads us back to Peter Strick's wagging finger. Was his choice to gesture with his pointer finger an outcome dictated by genes and experience? If so, what choice remains?

"If you want to go about debunking the stimulus/response theory, you can say, 'Well it seems that there isn't anything around me that's causing me to raise one finger rather than another,'" Sullivan says. There's no reward ahead, no fear of punishment. Unless, of course, Strick had extended his middle finger. That could upset someone.

But Strick insists offensive gestures are simply not in his repertoire; nor were they ever. "My mother raised me right," he says.

Is that the echo of determinism? ■

The Psychiatrist
Our Choices Are Real

Genetics and experience are important, of course, in molding the individuals we become. No reasonable person would argue that point. But when it comes to making conscious decisions, says Mary Phillips, they're certainly not the only determining factors.

Phillips, an MD, came to the University of Pittsburgh last year as a professor of psychiatry and member of the CNBC, having previously served as a visiting professor, on loan from the Institute of Psychiatry, Kings College London, where she maintains a research group. Phillips directs her department's functional imaging program; she uses the technology to sort out the neural mechanisms involved in normal emotion, a pursuit that's given her some insight into the nature of choice and will.

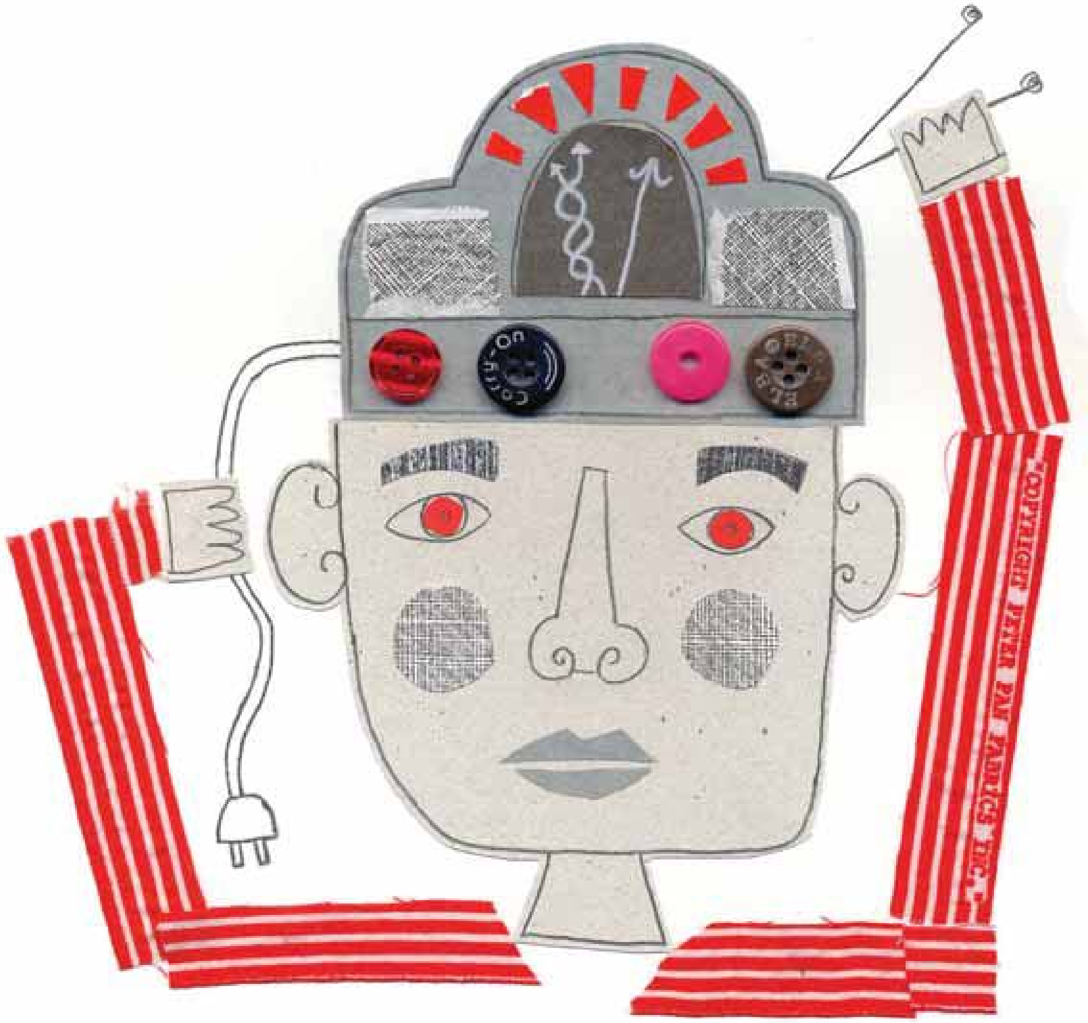
What we are genetically, and what we've experienced over the course of our lives, she says, do not constrict us to the degree that we should toss the concept of free will off the Cathedral of Learning.

"We still have some control," she asserts.

"We have decision-making control. Our genes and environment just limit our choices." Our choices may be limited, she says, but they are real.

The brain, she notes, behaves differently when it, consciously or unconsciously, perceives an element of control over a situation. Phillips recounts an experiment performed in London:

"It's called the 'tickling experiment.' They rigged up this machine and, basically, the person—the poor, unsuspecting person in the scanner—will pull a lever, and they either get a tickle in the direction they expected, or a tickle in the opposite direction, or no tickle at all."



Our brains behave differently when we perceive that we have control over an outcome.

Eventually, Phillips says, the subject figured out a pattern and had some ability to predict what would happen when she pulled the lever. At this point, activity was observed in different brain circuitry than when the subject wasn't wise to the pattern.

"It's just that when you become aware of self-control, there's something that kicks in as opposed to when things are done to you," Phillips explains. The brain, Phillips says, seems to know the difference between when it is acting and when it is being acted upon.

"Think about psychiatric symptoms such as delusions, hallucinations, imaginary voices," she says. "There's a free will issue here. People don't choose to have those experiences. It turns out that hallucinations and true sensory experiences involve different brain responses. Similar and overlapping, but different."

In such cases, Phillips says, "There's always an abnormality within the basal ganglia as well as the cortex. We always find some kind of functional abnormality in the basal ganglia."

Phillips thinks that Strick's circuits that pass through the basal ganglia all play a role in allowing us to consciously choose how we behave, which begs the question, "Are the basal ganglia involved with free will?" Answering the question, Phillips says, "What I can say is the basal ganglia are very important for helping us actually experience emotion consciously. The basal ganglia are a very crucial part of our cognitive, behavioral, and emotional circuits."

A few regions show increased activity when our brains are making decisions, Phillips says: Don't forget the prefrontal cortex—which communicates with the basal ganglia and is active when people attempt to coordinate thoughts and actions with internal goals. Or the cerebellum (also on the Strick basal ganglia circuit), which is involved with behaviors that border on the automatic, like driving a car or the motions of an experienced musician. Or the amygdala—a component of the basal ganglia that helps regulate emotion. So, then, in which neighborhood of the brain does free will reside—if it can be located?

No one knows, of course. Phillips' comments suggest less of a location and more of a perpetually forwarded address.

"Inevitably, free will is going to involve so many complex interactions between the cortical [outer portion of the brain] and the subcortical [nested inner regions]," she says.

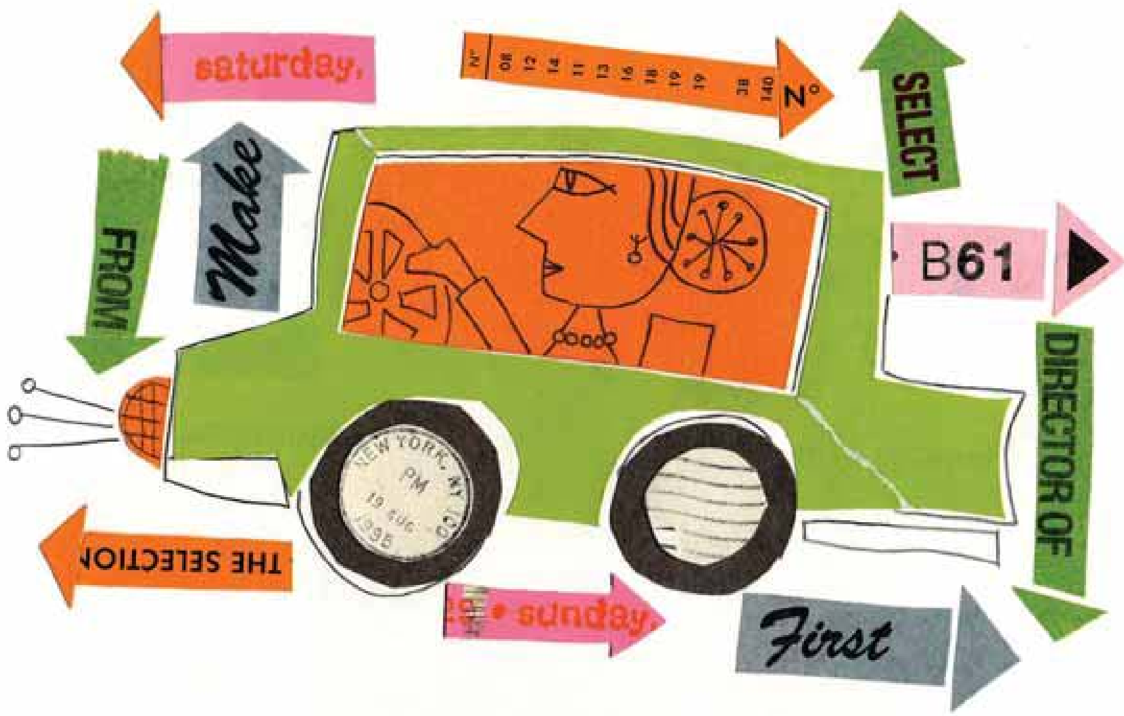
"But I'm sure we're going to get there eventually.

"What you'd have to do is design an experiment where you can single out the one component that's free will, as opposed to being forced to do something. And then you've got to design it so well that you can show that any differences you see in brain activity have to do with free will. That's a very difficult thing to do."

There are technological challenges to overcome, more refined and directed questions to ask about the brain—"Your question, that's a biggie," Phillips says. "It's metaphysical and nebulous"—and there are even seemingly simple matters, such as agreeing on definitions.

"People have different meanings for free will," she says. "How do you measure it?" ■

We seem to have a deep-seated impulse to behave as though we're independent actors.



The Psychologist
An Illusion of Control

Julie Fiez has also delved into what happens, in a hard-wired way, when we try to control outcomes.

Her lab showed volunteers, as part of a group of studies, a series of numbers, asking them to predict if each would be greater or less than five. If the guess was correct, a green arrow would appear, indicating that the subject won money. If incorrect, the subject saw a red arrow, denoting a loss. The volunteers were hooked to neuroimaging machines that revealed the striatum was active when they made these predictions. The striatum is a region of the basal ganglia that's part of the dopamine pathway and involved in circuits associated with volition.

In other situations, where the volunteers were not asked to predict an outcome, the striatum didn't light up.

"This suggests that [the striatum] really is only active when subjects perceive a contingency between their actions and the outcome," says Fiez.

In the first experiment, Fiez reports, there was no way for the subjects to improve the likelihood of winning money: The sequence of the numbers presented to them was random and volunteers were told so beforehand. Yet participants reported after the scan that they had developed a strategy or thought that they had detected a pattern.

They thought they were in control and their brains acted like they had control even though they didn't.

Fiez is a PhD associate professor in the Department of Neuroscience and Department of Psychology at the University of Pittsburgh, a member of the CNBC, and a research scientist in the University's Learning Research and Development Center. Her interests are the neuroscience behind language processing, as well as behind reward and motivation.

Her experiments tell her that we seem to have a deep-seated impulse to behave as though we're independent actors.

"It's surprising that people still seem to be

PATHS TO OBSESSION

The symptoms of obsessive-compulsive disorder are easily observable. The man who washes his hands every time he touches something. The woman who repeatedly goes back to make sure she made the coffee for the next morning. The guy who has stashed away every *Pittsburgh Post-Gazette* he's ever bought. The "why" of such behaviors is much more mysterious.

University of Pittsburgh professor of psychiatry Mary Phillips uses functional magnetic resonance imaging (fMRI) to associate such behavior with specific neural pathways. Her research findings may one day help pharmaceutical companies make targeted drugs or help doctors make more informed decisions on therapy.

Phillips' team showed compulsive hand washers pictures of dirty objects and told them to imagine they'd come in contact with the objects but wouldn't be able to wash afterward. The hand washers exhibited greater activity in areas of the brain associated with processing emotions, specifically disgust, than their control counterparts.

Phillips' lab tied checking—think of someone repeatedly going back to make sure he turned off the oven—with regions of the basal ganglia important for motor and attention functions, particularly the inhibition of unwanted impulses.

Obsessive hoarders were a bit more difficult to figure out. They showed higher than usual activity in the motor cortex and right orbitofrontal cortex, which is involved in decision making. Other experiments show that heightened activity in the right orbitofrontal cortex indicates that such patients may be more responsive to antidepressant medication. —*JM*

going through a decision-making process," she says of the experiments.

"Even if I know the program's going to pick an outcome after I press a key to give me the predetermined reward or punishment," she adds, "the brain nevertheless wants to make a decision.

"There's something very powerful there."

She suggests it shows that there's a strong desire for agency embedded in our brains.

Fiez makes a leap into the theoretical. She thinks that our apparent desire to claim some kind of independent involvement in decision-making factors heavily in learning. We may be able to set a goal for ourselves at a specific moment in time, but whatever we choose as a goal is predicated upon what came before. Yet we think we have agency, control.

"I guess the argument [for this determinist line of thinking] would have to be something like—it's the set of prior experiences that caused you to engage the prefrontal cortex in a way that perceives this to be a goal and perceives you to have contingency upon others.

"You have this illusion of control," Fiez says.

So if that's the case, what accounts for so many of us being sure that we are independent actors hacking our way through the jungle to cut out a life of our own, on our own?

Fiez thinks it could be because so much happens to us over the course of our lives that we're unable to trace what appear to be choices back to the experiences that determined the outcomes.

"I keep emphasizing in my cognitive [psychology] class that every single moment of cognition leaves a trace somehow," she says.

"So when do you ever have a choice?" she asks.

"I don't know. You certainly feel like you have a choice, and you certainly feel like sometimes you do struggle with something.

"If you had a computer simulation that could keep track of every single thing that you experienced, that could somehow get us to that exact point [of decision] and show that every single time this is what the person does, that would prove the illusion of control.

"As a neuroscientist, there's a part of me that sort of thinks you are the sum total of what you started out with and all the experiences you've had.

"But at an individual level, a subjective level, it feels very powerfully like you have a choice, and it would seem kind of ludicrous that you don't."

The Patient
Eroded Freedom

Jim Cordy doesn't have a choice. At least he feels like he doesn't.

Like that day the Squirrel Hill resident was up near Pitt's Petersen Events Center. That afternoon, he spotted Chancellor Mark Nordenberg on the corner by the Pete. Now, Nordenberg's a pretty recognizable person, particularly on the University of Pittsburgh campus, but crowds of people were passing him by, no one stopping to engage him in conversation. Cordy had met Nordenberg a time or two at Pitt basketball games, but the two didn't really know each other, at least not well. Cordy considers himself the shy and retiring type, certainly not a guy who would just walk up to the Chancellor and start talking to him. He had no reason to chat up Nordenberg and no deep-seated desire to meet him again.

"But of all those people crossing the street, only one person had the chutzpah to go up to him and say, 'Hey, Mark, how are you doing?' and it was me."

Cordy says he never would have done something like that before Parkinson's set in.

The disease has changed him. To some degree, he feels that his freedom has been eroded, both by the ailment and the treatment. When he takes levodopa to replace the dopamine drained away by Parkinson's, he acts in ways that seem foreign to him, engages in compulsive behaviors that he finds embarrassing. If he takes too much, he develops dyskinesia—his limbs make wild, flailing movements. If he fails to take the drug, or doesn't take enough, commonplace tasks such as getting out of the car, tucking in his shirt, or putting on his socks are all but impossible, no matter how strongly he desires to do them.

Cordy, 58, was diagnosed with Parkinson's 18 years ago.

"It's progressed continually," he says. "Movement deteriorates. I have a hard time getting out of the tub; I tend to freeze. Fine motor skills are shot. Short-term memory is shot."

Conversation with Cordy is like playing Whack-a-Mole at an arcade. He jumps from topic to topic. What he wants and what he does, or can do, are distant from one another. Though Cordy clearly wishes his circumstances were otherwise, he lacks self-pity.

"Things range from the mildly annoying to the debilitating," Cordy says.

But, he adds, the disease and the treatment—which have rendered him unable to make his limbs do what he wants them to do and make him behave in ways he most assuredly would choose not to—have also allowed him some freedoms: the ability to take chances.

He does so as founder and president emeritus of the Parkinson Chapter of Greater Pittsburgh. In that capacity, he has spoken at Congressional hearings, lobbied for money for Parkinson's research, and promoted the pursuit of stem cell research. And he has done so relentlessly.

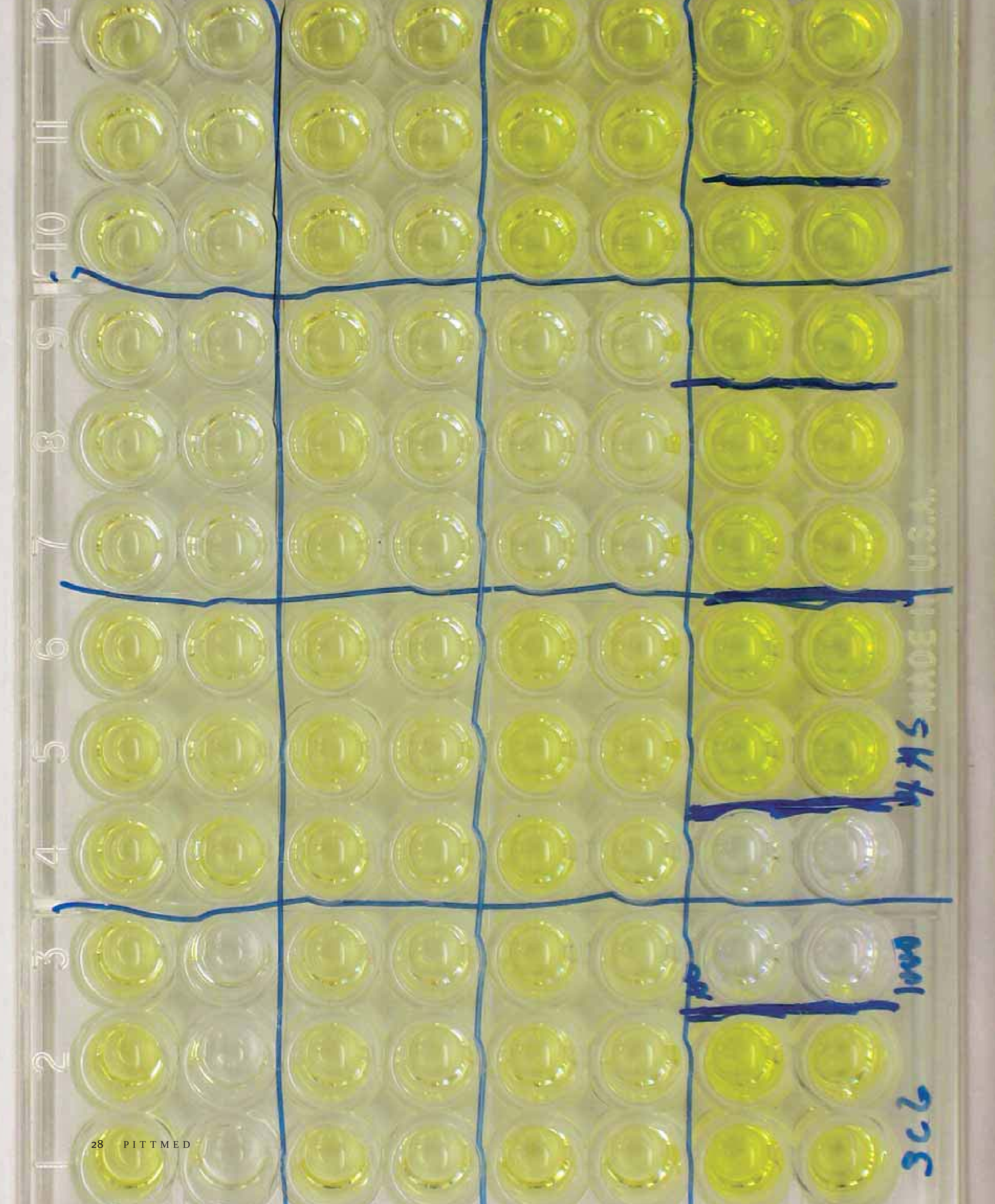
"I wouldn't have done anything like this before. [Levodopa] just makes you more compulsive; you just do things.

"I'm an empowered person with Parkinson's," he says.

The predispositions and decades of pre-Parkinson's experience that guided Cordy's behavior for the first 40 years of his life seem to have been rendered impotent by the disease.

Can this be construed as evidence that will amounts to no more than a function of biology, chemistry, and electrical impulses in the brain? On the other hand, can biology actually free some of us? Cordy says he has no idea.

What he does know is that he'd dearly like to be as he was.



CAN OUR OWN IMMUNE RESPONSES TAKE ON CANCER? | BY ELAINE VITONE

RIGHT UNDER OUR NODES

He could not eat. Two months earlier they'd pruned an orange-size tumor from his neck, but again the cancer was thriving, all but choking him as it spread, taking root in his tonsils and hanging grape-shaped growths below his left ear. In his tenement bed on the Lower East Side, Mr. Zola lay waiting to make medical history, though history would not remember this poor Italian immigrant's full name.

It was October 1891, "The Golden Age of Quackeries," when cancer therapy employed such barbarisms as mercury, quicklime, and electrocution. As Zola lay dying, a young doctor named William Coley visited his home to conduct an experiment so dangerous that New York Hospital would not allow it on its campus—injection of a killer bacterium known today as *Streptococcus pyogenes* directly into the tumors in Zola's neck. He'd been trying to infect Zola for months to no avail, but this time, within hours, chills, vomiting, and fever roared through Zola, and his skin turned bright red. For a man in Zola's condition—or anyone in this prepenicillin era—this could have been a life-ending act.

Olivera Finn is convinced the immune system is our best cancer watchdog. Case in point: The bottoms of the wells on this plate are coated with tumor antigen and filled with serum from cancer patients. The brighter the yellow, the higher the concentration of antitumor antibody in the serum. This tells Finn that the immune system is trying to control tumor growth.

PHOTO COURTESY FINN LAB

But Olivera Finn, chair of the University of Pittsburgh Department of Immunology, thinks of Coley as a hero.

Coley was attempting to duplicate the success of a single, fluke case he'd read of in the hospital's medical records. A cancer patient had suffered a violent *Streptococcus pyogenes* infection—St. Anthony's fire, as it was commonly called—and once it subsided, he went into remission.

It was a shot in the dark, but it worked. Zola survived, barely. His tumors shrank, his airway cleared, and as long as he continued taking Coley's treatments, his cancer ceased to spread. Zola lived another eight and a half years before cancer finally won. Coley had abetted an elusive phenomenon of the body known as immunosurveillance.

To grasp the concept, you must first entertain a thought even scarier than 19th-century medicine: Cancer's predecessors may be far more prevalent than you imagine. As you read this, the smallest seeds of cancer may be hiding in people all around you, or even struggling to make a vineyard out of your throat. But Finn says that if you're healthy—especially if your immune system is in top shape—you're likely to render your tumors harmless, or even kill them before they have the chance to form. Immunosurveillance is an unheralded success of the body that probably happens more often than you'd ever want to know.

Finn is the immune system's biggest fan, and when she's excited about something, it shows. While a student at Stanford University, she shared a lab bench with the late Shraga Segal, who was a postdoctoral fellow at the time and later became a leading cancer immunobiologist. Finn would rush home to nurse her son while waiting for results of experiments. Before she left the lab, she would make Segal promise not to check the results until she returned.

"I wanted to see it together," says Finn. "I didn't want to be the second. It's like when a child starts walking."

Finn recalls that when she and Segal worked together in the '70s, and immunology was a newly developing field, he believed that every experiment held the promise of teaching them something important. Segal couldn't imagine doing anything other than immunology, and Finn feels the same way now.

"Whatever I love, I advocate," she says, and advocate she does, as a member of the Immunology Task Force for the American Association of Cancer Research; council member of the International Union of Immunology Societies; president-elect of the American Association of Immunologists; and senior editor for immunology for the world's premier cancer-research journal, *Cancer Research*.

Finn hopes that once the rest of the world catches on, maybe it will become commonplace to see immune response as she does—not only as a system that engages in the well-known role of warding off invaders, but also as a promising means of both detecting and defeating cancer.

Even the immune system's biggest fan knows that the system isn't perfect. Finn says that all too often, cancer can win for a number of reasons. For one, the immune system may be hindered by genetic predisposition, environment, immunosuppressive drugs, or age. For another, genetic mutation in either the patient or the cancer can cause the immune system to respond in ways that may only control the cancer temporarily. And sometimes, the immune system mounts a less-than-ideal response that ultimately gives cancer the upper hand.

Robert Schreiber, a professor of pathology and immunology at Washington University in St. Louis, explains that in its fight to eliminate tumors, the immune system alters the type and amount of antigens cancer uses to attack the body. Schreiber has recoined immunosurveillance "immunoediting," finding the moniker better suited for the "seesaw" relationship between the immune system and tumors.

Although it's true that immune response is a mixed bag, laboratory evidence (including Schreiber's) shows that healthy mice grow tumors, but immunocompromised mice grow bertumors. We're better off with a fl awed champion than no champion at all, Finn would say.

Finn points out that to date, only one laboratory test has been recommended by the American Cancer Society—PSA, which measures increased levels of prostate-specific antigen.

Unfortunately, benign functions of the prostate can cause spikes in PSA levels as well. The result: overdiagnosis and unnecessary biopsies. Finn calls PSA "antique."

Yet, although we still use poisons and knives to try to defeat cancer, we've come a long way since the Golden Age of Qackery. Today researchers are developing early detection methods using advanced molecular technologies. Bill Bigbee directs the University of Pittsburgh Cancer Institute's (UPCI) Clinical Proteomics Facility. He says we're in the midst of an "omics revolution" in cancer research initiated by the Human Genome Project. Researchers continue to develop new "omics" approaches; they started with genomics, which gives an analysis of cancer-cell genes and their expressions. Then came proteomics, peptidomics, metabolomics—"and the omics keep coming," he says, including—you guessed it—immunomics.

However, Finn wrote in a *New England Journal of Medicine* (*NEJM*) editorial last September, these applications "are not being developed fast enough."

Investigators are using proteomics to try to find useful cancer biomarkers. But generally, by the time the tumors are substantial enough to produce cancer-specific proteins that these tests can detect, doctors can tell the patients are sick just by looking at them, Finn says. The challenge is detecting cancer early enough to be able to do something about it.

Bigbee notes that a number of candidate biomarkers—products of genomics and proteomics studies now in the evaluation and validation pipeline—appear to be sensitive in early stage patients.

He says that a couple of years ago, he would've agreed with Finn's skepticism of things "omic," but considering the rapid pace at which the technologies are emerging, he's now thinking we should cast as wide a net as possible. Yes, it's costly; and yes, it's technically and intellectually challenging.

"But that's what we're about," he says. "That's modern science."

But perhaps it doesn't have to be that way, Finn suggests. She believes we've lost sight of the fact that cancer doesn't happen in a vacuum, but within the complexities of a living host. We have everything to gain from studying the battle between tumor cells and our own bodies, Finn says. As the immune system encounters the earliest inklings of cancer, it releases antibodies—air raid warnings. Perhaps the world's most effective cancer detection method has always been right under our nodes.

Last year, Finn and John McKlanis, a research associate in the Department of Immunology, collaborated with Harvard University researchers. The group compared ovarian-cancer patients to a control group. They looked for evidence of immune response to MUC1, an antigen associated with ovarian tumors as well as lactation, pregnancy, oral-contraceptive use, and pelvic surgery, among other events. The researchers found that the

COURTESY CANCER RESEARCH INSTITUTE

William Coley (top) used a deadly bacterium to kill an advanced cancer in Mr. Zola (bottom).

more MUC1-antibody-producing events these women experienced early in life, the lower their risk for ovarian cancer. The immune system responds to new threats more effectively in youth. If a woman generates anti-MUC1 antibodies for the first time at a later stage in life, it could mean cancer is on the way.

A team at the Scripps Research Institute in La Jolla, Calif., pursued a study examining seven tumor-associated antigens. The antibodies worked as biomarkers in 92 percent of the patients and even specified the types of cancer in 91 percent. The study supports Finn's credo, which she wrote in her *NEJM* editorial: "There is no detection instrument that rivals the sensitivity and specificity of the immune system." She's eager to see the Scripps researchers draw more attention to their study—typical Finn zeal. Schreiber credits her as "one of the true public voices" of the field.

"[A] public voice or a loudmouth?" Finn jokes. She admits she can't help goading people. "I get them all busy."

More than an ideal biomarker, immune response is a bio make-or-breaker—a key player in the battle for your life. Finn says, "You can either let it do what it does, or you can make it do it better"—meaning you can take a lesson from Coley's experiment.

This may sound foolhardy. After all, Coley nearly killed Zola and, in fact, did kill two of his first 12 test patients with his live-bacteria injections. However, Coley subsequently tempered his methods, opting for a mixture of innocuous bacteria instead, and in at least one case, it worked.

As a deathly ill German immigrant with an eggplant-sized tumor on his abdomen fought off a Coley-induced infection, he shrunk his tumor by 80 percent in less than three months. He lived another 26 years before dying of a heart attack.

Unfortunately, no one could duplicate the results of that singular case. Coley was dismissed as just another quack.

Finn and Chandra Belani, professor of medicine and codirector of the Lung and Thoracic Malignancies Program at UPCI, hope to harness the mechanisms behind Coley's infrequent successes, boosting and/or initiating immunosurveillance.

They've secured funding for clinical trials of a lung-cancer prevention vaccine as part of the Specialized Program of Research Excellence in Lung Cancer. The vaccine is designed to prevent recurrence by boosting immune response to cyclin B1, a lung-cancer antigen Finn has been investigating for years.

Preliminary data from the study indicate early-stage lung-cancer patients with anti-cyclin-B1 antibodies are able to fight off recurrence longer than other patients. Out of seven antibody-producing patients studied, only one developed cancer again in the first 22 months after surgery; of the nine antibody-negative counterparts studied, six experienced a recurrence.

Finn also would like to pursue clinical trials of a vaccine designed to boost immune responses to chronic pancreatitis (linked epidemiologically to pancreatic cancer) and advanced autonomous polyps (precursors to colon cancer). Such trials would be the first to test a cancer vaccine on nonvirally caused cancers.

If this amazing, diagnosing, remission-prolonging, and even curative device—the immune system—is as close as our own lymph nodes, why does it get so little attention?

"I think that a lot of people like gadgets," Finn says with a laugh. "I think gadgets win over ideas every time." She adds that bias has a lot to do with it as well.

Critics used to say that because cancer is born within the body, the immune system cannot react to it. It's clear that the immune system reacts to cancer, says Finn. Now critics contend that the immune system is no match for it.

Not enough was known about the immune system to test the immunosurveillance hypothesis effectively when it was first proposed in 1957. In the next several years, researchers tested control mice against immunocompromised mice, but unbeknownst to them, the latter turned out to be immunocompetent after all, so both groups developed cancer at the same rate. Animal studies have since made a strong case for immunosurveillance, but skepticism remains.

A group at Rockefeller University is studying the first documented cases of successful human immunosurveillance. The reason these cases were noticed at all is unfortunate. The patients' immune responses caused rare autoimmune diseases known as PNDs—paraneoplastic neurologic syndromes. Doctors detected breast, ovarian, and small-cell lung tumors in the patients during PND diagnosis—tumors that were kept in check without anyone's notice until neurological problems compelled the patients to visit a hospital. Some patients had no sign of cancer whatsoever—they did, however, present antitumor antibodies, signs of battles won.

Some might consider this story a cautionary tale, a reason to rule out cancer immunotherapy as too dangerous. When the subject comes up, Finn acknowledges that immunotherapists must be selective in choosing their targets. In the same breath she says the Rockefeller group's findings are good news—proof that immunosurveillance exists.

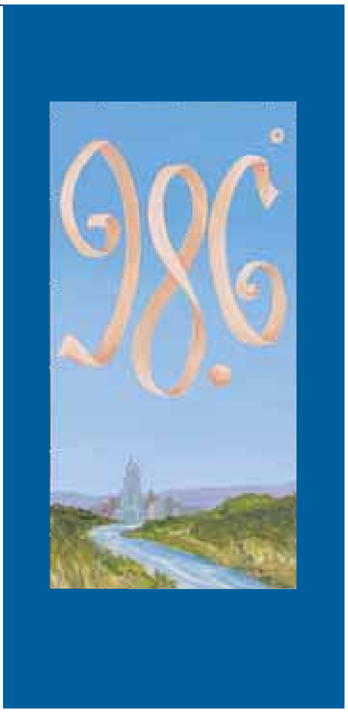
Finn is not interested in talking about the legitimacy hurdles her field has scaled since Coley's day. She's focused on the future: one-stop shopping for diagnosis and treatment at a fraction of the time, expense, and inconvenience. As an alternative to colonoscopies, perhaps one day doctors will detect the smallest germs of cancer in blood samples, then immediately administer vaccines. And if cancer is detected in malignant stages, once the tumors are removed, perhaps doctors will prevent recurrence by boosting antibody levels as needed.

She thinks big.

In underdeveloped countries where widespread papilloma-virus infection causes cervical-cancer epidemics, it will be much easier for health workers to collect drops of blood from women than do pap smears. Then, they'll be able to zero in on women with the highest risk, manage their antibody levels with a vaccine, and save lives. Someday.

In the meantime, there's work to do. Finn sifts through manuscripts, rushes from one conference to another—advocating, goading. "All for the cause," she says. ■

People and programs that keep the school healthy and vibrant



"PLEASE BE NICE"

INDEBTED STUDENTS CALLING

BY JEN DIONISIO

Sarah Carter nervously twirls the telephone cord in her fingers as she waits for an answer on the other end of the line.

"Please be nice," she asks out loud, perhaps thinking back to a physician she called earlier. He was irate at being interrupted in the middle of the November afternoon during a Steelers game. This time, when Carter gets the person she's waiting for on the line, her voice rises an octave as she nervously begins: "My name is Sarah. I'm a medical student at the University of Pittsburgh. …"

Carter is one of nearly 100 Pitt med students volunteering for the med school's first student phonathon. For five days, they've shuffled through a 3-foot-tall stack of alumni names and numbers, raising funds for Medical Alumni Association (MAA) scholarship programs. The Alumni Relations Office for the Schools of the Health Sciences and the MAA organized the event, believing that these students would put a sympathetic face (bright, promising, perhaps in debt) on an issue that has grown more important since most Pitt med grads left campus.

The cost of attending medical school has risen dramatically around the country, and about 85 percent of graduates are in debt. The average indebted graduate enters a residency program owing $120,000. The average is more like $138,000 for those graduating from private schools. Pitt med graduates are likely to end up with debt loads similar to those of graduates from comparable top tier private schools, because the Commonwealth of Pennsylvania's support for medical education is exceptionally low, notes Arthur Levine, dean and senior vice chancellor, health sciences.

Deferring payments until after residency can significantly raise a graduate's total debt load. (A 10-year repayment schedule, at projected interest rates, can mean paying $226,000 for a $120,000 loan.)

So can paying out-of-state tuition, as another phonathon participant, Dan Brown (Class of '06), is learning. Brown is from New York. He gets by with a mix of subsidized and unsubsidized Stafford loans. But, leaning back in his chair at an Oakland coffee shop after the phonathon, he points out that the loans don't cover all his costs, as is the case for most borrowing students. Fortunately, the MAA granted him a low-interest loan in his first year, which spared him the high-interest private loans and credit card debt that are last-resort options for some students. It also motivated him to participate in the phonathon to help other students.

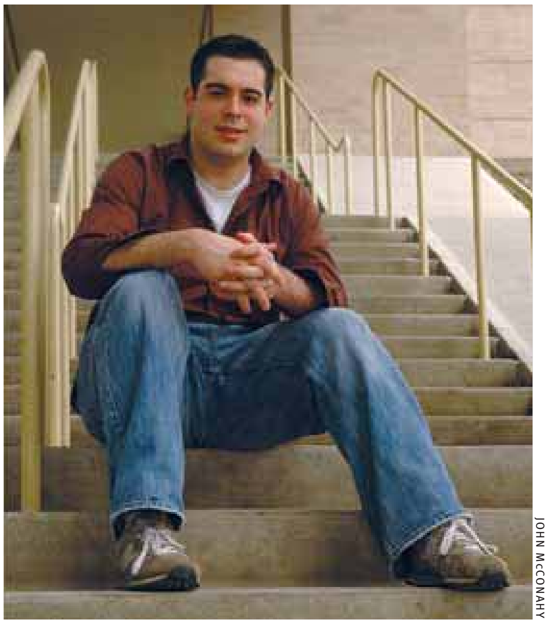
In addition to loans, the MAA offers a limited number of tuition scholarships and supports students who want to perform service-learning projects over the summer. In 2005, five Pitt med students received summer stipends to care for patients in the developing world—four in Africa and one in South America. The stipends ranged from $1,000 to $2,000—enough to encourage students to do something important with their summer break without going further into debt. This summer, the MAA will offer $20,000 in stipends.

How did medical schools get so expensive? Levine notes that the costs associated with running a med school—like staff salaries and just keeping the lights on—are driving tuition up everywhere. To help combat the problem, in the past couple of years, he has more than doubled his office's commitment to full-tuition, merit and need-based student scholarships to $6 million during the current year. Scholarships require no payback.

Levine's goal is to provide full tuition scholarships to 20 or 25 percent of each class, but meeting this goal will depend heavily on philanthropy.

"Pitt's stepping up the effort to give out more scholarship money," Brown says. "It really benefited me a lot."

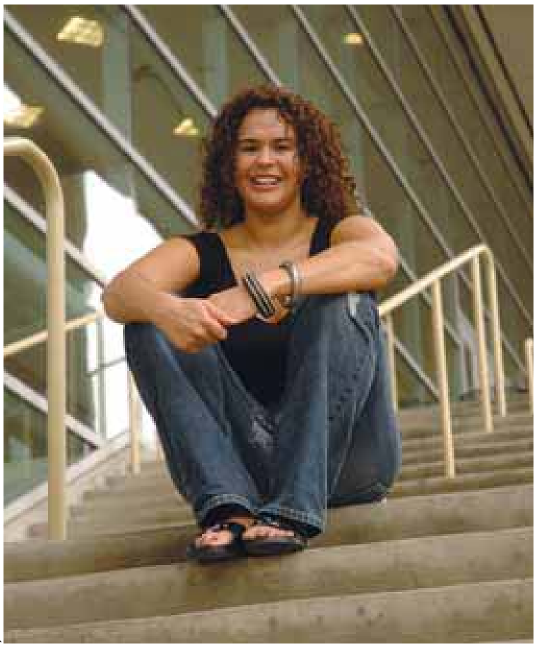
As he graduates in May, Brown's first loan payments are creeping closer but he has no regrets about his choice to enter the medical profession. Yet he notes, "If I went to business school or finance school, I could be making a lot of money right now."



JOHN McCONAHY

A low-interest loan from the Medical Alumni Association helped Brown.

Kristin Cochran (Class of '07) received some unexpected support this year from the MAA—a $10,000 scholarship awarded out of the blue, based on her financial need and academic performance in her first two years. The scholarship was especially welcome because it came shortly after her father's death. Cochran


JOHN McCONAHY

Carter, one of nearly 100 med students who volunteered to raise scholarship funds.

says the scholarship allowed her to give loan money back to her lending institutions this year. (Students are often advised to borrow as little money as possible.) To save money for med school, she worked at a boarding school before coming to Pitt.

"I think a lot of us students are in denial," Cochran says. "Payment feels so far off." She adds that she and her classmates get a dose of reality when their professors announce that they have finally finished paying off their loans.

Cochran plans to pursue emergency medicine at an academic medical center, though she realizes that path may make it difficult to pay off her loans in a timely manner. It's the sort of dilemma shared by medical students around the country. Studies show that students at the highest levels of debt may choose specialties based on financial concerns. Jeannette South-Paul (MD '79), chair of the Department of Family Medicine, is concerned about the implications of students basing important career choices on money worries. South-Paul's field, family medicine, pays among the lowest to new doctors. Many communities are feeling the effects of those economics, says South-Paul.

"The healthcare status of our community is not dependent on the number of ICU beds you have in a community. It's not dependant on the number of x-ray units you have in the community. It's dependent on your [access] to a primary care physician," South-Paul explains.

Access becomes a major issue in traditionally underserved rural and urban areas. Patients end up avoiding care until they can no longer function.

Brown, who will soon embark on a career in internal medicine, and others at Pitt are looking out for future patients and medical students by working on long-term solutions as members of the American Medical Association (AMA) Task Force on Student Debt. The cochair of the AMA's task force, Pitt MD/PhD student Alik Widge, says, "It makes your head hurt just thinking [about] what has to be done."

Widge braves the headaches long enough to describe a future medical school system that is self-sustaining. He suggests, for example, the federal government could pay for medical school in exchange for a few years of service where physicians are most needed. Pitt's Carl Sirio, associate professor of critical care medicine, is working on the AMA's Initiative to Transform Medical Education, proposing a top-to-bottom refurbishing of the entire system, an effort last attempted in the early 1900s.

In the meantime, short-term solutions prove more complicated than they sound. Brown suggests more deferrable subsidized Stafford loans—a tough sell in lean budget years. The question remains as to where the money will come from for such programs. From the likes of Dan Brown's pockets? There's not much in those pockets today. He thinks hard about when the next check will come before buying a beverage at the coffee shop.

The task force's suggestion that schools raise money to help students seems the most promising option at this point. Brown says the MAA phonathon, for example, was a success, especially considering that students were calling some alumni who had never donated to the University. The students raised $55,000 in pledges in one week.

For the time being, Brown has started a part-time job teaching science, which he plans to keep until he starts his residency. But someday he may find himself on the opposite end of a phonathon—the side that pledges to cut a check that will ease the plight of a worried med student. When that day comes, a debt-free Brown can laugh that he briefly worried he'd celebrate his graduation by saying, "Good evening, I'm Dr. Brown, and I'll be your waiter this evening." ■

BOOSTER SHOTS

Charles Hefflin (MD '74) was medical director for the only Black nursing home in the Pittsburgh area and mentored med students from many backgrounds. He died in November 2004, and a scholarship fund for disadvantaged students has been named for him. His son, Brockton Hefflin (MD '90), envisions the scholarship going to a needy student who, aside from having an outstanding academic record, furthers the community and causes his father championed.

Of the 10 leading causes of death in the developing world, five are communicable diseases—HIV/AIDS, infectious diarrhea, malaria, tuberculosis, and measles. In developed countries, only tuberculosis makes the top 10.

A vaccine research and discovery lab in Biomedical Science Tower 3 has been named for **Richard Raizman**, who with his wife, **Dorothy Raizman**, made the largest gift yet for the new building. The lab will help develop cost-effective prevention methods for infections that affect many of the world's peoples. Raizman (MD '71), who has volunteered in clinics and hospitals on several trips to Northern India, says, "When you spend time in third world countries, you realize that your clinical efforts, no matter how intense, will fade once you leave. Whereas prevention can have global effects." —*Sydney Bergman*

FOR INFORMATION ON GIVING: 412-647-9071 or LMICHAEL@PMHSF.ORG

NOBODY COMES HOME THE SAME

TREATING THE COMBAT VETERAN

BY CHUCK STARESINIC

The day before West Virginia's archery deer season opened, Keith Thompson packed his bag to head for the family hunting camp. The next day, he would wake up surrounded by a few hundred acres of autumn forest. Nothing could be sweeter. A year earlier, he'd been in Iraq with his fellow marines, and missing hunting season was worse than missing Christmas.

When his bag was packed, he couldn't find his hunting license. He swept everything off the top of the dresser. He tore through the drawers and threw all the clothes on the floor. Then he ripped every room apart. He spooked his dog so badly that it tried to hide under a car out back. In the kitchen, he picked up a stool by its legs—he was screaming and cursing now. He swung it over his head and slammed it hard on the floor. Again. Again. Again. He left it in too many pieces to count. Then he wondered what he was doing.

Welcome home, soldier.

After more than three years of war in Iraq, there are now many thousands of American combat veterans who have witnessed, suffered, and inflicted more violence than the typical American will see in a lifetime. They have lived on edge for months at a time. Many have escaped death by inches and by chance; others have been maimed and crippled by the same margins. They have killed. They are not always certain that they killed the correct people. Some have tried to save the lives of their friends and failed. Thompson (not his real name) watched a fellow marine walk away on patrol one night. Minutes later, he came back in an ambulance, burnt black, minus an arm and a leg. He died the next day. Later on that same tour, Thompson suffered permanent damage to his leg from a roadside bomb. His leg was treated immediately, of course, and he continued with physical therapy when he returned home. But it was many months before he sought help for his psychological symptoms.

Soldiers are taught that they are invincible, so it's not unusual for them to avoid asking for help. At the end of the Vietnam War, post-traumatic stress disorder (PTSD) had yet to enter the psychiatrist's diagnostic manual; it did not become an official diagnosis until 1980, when Vietnam veterans had been home for at least five years, and some longer than 15 years. Many with PTSD didn't get help until they had ruined a few marriages, lost a dozen jobs, developed addictions to hide the pain, or wound up homeless. Many committed suicide. Many never got help.

This time, the Veterans Administration (VA) is more prepared, and soldiers in this area are getting help early from Pitt-trained psychiatrists.

"I think the military is doing a better job of screening early on," says Jeffrey Peters (Res '84, Fel '86), a Pitt associate professor of psychiatry and vice president for behavioral health with the VA Pittsburgh Healthcare System. Peters sees dozens of combat veterans who have served in Iraq and Afghanistan at the VA's PTSD clinic. So does Barry Fisher (Res '90), the medical director of the clinic. Some veterans attend individual therapy sessions and take medication to control anger and depression. Many attend group therapy sessions. Peters estimates that of approximately 2,000 veterans who have returned to the region, 600 have been seen at the VA's primary care clinic, and half of those for behavioral health. Because behavioral health is part of the primary care clinic, he says, they've had success getting veterans to take the critical first step: asking to talk to someone about emotional issues.

"They get a red haze, some of them, because in combat, there is only one emotion that seems to help these guys. It's anger."

Not long after he tore up his apartment looking for his hunting license, Thompson took that step at a physical therapy session. He'd been arguing with his girlfriend regularly and simply wasn't himself, he says: "It was summertime, and I didn't want to go out. I didn't want to do anything. After months of thinking it would just get better, I said, 'I can't take this anymore. I've got to talk to someone.'"

"Guys talk about literally seeing red," says Joseph Fetchko (MD '93), Thompson's psychiatrist, who has worked in the PTSD clinic for eight years. "They get a red haze, some of them, because in combat, there is only one emotion that seems to help these guys. It's anger. Sorrow is discouraged, and the fear is channeled into anger."

Thompson began to feel better driving home after the first therapy session, he says. He began to believe that therapy could help him have a more normal life again. Maybe he'd be able to stop flying off the handle over little things and stop checking for snipers everywhere he went. Maybe he'd be able to hear a few firecrackers go off without freaking out.

At a recent session, Fetchko asks how he's doing.

"I've definitely got my stride back," he says. "I want to go out. Don't want to stay home. I'm still on alert, but it's mild. I'm not getting pissed all the time—I haven't gotten mad for a while."

The other day, his dog ripped his slippers apart, he says with a smile. He got mad, but not like he would have before.

Thompson's unit may soon be sent back to Iraq for a third tour. The desire to never be separated from your fellow marines is powerful, and when Thompson begins to talk—hesitantly—about going with them on limited duty, Fetchko jumps in, saying: "I've treated hundreds of vets. I can count on one hand the guys who've done two tours. You've done two tours. We're indebted to you. …

"I would recommend at this point that your job is to take care of your health and to move on with your life."

Thompson knows his doctor is right. He has heard it before. And he has accepted the fact that he'll get a medical discharge soon. Still, he can't help but think about being with his buddies when they deploy.

"This is the time to really work on your health and your future," says Fetchko.

Thompson quietly nods at Fetchko, considering the mission ahead of him. ■

GETTY IMAGES

CLASS NOTES

’50s **Edwin Azen** (MD ’55) has been on the medical faculty at the University of Wisconsin, Madison, for quite some time, but he has been a lifelong student. At Pitt, Frank Dixon, the longtime chair of pathology, stimulated Azen’s desire to uncover secrets in the lab during summer research. Azen followed that interest to an internal medicine residency and a hematology fellowship at Wisconsin. He cared for patients with blood abnormalities for many years. But in the early 1980s, he took a sabbatical to work in the lab of renowned geneticist Oliver Smithies and learn as much as he could about molecular genetics. Azen turned that midcareer switch into a slew of important publications on the genetics of salivary proteins, not to mention a 10-year National Institutes of Health MERIT award, which he received in 1991. In 2001, he became a professor emeritus of medicine and medical genetics at Wisconsin.

’60s Medical school in the 1960s had a more formal atmosphere than it does today. So at the end of a lecture, **Donald Nevins** (MD ’67) didn’t expect his classmates to applaud suddenly and effusively. But the speaker was Arthur Mirsky, Pitt professor of psychiatry and renowned expert in psychosomatic illness, and that’s what they did. “This had never happened before or after,” Nevins says, and that spontaneous response to a teacher, along with the example his professors provided as compassionate clinicians, has stuck with him. Nevins is now a clinical professor of psychiatry at the University of California, San Francisco. He was recently elected a fellow of the American College of Psychoanalysts.

’70s When **Charles Whitaker III** (MD ’70) was president of the Parkersburg Academy of Medicine in 2003, malpractice tort reform was a big issue in West Virginia. Premiums were so high that doctors were leaving the state. For Whitaker, who won his state’s American Academy of Pediatrics Pediatrician of the Year Award in 2004, it wasn’t a pocketbook issue; it was a patient care issue. So he lobbied. He took a busload of medical professionals to Charleston. With physicians from all over the state, he spoke out, wrote letters, met with representatives. The reforms passed, and premiums are inching back down.

Most med students interviewing for residencies don’t get much time with the chair of the department. But **Barry Hirsch** (Otolaryngology Resident ’79) remembers walking around campus with Eugene Myers, then head of the Department of Otolaryngology. Over coffee at a ’60s-style counter, Myers related his ideas and vision for the department he would lead for years to come. The experience sold Hirsch on Myers and Pitt, where, apart from a brief stint at Georgetown University and a fellowship in Zurich, he has remained ever since. As an associate professor of otolaryngology, he specializes in neurotology, the neurological study of the ear. Despite the seemingly relaxed interview, Hirsch fondly remembers it as a formal cup of coffee: “We held our pinkies up,” he says.

John Sassano was between patients and pressed for time when an unexpected call came from Pittsburgh—a *Pitt Med* writer asking him to reminisce about working with Tom Starzl. Sassano (Anesthesiology Resident ’80) grew quiet and contemplative. “I just get speechless when I think about the days that I worked with him. I miss them. They were

A FAMILY AFFAIR

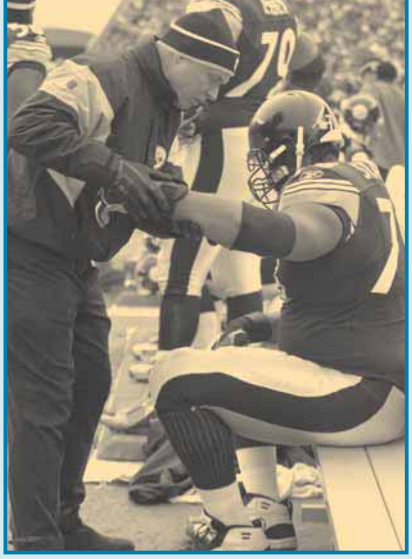
TAKE TWO BERGS AND CALL US IN THE MORNING

Debra Berg’s (MD ’85) Thanksgiving dinner is not for the faint of heart. Hers is a family of 17 doctors, 13 of whom graduated from the University of Pittsburgh School of Medicine. Not surprisingly, medicine is a popular topic of conversation. Napkin on the lap, fork perched over the turkey, a guest is likely to be a captive audience for Berg’s father, George Berg (MD ’55). The urologist has been known to offer riveting (and digestively challenging) descriptions of the kidneys he sees in surgery, from the simply diseased to those that have declined into a “decayed mess.”

Berg’s School of Medicine pedigree starts with her maternal grandfather, Albert Berkowitz (MD ’24), and his brother-in-law Isadore Lichter (MD ’28).

She recalls that her grandfather, who played piano for silent film screenings to pay his way through med school, was “an idol” to his sons (who truncated the family name), Myles Berk (MD ’53) and Robert Berk (MD ’55, winner of Pitt’s 1986 Hench Award). Berkowitz, who practiced on the Northside, sometimes operated on a barter system with his patients, accepting chickens or vegetables as payment.

Debra Berg’s father, George Berg (MD ’55), married into the Berk family after meeting the Berk brothers while in med school. Robert Berk introduced George Berg to his sister, Betty, Berg’s future wife. Two of their children would go on to graduate from



James Bradley is head physician for the Steelers.

phenomenal," he said. (Read the full story starting on p. 12.) The discussion brought back memories of another Pitt giant, Peter Safar. Sassano, now the medical director of North Florida Pain Specialists, trained under Safar. "Peter and Tom were not afraid to be great because they were not afraid to be wrong."

'80s

Twenty years ago, there was only a four-hour window from the time a cornea became available to perform a corneal transplant. **Jean Harwick** (Ophthalmology Fellow '84–'85) would scrub in at midnight or later. Now an ophthalmologist at West Penn Hospital in Pittsburgh, Harwick dabbles in another of her passions, art history. She felt some professional pride seeing Monet's water lily series at a Paris exhibition. Monet went from bright greens to muddier browns as he developed cataracts; the work became clear and colorful again after his removal surgery.

Most people would choose Hawaii over Detroit. **James Bradley** (Orthopaedic Resident '87) preferred the latter. Bradley is head physician for the Pittsburgh Steelers—in case you didn't hear, that team earned a trip to Detroit for Super Bowl XL by winning the AFC Championship Game. (The physician for the losing team got the consolation prize of working the Pro Bowl in Honolulu.) Outside his Steelers duties, Bradley is a Pitt clinical associate professor of orthopaedics, conducting research on the success rate of arthroscopic surgery for instability in athletes' shoulders. Quarterbacks and baseball pitchers alike sustain repetitive small traumas to their shoulders, which can stretch ligaments. Bradley is working to find less invasive surgical options, helping injured athletes return to their sports quickly.

'90s

A mother rushes through the doors of an urgent care clinic in California, carrying her child. The girl is wheezing—she can't speak, and the mother speaks only Spanish. **Lisa Roberts** (MD '98) and a team of nurses deliver oxygen, albuterol, and epinephrine to open the girl's airway and calm the angry red hives on her skin. The mother reveals her daughter is allergic to penicillin and had been prescribed amoxicillin. Roberts, who majored in Spanish at the University of Virginia, explains how to inform her doctor of the allergies. After the mother and child leave, Roberts won't ever see them again. She worked in urgent care clinics for a year after her Stanford residency but left the West Coast seeking greater continuity of care with her patients. She has found it in northeastern Atlanta, as a general pediatrician.

'00s

A newborn's trachea is only 7 millimeters in diameter; even the smallest obstruction can compromise her ability to breathe. If, in her airway, she develops a hemangioma—a nonmalignant tumor that often grows for the first year of life, then shrinks on its own—doctors have traditionally installed a tube in a hole in the windpipe and neck and waited it out. But having the tube in place can come with its own complications, including infection. So **David Mandell** (Pediatric Otolaryngology Fellow '03) began performing open excisions of these hemangiomas—a first at Children's Hospital of Pittsburgh. While all have been successful, he doubts that this treatment will become standard; babies are kept asleep in the ICU for a week afterwards. Mandell, a Pitt assistant professor of otolaryngology, credits excellent anesthesiologists and postoperative care for making the treatment feasible at Children's.

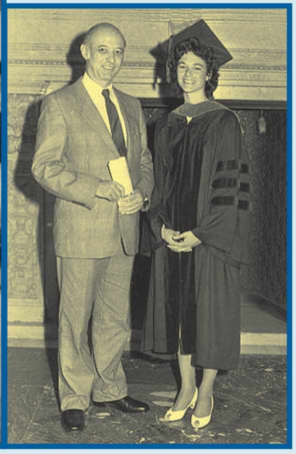
The 6.6-magnitude earthquake may have struck in December 2003, but its devastating effects are still felt in Kerman, a region in southeastern Iran. **Ali Sajjadian** (Plastic and Reconstructive Surgery Fellow '03) returns regularly to his native country to perform reconstructive surgery on those injured in the quake, as well as on people with congenital malformations. He also helps doctors there through lectures, donated books, and videotapes. In addition to these projects, Sajjadian, an assistant professor of plastic surgery at Pitt, codirects UPMC's aesthetic plastic surgery center, where he specializes in rhinoplasty.

—Sydney Bergman and Chuck Staresinic

Pitt's School of Medicine: Berg and her brother James (MD '86). Other familial Pitt grads include cousins David Benjamin (MD '74), David Berk (MD '78), Larry Berk (MD '88), William Lichter (MD '42), David Solomon (MD '58), and Ronald Wasserman (MD '69).

A warning to potential Thanksgiving guests: A thorough discussion of bird flu is sure to come up at this year's dinner.

Debra Berg serves as medical director of the Bioterrorism Hospital Preparedness Program for the New York City Department of Health and Mental Hygiene. She plans and coordinates the city's emergency response to major public health threats. With her colleagues, she's preparing for a potential pandemic influenza. Last fall her program sponsored a citywide tabletop exercise with nearly 300 participants to build a strategy for identifying, quarantining, and treating infected patients in the event of an outbreak. *—Jaclyn Madden*



COURTESY D. BERG

Debra Berg's (MD '85) family legacy of 13 Pitt med grads dates back to Albert Berkowitz (MD '24)—shown top left with his wife, Nellie Berkowitz, and to the immediate left in his med school class photo (highlighted in yellow). Berg's dad, George Berg (MD '55), was all smiles at her graduation (above).

THE WAY WE ARE
AT THE WINTER ACADEMY

The first Winter Academy, held in Naples, Fla., brought together 175 alumni and friends.

For a couple of days in February, it was as though the University of Pittsburgh had established a satellite campus in a place where folks never have to scrape ice from their windshields or shovel the walk. **Jack Tomley**, who was on the host committee for Pitt's first Winter Academy in Naples, Fla., says Pitt grads came from as far away as northern Florida and points farther up the East Coast to attend the program. (Tomley has a seasonal residence nearby.) The weekend-long event was open to all Pitt graduates and friends (175 of whom attended). It featured presentations by some of Pitt's most accomplished scientists from the schools of the health sciences.

Tomley (MD '55), whose own class is famously cohesive, got a lot out of mingling with other health sciences grads. The location of the Academy wasn't bad either. (It may be home, but Pittsburgh in February can't compete with the outstanding climate and atmosphere of the Gulf Coast, he points out.) Tomley calls himself "90 percent retired." The thing he misses most about running his own pediatric practice? His patients. With the infants and toddlers, he learned to take his time and put them at ease, using the stethoscope on himself and the parent before touching the child. He'd gladly do an entire exam with the child never leaving her mother's arms. For the older kids, he performed magic tricks, often pulling coins out of their ears (no otoscope required).

Loren Rosenbach (MD '54) was a practicing hematologist and a clinical assistant professor in the medical school for years, but the presentations by Pitt researchers at Winter Academy gave him a new appreciation for what goes on in the School of Medicine. (Among other highlights, Fadi Lakkis, professor of surgery and immunology and scientific director of the Starzl Transplantation Institute, described the future of organ transplantation.) His wife, Barbara Rosenbach, a retired UPMC lab technologist, was so intrigued by the groundbreaking Alzheimer's research of Chester Mathis and William Klunk (both Pitt School of Medicine faculty) that she spoke with them after their talk and was inspired to volunteer for one of their studies.

Walter Telesz (MD '65) says that he would love to see his future class reunions acheive the attendance he saw at the Winter Academy. The general surgeon, who started his own practice from scratch in 1970 near Canton, Ohio, recently retired. He probably would have stuck around his practice longer but for two things: He wasn't too eager to cover emergency calls at his age, and "You can't work part-time and cover $100,000 malpractice insurance payments," he says, lamenting.

Telesz's classmates have a few years to organize themselves for their 45- and 50-year reunions. In the meantime, they may want to warm up at the next Winter Academy. Organizers intend to hold one in Naples again next year. And, rumor has it, the Alumni Relations Office for the Schools of the Health Sciences is scouting Arizona for a second location—call it Winter Academy West. *–CS*

IN MEMORIAM

'40s

JULIUS W. AMBROSE
MD '43A
JAN. 28, 2006

NORMAN DAVIS
MD '43A
JAN. 20, 2006

HARVEY W. ROSENBERG
MD '45
FEB. 5, 2006

'50s

LOUIS SIGNORELLA
MD '50
JAN. 5, 2006

RICHARD J. ADLER
MD '53
DEC. 16, 2005

'60s

ARDEN J. TIESZEN
MD '61
FEB. 23, 2006

THOMAS E. CHVASTA
MD '66
FEB. 2, 2006

FRANK B. KERN
MD '66
JULY 13, 2005

RONALD D. WILBUR
MD '68
FEB. 27, 2006

EDWARD CURTISS
AUG. 8, 1938–FEB. 15, 2006

Curtiss

Nobody took pride in the annual white coat ceremony quite like Edward Curtiss. Sure, parents are proud when their son or daughter dons the white coat of a Pitt med student for the first time, but Curtiss, the School of Medicine's senior associate dean for admissions and financial aid, had championed every one of those students. "He read every application to the medical school," says Barry London, associate professor of medicine, cell biology and physiology, and chief of the cardiology division. Curtiss died this winter of a heart attack at age 67.

"He had a strong commitment to social justice," says Paula Davis, the assistant dean of admissions, financial aid, and diversity, "and that's why he championed women and believed that underrepresented minorities deserved a place at the medical school."

Zelda Curtiss explains that when she told her husband that she wanted to go to law school at age 34 with two young girls at home, he replied, "Great. We'll make it work."

"He saw what women can accomplish," she adds.

"Because of Ed, our student body is one of enormous diversity," says the dean of the medical school and senior vice chancellor for the health sciences, Arthur Levine. "Not just in the traditional senses of race, ethnicity, and gender, but also in the sense of looking at individuals who came from eclectic backgrounds but had somehow developed a passion for medicine."

Curtiss was once an atypical med student himself at New York University, with an undergraduate major in American history. He had been diagnosed with juvenile diabetes at age 13 and eventually suffered all the ravages of the disease, including heart problems and vascular damage that caused him to have both legs amputated in the last few years. An award-winning professor of medicine, he overcame this near-fatal episode to return to his specialty, teaching Pitt's cardiology fellows and students the art of reading electrocardiograms, as well as assembling the next med school class.

"Those new generations of competent, caring physicians," says Levine, "are Ed's greatest legacy." *–CS*

NICHOLAS BARBARO: EPILEPSY AND THE GAMMA KNIFE

BY CHUCK STARESINIC

When Nicholas Barbaro (MD ’79) was a student at Penn Hills High School, he decided that he needed to begin preparing himself for some sort of career in medicine. So he wrote a letter.

“I’m not even sure where I mailed it,” says Barbaro, now a professor of neurological surgery at the University of California, San Francisco (UCSF). “It was one of those things like ‘Santa Claus, North Pole.’ I sent it to the medical center.”

He must have written something about surgery, because he got a note back from a Pitt surgical resident named Marshall Webster (Res ’70), who invited him down for lunch and a little tour of Presbyterian University Hospital. There was a dollar or two in the envelope for bus fare. (Barbaro says he got a ride to the hospital and pocketed the cash.) Webster, who is now the Mark M. Ravitch Professor of Surgery at Pitt, took him up to the dome, where they looked down on cardiac surgery in process.

This was the first of many small acts of encouragement that Barbaro encountered at Pitt, where he returned as a med student in 1975.

He did research with Dave Tomko, who retired as a research associate professor of physiology. Peter Jannetta, then chair of neurological surgery, gave enthralling lectures on brain surgery complete with films, which were more of a novelty in the classroom then. The cumulative result: Barbaro graduated with a significant boost to his new career in academic neurological surgery. He’s now the principal investigator on a National Institutes of Health grant exploring the use of noninvasive techniques to perform brain surgery on epilepsy patients.

Nearly a million Americans suffer from epilepsy that originates with abnormalities in the temporal lobe. Many control their seizures with medication, but some patients don’t respond to the drugs. For several decades, the standard treatment for them has been craniotomy and lobectomy—open up the skull and remove the abnormal tissue from the brain. As brain surgery goes, it’s a relatively safe and effective treatment.

Barbaro was inspired by a visit to France, where a colleague was having success treating temporal lobe epilepsy with the Gamma Knife, which uses low-dosage gamma radiation from some 200 different sources to target one spot in the brain.

He put together a clinical trial of 30 patients—the first in the United States—to establish the most effective dosage. Three other centers, including Pitt, participated in the trial. Douglas Kondziolka (Res ’91, Fel ’92), Pitt’s Peter J. Jannetta Professor of Neurological Surgery and Radiation Oncology, is one of Barbaro’s coinvestigators. In the next phase, they’ll randomly assign 200 patients to craniotomy or radiosurgery, as the Gamma Knife procedure is called. The goal is to see whether radiosurgery is equally effective.

Clearing the way for a noninvasive approach to treating otherwise intractable temporal lobe epilepsy would be a major advance, especially for patients who can’t undergo the open procedure because of bleeding disorders or heart conditions. It would create an option that forgoes a long hospital stay or risk of infection.

There are tradeoffs. For example, the open procedure eliminates seizures on the day of the surgery while radiosurgery takes an additional 12 to 15 months before the radiation has had its full effect. Yet, given the choice, most patients would opt for the noninvasive approach, Barbaro believes.

Barbaro now has his own hand in the next generation of neurosurgeons. He directs UCSF’s neurosurgical residency program, and interested students seek him out early and often. The program has just accepted Pitt’s Brian Jian (MD/PhD Class of ’06) as a neurological surgery resident. ■

COURTESY UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Barbaro looks over the Gamma Knife he uses to treat epilepsy.

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CAMI MESA

Robert Phillips (center) turned 80 in December, but he likes to say he's 43. He's got two birthdays, you see. Forty-three years ago, in January 1963, Tom Starzl sewed Phillips' sister's kidney into his body and got rid of Phillips' own kidneys, which were making him sick. Phillips is the world's longest surviving organ transplant recipient. He remembers how Starzl offered him a job in his lab while he was recovering—"Dr. Starzl told me to work when I wanted to. ... He has a lot of compassion for his patients. That means a whole lot of beans."

Phillips joined four other former Starzl patients on March 10 to mark another birthday—Starzl's 80th. Clockwise from left: liver transplant recipients Austin Szegda (age 22, transplant 1984), Kim Hudson Rasmussen (age 40, transplant 1970—the world's longest surviving liver transplant recipient), Betty Baird Lewis (49, transplant 1979), and Jerri Williams (37, transplant 1974).

CALENDAR

OF SPECIAL INTEREST TO ALUMNI AND FRIENDS

Unless otherwise noted, for information on an event contact the Medical Alumni Association: 1-877-MED-ALUM
medalum@medschool.pitt.edu.

SIMMONS LECTURE

MAY 3
8 a.m.
Room S100
Starzl Biomedical Science Tower
Michael T. Longaker, MD, Speaker
For information:
www.surgery.upmc.edu

MEDICAL ALUMNI WEEKEND 2006

MAY 19–22
Classes Celebrating:

1941	1976
1946	1981
1951	1986
1956	1991
1961	1996
1966	2001
1971	

SCOPE AND SCALPEL

MAY 19 & 20
7 p.m.
The Antonian Theater
Carlow University
Pittsburgh
For information:
www.scopeandscalpel.org

SENIOR CLASS LUNCHEON

MAY 19
11:30 a.m.
Twentieth Century Club
Pittsburgh

SCHOLARSHIP APPRECIATION TEA

MAY 19
3:30 p.m.
Pittsburgh Athletic Association
Pittsburgh

ALUMNI CHAMPAGNE BREAKFAST & REUNION GALA

MAY 20
8:30 a.m. & 6 p.m.
Omni William Penn Hotel
Pittsburgh

GRADUATION CEREMONY

MAY 22
10 a.m.
Carnegie Music Hall
Pittsburgh
For information:
Student Affairs Office
412-648-9040
student_affairs@medschool.pitt.edu

CLASS OF 2010 WHITE COAT CEREMONY

AUGUST 13
3 p.m.
Auditorium 6, Scaife Hall
Student Affairs Office
412-648-9040
student_affairs@medschool.pitt.edu

TO FIND OUT WHAT ELSE IS HAPPENING AT THE MEDICAL SCHOOL, GO TO www.health.pitt.edu

RACHEL EDWARDS HARVITH AT CEDAR POINT, SANDUSKY, OHIO, IN 1980. PHOTO BY HER FATHER, JOHN HARVITH, SENIOR ASSOCIATE VICE CHANCELLOR FOR UNIVERSITY NEWS AND MAGAZINES. © JOHN HARVITH

NO STOPPING HER?

How do you keep the best and brightest on the med school track? A planned gift to the School of Medicine can be directed toward scholarship funds or other meaningful projects. In the meantime, it can provide an annual income stream for you or a loved one. (If the School of Medicine is already in your will and you haven't let us know, please contact us so that we can make sure your gift is used as you intend it to be.)

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