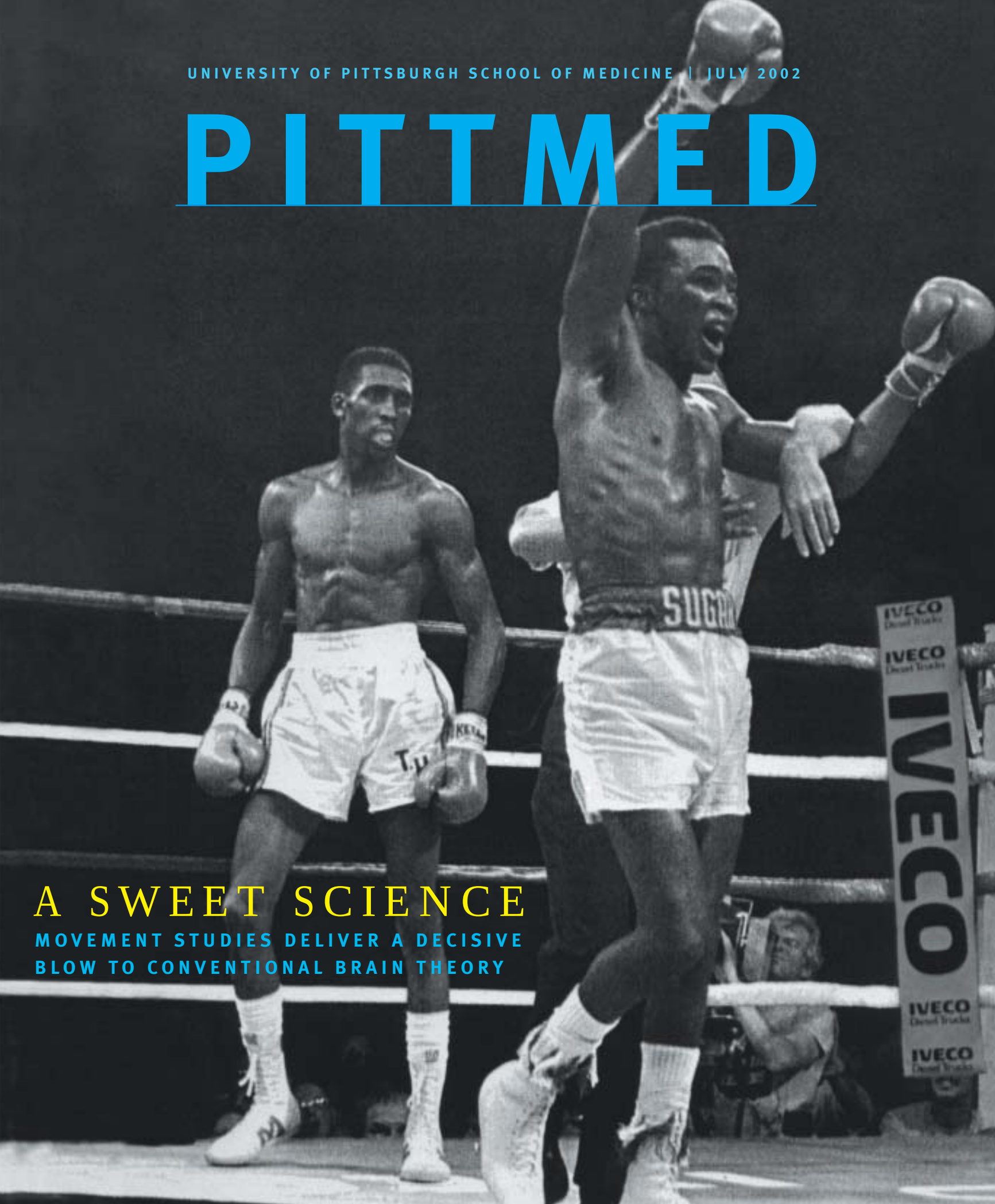
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | JULY 2002

PITTMED



A SWEET SCIENCE

MOVEMENT STUDIES DELIVER A DECISIVE BLOW TO CONVENTIONAL BRAIN THEORY

THE FERGUSON DYNASTY CONTINUED

We feared that we missed a few stars in our search for chairs who trained under orthopaedic legend Albert Ferguson. Sterling Williamson, Res '70, now semiretired, called to say he studied under Ferguson and later, during the '80s, became chief of pediatric orthopaedics at Children's Hospital of the King's Daughters in Norfolk, Virginia. He's known for treating inoperable spine problems.

SURGEON/MUSIC MATCH

ANSWERS TO OUR "LAST CALL," PAGE 40:

Giselle Hamad—John Coltrane, Miles Davis, Roy Hargrove, Led Zeppelin, The Police. **Robert Goldwyn**—Edith Piaf, Paganini, Brahms. **Jeffrey Upperman**—Mendelssohn, Jean-Luc Ponty, Alicia Keys, Dave Matthews Band, India.Arie. **Peter Ferson**—Preifers silence. **Robert Bragdon**—Bob Seger, John Mellencamp, Matchbox Twenty, Barenaked Ladies. (Note, some of these docs take patient requests.)

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

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2002 MAGAZINE HONORS

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Gold Medal, Best Article of the Year
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Silver Medal, Periodical Staff Writing
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Honorable Mention, Magazine
Women in Communications
Pittsburgh Professional Chapter

Matrix Award, Best Article of the Year
Women in Communications
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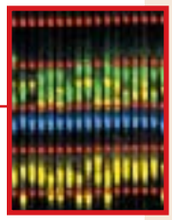
PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE | JULY 2002, VOL. 4, ISSUE 3

DEPARTMENTS



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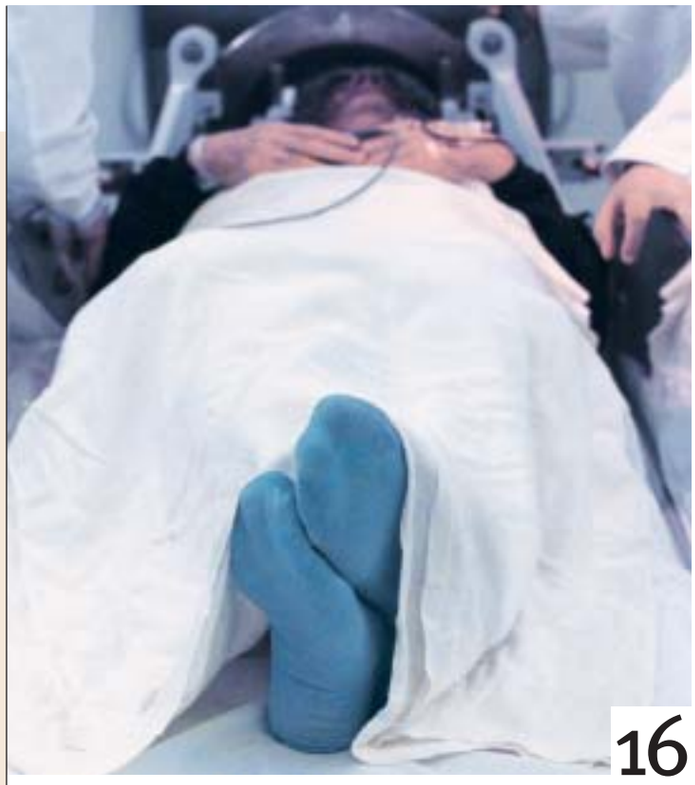
TOM ALTANY—["Mt. Olympus Goes Techie"] Pittsburgh native Tom Altany is an uncommon food expert. He once left home for adventure only to end up selling scrapple, chicken fingers, and the like to road diners along the northeastern Pennsylvania-New York border. Later, as a photographer's assistant, he set up photo shoots of Bengal tigers as well as table food for corporate clients like Pillsbury. In Pittsburgh Altany has worked for, among others, *Pittsburgh Magazine* and the *Pittsburgh Tribune-Review.* He dreams one day of returning to corporate work, but not necessarily food. "If you shoot food in New York, you have to specialize. If you shoot ice cream and become known for it, that's probably all you'll shoot." JOSIE FISHER—["Zane Gates: On Magical Powers"] Josie Fisher is an occasional writer for this magazine who will be missed as she moves on to Corvallis, Oregon, land of bike lanes, smoke-free restaurants, and big trees. She's also an occasional artist, whose work has appeared in the Three Rivers Arts Festival juried show. Her most current medium: recycled light-switch plates. Fisher's many talents have put her in the role of ophthalmologist's assistant, theatre director, hair stylist, and dog sitter. Way back when she pursued her undergraduate degree at Pitt, she liked to park in Chancellor Wesley Posvar's reserved space.

COVER

Knock-out science: Peter Strick and friends' movement studies deliver decisive blows to conventional brain theory. (Photo: 1981. Sugar Ray Leonard defeats Tommy Hearns for the welterweight title. © Bettmann/CORBIS.)



16

FEATURES

PITTMED

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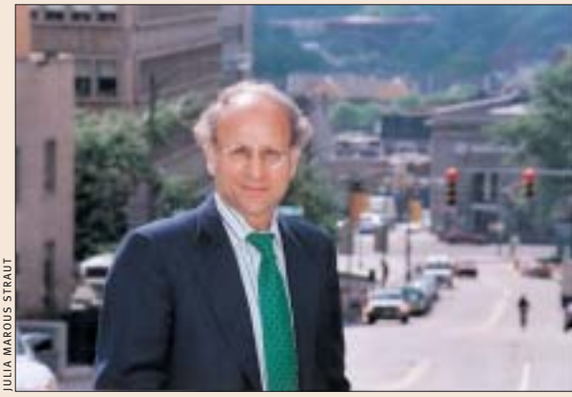


JULIA MAROUS STRAUT

Recently, I had dinner with Dr. Antonio Gotto, dean of the Cornell Medical School, who described a new course in his school whereby medical students spend time each week in the Metropolitan Museum of Art, learning how the painter's view of life can inform the scientist and the clinician. This accords with my own experience: For all of the days of my marriage, I have come home each evening and spent my first few moments studying the art that my wife, a painter, has created that day. Her work is abstract and, I believe, quite elegant—not unlike the contemporary distillate and aesthetic of the cell biologist. In ways that I cannot always articulate, I see in each period of painting a way of viewing our world that seems to have also informed the science of the time. In fact, the scientist and artist are more similar than not. I don't say this just because literature, writing, and theatre took up so much of my interest and effort in another, earlier, life. I'm speaking of the two species more transcendently. Many observers have noted that the works of both the artist and the scientist are measured by the height of their creativity. Even our parlance finds common ground. The tools and theories that scientists use to understand and describe the world are, ideally, "beautiful" or "elegant." And in the end, both pursuits seem to me to be attempts to get beyond our own mortality. Both the artist and the scientist seek to defeat their common antagonist by elaborating meaning in what otherwise appears to be an indescribable void, "a universe of apparent meaninglessness," as neurosurgeon and poet Michael Salcman noted. Or as the great social anthropologist Ernest Becker put it, "the wellspring of all human activity is the fear of dying."

Whether or not you subscribe to the idea of a *Zeitgeist*, that there is an evolving social intellect explaining how, for instance, Picasso's new spatial realities arose just as physics was independently spawning relativism, it's hard to deny that art and science are enriched when they pay attention to each other. I challenge any choreographer not to become entranced by the exquisite ballet that takes place when membranes traffic within a cell. And themes of time certainly suffused the artistic mindset of Einstein's generation, just as the helix, figuring prominently in the work of many post-impressionists, surely did not escape the notice of Watson and Crick.

Many of our own medical students don't need to be reminded of what the arts offer them. In this issue, you'll meet students who sing with the Mendelssohn Choir of Pittsburgh, and there are many others who've made sure that the arts continue to be a part of their lives. Singing, dancing, sculpting, or writing no doubt provide a much-needed release from the often frenetic pace of med school. Moreover, the imprint of the arts on the imaginative mind surely fosters "thinking out of the box"—a characteristic of our best diagnosticians. I wonder though, what other fruits these pursuits will bear. Perhaps someday we'll hear about how the harmonic interplay of Brahms' Requiem or Bach's *Kunst der fugue* inspired a young academic physician to, for example, build an accurate model of channel gating that finally reveals just how anesthetics work their molecular mysteries.

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

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

PATTY NAGLE

Schwartz

Moving Easier

Just as people are right- or left-handed, some neurons have a "preferred direction." If you reach your arm straight in front of you, for instance, motor cortex neurons whose preferred direction is straight ahead will be more active than neurons whose preferred direction is to the right or left. Using electrodes to track the activity of hundreds of neurons in the motor cortex, Andrew Schwartz found that when lab animals use their brains to control a prosthetic limb, their neurons' preferred directions actually change. After the change, the animals are able to control the artificial limb much more smoothly. His findings were reported in *Science* on June 7. Schwartz arrived at Pitt this month as a professor of neurobiology. For the past six years, he has held appointments at Arizona State University and the Neurosciences Institute in California. His remarkable findings may one day lead to tools that enable paralyzed people to direct robotic arms through electrodes implanted in their heads. —*DH*

FOOTNOTE

The creators of Scope and Scalpel 2002 offer this definition in their program glossary–

Carpal tunnel: The only tunnel in Pittsburgh that doesn't cause a traffic jam.

HEADS UP

The American Society for Clinical Investigation (ASCI) has admitted its first otolaryngologist—Jennifer Grandis, MD '87, associate professor of otolaryngology and pharmacology. Grandis is Pitt's latest inductee into the prestigious ASCI, whose members must be admitted before the age of 45. Mark Zeidel, chair of the Department of Medicine, says that Grandis is one of only a handful of people in the country studying the basic science underlying head and neck cancer. "She has really gone into mechanism: Why do cells grow aberrantly?" says Zeidel. "She's also been actively involved in clinical trials to enhance the therapies we use." Grandis says her multiple roles—as clinician, clinical investigator, basic scientist, and teacher—are not that taxing for her. Her clinical practice motivates her to find better ways to help her patients. Three grants from the National Institutes of Health support her research. "I just have a passion," she says. "I have a wonderful life." —*DH*

Grandis

Faculty Snapshots

In 2000, David Satcher, then the surgeon general, set health goals for US racial and ethnic minorities that were the same as those for US whites—*for the first time in his office's history.* Previously, surgeons general had resigned themselves to set lower goals for the health of those minorities. Recent reports compiled by Pitt researchers attest to the need to end racial health disparities. Black men in Allegheny County die an average of 5.7 years younger than white men; among women, blacks die 3 years younger than whites. Diabetes death rates for blacks in Allegheny County are twice those of whites. Blacks are 1.5 times as likely to die from unintentional injury as whites. **Ralph Bangs**, research associate at the Center for Social and Urban Research, compiled the reports, called the *Black Papers,* with the help of **Ken Thompson**, associate professor of psychiatry.

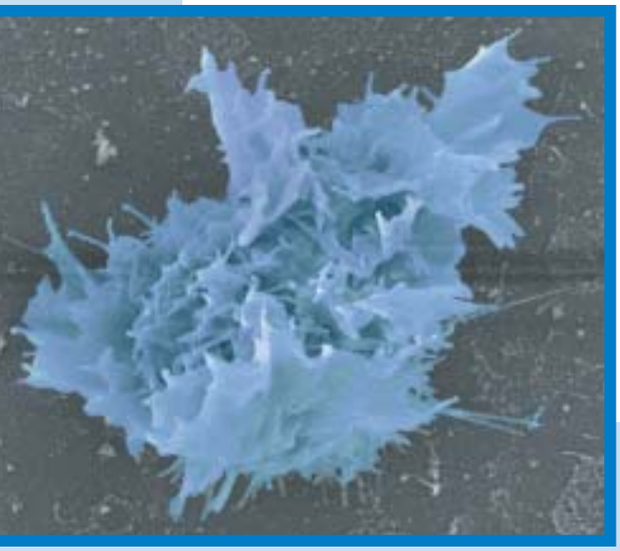
"The *Black Papers* are a call to action," says Thompson. "I'd like to see Pitt be known for an extraordinarily rich system of providing health care to people in communities where health is most threatened." The Neighborhood Physicians and Practitioners Forum, created by Thompson, is one way the physician seeks to address issues of local health inequalities.

FOR MORE INFORMATION ON THOMPSON'S NEIGHBORHOOD FORUM: thompsonks@msx.upmc.edu

Scantlebury

Yeager

Transplanted kidneys are inevitably destroyed. While the body may tolerate the organ for a few years or for nearly two decades, eventually the immune system will turn the organ into scar tissue, a slow process called chronic rejection. **Velma Scantlebury**, associate professor of surgery, and **Andrew Yeager**, professor of medicine and pediatrics, recently tested a new procedure that may lengthen the functional life of transplanted kidneys. Yeager used a granulocyte colony-stimulating factor to stimulate production of stem cells in the bone marrow of a person donating a kidney to a sibling. (In the procedure, the marrow produces so many stem cells, they spill out into the blood. The stem cells are then removed from the blood and frozen.) Scantlebury transplanted the kidney; three days later, Yeager's team infused the stem cells into the recipient. The doctors hope that the stem cells will foster organ acceptance so the patient won't need to be as reliant on immunosuppressive drugs. The patient is doing well, but it is too early to assess the effects of the stem cell transplantation.



Langerhans cells

In a recent study published in *Nature Immunology,* **Louis Falo**, professor and chair of the Department of Dermatology, identified the precursors of epidermal Langerhans cells (LCs). LCs are skin cells that help to stimulate and control the body's immune response. Scientists hope that by manipulating LCs, they may be able to intensify, mute, or turn off the immune system. Falo plans to use LCs in designing vaccines against melanoma. *—DH*

D'Ambrosia (left) and Billiar

KNOWING YOURSELF

The children drifted toward the American air base in Thailand during the Vietnam War, tattered, starving, homeless. Robert D'Ambrosia, a flight surgeon, was compelled to help build an orphanage.

"Humanitarianism lets you know what kind of professional you are," says D'Ambrosia (MD '64, Res '70, Fel '70), who'll become chair of orthopaedic surgery at the University of Colorado in September after running the department at Louisiana State University for 26 years. "It takes you away from thinking about the dollar."

D'Ambrosia shared that message with the Class of 2002 in May while accepting the Hench Distinguished Alumnus Award, an honor bestowed by the Medical Alumni Association. He let his audience know that he learned much about serving others from his mentor, Albert Ferguson, the former chair of orthopaedic surgery at Pitt. *–DRE*

THE RIGHT QUESTIONS

Rarely does Timothy Billiar (Fel '90, Chief Res '92) break stride. However, in accepting the 2002 McEllroy Award, given by the Medical Alumni Association to recognize outstanding physicians who trained at Pitt, Billiar stoically said that former residents of Crete, the humble Nebraska town of his youth, were known as "ex-Cretans."

More commonly, Billiar, chair of surgery at Pitt since 1999, is known as a reserved scholar immersed in his work. Throughout his career, he's been a key player in understanding nitric oxide—a molecule essential to the healing process, among other benefits.

A good researcher understands the difference between knowing the answers and asking the right questions, he says. "As students, we are all programmed to do the former, but to become a successful researcher, you must be able to do the latter." *–DRE*

TOP RIGHT: JEN URICH. BOTTOM LEFT: COURTESY WATKINS

Match!

By Jessica Mesman

Deans Steven Kanter, Joan Harvey, and Paula Davis stand before the Class of 2002 with a stack of white envelopes.

For the past few years, an average of 83 percent of Pitt medical students have been assigned residencies with one of their top three institutions of choice. Today, Match Day, graduating students find out where they will end up. Each time the deans present a new envelope, there's a collective holding of breath.

Those whose names are called might take the steps two and three at a time, tear open their envelopes right away, and yell or dance or kiss the papers they find inside. But Peter Le clutches his envelope until he's back in his seat, where he unfolds his letter deliberately.

Cheers and congratulations ring through the auditorium: *Cornell! That is huge! I'm so psyched for you!—DC, baby!* Some yell into cell phones: *Mom! I got my first choice!* But Le, goose bumps on his forearms, is quiet. He hugs a friend in the neighboring seat.

"I'm going home," he says, and he smiles. Home means Orange County, University of California, Irvine Internal Medicine. And it means family and a large Vietnamese community. He rests his head on his knees and rocks back and forth in his seat.

Behind him, a blond woman jumps into a friend's hug and wraps her legs around him. "It's like getting into college all over again!" she yells. "It's awesome."

THIS PAGE: PHOTODISC

HEALTHY ENVIRONS

Last year, Children's Hospital of Pittsburgh was deemed fourth best pediatric hospital in the nation, according to *US News & World Report*. A new building program will help keep Children's ahead of the pack. David Perlmutter, chair of pediatrics for the School of Medicine, loves to tell potential residents about the great future he envisions as the hospital plans a sorely needed new facility, making room to expand critical care, cardiac care, and other programs. Promise of a new clinical home helps Perlmutter woo top doctors to join the department, too, like Raphael Hirsch from Cincinnati Children's Hospital Medical Center ("the best person in the country for academic pediatric rheumatology," Perlmutter notes). Children's is also planning a new ambulatory care center. *—EL*

Olympian Rewards

The skis, poles, and racing gates weighed on the Icelandic men's Olympic ski team as they labored uphill across the snowy Utah mountains. Ian Greenwald and Eric Jensen, University of Pittsburgh residents in emergency medicine, felt sorry for them and helped. As a thank-you, the women's Icelandic team gave the two kisses on the cheek. And the men's team gave them Iceland pins. (Country pins are coveted items at the Olympics.)

It wasn't all pins and kisses for Greenwald and Jensen though. The residents were there to help in medical emergencies and disaster management at the 2002 winter games.

Other Pitt doctors made Olympian efforts, too: Chip Burke, team physician for the Penguins, was the doctor for the US men's hockey team. And Savio L-Y. Woo heads the International Olympic Committee's Olympic Academy on Sport Sciences. *—MH*

KEITH HODAN

The president came to Pitt to announce his proposal to defend the nation against biological terrorism.

Presidential Witness

With the events of September 11 very much a point of discussion, in February President George W. Bush made the first visit by a sitting president to the University of Pittsburgh. He came to witness the Real-time Outbreak and Disease Surveillance system (RODS). Developed by School of Medicine researchers, RODS monitors data from 1,200 daily patient visits to western Pennsylvania hospitals, looking for symptoms of flu, respiratory illnesses, diarrhea, and skin rashes. A sudden increase in any of these symptoms might indicate a bioterrorist attack. (A few weeks after Bush's visit, RODS covered Salt Lake City during the winter games.) Bush called the system the modern "DEW line," referring to the Distant Early Warning radar system employed during the Cold War to guard against Soviet attack. "I've come to realize," he said, "that while Pittsburgh used to be called Steel Town, you need to call it Knowledge Town." *—DRE*

Appointments

Husband and wife, epidemiologist and pathologist, discoverers of KSHV, the virus that causes Kaposi's sarcoma—**Patrick Moore** and **Yuan Chang** arrived at Pitt this month from Columbia University. Moore is program leader for the molecular virology program at the University of Pittsburgh Cancer Institute and professor of molecular genetics and biochemistry; Chang is professor of pathology. The researchers' first paper on Kaposi's sarcoma, the most common cancer in people with AIDS, was published in *Science* in 1994. The scientists went on to show that KSHV causes not only Kaposi's sarcoma, but also primary effusion lymphoma and multicentric Castleman's disease (a rare tumor-inducing disease of the lymph node tissue). The MD researchers will jointly manage a Pitt lab at the Hillman Cancer Center. They currently study specific KSHV genes that are expressed in tumors and try to determine how the proteins encoded by these genes interact with the cell. "If we can find out more about how KSHV causes cancer, we may be able to apply this knowledge to other cancers, even cancers that aren't caused by a virus," says Moore.

Steven DeKosky, a professor of psychiatry and neurology at Pitt since 1990, has been appointed chair of the Department of Neurology. DeKosky holds the largest single grant ever made by the National Institutes of Health's National Center for Complementary and Alternative Medicine. The grant supports a multicenter investigation into whether ginkgo biloba prevents the onset of dementia in older people. DeKosky also is known for clinical and basic science research on Alzheimer's disease. *—DH*

DeKosky

THE MIDDLE PATH

Steven Kanter and Jon Rittenberger have a dream. Really, it's a twinkle in the eye: They would love for all US middle school students to learn CPR, including how to use Automated External Defibrillators, and also be able to make informed decisions about their health. Well, they're one middle school closer. This spring, Marshall Middle School students from Pittsburgh's North Hills came to Pitt for a day. Kanter, senior associate dean (above, right), and Rittenberger (MD '02) enlisted other fourth-year med students and faculty to run sessions like CPR, Where's Waldo in Radiology, and the Host/Defense Game for the kids. "They got to see how doctors use their senses (sight, hearing, touch) in coordination with high-powered technology to help patients," says Rittenberger, who helped with the patient simulator station, Sim Man. *—EL*

PATTY NAGLE

TERRIFYING AND THRILLING ADVENTURES IN SONG

BY DOTTIE HORN

Annie Lee, Paul Bryson, and George LaVerde

One Sunday last January, Annie Lee was worried. The following weekend, she would be performing with the Mendelssohn Choir of Pittsburgh. But, before the concerts were rehearsals on Sunday, Tuesday, Wednesday, and Thursday—for a few hours each night. She had a reproductive and developmental bio exam on Saturday. The weekend following the concerts, she would be going to a conference, giving a talk on her otolaryngology research. How was she going to study for her exam, go to class, prepare her talk, and sing six times in one week?

Then she went to rehearsal, and her mood changed. "While you're singing, you forget about med school. It's energizing," she says. As she drove home, she put in a Brahms tape, the piece they would be performing.

"I was humming. I was singing along," she says. "I was just totally immersed in the music."

For third-year University of Pittsburgh medical students Lee and Paul Bryson and MD/PhD student George LaVerde—all members of the Mendelssohn Choir—it's hard to imagine life without singing. They've gained so many friends and opportunities through music: Bryson traveled to Russia, Estonia, and Finland last summer as part of a choral group. And singing is such a refreshing emotional release, a balance to medicine. If Lee doesn't sing, she gets cranky.

Weekly three-hour rehearsals are a part of their lives; and concert weeks are much more intense. The demanding practices are led by Grammy Award-winning music director Robert Page, whom the students describe as good-natured, unforgettable, creative, comical—and occasionally terrifying.

"He requires an enormous amount of focus and concentration," says LaVerde. "If you can't muster the energy that night, he'll know it."

"And he'll let you know that he knows it," adds Lee.

Page challenges them without singling out individual choir members. At a typical rehearsal, if the choir doesn't sound energetic enough, Page might say, *Don't sit there like a puddle of flesh.* If singers are looking down at their music rather than watching him conduct, *Why are you looking at your crotches? I'm not down there.* He often has the choir repeat phrases in the music until he's satisfied, and if the singers are not producing the desired change, he quips, *Don't do the same thing and expect a different result.*

The demands of rehearsals build up to the thrills of performance—the adrenaline of stepping onstage in a packed Heinz Hall, the delicate passage in a requiem that a performer can't get through without a teary eye. "Sometimes, there's just a very soft, gentle moment in a piece where every single singer gels together into one sound, and you're lifted up," says LaVerde.

And there are the reminders, with every concert, that each performance is fleeting:

As the choir breaks off its final note, there is silence, but the show is not over. The conductor has not yet put down his baton. He has not given the audience leave to respond. Every performer is focused on his hands. The choir members may feel tired, may feel a little relief that it's over, and they got through. Their conductor glances at them with a nod or smile. That silent instant is tense, magical, frozen in time.

The baton lowers. The audience cheers.

FLASHBACK

Allegheny County Coroner Cyril Wecht (MD '56) was lecturing to med students at Scaife Hall during the mid '70s when a streaker (mit paper bag over his head) ran across the stage. The bag probably obscured the naked runner's vision, causing him to trip over slide projector wires. The mortally embarrassed streaker limped away, and Wecht didn't miss a beat: "I seem to have damaged my pointer," he deadpanned. "I hope the same can't be said for that young man."

WANTED: MORE ISLETS

BYPASSING THE PANCREAS DONOR SHORTAGE | BY ERICA LLOYD

His brain just sort of "clicked off," he says. About 10 years ago, Richard Gurwitz was driving on the interstate outside Atlanta, heading to work. The next thing he knew, he was standing in a ditch next to the highway, and a police officer was shaking him.

"I'm diabetic," Gurwitz said as he came to. The officer got him some food, then told him how he ended up in the ditch, according to the employees at the McDonald's nearby—the one Gurwitz went to every workday morning for breakfast. They said Gurwitz stopped at the drive-thru, ordered, then proceeded without paying. They watched him get onto the highway, then back his car into the ditch. But Gurwitz has no recollection of any of that. The last thing he remembers, he was driving on the interstate about *five miles* before his regular McDonald's stop. Somehow he was able to traverse those miles, even order breakfast, without knowing what he was doing.

A couple of other times while he was driving his brain clicked off like that, too.

Still Gurwitz, 37, managed to live a fairly normal life with type 1 diabetes. Daily insulin shots enabled him, for the most part, to stabilize his metabolism and stay active. He helps run a Kinko's in Fort Lauderdale and amuses himself in his free time kayaking in the Everglades looking for wildlife (where he has seen lots of mosquitoes but no alligators). At 5 feet 4, he plays basketball with lots of heart, if not the heft of the big guys. Decades of diabetes have taken their toll, though. He required five laser surgeries on his eyes to preserve his vision. He counts his lucky stars that he hasn't suffered kidney failure.

Gurwitz figured he would be diabetic all his life. Happily, it looks like he was wrong. In the fall, he underwent an experimental islet cell transplant at the University of Miami. Doctors have met with success with this minimally invasive procedure only recently.

Normally, beta cells within what are known as the islets of Langerhans in the pancreas produce insulin. In people with type 1 diabetes, the islets are destroyed, and their bodies are no longer able to convert food into fuel automatically. Diabetes is the Greek word for siphon, in reference to the unquenchable thirst and hunger met by those who could not process nutrients but only urinate "like the opening of aqueducts," as Aretaeus of Cappadocia put it. Aretaeus, born in 30 BC, named and described the disease. ("Mellitus,"a Latin word added later to the name, refers to the honey-like smell of urine common among untreated diabetes sufferers.) Until the 1920s, when researchers at the University of Toronto developed insulin therapy, type 1 diabetic patients usually withered away and died, often in their youth.

As an adult, Gurwitz required 58 total units of insulin, administered in two shots each day. Since the islet transplants, he no longer needs those shots; his body now produces enough insulin on its own. He feels great: "I'm like a normal person. I can do anything I want!"

Gurwitz's good health is great news to the more than one million suffering from type 1 diabetes in this country alone. Yet transplants like his can require two to four pancreases worth of islets, and there aren't enough donated organs to go around. Researchers at the University of Pittsburgh are closing in on a solution.

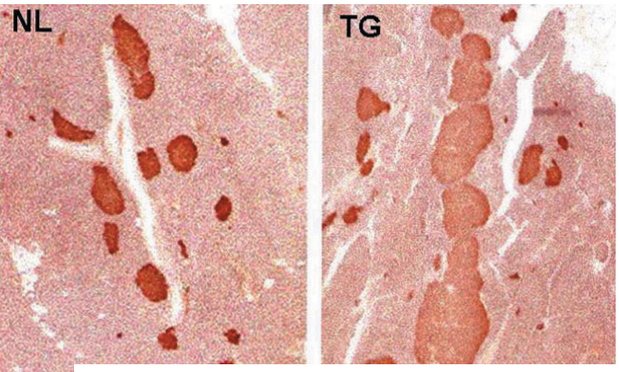
Before Rupangi Vasavada, a PhD molecular biologist in Pitt's Division of Endocrinology and Metabolism, became interested in diabetes, she was studying a gene called PTHrP, which scientists now understand is expressed in almost every tissue in the human body. Knockout mice created without PTHrP die very young. In 1996, when Vasavada was working in the lab of Andrew Stewart at Yale University (Stewart is now her division chief at Pitt), she learned that PTHrP is also made by the islets. She wondered what the protein was doing there—if anything. So she genetically modified mice to produce large amounts of PTHrP in the islets. To her surprise, she'd created hypoglycemic mice. Somehow, all of that extra PTHrP had caused an increase in beta-cell mass, spilling insulin into the animals' blood at a hyper rate. Glucose levels dropped. The opposite happens in diabetic models.

"To us, it was very exciting at the time," notes Vasavada. She'd found a potential growth factor for beta cells. But how did PTHrP increase beta-cell mass? At this point, she has narrowed the mechanism down to two possibilities: Either PTHrP plays a role in decreasing the normal rate of beta-cell death or the protein affects precursors to beta cells. Her colleagues in the endocrinology division, Adolfo Garcia-Ocana, Karen Takane, Ana Cebrian, Juan Carlos Lopez-Talavera, and Stewart, are pursuing other promising islet growth factors as well.

As they get closer to offering the world a new supply of insulin-producing cells, Gurwitz is likely to be getting ready for his next Everglades trip: strapping the kayak to his truck, settling in behind the wheel—alert and ready for the adventure ahead. ■

LEFT: COURTESY GURWITZ. RIGHT COURTESY VASAVADA

LEFT: Richard Gurwitz has been cured of diabetes.



Rupangi Vasavada was surprised to discover she had created hypoglycemic mice. That finding could lead to a new source of islet cells, so that many more diabetic patients can undergo islet cell transplants like those that helped Richard Gurwitz (shown kayaking, left). Vasavada's happy finding came after creating transgenic mice that overexpressed a protein called PTHrP in their islets. She found more and larger islets (stained brown) in the transgenic mice (TG, right) compared to islets in normal mice (NL, left).

NAYSAYER BECOMES BELIEVER

THIS SEASON'S HOTTEST SHOW—INSULIN RELEASE CAPTURED | BY DOTTIE HORN

In 1981, when he was a graduate student, Peter Drain took a course on fluorescence imaging. *A picture is worth a thousand words,* he decided. To him, the saying had an atypical meaning: It was definitely *not* about a picture's value relative to words. Rather, the phrase encapsulated the worthlessness of both. "A thousand words are a bunch of flowery embellishment," he says. Pictures, he thought, were extraneous, extravagant. Especially if you were interested in quantitative information. What mattered were numbers.

Since then, new equipment has made fluorescence microscopy semiquantitative. Researchers have developed new methods to more accurately label cell components with

fluorescent markers. With these advances, Drain, now an assistant professor of cell biology and physiology at the University of Pittsburgh, has changed his mind.

These days, the former naysayer is devising some new imaging methods himself.

Working with other Pitt researchers, Drain contributes to the development of new therapeutic approaches to diabetes. The group, led by Massimo Trucco, the Hillman Professor of Pediatric Immunology, recently received a $10 million grant from the Juvenile Diabetes Foundation.

In an attempt to cure type 1 diabetes, some researchers have tried to transplant into diabetic patients the islets of Langerhans. Scattered throughout the pancreas, the islets are clumps of cells that secrete insulin and regulate its release. In 1999, researchers successfully transplanted islets for the first time—blood glucose levels in the recipients became normal, although patients had to be placed on a regimen of immunosuppressive drugs. (Trucco's group recently applied for approval from the Food and Drug Administration to perform the experimental procedure at Pitt. His colleagues and sometime collaborators at the University of Miami are among the handful of clinicians who've performed these procedures successfully—see "Wanted: More Islets," page 8.)

While transplants seem to hold promise, many questions surround them. For example, to achieve normal glucose regulation in the recipient, perhaps three persons' worth of islets must be transplanted. Why does it take so many islets? Are some of the cells dying after transplantation? Are the cells producing a normal amount of insulin? Is the insulin being released normally in response to glucose? No one knows.

Mouse models, thought the Pitt scientists, might provide answers.

Wouldn't it be revealing, they thought, to transplant islets into a mouse and then later perform a biopsy of the transplanted islets? They could use a special microscope to measure, in the living cells they had extracted, how much insulin was being produced and released in response to glucose. Better yet, what if they surgically implanted into a mouse a skin flap, with a window for a microscope underneath? They could position the flap so that they could simply pick up the mouse and look directly at the islets (which are transplanted into a transparent pocket that surrounds the kidney). Using a handheld microscope, the scientists could then measure the function of the transplanted islet cells inside the living animal.

A major stumbling block prevented them from doing the experiments. For seven years, scientists had tried to fluorescently label insulin in living cells. Nothing worked.

Drain got to thinking.

Once insulin is made in the cell, it goes to the Golgi apparatus (a protein refining factory). As it leaves the Golgi (in an immature form), it becomes sealed inside a granule, where it remains until it is taken to the cell membrane and released outside the cell.

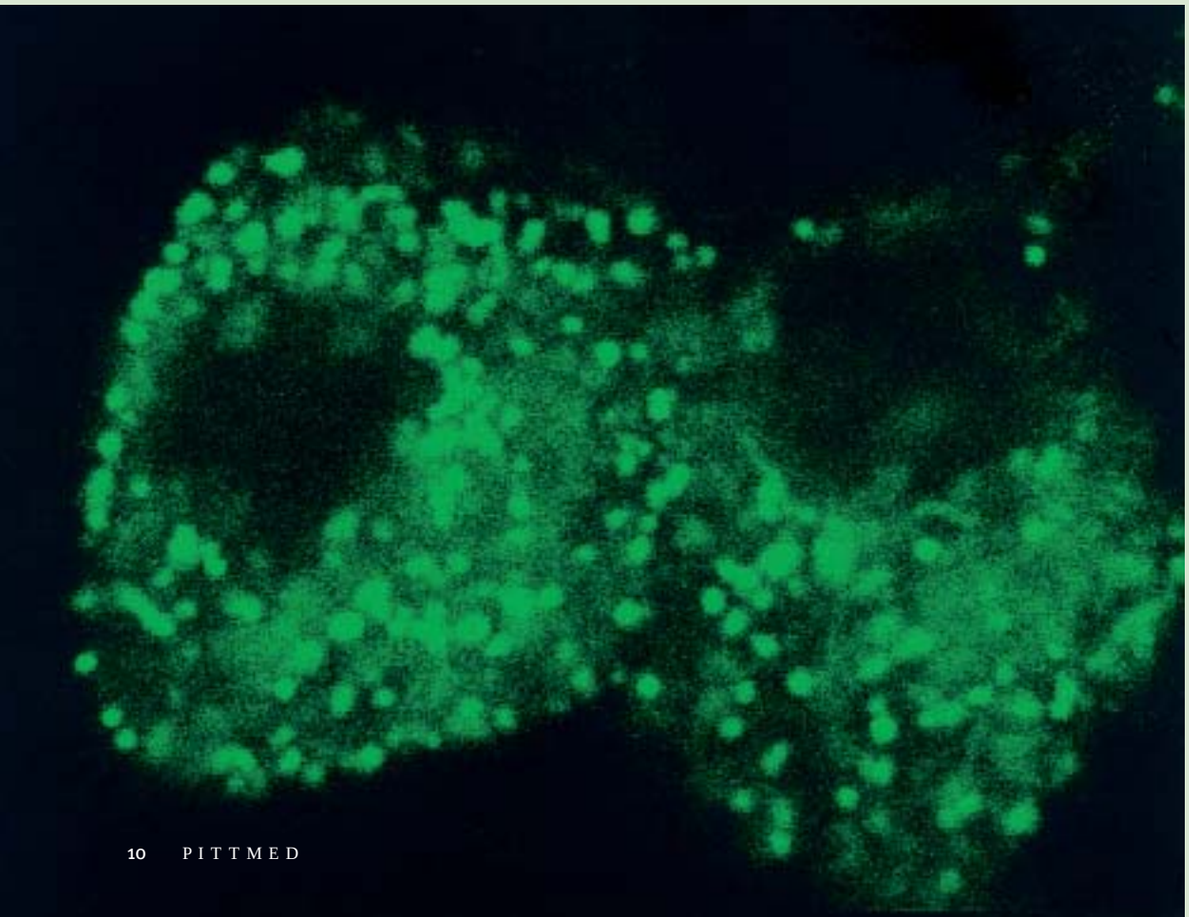
Once inside the granule, the immature form of insulin matures—part of the protein, called the C peptide, is cut away. Other scientists had tried labeling mature insulin, but found that the labeled insulin no longer functioned normally. Drain thought: *Why not label the C peptide instead?* The C peptide remains in the sealed granule. Since there is one C peptide for each insulin molecule, researchers would be able to measure the amount of insulin in the granule.

Drain tried the experiment. It worked.

One afternoon in his office, he shows a video of insulin secretion in a living cell. The cell is just beginning to respond to an increase in glucose levels. The cell moves. Its insulin granules move. Some granules head toward the cell membrane. A couple pop out of the cell; the fluorescence abruptly disappears as the granule ruptures, dispersing its contents. "This is as good as it gets," he says.

"My favorite thing about science is realizing that I'm completely wrong on something I was completely convinced of," says Drain. He was wrong, he admits, about a picture's worth. ■

For years, scientists dreamed of pictures like this one—of insulin granules fluorescently labeled in a living cell. But, no one could figure out how to label insulin—until Peter Drain got involved.



COURTESY DRAIN

GENE RACES

MATCHING CHROMOSOMES WITH CROHN'S DISEASE | BY TRINA WOOD

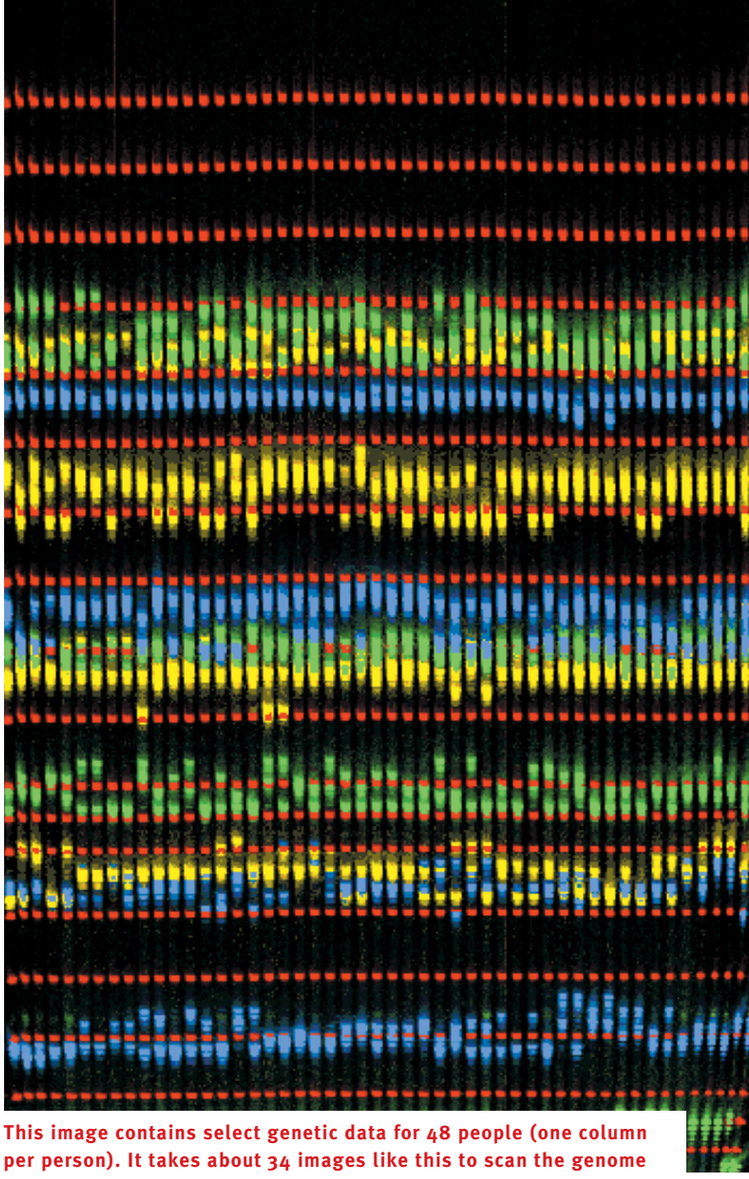
During an episode of inflammatory bowel disease (IBD), diarrhea and abdominal pain can be so severe that normal daily routines are impossible. IBD can lead to a blocked intestine, intestinal infections, nutritional deficiencies, and other complications.

A 1996 finding from a group of French scientists provided hope for a better understanding of the causes of IBD. In 1996, the French scientists published a paper in *Nature* showing a link between a region of chromosome 16 and Crohn's disease (ulcerative colitis and Crohn's are the two forms of IBD). The paper set in motion an international race to find the first gene for Crohn's.

Shortly after Richard Duerr, assistant professor of gastroenterology, hepatology, and nutrition at the University of Pittsburgh, heard about the French study, he joined forces with collaborators at the University of Chicago and Johns Hopkins University. Working together, the scientists decided, they would have a better chance of finding genetic causes of IBD, which affects about 2 in every 1,000 people in Western countries.

As collaborators, Duerr and the other scientists would share DNA samples from affected families. Although Pitt has one of the largest collections of IBD DNA samples in North America, with data from 1,700 members of 350 families, far more samples were needed. "To find human disease genes in a complex trait like inflammatory bowel disease, we need many, many samples. A few hundred families by themselves are generally not enough to find genes," says Duerr. Joining forces gave Duerr access to samples from an additional 1,500 members of 388 families. When the collaboration formed, each group focused on a different region of the genome. The 1996 discovery linked Crohn's to chromosome 16, the University of Chicago's turf, so Duerr's collaborators in the Windy City began looking for the gene on the implicated region of chromosome 16.

Judy Cho was leading the Chicago effort. One day, she got a phone call out of the blue from a stranger—Gabriel Nuñez, a scientist at the University of Michigan. Nuñez studied a gene called NOD1. He had been looking for genetic sequences that might be similar to NOD1 and found a similar sequence—on chromosome 16. It was in the middle of the region linked to Crohn's disease. A light bulb went on. Nuñez knew the predominant theory of the cause of IBD: that normal gastrointestinal bacteria somehow stimulate the immune system into a chronic inflammatory response. NOD1 was involved in immune system signalling and bacteria sensing, and this region appeared to be as well. Could the genetic sequence he had found on chromosome 16 be involved in Crohn's? He learned of Cho's work on IBD and eventually picked up the phone.



This image contains select genetic data for 48 people (one column per person). It takes about 34 images like this to scan the genome for every 48 people in a genome-wide search for disease genes.

COURTESY DUERR

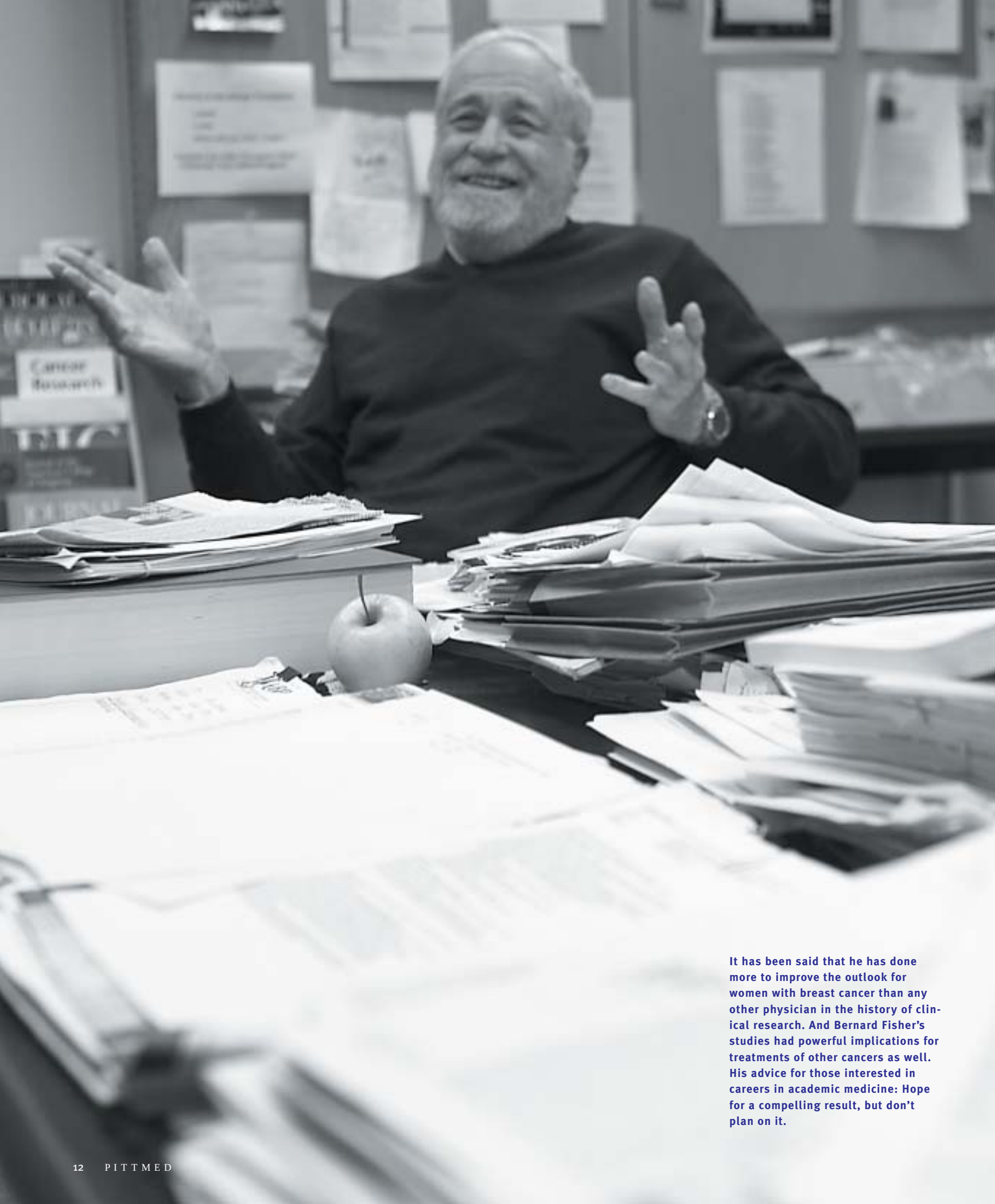
Together, Cho and Nuñez looked more closely at the region of chromosome 16 that Nuñez had identified. Using the collaborative group's DNA samples, including those from Pitt's large collection, the two scientists discovered a gene (now called NOD2), which has three different mutations that are significantly more common in people with Crohn's. At the same time, the French group that had initially reported the chromosome 16 linkage uncovered the same NOD2 mutation. Papers from the two groups, jointly announcing the discovery of the first Crohn's gene, were published side-by-side in *Nature* on May 31, 2001.

"This discovery goes beyond the study of Crohn's disease," says David Whitcomb, chief of Duerr's division at Pitt. He speaks admiringly of how the collaborators, using sophisticated statistical genetic techniques, localized the chromosomal regions where individual mutated genes lie, and then, using knowledge of the biology of the disease, identified culprit genes.

"It is likely that the same techniques and methods will be successful in discovering the underlying genetic causes of other complex diseases," Whitcomb adds.

Since the 2001 discovery of the first Crohn's gene, other researchers have confirmed the association with Crohn's. But, only 20–25 percent of those with the disease have any one of the three known mutations. That means other genes are yet to be found.

These days, with the help of a $1.4 million grant from the National Institutes of Health, Duerr is looking for an IBD gene on chromosome 3. He also recently discovered that a region on chromosome 12, which had been previously linked to IBD, seems more related to ulcerative colitis than to Crohn's. He's hot on the trail of more IBD genes. ■



It has been said that he has done more to improve the outlook for women with breast cancer than any other physician in the history of clinical research. And Bernard Fisher's studies had powerful implications for treatments of other cancers as well. His advice for those interested in careers in academic medicine: Hope for a compelling result, but don't plan on it.

IT DOESN'T HAVE TO BE A BLOCKBUSTER

BERNARD FISHER

IN CONVERSATION

A dreamy photo of dancer Betty Bloomer, circa 1945, shows her splayed on the ground, back arched against a grassy lawn, her sweeping skirt in a splendid fan surrounding her. Others show the lithe woman, who performed and studied under Martha Graham's direction, slicing the air with a dramatic lean or whirl, at once a picture of strength and vulnerability. Decades later, in September 1974, First Lady Betty Bloomer Ford had a radical mastectomy, again a dramatic display of strength and vulnerability: Her very public surgery is credited with doing much to advance a vital health issue that Americans had shied away from discussing in anything but whispers.

While the first lady underwent surgery at the Naval Medical Center, across the street, at the National Institutes of Health, Bernard Fisher, MD '43, of the University of Pittsburgh, reported findings from studies that would have a profound effect on the treatment of breast cancer for the next 30 years.

PHOTOGRAPH | ROY ENGELBRECHT

PHOTOS THIS PAGE: COURTESY FISHER

"I felt at an early point in my career that cancer is not a surgical disease any more than is arteriosclerosis a surgical disease," notes Fisher. (LEFT AND ABOVE, circa 1970)

Fisher's report showed that less-extensive surgery was just as effective as radical mastectomy. He also reported findings from the first clinical trial ever carried out to evaluate the value of postoperative chemotherapy, indicating that a single agent (L-PAM) after surgery led to a better outcome. The first lady was prescribed L-PAM as a result of Fisher's findings; it was too late for her to receive the less radical surgery.

The day before Fisher's announcement, radical mastectomy was the *accepted treatment for breast cancer; it involved removing not only the breast but also the chest wall muscles, the nearby lymph nodes, and sometimes even both breasts. This treatment was based on the Halstedian hypothesis, derived from anecdotes and induction. The Halstedians proposed that cancer spreads in an orderly way, progressing from one anatomical site to another: Thus, stopping cancer's progression necessitated extensive surgery. But anecdotes to the contrary were common. Women who'd undergone radical mastectomies were still dying from cancer.*

In a meeting held during the late '50s, Fisher and fellow surgeons from across the country discussed why radical mastectomy so often failed to improve the outcome of patients. To that group, which eventually became the National Surgical Adjuvant Breast and Bowel Project (NSABP), it seemed that, rather than prevent the spread of cancer, surgery might actually stimulate *its progression: "One of the weak links of surgery was that, while you were trying to get a tumor out," Fisher explains, "some tumor cells got disseminated." The spread of those cells, or metastasis, was an understudied field at the time, though the phenomenon intrigued Fisher. With his brother Edwin Fisher, a member of the faculty of medicine and also a School of Medicine graduate (MD '47), he studied the biology of metastasis throughout the next decade. Their laboratory studies showed "dormant" tumor cells exist and altering a host can result in lethal metastases—challenging the then widely accepted notion that cancer was autonomous from its host. Findings coming out of the brothers' lab suggested a thesis that, unlike Halsted's, was biologic, rather than anatomic and mechanistic.*

Fisher proposed that cancer spreads unpredictably, and metastases occur because of the individual characteristics of the tumor cells and of the individual patients in whom they exist.

By 1967, the NSABP needed a new chair and an infusion of energy. Fisher, among the group's founders, certainly had the qualifications, but he resisted because "it didn't look like a very promising thing to devote your life to." His colleagues pressed. The NSABP got a new chair.

Fisher soon realized that members of the NSABP could help him test this new hypothesis and, at the same time, determine the value of less-mutilating surgery. The first clinical trial he designed was to compare radical mastectomy with removal of the breast without removing the muscles or lymph nodes. A second compared the efficacy of removing the tumor by lumpectomy with more radical operations. The operations were all found to be equally effective. In more than 25 clinical trials involving more than 50,000 women, Fisher's group would go on to prove the effectiveness of new therapies and combinations of chemotherapy and tamoxifen. These latter two systemic treatments eliminated tumor cells that circulated in the blood or that remained undetected within organs, out of the reach of the Halstedian's knife.

It turned out that tamoxifen, which became available in the '80s, not only was an effective therapeutic, but could be employed for breast cancer prevention. This 1998 finding is among the more recent Fisher breakthroughs.

Fisher is now 82, and most of the horizontal space in his office is covered by papers and folders relating to his current projects. He indulged us with an interview this spring, during which he reflected on his career (including some 40 years of research at the University), deliberated on the future of breast cancer treatment, and meditated on the academic life. Excerpts follow.

I was a reader as a kid and was fascinated by books such as Paul de Kruif's *Microbe Hunters*. Plus, I had every contagious disease known to mankind: measles, mumps, whooping cough, scarlet fever, you name it. It was a different time, when the public health nurse would come along and put a little sign on the door, and your house was quarantined; nobody came in or went out. It was a rather interesting immersion experience. In retrospect, it gave me an opportunity to read and to fantasize about my future.

A great-uncle of mine, Julius Rogoff, was a very well-known physiologist who started off his career as a surgeon, then became an academic.

"I speak, I write, others tell you what I mean. Prejudice can alter perception more profoundly than hallucinogens."

As chance would have it, in the '40s he came to the University of Pittsburgh, where he became the first research professor of experimental endocrinology. I had an opportunity to work occasionally in his laboratory.

[*In the '50s, Fisher investigated blood vessels, liver regeneration, and hypothermia in his surgical research lab at Pitt.*] In those days, being a clinician and an investigator was an unusual combination. I was difficult to categorize. Clinicians looked upon me as an animal doctor and basic researchers looked upon me as a clinical doctor. As a result, I was often asked, "What are you going to do when you grow up?"

Around 1955, I got a call from Dr. George Moore, who was chief of surgery at Roswell Park in Buffalo. He was creating a cancer institute and asked me if I would be interested in going there as a surgical oncologist. And I said, "Well, I am not really interested in cancer." In 1958, I got a call from Dr. I. S. Ravdin, who had been my mentor at Penn. He said, "We're having a meeting in Washington at the National Institutes of Health, and I want you to be there. We're going to set up a clinical trial involving women with breast cancer." I said, "I'm not in the least bit interested. I'm doing what I want to do in the laboratory here at Pitt." He said, "I'm telling you to be there." Well, you don't refuse a two-star general who . . . had operated on Eisenhower, and who was known the world over.

To me, a clinical trial is like a flow cytometer or an electron microscope. It's where you put something in and get something out. What you get out relates to the quality of what you put in. The chance of obtaining important results from a clinical trial depends upon the strength of the hypothesis being tested.

While the clinical trial mechanism is accepted today, when I began my clinical trials, it was difficult for me to get women and physicians to participate in them. When radical mastectomy was being evaluated, the idea of performing less-extensive operations was considered, in some institutions, to be equivalent to malpractice.

To get a woman to participate in a clinical trial where she was going to have her breast off or have her breast not taken off, that was a pretty difficult thing to do. Not like testing Drug A versus Drug B. In time, as more trials were being done, it became easier to attract participants. Those women who did participate in our studies felt that they were making a contribution that would be of value to their progeny and to other members of their family. The women themselves are the heroes.

Our 1998 report indicating, for the first time, that breast cancer could be prevented with tamoxifen was probably the capstone of my career. Certainly, in 1958, when I began this journey, the idea of using an agent to try to prevent breast cancer was . . . science fiction.

During my scientific life, I have been trying to make a contribution toward bettering the lives of women with breast cancer. Others will have to assess the worth of my accomplishments. Unfortunately, after four decades of investigation, I've recognized that discovery is not always triumphant. There's a sign right there. [*He points to the cabinet across the room, papered with his own maxims.*] It says, "I speak, I write, others tell you what I mean. Prejudice can alter perception more profoundly than hallucinogens."

I have always believed that the research we were doing was not only related to breast cancer but to other cancers like colon or lung cancer, or to all other tumors where unbelievably extensive operations were being done—forequarter, hindquarter amputations, and so on.

The understanding of the disease has changed, and that's the important thing. Now we're entering a new era in which there are molecular or genetic kinds of approaches, which have a great deal of promise. We may have reached the end of what we're going to get with chemotherapy. There are people who are talking about the use of immunologic agents, about finding genetic mechanisms that can be interfered with. Those will be the new systemic therapies of the future. Hopefully that will occur, because, if it doesn't, then we're not making any progress.

I felt at an early point in my career that cancer is not a surgical disease any more than is arteriosclerosis a surgical disease. With regard to the latter, what one does is to use coronary artery bypass, or stents, or to resect aortic aneurysms, but you're not curing arteriosclerosis. You are nowhere near preventing or eradicating that process. And the same thing applies to cancer.

I've recently become interested in the mammography controversy. We can demonstrate from all of our trials that women with small tumors—really small tumors—do better than women with big tumors. Almost all of those small tumors were detected by mammography. Screening is still appropriate. It's not so much how many tumors you find; it's what kind of tumors you're able to detect. Incidentally, in 1974, I established, at Pitt, the first breast cancer detection center in Pittsburgh.

My advice to those who are going into academic medicine is that they should pick something important to work on, something that could make a difference. And then, do it with passion. Hope for a compelling result, but don't plan on it. But even if they make some contribution, that's worthwhile. It doesn't have to be a blockbuster. I think that's the thing that they should aim for, but they should realize that they're going to be disappointed more often than not.

Whatever contribution I have made has only been possible because of both my family, who have been entirely devoted to my career, and the thousands of people who worked with me over the years. They were committed. Totally committed.

It's been an interesting life. And it isn't over yet. I still have a full briefcase! ■

Interview by Leah Kauffman

A SMARTER O.R.

PHOTOGRAPHY BY TOM ALTANY

TEXT BY DAVID R. ELTZ

MT. OLYMPUS GOES TECHIE

In the observance of ingenuity there is subtle elegance. A flashlight beam passes over a man's neck, and in the pale blue glow his jugular appears to rise from within muscle and tendon and float across flesh like a whale surfacing for air. Elsewhere, Zeus is summoned to assist mere mortal hands, Hermes delivers more than messages, and invisible knives carve away deadly masses.

At the University of Pittsburgh, technology and surgery commingle; technique and gadgetry intertwine. In trained hands, procedures become more precise, less painful. Lives hang less in the balance, and we dance decisively toward better health.

INNER WORLDS

"You are, in essence, looking into the skin, seeing what's inside," George Stetten says of his sonic flashlight, so named for its pale incandescence. The handheld device sends ultrasound into the body. As the echoes bounce back, a semitransparent mirror reflects an image of blood vessels and tendons within.

Stetten, an assistant professor of bioengineering at Pitt and a research scientist at Carnegie Mellon University, envisions the device, now under patent application, as a guidance system for inserting central lines into deep veins for delivery of chemotherapy agents, for invasive procedures like amniocentesis, and for biopsies of tumors. "It's cheap and safe and portable and small, and it's very fast," he says, pushing the scanner against the top of a water balloon while his hand presses the balloon's underbelly.

"Here's my finger coming in from the other side of the balloon; you can see the joint. I wonder if you can see my ring? Oh. There's my wedding ring. That's cool!"

BATTERIES NOT INCLUDED

Silky music eases from Giselle Hamad's iPod MP3 player like some acoustic anesthesia. The medical director of bariatric and minimally invasive general surgery at Magee-Womens Hospital, Hamad is an avowed tech geek. In this OR, which she helped design, she's home.

At the operating table, Hamad commands Hermes, a voice-activated computer system, to tilt the table 45 degrees. A camera looms above, inside the operating light, and Hamad puts it to work: "Hermes, overhead camera, zoom out." The bird's-eye view of the patient, displayed across the room on a 42-inch digital plasma television screen, pulls back. The screen, one of six monitors here, is part of a video-router link that receives and broadcasts operations to residents and students at Pitt's new Charles G. Watson Surgical Education Center and the world beyond.

Around the table, pneumatic booms descend from the ceiling, hoisting suction and CO_2 machines off the floor, clearing the surgical staff's path. An endoscope guides Hamad through the patient's abdomen, where she performs stomach reduction surgery. A wireless digital headset displays the endoscopic image on a tiny monitor inches from her eyes. Hamad takes a second to pan the room beyond her headset; wide-eyed she says, "This is like Best Buy."

INVISIBLE KNIVES

Inside the gamma knife at UPMC Presbyterian, 201 beams of radiation vanquish a tumor that once prospered behind a man's eye. As he slid into The Oven, as the hulking device is known by some, the man smiled—a reaction common among those about to undergo this procedure. For it is extremely successful. And a marvel of precision: Through holes in a steel helmet bolted to the patient's head, the gamma knife delivers slivers of radiation through skin, skull, and into his brain, forming a three-dimensional confluence of therapy intersecting powerfully at the tumor. It's a little bit like filtering the sun's rays through a magnifying glass to burn a hole in paper.

The device was first used for treatment in the States in 1987—at Pitt. Some 5,000 procedures later, a robotic model positions the head at predetermined coordinates before zapping the offending tissue—another first for the nation and Pitt. "Much of the science behind the use of this technology has come from our institution," says Doug Kondziolka, a professor of neurological surgery and radiation oncology. More people come here for treatment of brain tumors, unstable tangles of blood vessels, and the tremors of movement disorders than anywhere else. The technology is about 90 percent effective in treating most of these conditions, though the rate drops to 35 for aggressive malignancies.

Most patients return home within 24 hours. Most never require treatment again.

ZEUS SUMMONED

Inventors set out in the early 1990s to create an omnicompetent robot that earthbound surgeons would use to perform procedures in space. The concept, however, gave way to a more practical use, heart surgery—on this planet. For Marco Zenati, director of minimally invasive cardiac surgery, the results have been especially rewarding: "It allows me superhuman capacity." Last year, Zeus assisted Zenati during the nation's first robotic coronary bypass on a beating heart.

Zeus, approved for investigational use only, is a command center on wheels. During surgery, Zenati sits at a console directing two robotic arms through joysticks, as if he were the robot's namesake. His brain fires instructions across synapses, his fingers twirl the controls, and electronic impulses hurl across the room through fiber optics. Inside the patient, mechanical wrists twist and thread sutures into a beating heart, moving one-tenth of an inch for every inch Zenati's wrists turn. Zeus eliminates hand tremors that one might experience while performing microsurgery with mere mortal hands.

On Mount Olympus the gods smile. ■

20 BATHHOUSE VISITS, 1,300 VOLUNTEERS, 17 DRUGS, AND 20 YEARS LATER

BY DOTTIE HORN

THE VIRUS KEEPS HIDING

In 1982, men would sometimes line up outside the Scaife Hall laboratory of immunologist Charles Rinaldo. Their hands grasped semen samples covered with plastic wrap or placed in glass jars, specimens they had brought from home. They were waiting so that second-year med student David Lyter could draw their blood in Rinaldo's tiny office. The immunologist had scraped together some money and joined forces with the student—they put out flyers and gave talks in local gay bars, asking men to come in and donate samples for a study. A mysterious new disease which seemed to target gay men had first been reported the year before.

JACK HOLLINGSWORTH | PHOTODISC

Charles Rinaldo posed for this cover of *Out*, a local gay newspaper, in 1983. His goal was to recruit 10,000 men into a study of AIDS. (The goal was later scaled back; about 1,300 men enrolled in a national study.) Those volunteers made possible 800 scientific articles.

Soon, Rinaldo, now a PhD professor of pathology at the University of Pittsburgh School of Medicine and chair of infectious diseases and microbiology at the Graduate School of Public Health (GSPH), had garnered funding from the National Institutes of Health (NIH) to study the new disease, which had come to be called AIDS. The Pitt Men's Study, housed in GSPH, was born.

Rinaldo and his team began recruiting gay and bisexual men into the NIH study in 1984. One or two nights a week, they would go to gay bars, coffeehouses, bathhouses. One of their haunts was the nightclub Pegasus. Arriving around 10 p.m., the researchers would walk past the dance floor, with its glittering disco ball and flashing, colored lights, to a back room, normally used for storage or as a dressing room for drag shows. The team would set up shop—taking out their informed consent forms and blood-drawing equipment. The club owner would announce that the Pitt Men's Study was there for the night. In some venues, the researchers would draw blood from an arm extended along a pool table or a keg of beer, all the while hearing the pounding beat of dance music through the walls. The recruiters usually stopped enrolling participants around midnight, but sometimes stayed until two in the morning answering questions.

In the clubs, standing on the edge of the dance floor, Rinaldo often wondered: *How many of these men will be alive in a few years?*

"I felt that we had to do something to stop the spread of this epidemic and learn more about it," he says.

The initial recruitment period lasted 12 months and resulted in the enrollment of 1,300 men. Every six months for the past 18 years, the study participants have come in for clinic visits. Since 1983, Rinaldo's study has received more than $47 million from NIH and has been used for more than 800 scientific articles—both epidemiological and biomedical. His is one of four sites in NIH's Multicenter AIDS Cohort Study, which is the largest study of AIDS among gay men in the United States.

In 1981, Rinaldo learned that the mysterious new disease involved T cell destruction, relating directly to his area of expertise. "To study the disease, I had to have volunteers giving us samples. Starting the Pitt Men's Study was a perfect opportunity for me as a scientist to do something constructive and important with this disease."

With the samples he has collected, Rinaldo studies how to give the immune system a better chance against HIV.

When the body is infected with a virus, the immune system's dendritic cells go into action, engulfing a few of the foreign invaders, tearing their proteins into small pieces. The dendritic cells then present these pieces of protein to the T cells, whose job is to hunt down and destroy the invader. The cells set out on a search mission, knowing what to look for—the piece of protein that the dendritic cell has shown them.

But, if the virus is HIV, the immune system can't get rid of it, not even with the help of drugs. If the patient is treated, the HIV simply goes into hiding. Rinaldo believes the T cells, in effect, can't see the hiding HIV. He wants to engineer the dendritic cells so that the immune system can better locate the virus.

The end result, he hopes, will be a treatment tailored to each individual: Extract some of a person's residual HIV, along with some of their dendritic cells. Expose the dendritic cells to bits of HIV protein that are not normally exposed to the immune system inside the body: Give them new ways to identify the lurking HIV. Put the dendritic cells back into the person's body. The theory is that the engineered cells will be better able to show the T cells how to find the hiding HIV.

Later this year, Rinaldo hopes to begin a Phase I clinical trial of the experimental treatment.

"We want to turn the T cell system on against this virus in a more potent and broader way," says Rinaldo.

The current standard of care for HIV infection is highly active antiretroviral therapy (HAART). For 50 percent of patients being treated with HAART, HIV infection is a chronic disease—requiring a lifelong regimen of multiple drugs, all of which are toxic and pose potential side effects like anemia and disturbances to the peripheral nervous system. If the patient stops treatment—even if the virus has been suppressed to barely detectable levels for years—the virus will come roaring back, wreaking destruction, within weeks. Even so, in half of the patient population, the treatment is controlling the virus so far.

In the other half, the HIV has mutated and become resistant to the drugs being used, and therapy is less effective. In these cases, clinicians experiment with the patient's drug regimen, trying to find a treatment to which the patient will respond. Some patients now have what is called multidrug resistant HIV—implacable to all of the 17 drugs currently available to treat the disease. The number of patients with multidrug resistant HIV is low, but growing.

More chilling: Some people are passing along multidrug resistant HIV to others.

"These patients, they're newly infected, they never had any drug exposure, but they're already precluded from any drug regimen because they have a virus which is resistant," says Michael Parniak, professor of medicine at the University of Pittsburgh School of Medicine.

"If we start getting widespread transmission of multidrug resistant virus, we're going to be back, possibly, to where we were in 1984, when people had a short life span once they were diagnosed, because there was no effective treatment,"

In the clubs, standing on the edge of the dance floor, Rinaldo often wondered: *How many of these men will be alive in a few years?*

says Parniak. "I'm getting scared. It's potentially a very devastating scenario."

Current drugs available for use against HIV target one of two viral enzymes—viral protease or reverse transcriptase. In an effort to stop multidrug resistant HIV, researchers are looking for new targets within the virus.

Parniak believes he has found a new target—even though it doesn't sound new.

It's reverse transcriptase.

Once HIV infects a cell, reverse transcriptase goes to work. First, it produces, from the virus' single strand of RNA, a corresponding strand of DNA. Then, reverse transcriptase degrades the RNA, which enables a second matching strand of DNA to be produced. (These double strands are then inserted into the cell's DNA, where they produce viral proteins.)

"Quite frankly, reverse transcriptase is the most beautiful enzyme I've ever come across," says Parniak, a PhD who first became fascinated with the enzyme under the auspices of Canada's Lady Davis Institute, directed by leading AIDS researcher Mark Wainberg.

Existing reverse transcriptase inhibitors target the part of the enzyme that performs the first job—producing the strand of DNA. But, the second job—degrading the RNA—is performed by a distinct and separate region of the enzyme. That region is called ribonuclease H.

Working with Pitt chemistry professor Dennis Curran, Parniak has found compounds that inhibit ribonuclease H. In initial studies, the inhibitors have proven effective against all known mutations of resistant HIV. The scientists hope to compile enough information to interest a pharmaceutical company in trying to develop a drug.

Such a drug, or a treatment involving Rinaldo's genetically engineered dendritic cells, would likely offer little hope in developing countries that cannot afford the drugs currently available in North America and Europe. Parniak believes the greatest promise for stemming the worldwide epidemic lies in prevention—and reverse transcriptase may be relevant there, too.

A few years ago, Parniak investigated an experimental reverse transcriptase inhibitor. He treated cells with the compound and then washed it off the cells. Then he tried to infect the cells with HIV.

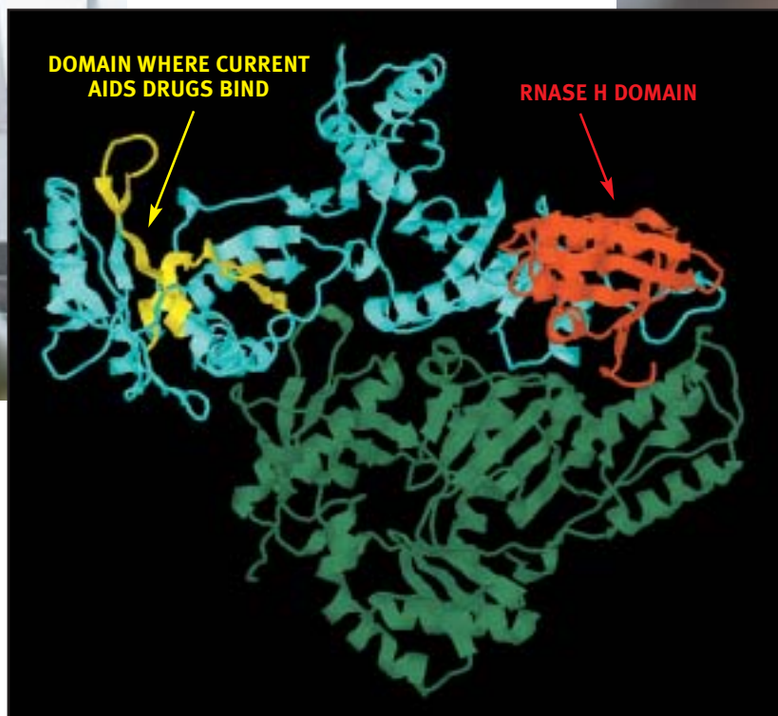
The cells were protected against infection.

"The compound turned out to be spectacular, unbelievably good," says Parniak.

Parniak's hope is that the compound can be used as one component of a vaginal cream that would prevent infection by the virus. A team of Pitt and other researchers recently has formed to work on the project.

Parniak believes such a cream could help control the epidemic. Heterosexual transmission is the primary mode for the spread of HIV worldwide; women account for 48 percent of those infected. "In a lot of relationships, a woman doesn't have a lot of say in whether the man uses a condom," he says. "A microbicide, like a cream, could be used by the woman to

PORTRAIT: CAMI MESA. DIAGRAM: COURTESY PARNIAK



Seventy percent of the drugs currently available to treat HIV infection target the viral enzyme reverse transcriptase, the molecular structure of which is depicted right. Existing reverse transcriptase inhibitors affect the part of the molecule shown in yellow. Pitt's Michael Parniak (above) and collaborators discovered compounds that disable another region of the molecule, called ribonuclease H (RNase H), shown in red. Because the new compounds target a different region of the molecule, they may prove effective against strains of HIV that are resistant to existing drugs.

provide a degree of protection even in the absence of a condom." A vaccine would be ideal to stop the spread of HIV, yet the possibility is years away. "A microbicide is a potential stop-gap measure to minimize the spread of the disease until an effective vaccine can be developed," he says.

The company licensing the drug believes it can go into clinical trials with the compound in about a year. Parniak is almost afraid to hope. "It's possible it'll go into clinical trials," he says. "One side of me is saying—*Please let that be the case*. The other side is saying—*We'll be real lucky if we get there*. But I'm leaning toward the optimistic side right now."

In dim rooms with dance floors and flashing strobes, Rinaldo in 1984 wondered how many in the local gay community would survive the new disease. Soon enough, he would get an answer. About one in five men who enrolled in his study (251 men) have died of AIDS.

Worldwide, the disease has claimed 22 million lives. Forty million alive today are infected with HIV. In some African countries, close to 40 percent of the adult population is infected. "I don't think we've even begun to scratch the surface in the devastation that this disease will cause," Parniak says.

In the United States, the number of those infected climbs every year. "There can be a feeling among some of the at-risk populations that because the drug regimens are so effective that there is actually a cure for HIV, and so there's less effort spent on prophylaxis," says Parniak.

The increasing rates of infection, the emergence of multidrug resistant virus, these are some of the reasons why the Pitt Men's Study, after 18 years, is enrolling participants again. With the help of a $4 million NIH grant, Rinaldo's study will expand to look at AIDS in young people and African Americans. (In the United States, 50 percent of new infections are in African Americans, who make up 12 percent of the population.)

Contrary to US public perception, AIDS is not under control, says Parniak—not even at home. "In the developed countries, I think we place too much faith in research—that we're always going to have a treatment. That may not be the case. This virus has proven to be unbelievably plastic. It gets around everything we've thrown at it," he says. "You don't know who's infected. Be cautious." ■

More chilling: Some people are passing along multidrug resistant HIV to others.

TAKE NOTICE, URGES JOHN MELLORS

One Saturday morning in 1985, John Mellors, who was then medical director of the emergency room at Yale-New Haven Hospital, was working when his brother-in-law Ruddy walked in. Ruddy, the youngest member of the family, was in his early 20s. Mellors evaluated him and immediately became worried. Ruddy had a cough and recurrent fever. That weekend, he developed *pneumocystis carinii* pneumonia. On Monday, blood test results came in, showing that Ruddy had no T cells. He was diagnosed with AIDS. At the time, there was no treatment for the disease. "He unfortunately passed away a little over a year after he was diagnosed," says Mellors, hesitating slightly as he tells the story. "That inspired me, the loss of my brother-in-law, to work on AIDS.

"I set out on what in retrospect was a naive course of events to become an HIV researcher," says Mellors. "I basically taught myself everything. *Here's the autoclave, here are the gloves*—that was my training, along with instruction in some rudimentary techniques in a virology laboratory."

Mellors came to the University of Pittsburgh School of Medicine as a professor of medicine in 1991. Soon after, he began looking at data collected on 180 men in the Pitt Men's Study. Using frozen samples, he measured the amount of HIV in study participants' blood (the viral load) from the early '80s. With coinvestigators in the Men's Study, he discovered that viral load correlated with the clinical outcomes of patients throughout the next 10 years.

"It showed that you could tell the probability of developing AIDS over a decade by one measurement," says Mellors.

"John demonstrated that it was a continuum—the lower the viral load, the better the clinical outcome," says Emilio Emini, senior vice president for vaccine research at Merck. Mellors' breakthrough gave clinicians the ability to gauge prognosis; it also told researchers working on drug development what to aim for—a lower viral load.

His current research focuses on trying to understand why treatment fails in some AIDS patients. Mellors is looking at the molecular level to find out how the virus changes so that it can bypass the destructive action of the drug.

Ultimately, Mellors believes, research and human ingenuity will develop a solution to AIDS, but he's not optimistic the epidemic will be controlled in his lifetime.

"AIDS is a test for humankind, and so far, we as a human race are not dealing with it very effectively," he says. "We're in slow motion."

The crisis, he believes, calls for a sustained, unified, well-led global strategy, the cooperation of governments, and billions of dollars. It also calls for reinforcements among the ranks of researchers. Whenever he has a chance, Mellors tries to inspire students to focus their careers on AIDS: "For this generation, born into a world impacted by AIDS, the question is, not having seen it evolve and spread from nonexistence to global pandemic, will they be more complacent about it?"

Many Americans, he notes, are dispassionate about the disease because they've never had a friend or family member die of AIDS—the majority of the three million who died last year from HIV/AIDS were in other countries (20,000 died in North America). Or Americans think AIDS is practically cured with the right medications.

"Here, sitting in Pittsburgh, most people can't relate to it," he says. "We're amazing creatures. Unless we have to step over the bodies on the way to work, we don't notice." *—DH* ■

CAMI MESA

America has become complacent about AIDS, believes John Mellors.

The brain may be one of the last great frontiers, but scientists thought they at least knew this much—such-and-such region controls thought, another controls emotion, another movement. . . . But there's much more interaction among regions than people thought. Pitt's Peter Strick, an expert on voluntary motor control, knocked the neuro community off its feet with his findings.

BRAIN STUDIES DELIVER DECISIVE BLOWS TO CONVENTIONAL THOUGHT | BY EDWIN KIESTER JR.

THE SWEET SCIENCE OF MOVEMENT

The first punch, high on the cheekbone, snaps the boxer's head back. Instinctively, he raises his gloves to protect himself. Welterweight champion Sugar Ray Leonard immediately seizes the opening to punish his opponent. Left-right-left-right-right, the flurry of punches coming so quickly the other man, flustered and knocked off balance by the fusillade, lowers his hands to shield his body. At that moment, Leonard throws a rocket-like right to the head. The opponent goes down.

To aficionados of what the writer A. J. Liebling called "the sweet science," that exhibition by Leonard, one of the fastest and most skilled boxers of his time, was a classic example of what used to be termed "the manly art of self-defense." To the University of Pittsburgh's Peter Strick, who's also a boxing fan, Leonard's rapid-fire five-punch combination represented something more—a shining example of a subject to which he has devoted a 30-year research career.

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Lightning-fast Sugar Ray Leonard rejoices after defeating Tommy Hearns to win the 1981 welterweight crown.

PHOTOGRAPHY | JEN URICH
EXCEPT WHERE NOTED

FROM LEFT: **Nathalie Picard, Donna Hoffman, and Richard Dum with Strick at his breakfast meeting haunt, Foster's in Oakland.**

In fact, Strick likes to show medical students video footage of Leonard throwing flurries of punches almost too fast for the camera to catch.

"When Sugar Ray hit a speed bag, obviously he wasn't thinking, 'Now I'll throw the left, now the right,'" Strick says. "The bag moved too fast for that. The punches were all part of one swift, sequential movement that was entirely preprogrammed somewhere in his brain."

Strick, a personable 55-year-old who discusses boxing and basketball as readily as neurons or glial cells, has built an international reputation as an expert on the brain's role in voluntary, automatic, sequential movement, the kind we perform fluidly, almost without thinking of the individual movements, like writing a signature, playing a glissando on the piano—or throwing a five-punch combo.

Strick's mouthful title is codirector of the University of Pittsburgh/Carnegie Mellon Center for the Neural Basis of Cognition (CNBC), senior research career scientist at the Research Service, VA Medical Center, and Pitt professor of neurobiology, neurosurgery, and psychiatry.

He's also a cartographer of sorts. By inserting a mild virus (such as herpes simplex) into an animal's brain and following its progress via staining techniques, his group has been able to watch the virus travel from nerve cell to nerve cell. The result has been a much more complete and detailed map of the brain's circuitry, disclosing previously little-known links between different brain regions.

"The conventional way of tracing brain connections told us which region of the brain connected to which other region, one connection at a time, the immediate inputs and outputs," Strick says. "But imagine trying to understand the New York City subway system or the London underground by only knowing where the train's coming from one stop before yours, and where it's going one stop afterward.

"The virus moves from neuron to neuron, over as many as five connections, and in that way we can look at the network of connections in ways never before possible. It's changing the way we think about the brain and certain areas of the brain.

"You can get a great deal of insight into the function of different brain regions by looking at how they're connected."

"Peter," says W. Thomas Thach of Washington University in St. Louis, a prominent expert in cerebellar research, "has made a cornerstone contribution to a fundamental area of cognition. The sophisticated viral tracing he developed was the pivotal step in what we now know about the field." Mark Hallett of the National Institute of Neurological Disorders and Stroke adds, "Peter is among the best investigators in the world on how the motor system works. His virus work is only his most recent contribution. He was already at the head of the pack before that."

Strick came to Pittsburgh in 2000 from SUNY Upstate Medical University in Syracuse, New York, bringing with him three longtime colleagues as principal investigators: the husband-wife team of Donna Hoffman (an expert on brain control of arm movement) and Richard Dum (renowned for his work on the spinal cord) as well as Nathalie Picard (whose discoveries have lent insight into how motor learning affects and changes regions of the brain). He also brought with him a primate colony, many of whose inhabitants, he notes, "have lived with us 15 years."

When Strick emerged from graduate school, what intrigued him most was the brain's role in voluntary movement, particularly movement of the hand. As his colleague Dum eloquently

"When Sugar Ray hit a speed bag, obviously he wasn't thinking, 'Now I'll throw the left, now the right.'"

points out, how we humans use our hands is what distinguishes us from other creatures, and what we use to make our world unique. Skillful hands allow us to create tools, build houses, paint pictures. The hand can perform hundreds of simple and complicated movements, from grasping and gesturing to playing a Beethoven sonata. Yet humans mostly use their hands automatically, without consciously thinking about the individual movements and without connecting movements to what signals are sent down from upstairs. A concert pianist does not deliberate about which finger strikes which key, but concentrates on phrasing, tempo, fortissimo, and diminuendo. The keystrokes are almost automatic, the result of trained fingering.

Strick's interest in voluntary movement, he acknowledges, may stem from his days as a schoolboy athlete. He attended high school in Philadelphia, where he was a basketball teammate of Reggie Jackson's (the same Jackson who turned to baseball and became known as "Mr. October" for delivering clutch home runs for the A's and Yankees in the World Series).

"Reggie wasn't too tall then, he grew after high school, but he was a strong forward with an incredible vertical leap, and he had an old-fashioned two-hand set shot from the top of the key. He was fascinating to watch. He was one of the few in those days who had learned how to dunk."

By the time Strick earned a PhD in neuroanatomy at the University of Pennsylvania, his own hoop time was relegated to the playground, half-court variety. After four years at the National Institutes of Health, in 1976, he went to Syracuse, where he held joint appointments in neurosurgery and physiology. There, he assisted neurosurgeons with the treatment of intractable movement disorders, like Parkinson's disease.

Then and now, most scientists pursued one or two techniques for investigating brain function. For example, some observe brains damaged by stroke or experimentally lesioned animal brains. Some electronically stimulate the brain and monitor what happens. . .

Strick prefers to pursue many approaches: "No one approach can give you the necessary breadth and perspective.

"Suppose one were to rely solely on the lesion approach to unravel the function of a brain region." He compares the lesion method to taking away a car's spare tire. "Remove the spare. What do you learn? One could come to the conclusion that the spare tire has no function because immediately after its removal, the car suffers no negative consequences. Obviously, the spare is needed for a certain specific set of circumstances. Unless we test those conditions, we learn very little about the function of the spare. The same is true for some brain lesions."

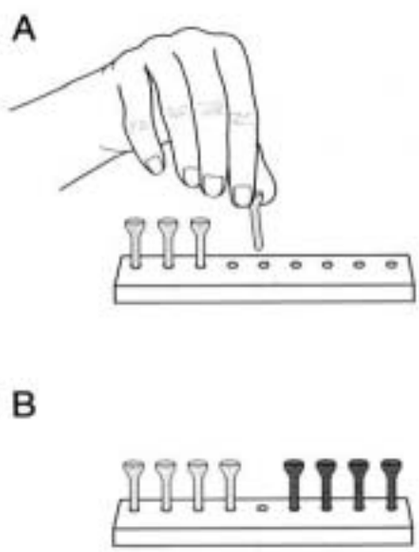
Among his many investigations in the '70s and '80s, Strick explored how the normal brain made fluid movement, like Jackson's dunk shot, possible.

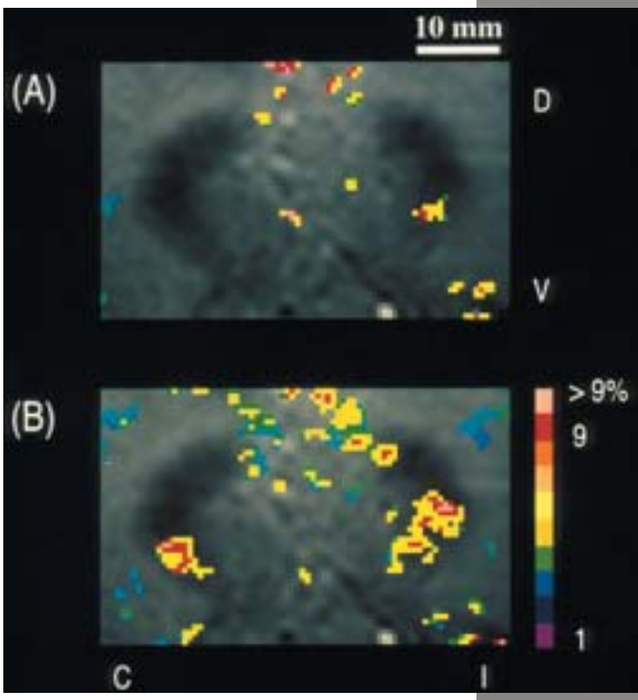
Eventually, he became interested in tracking brain connections. He tried several methods of injecting dyed substances into individual neurons and then monitoring the substances' movement. Then, in 1986, he came upon the viral tool.

Viral tools for tracing brain circuitry had actually been devised years earlier, set aside, and then revived by the late Hans Kuypers at Cambridge University in England. Kuypers injected a virus to chart brain connections in laboratory mice. Strick felt the method could be adapted for primates, and thus could have greater application for humans. He spent a couple of sabbaticals studying with Kuypers in Cambridge, then returned to Syracuse to put his lessons into practice.

Perfecting the technique took years; but he and a graduate student, Frank Middleton, reported success in primates in 1994. Their paper in *Science* was a heads up to cognitive investigators throughout the world, Thach recalls. Using viruses and antibody tracers attached to them, they were able to trace a multineuronal pathway to the prefrontal cortex, an area involved in higher executive functions and working memory, from the cerebellum—supposedly out of the thinking/emotion loop. In experiments with other students, Strick later showed that the prefrontal cortex and cerebellum were part of a closed loop circuit that continuously communicates information back and forth between the two remote structures.

Then in another eye-opening experiment,





With colleagues in Minnesota, Strick was among the first to report that the computational power of the cerebellum is applied not only to controlling movement but also to cognitive functioning. In A (above), study participants were asked to perform a straightforward task—i.e., moving the pegs, one by one, from one end of the board to the other—which slightly activated the dentate nucleus of the cerebellum, not surprisingly. When the participants were presented with a puzzle (B) that was much more difficult to execute, activation in the dentate nucleus was three to four times larger.

If you try to write your signature with your opposite hand, that hand will still follow the same pattern of movements to form the letters, however illegible the result.

Strick collaborated with Seong-Gi Kim and Kamil Ugurbil at the University of Minnesota. The group was the first to use functional magnetic resonance imaging at high magnetic field strength to examine the activity of the dentate nucleus of the cerebellum in humans. During scans, all subjects displayed substantial activation of the dentate during attempts to solve a pegboard puzzle. The area activated was three to four times greater than when activated during simple movements of the pegs. These results provided unmistakable evidence that the cerebellum was plugged into the thinking process.

Remember, the cerebellum—the fist-sized brain structure at the back of the head that sits atop the spinal cord—traditionally had been considered a lower brain center. Most thought it was concerned with such basics as coordination and balance, primitively signaling via the spinal cord when and how the muscles should act and move. It was thought to be removed from more sophisticated matters such as thinking and feeling.

Looking back, Strick offers a perspective on the cerebellum in terms that would sound familiar to anyone who has sipped a second martini: "Some cerebellar neurons are quite sensitive to alcohol, and if you drink too much, you can experience wobbliness, dizziness, unsteadiness, what is called 'ataxia.' Your speech becomes slurred, uneven. The alcohol reaches your cerebellum and affects your balance and motor movement. But there are also changes in behavior. You may become less inhibited. You may become aggressive. Your judgment is impaired. Maybe you make bad decisions. Now we're not just talking about simple movement and posture. What we call executive function has been interfered with.

"Clearly that portion of the cerebellum is involved with more than how you stand or move."

Strick's work substantiated what a rather unlikely pair of neurological commentators had been stating, to sometimes disdainful hoots, for several years. "Peter," says Henrietta Leiner, "confirmed in experimental work what we had been saying theoretically." Henrietta and Alan Leiner, who are married, both 88, and living in a retirement home in Palo Alto, California, are not neuroscientists by training but computer scientists. They became intrigued by the resemblance between computer wiring and brain circuitry. After her children had grown, Henrietta Leiner enrolled as a nondegree student at Columbia University to study neuroanatomy, bringing home armloads of texts to pore over diagrams of how the brain was put together. The couple concluded the role of the human cerebellum in human behavior had been vastly underestimated.

"You could clearly see that a huge number of fibers connected the cerebellum to the so-called higher brain centers," Henrietta Leiner, the more talkative of the two, said recently.

"When you see such a cluster of wiring in a computer, you know that a great deal of information is being communicated." Scientists had been using the monkey brain as a model, but it has far fewer such fibers than the human brain. In humans, the fibers are denser, and the dentate nucleus is larger. "The human cerebellum is clearly different," Leiner continues, "and much more involved than anyone believed. We call it 'the treasure at the bottom of the brain.'"

Strick read the Leiners' article, "Does the Cerebellum Contribute to Mental Skills?" when it was published in collaboration with neurologist Robert S. Dow in the journal *Behavioral Neuroscience* in 1986. Strick was, shall we say, skeptical of the paper: "I thought they were nuts." But when his own laboratory outlined the very connections between cerebellum and "higher centers" as the Leiners had predicted, he became a believer. Repeatedly, in experiments like the peg game, the cerebellum "lit up like a Christmas tree" (as Leiner likes to say), not only when the subject was actually moving pegs, but when mulling over the next move, brow furrowed, but hands still.

ERICA LLOYD

Henrietta and Alan Leiner

"The most important thing Peter has contributed," Leiner says, "has been to show for the first time that the cerebellum not only sends fibers and information to some prefrontal areas of the cerebral cortex but also receives fibers from these same areas. No one had ever seen that before. That means the cerebral cortex can talk to the cerebellum and exchange information. That kind of feedback loop is central to the computer.

"That concept led to a whole 'engineering way' of looking at the brain."

"The conventional view of the brain used to be one of localization," Richard Dum says. "This part of the brain controls movement, this part controls thought, this part does feelings. They each have their own discrete roles. But there is a lot more interaction and cooperation going on than was once believed. We have seen that the brain is much more complex than people thought."

Those complexities between voluntary motor movement and other regions of the brain are what intrigue Strick.

He cites an example. When you write your signature, you do it in one swift, practiced, fluid movement, like Sugar Ray Leonard throwing his combination of punches. You don't think about how to form the loops of the Es or when to cross the Ts. And if someone interrupts you midway through your scribbling, you may have to go back and start over. You can't just pick up where you stopped.

So what part, or parts, of the brain guides the pen?

If you try to write your signature with your opposite hand, that hand will still follow the same pattern of movements to form the letters, however illegible the result. Same if you hold the pencil between your toes and try to write that way. It won't exactly match your signature on a check, but, Strick says, "a handwriting expert comparing them would say they're by the same person. It's the same if you hold the pencil between your teeth. So it's not just a matter of hand and arm movement. The blueprint for that skill is stored somewhere within the brain."

But where? And in what form? Is the blueprint located in one place or throughout? Does that blueprint inflict structural changes, chemical changes, changes between the neuronal connections, changes in the way neurons reach out to each other? Those questions remain to be answered.

"That is," says Strick, "why I still have a job." ■

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Phitayakorn, Roy
University Hospitals of Cleveland, OH
Rosales, Carlos
University of Texas—Galveston, TX
Sorce, Damian
New York Presbyterian Hospital—Cornell, NY
Valenzuela, Yunuen
University Hospital Cincinnati, OH

SURGERY — PRELIMINARY
Davido, Helen
Ohio State University Medical Center, OH
Latt, Leonard
University of California, San Francisco, CA
Remy, Ludmio
Beth Israel Medical Center, NY

TRANSITIONAL MEDICINE
Williams, Sherida
St. Francis Hospital, PA

UROLOGY
Fletcher, Sophie
University of Virginia, VA
Ordonez, Maria Alexandra
SUNY Health Science Center—Brooklyn, NY

In July 1956, Chicago had already reported 169 cases of polio before the city made free shots of the long-awaited vaccine available.

IT WORKS!
THE VACCINE WORKS!

BEHIND THE HEADLINES

BY EDWIN KIESTER JR.

In these days of media saturation, it is difficult to picture what happened to John Troan 50-plus years ago. The young reporter for the *Pittsburgh Press* was assigned to "fill in around the ads" in the *Press*' annual health supplement. He "filled in" such good stories, Troan recalls, that he was conscripted as the paper's first medical writer. This was the early 1950s, when doctors in private practice were not allowed to talk to the media (it was considered unethical self promotion), though medical researchers could. At that time, Pitt's medical school didn't have much of a public-relations operation, Troan recalls. "Nothing," agrees Patricia McCormack, medical writer for the old *Pittsburgh Sun-Telegraph*,

Troan's crosstown competition. Not that Pitt was so different from other schools in that regard. Stanford, for instance, didn't institute a medical-school PR office until 1959. Until then, as at Pitt, press releases on such matters were covered by a small university PR office, written by whichever staff member caught (or didn't avoid) the boss' eye that day.

Troan's career eventually had him covering science in Washington, DC, for Scripps-Howard, then serving as editor of the *Press* before its demise. But first, he got the inside story of a lifetime at Pitt, as he recalls in his memoir, *Passport to Adventure* (Networks Press).

In his search for a good story, Troan regularly visited the office of Campbell Moses, MD '41, director of Pitt's Addison Gibson Laboratory. One day Moses suggested Troan look up "that young whiz the dean [William S. McEllroy] brought in from Michigan to set up a virus-research lab." Jonas Salk was working on an experimental flu vaccine and about to test it on 15,000 soldiers in New Jersey. Troan approached the researcher, who finally agreed to let him write about the test, but wanted to approve the article before publication (a proposal that would be handily dismissed today by most major dailies). Troan argued that Salk wouldn't be able to read it in time for the Sunday edition. "I'll make a deal with you," he told Salk. "If I foul the story up, you never need to talk to me again." Sunday afternoon, he received a telegram: *You did a splendid job. Jonas E. Salk.* Thus began a relationship in which Troan helped to write the parental consent form for the first polio vaccine field trials, edited Salk's statement when a batch of contaminated vaccine caused 200 cases of polio, and was generally the consummate insider—to the chagrin of his competition, who considered the relationship too cozy.

Polio was every parent's dread; 57,000 cases—mostly children and young adults—hit the United States in 1952, resulting in 21,269 deaths. The nation was frantic for a vaccine.

In 1949, Harvard's John Enders and colleagues found a way to cultivate the polio virus in a test tube—the key step that could lead to a vaccine. (They received the Nobel Prize in 1954.) Salk was diverted from his influenza research.

"Everybody was fooling around with the polio thing, and I thought I'd play around, too, and maybe get some experience," he told Troan. Pitt was among the universities commissioned the tedious work of classifying the various polio viruses; it was found they could be sorted into three main strains. Salk then began to investigate a potential vaccine using viruses from the three strains. Salk's associate Julius Youngner managed to exponentially increase the amount of virus they could grow and work with; his group then killed the virus with formaldehyde, while stimulating the production of antibodies against the disease. Researchers led by the University of Cincinnati's Albert Sabin dismissed the idea and were exploring a live virus vaccine.

One evening in May 1952, Troan met Salk just before a School of Medicine fund-raising dinner. Salk "casually" told Troan that he would soon begin tests of a vaccine on humans; it had already been successfully tested on monkeys, he said.

Salk "casually" told Troan that he would soon begin tests of a vaccine on humans.

"It is the first indication that science is so close to its goal of wiping out the scourge of infantile paralysis by vaccination—the way smallpox has been eradicated," Troan wrote for the next day's *Press*, and wire services soon took the electrifying story around the world.

In the next months, Troan reported on the first human tests comparing antibody levels in children undergoing treatment for polio with polio-free children who had been vaccinated. He then covered a small study in which 161 Pittsburgh schoolchildren were given the vaccine and others a placebo. (Eventually that test included 7,000 Pittsburgh children.) Before the Pittsburgh test, Salk inoculated himself, his three children, and his wife. All tests showed the killed-virus vaccine to be effective, and safe. The stage was set for a massive field trial of the vaccine.

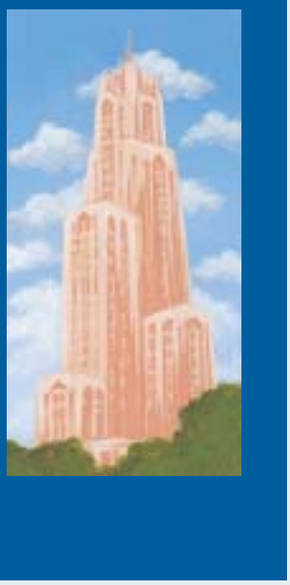
The trial began in April 1954 and included 1.8 million children in 12 states. In the double-blind study, 425,440 children received three injections of vaccine, another 203,206 received a placebo, and others were considered controls. Researchers monitored the children throughout the polio season; the final results were evaluated by a team at the University of Michigan led by respected epidemiologist Thomas Francis. The final evaluation was to be announced in Ann Arbor on April 12, 1955. But on April 3, Troan's pipelines revealed enough for him to announce, via the *Press:* "The Salk vaccine will be released for general use—probably within 10 days."

On April 12, he was in the huge throng that descended on Ann Arbor. "The formal verdict on the Salk vaccine was disclosed today amid fanfare and drama far more typical of a Hollywood premiere than a medical meeting," wrote William Lencde for the *New York Times*. Indeed, the news release distributed by the University of Michigan News Service caught the drum-beating atmosphere—"The vaccine works. It is safe, effective and potent." Troan's own story, dictated over telephone to the *Press*, ran under, as he puts it, the "most satisfying headline of my reportorial career: 'Polio Is Conquered.'"

As news poured out of Salk's laboratory, Pitt had established its own medical public-relations office, directed by the late Tom Coleman. Coleman, as Troan recalls, was on hand for the Ann Arbor "feast." But neither he nor Salk nor anyone else was prepared for the clamor that followed. The scientist was in huge demand for interviews, TV and radio appearances, presentations, awards, even a White House visit. One college, unable to get Salk to accept an award personally, asked Troan to appear in his stead. (Troan demurred.) Coleman was assigned to deal with the onslaught. He fielded so many requests that he lost his voice.

In his memoir, Troan reports that with Salk's encouragement, the medical news service attempted to rename the "Salk vaccine" the "Pitt vaccine," but the idea never took, even with Troan: "As a personal favor, I did switch . . . but gave up when 'Salk' exhibited greater staying power."

Still, by whatever name, the vaccine had put Pitt medical research, its media relations program—and Troan—into the big leagues. ■



CLASS NOTES

'50s

Melvin L. Cohen, MD '53, is the director of medical education at Phoenix Children's Hospital, a position he's held since the hospital was founded in 1983. For the majority of the hospital's history, Cohen was the only pediatric nephrologist, which means, among other things, that he knows what it's like to cut short a fishing vacation to tend to a patient in critical condition. It's rewarding for him to do little things for the kids in the hospital; for one child, he obtained a basketball autographed by the Phoenix Suns. The hospital's new conference center recently was named in his honor.

'60s

Richard Trackler, MD '61, recently published the novel *The Roll Call Vote* (Pentland Press, Inc.). The book follows a US president's struggle to confirm a controversial Supreme Court candidate. Trackler, who was a radiologist and founding member of the San Diego Diagnostic Radiology Medical Group, retired recently after 22 years of private practice, which he began after working at several universities.

Harvey Golomb, MD '68, has been chair of the Department of Medicine at the University of Chicago since 1998. He enjoys nurturing residents and younger faculty members, and he's proud of establishing four new clinical centers: an asthma center, a memory center, an emergency resuscitation center, and a cancer genetics center. Golomb says he moved the department's books to the black, adding that he developed his business skills selling toys for the Squirrel Hill Newsstand, which his parents once owned.

L. Gregory Pawlson, MD '69, is executive vice president of the National Committee on Quality Assurance, a Washington, DC-based organization. The group investigates everything from the quality of hospitals to HMOs to primary care physicians to specialists. He is the only medical officer in the organization.

'60s RESIDENTS AND FELLOWS

Gilbert A. Friday Jr. (Pediatrics Resident '62–'63, Allergy and Immunology Fellow '62–'67), recently retired from the University, where he'd been a professor of pediatrics since 1968. Now in private practice, Friday is conducting research indicating that intravenous gamma globulin can interfere with autoimmune antibodies in patients with polyendocrinopathy. Polyendocrinopathy is a rare autoimmune disease that produces symptoms such as hypothyroidism, the erosion of enamel from teeth, and a loss of pigment in skin. Gamma globulin has been used as therapy for some genetic diseases, such as multiple sclerosis.

1976 Owl

Robert Goldwyn, (Plastic Surgery Resident '61–'63) recently retired after 34 years as a plastic surgeon at Beth Israel Deaconess Medical Center; he still teaches at Harvard University. He recently completed editing the third edition of the textbook *The Unfavorable Result in Plastic Surgery: Avoidance and Treatment.* He says that some patients who opt for such surgery have unrealistic expectations. Surgeries that are "technical" successes may not meet the patient's standards. The intent of his book is to help doctors deal with the gap between expectations and reality.

'70s

Ira M. Weissman, MD '71, has been in private pediatric practice in Malone, New York, since 1988. His former classmates might recognize him from a recent segment of *60 Minutes.* One of his patients suffered recurrent, life-threatening seizures affecting regions of her brain controlling pulmonary and cardiac function. He believed the mother was smothering the child, especially since the girl's older sibling had similar episodes. Another set of doctors disagreed and gave the girl a pacemaker. The child died anyway, and investigators discovered that she, indeed, was smothered. Her mother was convicted of murder: A jury found she was trying to obtain Social Security money. Weissman was featured on the CBS show in January.

Kathy Helzlsouer, MD '79, is a professor in the Bloomberg School of Public Health at Johns Hopkins University. Until recently, she directed the Breast and Ovarian Surveillance Center at Hopkins. For several years

WE KNEW YOU WHEN | LOIS POUNDS OLIVER

Lois Pounds applied to the School of Medicine after five years of nursing. She was told, "We don't take trade school students." Yet she was admitted, and in 1965, she earned her MD from Pitt and moved smoothly into pediatrics. By 1972, Pounds was director of the pediatric outpatient clinic at Duke Medical Center, where she taught every Duke University med student—"the best way," she says, laughing, "to win a Golden Apple." Pounds returned to Pitt in 1974 as associate director of the ambulatory care center at Children's Hospital of Pittsburgh and soon married Tim Oliver, longtime chair of pediatrics. In the union she took his name and half of his Steelers season tickets.

In 1984, after several years on the School of Medicine's admissions committee, Lois Pounds Oliver became associate dean for student affairs. On her second day, she had to dismiss a student. The incident was an anomaly in her career. "It's a wonderful job working with young people,

Pounds Oliver 1964

Helzlsouer has run a large community-based study in Washington County, Maryland. One group gave blood in '74, the other in '89, and she uses their samples to determine if certain environmental and genetic factors contribute to cancer. Helzlsouer just finished another project investigating the effect of carotenoids, micronutrients including antioxidants like carotene, on reducing breast cancer. While preliminary results indicate they don't have an effect, Helzlsouer continues to search for preventive measures.

'70s RESIDENTS AND FELLOWS

Sandra Schneider, MD '75 (Internal Medicine Resident '75–'78), director of medical emergency services at Montefiore Hospital from 1981 to 1992, is chair of emergency medicine at the University of Rochester, New York. She put her work on poisonous mushrooms aside for administrative responsibilities, but now investigates ways to improve efficiency in the emergency department at Rochester's Strong Memorial Hospital. Before Schneider's arrival, ED doctors were spending a lot of time trying to notify primary care physicians about their patients in the ED. Since the ED added a "communication" nurse, these doctors now spend more time with patients.

David Mallott, MD '78 (Internal Medicine Intern '78–'79), is the associate dean of medical education and an associate professor of psychiatry at the University of Maryland School of Medicine, in Baltimore. He directs the school's problem-based learning program, which gives students a practical scenario to work out. (One group needed to treat a woman on welfare, so in addition to learning about her medical conditions they applied for welfare.)

'80s

Peter G. Gerbino II, MD '86, an instructor of orthopaedic surgery at Harvard Medical School, is examining whether football causes an increase in degenerative back problems. Although improper and excessive weightlifting causes some long-term effects, Gerbino says explosive spine hyperextension—which can occur when football players line up for the snap, shoot from crouching to standing positions, and crash into each other—causes many stress fractures, often leading to crippling back pain in older years.

'90s RESIDENTS AND FELLOWS

Laurence M. Katz, MD '87 (Emergency Medicine Resident '90–'93), is an associate professor of emergency medicine at the University of North Carolina, where he is conducting research on restoring neurological function in patients who nearly drown or suffer heart attacks. He suggests that inducing a "hibernating state" in such patients can reduce long-term brain damage. Katz's animal studies show that an investigational synthetic drug can induce a hibernating state and decrease brain damage after asphyxial cardiac arrest. His interest stems from his residency under Pitt's Peter Safar.

'00s

Hugo "Jamie" Pfaeffle, PhD '98, MD '00, shares a family story: When he was a child, Pfaeffle's father arrived home to find him blue, choking on his own vomit. Quickly, the elder Pfaeffle performed cardiopulmonary resuscitation, saving his son—one reason the younger Pfaeffle is now in medicine. As a resident in the orthopaedics department at Pitt, he recently received a grant from the Orthopaedic Research and Education Foundation. He will use the $10,900 grant to study improved treatments for the interosseous ligament. The ligament can be severed during extreme fractures, and current treatments sometimes disable range of motion. *—MH*

especially people as bright as medical students," she says. In 1987, the Olivers moved to North Carolina, where she accepted a similar position at Duke. She retired officially in 2000.

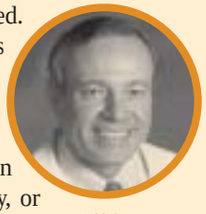
Today, Oliver is a docent at Duke Gardens. She refuses all conversation during Blue Devil basketball games. *—DRE*

Pounds Oliver with husband, Tim Oliver, and soccer champ, Kelsey

THE WAY WE ARE: CLASS OF '62

BY MEGHAN HOLOHAN

When John Hibbs (MD '62) was in med school, he thought he'd be an internist. After an internship in Oregon, Hibbs was drafted into the army. He was stationed in Panama when he heard the National Institutes of Health (NIH) was in Bolivia investigating a fever epidemic later shown to be caused by the Machupo virus. Patients were developing rashes, severe headaches, muscle aches, low platelets, and going into shock. Sixty percent of those infected were dying in Bolivia. They needed more Spanish-speaking doctors, so Hibbs volunteered to help. Those adventures convinced him of the importance of basic science that his professors at Pitt had emphasized. Hibbs has spent his career investigating macrophage chemistry, helping to understand its role in controlling inflammation and immune responses. He published the important discovery that macrophages release nitric oxide from L-arginine, indicating that nitric oxide production could be related to inflammation and cell-mediated immunity.



Hibbs

Barry Brenner (MD '62) left Pitt with a research career in mind. His work in nephrology led to his formulation of the well-known glomerular hypertension theory, or "Brenner's Theory." He recently retired as director of the renal division at Brigham and Women's Hospital and director of the Harvard University Center for the Study of Kidney Disease. Time for some new blood to run things, he noted, with high hopes for novel ideas the next generation might spawn.

Heidenreich with wife, Audrey Heidenreich, and grandchild

Hibbs and Brenner's classmate Fred Heidenreich (MD '62) left the School of Medicine with a sense of purpose. In the late '60s, he landed at Allegheny Valley Hospital, outside Pittsburgh, where he was instrumental in the development of the hospital's cardiology department. He recalled the excitement then of purchasing the latest technological advancements, like the echocardiograph. Medicine runs deep in Heidenreich's family. Three of his four children are doctors; two attended Pitt—Fred Heidenreich Jr. (MD '93) is a pediatric orthopaedic surgeon at Children's Hospital of Pittsburgh, and Michael Heidenreich (MD '96) is a vascular surgery fellow at the University of Maryland, Baltimore.

Brenner (the 1995 Hench Award winner) was unable to attend the June reunion, organized in part by David Jacobs, president of the Class of '62, a urologist in private practice in Pittsburgh, but Hibbs and Heidenreich did. When we spoke with Hibbs, he was looking forward to hiking some western Pennsylvania hills. Heidenreich planned to check in with his friend Bob Israel; the two met in 1958 in an undergrad Greek and Latin medical terminology class. How do you say "Hail to Pitt" in Greek?

ON THE ROAD: CALI

Bebe Miller (MD '55) and his wife, Gwen Miller, packed a few treasures for Pitt Med on the Road to California in May. Goodies from the "Bebe Bag" included Scope and Scalpel programs from yesteryear, to the delight of Mary Ann and Sam Aronson (MD '55), who were among the 40 alumni and friends attending the reception at the home of David Mendelson (MD '64) in San Francisco. Aronson recalled brainstorming for a school play, "something to bring the class together after their clinical years" with Frank Dixon; that conversation begot the first Scope and Scalpel. As guests thumbed through Bebe treasures, Harry and Winifred, Mendelson's 1-foot tall corgis, provided interventions if food happened to drop to the floor. Harry and Winifred had the advantage, since everyone was agape at the host's art collection.

Pitt on Pierce St. in San Francisco

Parag Nene, MD '01, who landed an internal medicine residency at the University of California, Davis, noted that he has been yearning to delve more into his artistic side. His new band, tentatively named Seventh Heaven, combines Western and Indian sounds: "We're going for a George Harrison kind of thing," Nene said.

Miller spoke about his experience as a senior mentor, a new Pitt program that reaps the talents of retired faculty by having them work with students during problem-based learning sessions. Miller, an ob/gyn, is not sure how he was picked for anatomy: "Regarding anything above the belly button and below the pubis, I keep quiet."

The ob/gyn ranks made a strong showing at the gathering. Per Sandberg, Res '96, remembered Miller as an attending—"always entertaining." Sandberg is now at the University of California at San Francisco (UCSF), where he specializes in critical care in pregnancy. His colleague, Sharon Knight, Res '98, came too; she works with women dealing with pelvic organ prolapse and incontinence. Rebecca Yee, MD '95, also in the UCSF group, was on call—but happily, not pulled away.

"That would have never happened at Magee," noted Miller. *—EL*

Big thanks to the California reception hosts: David Mendelson, MD '64, San Francisco; Robert Berk, MD '55, and George Leopold, MD '62, of La Jolla; and in Los Angeles, Elaine and Jeff Kamil (both MD '73)

ABOVE: Joseph Manzini, MD '83, and John Bednar, MD '66, in La Jolla. LEFT: Joanne and Lawrence Green, MD '68, at the LA fete.

ROBERT J. CORRY
DECEMBER 3, 1934–FEBRUARY 11, 2002

Corry 1978

His knowledge of the pancreas was legendary. While the organ frustrated some, for it contains powerful enzymes that can damage surrounding tissue during surgery, Robert J. Corry was undaunted. He developed techniques around the problem, tried to expand the national organ donor pool, and investigated ways that transplant patients' immune systems might better accept their new organs. In all, the University of Pittsburgh professor of surgery and director of the pancreas transplant program at the Thomas E. Starzl Transplantation Institute performed more than 350 pancreas, 180 kidney, and 50 liver transplants. The former president of the American Society of Transplant Surgeons also played an important role in the development of islet cell transplantation—which has been performed experimentally to cure diabetes. *—DRE*

GALAL M. ZIADY
AUGUST 21, 1939–MARCH 17, 2002

Galal M. Ziady came to the University of Pittsburgh from Egypt 15 years ago because his son needed a kidney transplant. By then, his wife, Laila Ziady, already knew she'd married a wonderful man. It wasn't that a father was giving his son a chance to live; he was like most dads, who would offer both kidneys if they could. It was something more—how Ziady, who eventually became director of clinical cardiology at the School of Medicine's Cardiovascular Institute, treated everyone like family. (On a professional level, he was also able to do something for his friend Thomas Starzl, by watching over his cardiac care.)

Ziady

His were simple but beautiful gestures. Like the time he gave money to a single mother who couldn't afford shoes. Or the way he would take a young resident under his wing. Or how he would talk with those he'd just met, as if they were old friends, listening, really listening, because he wanted to understand. "He was uncritical," says his wife, and for that people loved him.

Many friends have called Laila Ziady recently to tell her, "He was like my father." She thinks of one boy in particular who's now 14. He used to play chess with the cardiologist while his mother visited with Laila Ziady. On their way over, he'd say, "I hope that beeper doesn't go off." *—DRE*

IN MEMORIAM

'20s
RICHARD C. SNYDER (MD '29)
MARCH 26, 2002

'30s
JAMES C. DOBLER (MD '31)
APRIL 23, 2002

LEONARD B. VOLKIN (MD '35)
APRIL 12, 2002

'40s
ROBERT J. DEAN (MD '42)
JULY 15, 2001

'50s
JACK M. ULRICH (MD '52)
APRIL 12, 2002

THOMAS S. VATES (MD '55)
MAY 19, 2002

FACULTY
ROBERT J. CORRY
FEBRUARY 11, 2002

GALAL M. ZIADY
MARCH 17, 2002

NOTE: A PRIMARY SOURCE FOR DEATH NOTICES OF OUR ALUMNI, THE AMERICAN MEDICAL ASSOCIATION, NO LONGER PRINTS AN OBITUARY LIST. WE ENCOURAGE YOU, MORE THAN EVER NOW, TO LET US KNOW ABOUT ALUMNI WHO DIED RECENTLY. (ON THE INSIDE FRONT COVER YOU'LL FIND CONTACT INFORMATION FOR THE MAGAZINE.)

ZANE GATES: ON MAGICAL POWERS

BY JOSIE FISHER

MITCH KERN

At the clinic he founded, 90 percent of Zane Gates' patients are working but uninsured.

Zane Gates, MD '95, examines his first patient of the afternoon, a man who has lost 30 pounds in the two months he has had diarrhea. As Gates takes the patient's history, he hears a familiar litany: Full-time laborer. Several work-related injuries over the years. Last doctor visit—can't remember. "No health insurance," adds Gates. Ninety percent of his patients at Altoona's Partnering for Health Services free clinic (which isn't the first such clinic Gates has founded) are working people who cannot afford health insurance. "Yet, if a person makes 20 cents an hour over minimum wage," says Gates, leaning into his pet peeve, "they're not eligible for Medical Assistance."

The 34-year-old Gates grew up not far from here, in a housing project, where "we believed you had to have some kind of magical power to be a doctor," he says with a laugh. His sense of humor wanes when his next patient complains of recurrent chest pain and shortness of breath. The retired woman has a stent. Her blood pressure is up—she thinks it's the stress of caring for her husband, who has cancer. He's covered by the VA. She's not. "As if she's not part of him," says Gates. "Sweetheart, let's get you a test over at my office." Winding through a labyrinth of hallways on the way to Gates' family medicine practice, the patient starts to cry. Gates put an arm around her shoulder.

The staff at Gates' group practice compliment him on his tie, decorated with tiny red hearts and the words "nice and nasty," a Valentine's Day gift from the free clinic's nurse and office manager—who are that clinic's only paid staff, though Altoona physicians volunteer and area nurses and specialists help out a lot. The hospital supports the clinic as well. Between bites on a red cupcake from his private practice's kitchen, Gates notes that the clinic is the only area respite for an economic stratum of patients who otherwise might end up desperately ill in the emergency room, "where the hospital would pay for it anyway." He checks the EKG results, then gently approaches his patient: "Honey, how do you feel about going to the hospital?"

En route to the next exam back at the free clinic, Gates greets a woman checking out at the front desk. The 40-year-old mother of five would look 10 years younger with her strawberry-blond ponytail—except for the exhaustion that shows when she talks about trying to get health care: "It costs $100 per week per family on my husband's plan. There's no way we can afford that." Several years ago, her eye started swelling; because she was pregnant, she was eligible to see a doctor through the state program, Access. Diagnosed with Graves Disease, she began treatment and was in remission. Now, unable to afford thyroid medication for a year, a racing heart keeps her awake at night. Her Access card ran out with her son's last well-baby check-up, and she's not eligible for Medical Assistance. "I tried to fight it. I wrote my state representative—" She holds a referral from Gates for an ophthalmologist and lab and prescription vouchers. "I was so afraid I'd be denied here today."

"This," Gates says, referring to his clinic patients, "is not how they thought it would be after all these years." He remembers his own difficult times, like in medical school—when burnout hit like a brick wall. "I was gonna quit," he says with a laugh. But then he volunteered for Operation Safety Net to care for the homeless. Gates devoted one night a week to the program. The experience was defining: "This is the neat thing about being a doctor. I'm one man, but I can help these people during some of the darkest times of their lives—with just my time and my knowledge."

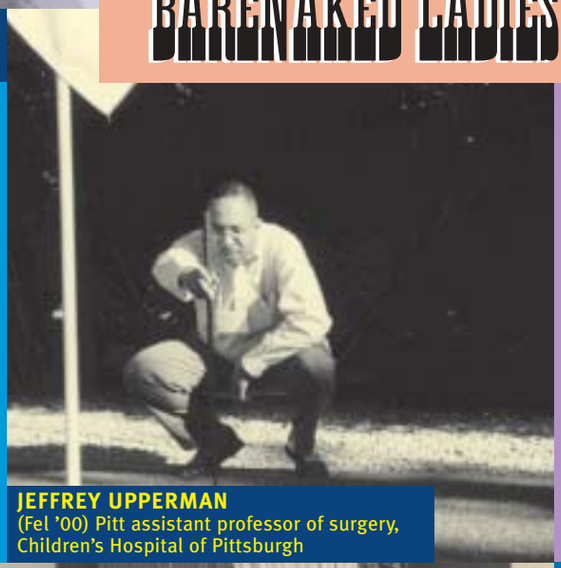
Gates has published a novel, The Cure, *a mystery about a boy whose blood cures cancer. Half of the proceeds go to the Gloria Gates Memorial Foundation for Children, which Gates founded in honor of his mother who died while he was in medical school. The foundation provides after-school programs for Altoona's Evergreen Manor Housing Projects.* The Cure *is available from amazon.com.* ■

GISELLE HAMAD
Medical director of bariatric and minimally invasive general surgery at Magee-Womens Hospital

BOB SEGER
JOHN MELLENCAMP
MATCHBOX TWENTY
BARENAKED LADIES

ROBERT GOLDWYN
(Res '63) Retired after 34 years of plastic surgery at Beth Israel Deaconess

JOHN COLTRANE
MILES DAVIS
ROY HARGROVE
THE POLICE
LED ZEPPELIN



JEFFREY UPPERMAN
(Fel '00) Pitt assistant professor of surgery, Children's Hospital of Pittsburgh

Edith Piaf
Paganini
and Brahms

PETER FERSON
(MD '73) Pitt professor, chief of thoracic surgery at VA Hospital

Silence.

music in the OR is "sacrilegious"

ROBERT BRAGDON
(MD '73) Private practice plastic surgeon in Pittsburgh, president emeritus of the Medical Alumni Association

Jean-Luc Ponty
Mendelssohn
ALICIA KEYS
DAVE MATTHEWS BAND
India.Arie

Another Pitt Med match: Guess who listens to what music in the OR. (And who prefers the sound of silence.)
Answers, inside front cover.

Music Illustrations | Michael Lotenero
Photography | Various

CALENDAR

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student_affairs@
medschool.pitt.edu

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Pittsburgh
For information
Bernard Michaels, MD '42
412-683-7005

DR. RICHARD N. HARRIS MEMORIAL GOLF OUTING
OCTOBER 7
Edgewood Country Club, 1:30 p.m.
Pittsburgh
For information
John G. Kokales, MD '73
412-647-4567
kokalesjg@msx.upmc.edu

SCHOOL OF MEDICINE HOMECOMING BREAKFAST
OCTOBER 26
University Club, 9 a.m.
Pittsburgh
For information
Jennifer Rellis
877-MED-ALUM
jrellis@medschool.pitt.edu

HOMECOMING GAME
OCTOBER 26
Pitt vs. Boston College
Time TBA
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Ross H. Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

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OCTOBER 25 AND 26

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Herbert Tauberg, MD '52
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CLASS OF '67
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Richard Raizman, MD '71
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Richard Kasdan, MD '72
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Freddie H. Fu, MD '77
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CLASS OF '87
Jon Levy, MD '87
412-441-7775

CLASS OF '92
Evan Baker, MD '92
412-464-1969

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NOVEMBER 15 AND 16
Peter Randall, MD, Speaker
For information
Ross H. Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

23RD PETER AND EVA SAFAR ANNUAL LECTURESHIP
NOVEMBER 21
Scaife Hall
Lecture Rooms 5 and 6, 4 p.m.
Lyn Yaffe, MD, Speaker
"Future Medicine—Biomedical Technology Systems for Victims of Combat and Terrorism"
For information
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I SEE A FUTURE

You will meet the average member of the School of Medicine's Class of 2002. You will learn the graduate has a debt burden of $128,000 and has decided a career in primary care medicine won't adequately pay the interest, let alone the balance. You will soon meet other recent med school graduates making similar realizations. And you will make a decision of your own: You will call 877-MED-ALUM to contribute to a scholarship fund for future medical students.

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