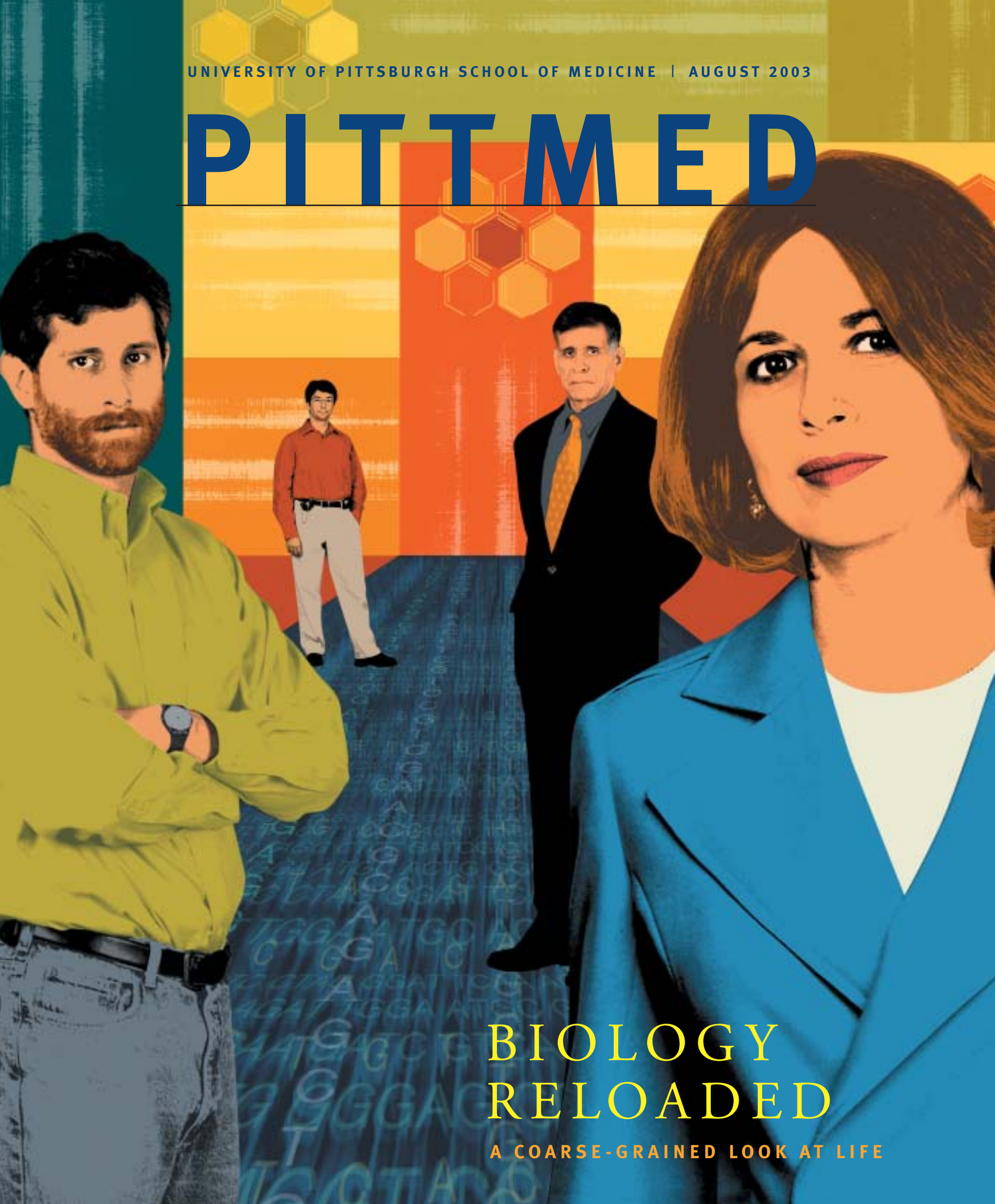
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | AUGUST 2003

PITTMED



BIOLOGY RELOADED

A COARSE-GRAINED LOOK AT LIFE



BE BRAVE, HE SAID

I quit surgery after one year of residency, and yet I will owe Dr. Henry Bahnson a debt of gratitude for the rest of my life. I'd lost my fiancée and my father within a week during my second year of medical school. Hank's kind instruction after that time both helped to distract me from grief and gave me inspiration to become a quality physician. When I told Hank 10 years ago that I would be leaving Pitt to train in psychiatry instead, I could have sworn I saw a tear in his eye. It wasn't that I was that good a surgery trainee; more likely he was disappointed because he'd put so much grandfatherly care into mentoring me and my colleagues. I was taking his kind investment elsewhere.

I'm now successful beyond my wildest dreams, and happy. When challenges come my way, I sometimes think of Hank's spirit, and why it is that I ever went into medicine. In the past decade I've slowly healed the bruises from that part of my life and am able to more clearly see and appreciate the people like him who gave so much to us.

This November, I had an urge to call Hank in particular and thank him. I didn't tell him I had a new challenge in my life, nor that I missed his grandfatherly advice. I just told him thanks for everything and that I hoped he was doing all right. He knew the passing of his wife was on my mind; he said, with a stiff upper lip, that he certainly missed her.

I never told him about the difficulty I had in reaching my current point in life. Still, he had a perfect "answer" for me. Before hanging up, he said something that surprised me with its unusual nature in phone conversation but made me think for a long time: "Be brave young man and trust in your training. Be brave."

I didn't know why I'd felt the sudden urge to call, until your recent tribute. His last words to Bartley Griffith were the very same as they were to me. He was a grandfather to thousands of physicians, and he lived his life true to his word.

Paul Dobransky (MD '93)
Denver, Colo.

LOOKING OVER THEIR SHOULDERS

The note on Davenport Hooker ("Last Call," May 2003) got my wheels turning. I think and speak of him often.

My contact with Dr. Hooker began in 1938, when I was a freshman in anatomy, and continued when I was a student assistant until 1941. He was a role model for most of us, commanded respect from all, yet was always fair and direct. He was always "Dr. Hooker" to us as we sat around the lunch table next to Drs. Donaldson, Hogg, and Humphrey, and he also brown-bagged it with us. He ran a tight lunch hour as he directed pointed questions about our projects as well as about the administration of the dissecting lab.

The last time I saw Professor Hooker was as an intern in 1943. I was in the accident room of Presbyterian Hospital, suturing a scalp laceration of one of his colleagues. He stood by my left shoulder, observing my technique. He kept in touch with each of us when we were overseas, and I still treasure his letters.

James F. Culleton (MD '43)
Mirror Lake, N.H.

On July 4, 1952, I had the good fortune of visiting Yale University specifically to seek out my University of Pittsburgh anatomy professor, Dr. Davenport Hooker (a Yale alumnus), then retired. He and I spent a delightful afternoon. We reminisced about the University of Pittsburgh School of Medicine and his favorite class—our Class of 1946. Dr. Hooker outlined his retirement plans to me and 50 years later helped me define my own retirement plans. I shall always recall that visit as being a most memorable event.

Carmello A. Ranii (MD '46)
Sharpsburg, Pa.

In September of 1943, as freshmen in the medical school, we were inducted into the Army Specialized Training Program as privates. We were required each afternoon to leave the anatomy lab, march to Shadyside Academy, and exercise in the hot sun for one hour. We then marched up the hill to the medical school, climbed the stairs several floors back to the anatomy lab, and attempted to resume our gross anatomy study. It was truly grueling.

One hot afternoon, Professor Hooker, 30 years our senior, joined us in this activity from beginning to end. He then convinced the army to stop this torture and allow us to continue our medical studies.

Martin H. Kalser (MD '46)
Miami, Fla.

OTHER LIVES MATCH

Answers to LAST CALL (p. 40)—
Forbes: minister; Johnson: oceanographer; Wall Street analyst, and urban redeveloper; Reichman: percussionist; Wilson Childers: sign language interpreter; Zeidel: salad chef

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

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PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE | AUGUST 2003, VOL. 5, ISSUE 3



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New light shed on miscarriages.
Breaking bones in the backcountry.

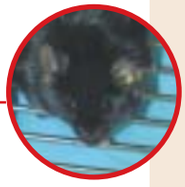
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You can take the oceanographer out of the doctor, but you can't take...





CONTRIBUTORS

ROBIN MEJIA — ["Addictive Research"] Around the offices of *Pitt Med*, we wonder if the FBI has a file on science writer Robin Mejia. She has a file on the bureau. In articles for the *Los Angeles Times* and *New Scientist*, Mejia has reported on the FBI's false assumptions about chemical analyses supposedly linking bullets from crimes with suspects' ammunition. Investigative reporting like this won the California-based freelancer a Soros Justice Media Fellowship this year. JOHN RITTER — [Cover and "Biology Reloaded"] Drawn by a spirit of freedom and rebellion, John Ritter embraced punk rock and skateboarding as a teen. As a freelance illustrator, he now enjoys the freedom of working for himself in his own studio. Ritter produces about 150 illustration projects a year for clients that include *The New Yorker*, *The Atlantic Monthly*, and *Men's Health*. And although he broke his hip skateboarding a year ago, the 38-year-old still skateboards almost every day. He lives in the Point Breeze neighborhood of Pittsburgh. GEOFFERY KURLAND — ["A Doctor's Run"] The writer and pediatric pulmonary specialist says some of his patients and their families have read his memoir of his experience with a rare leukemia: "It gives them insight. Though some say they learn more about me than they wanted to know." The best news: Kurland seems to be healthy these days, yet every time he qualifies for the arduous 100-mile Western States Endurance Run, he gets injured. A few days a week, Kurland runs from his home in Regent Square to Children's Hospital, taking detours through Frick and Schenley Parks, to make the run longer, of course.

COVER

We've mapped the human genome; what's next? Computational biologists at Pitt are looking for effective shortcuts to new cures. Clockwise from right: Ivet Bahar (in blue jacket), Dan Zuckerman, Takis Benos, and Hagai Meirovitch. (Illustration © John Ritter. Photos © Chuck Mitchell.)



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Susan Amara, Pitt's new chair of neurobiology, has run across some pretty tough characters in her work, including cocaine hijackers.
BY ROBIN MEJIA

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This time, he's the one with the disease.
ESSAY BY GEOFFERY KURLAND

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JULIA MAROUS STRAUT

In an enchanting tale by Gabriel García Márquez, children find the drowned corpse of a giant stranger that's washed onto the shore. "He has the face of someone called Esteban," the village women agree as they prepare the body for a proper burial at sea. In time, everyone in the small village falls in love with the corpse—even the men. They decide he is the strongest, most handsome, most sincere man ever to enter their town gates.

They also knew that everything would be different from then on, that their houses would have wider doors, higher ceilings, and stronger floors… they were going to break their backs digging for springs among the stones and planting flowers on the cliffs so that in future years at dawn the passengers on great liners would awaken… and the captain… pointing to the promontory of roses on the horizon, he would say in 14 languages, look there… where the sun's so bright that the sunflowers don't know which way to turn, yes, over there, that's Esteban's village.

Through Esteban, the villagers touched something much bigger than themselves. In the world of medicine and science, we are blessed—such moments aren't so infrequent. In this issue, Geoffery Kurland tells the story of his experience as a resident: A boy with leukemia whom he befriended hates bone marrow biopsies but tells "Dr. K" that it will be all right if Kurland performs his first biopsy on him. Such are the quiet stories of courage and generosity that transform us one at a time. The stories of medicine that can capture the imagination of a whole community—in effect, our Estebans—typically come from great research: *Yes, over there, that's Bernard Fisher, Thomas Starzl, and Jonas Salk's village.* The breakthroughs that do so much for human health have tangible effects on our medical school and the quality of education we offer. The headlines and renown attract other great faculty as well as top students. And surrounding students with stellar research minds encourages them to be rigorous, imaginative, and analytical in their thinking—traits you want in your physician.

Pittsburghers reap the benefits of a fertile medical community as well. The local population is privy to new therapies often years before they're commonplace. Further, medicine and medical research are fast becoming Pittsburgh's new "steel," creating high-quality jobs and helping ensure the economic future of this region.

Our own Drs. Patrick Moore and Yuan Chang this summer received the prestigious Mott Prize from the General Motors Cancer Research Foundation. This top international honor was awarded to the husband-and-wife team for their discovery of the virus that causes Kaposi's sarcoma. (Kaposi's is the most common malignancy in people with AIDS, and the virus offers cancer researchers extraordinary insights into oncogenesis and tumor cell biology.) As the nation's eighth-leading institution with respect to support from the National Institutes of Health, this university is rich with many other faculty members who've the promise of Drs. Moore and Chang. Though we take great pride in this, it also means we've much to lose. We don't want the next Jonas Salk moving on to California or anywhere else, yet the threat is real. Attracting and retaining outstanding faculty is a critical challenge. Hurdles such as declining reimbursements and the cost of providing care to 61 million under- or uninsured Americans have left academic medical centers in a precarious position. More than ever, we need the support of our community and alumni to sustain our momentum, so that—to borrow a García Márquez metaphor—we can build higher ceilings and stronger floors.

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

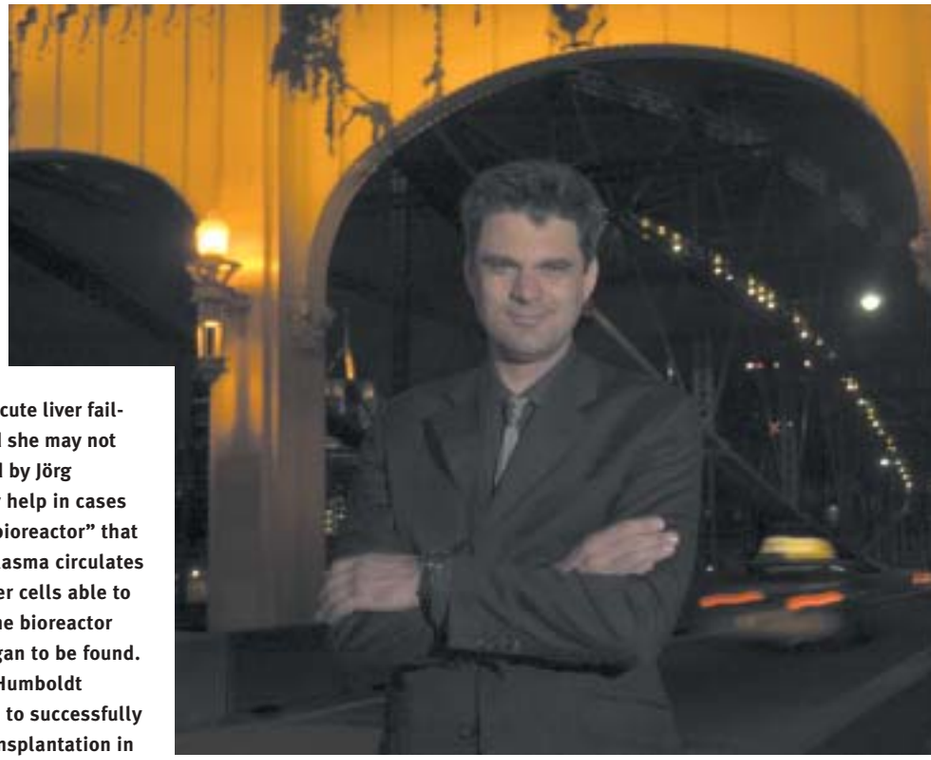


Devoted to noteworthy happenings at the medical school... To stay abreast of school news day by day, see www.health.pitt.edu

Bioreactor Buys Liver Patients Time

A woman has an unexpected side effect to a medication and develops acute liver failure. She is likely to die within days. Her only hope is a transplant—and she may not live until a liver becomes available. An experimental therapy developed by Jörg Gerlach, University of Pittsburgh professor of surgery, may eventually help in cases of acute and chronic liver failure. He has developed and patented a "bioreactor" that can provide temporary liver support outside the body. The patient's plasma circulates through the machine, which contains nearly two pounds of human liver cells able to perform many of the functions of a normal liver. Gerlach hopes that the bioreactor will buy patients time for their own livers to recover or for a donor organ to be found.

An MD/PhD, Gerlach arrived at Pitt in January from Humboldt University in Berlin. He has been able to successfully support liver function until transplantation in eight test patients. *—Dottie Horn*



Jörg Gerlach

TOP AND BOTTOM: C.E. MITCHELL

FOOTNOTE

There are the Pittsburgh Steelers, the Panthers. What would happen if the city received an NBA franchise—long a dream of local hoops fans? *Pittsburgh Post-Gazette* sportswriter Dan Gigler advises naming such a team the "Pittsburgh Physicians," predicting they would perform unnecessary surgery on their opponents. He rejected "Pittsburgh Nurses"—"didn't sound quite fierce enough," he says, but we've met some pretty tough nurses in our time.

LIFE-GIVING CARBON MONOXIDE?

Don't expect to see carbon monoxide bars opening anytime soon, but it appears that minuscule wafts of what is normally considered a dangerous gas may have beneficial effects.

With others at Pitt and Harvard University, Leo Otterbein, an assistant professor of medicine and a PhD, found that very low levels of the gas prevented excessive arterial cell growth in animals (specifically, rodents that had undergone angioplasties and blood vessel transplants). Among other benefits, the therapy altered the immune response after transplant: It appeared to block the activation of white blood cells that normally accumulate at the site of injury.

The animals were exposed to the gas at about 1/20th the level considered toxic and suffered no ill effects. (For you and me, that's roughly the carbon monoxide intake equivalent of smoking two cigarettes in a half hour.) Collaborators in Austria are testing the impact of similar doses in humans. *—Erica Lloyd*



CAMI MESA

A&Q

with Recruitment Team Leaders

Sometimes, students on the school's new Recruitment Team get asked unexpected questions, like, "Why didn't I get into Pitt last time?" Team members—including (from left, above) fourth-year students Neha Trivedi, Melisha Krejci, and Lestina Clay—represent the school at events across the country and organize Second Look weekends for those who have been accepted at Pitt but are still undecided. This year, 100 Pitt med students competed for the 40 team openings. Why is the team so popular? "If you're not from Pittsburgh, you get sucked in once you get here," says Clay. "You want to go out and tell people what you found in this special part of the world."

Stories they tell prospective students again and again:

Clay: "I [was flying back to Pittsburgh] and got stuck [overnight] in St. Louis. I was planning to miss the first day of biochemistry, so I missed the second day as well. I finally made it back, and they had lost my luggage. That was the last straw. I just started crying. The woman was like, 'We'll deliver it to you.' I said, 'When am I going to be home waiting for luggage?' I [called] Student Affairs. As soon as I heard [Suzanne Beardsley's] voice, I totally started crying and said, 'Hello, Suzanne. This is Lestina.' And she goes, 'Okay, honey, are you safe?' 'Yeah, I'm safe.' 'Okay, well just breathe. Now tell me what's going on.' So I told her everything. Suzanne talks to the counter person. Then Suzanne says, 'Now come on to school. It's all taken care of.' And I was like, *Oh, it's like what your mother would do.* That was so awesome!"

Trivedi: "Dr. Jamie Johnston was doing a review session, and I was studying [nearby]. That morning, I had started getting severe abdominal pain. It just got worse, and I started to get really pale. And it dawned on me, Jamie Johnston was right next door. Medical students were asking him questions. I waited in line, and it was my turn, and he looked at me and said, 'What's wrong?' He took me inside a PBL room, sat down with me, took his time, did an entire history. The fact that he took the time to sit with me when he had a thousand other things to do was pretty remarkable. I [thought], *Wow, this school rocks*."

On the most difficult question they are asked:

Trivedi: "Somebody asked me, point-blank, 'How much have you borrowed [for medical school]?' and I was like, 'Oh no, do we have to go there?'"

Krejci: "I always tell people, you have to decide what's going to make you happy, and how you want to invest your money. For me, I decided to invest my money in myself. I just explain my own story."

A question for the world:

Krejci: "When people go out and represent Pitt, what are the important points to sell or talk about?" —*Interview by Dottie Horn*

Faculty Snapshots

Say a woman wants to become pregnant but has already had three miscarriages. Her doctor might order an expensive battery of tests—to look at, for example, her hormone levels and the size and shape of her uterus. There's a smarter approach, says **W. Allen Hogge**, professor of obstetrics, gynecology, and reproductive sciences. The MD recommends first checking for chromosomal abnormalities with a karyotype test on tissue from the miscarried fetus. If the test detects abnormalities, there is an obvious explanation for the pregnancy loss. His study of 517 tissue samples from miscarried fetuses showed that 56 percent had chromosomal abnormalities—that number jumped to 82 percent if the mother was 35 or older. Because one in five pregnancies ends in miscarriage, many couples will have two or more miscarriages simply by chance. Yet, says Hogge—"Commonly, women with recurrent miscarriages are given things like injections of white blood cells from their partner or hormone medications, which have never been shown to be effective." His study found that couples whose miscarried fetus had chromosomal abnormalities had an 85 percent chance of having a successful pregnancy if they tried again.



Abnormal chromosomes detected by an advanced karyotype test

Although general anesthetics have been used for more than a century, scientists still don't understand how they work. "Even now there's no theory everybody can agree upon," says **Pei Tang**, a PhD and an assistant professor of anesthesiology. Researchers like Tang have shown that general anesthetics target ion channels in the cell membrane. Her latest evidence shows that, though the anesthetic molecules bind to a very particular part of the ion channel, they produce global effects on the entire channel. For example, the anesthetic actually changes the way the channel moves. Her findings were the cover story in the Dec. 10, 2002 issue of the *Proceedings of the National Academy of Sciences.* —*DH*



Tang's work was a cover story for PNAS.

PNAS COVER: © 2002 NATIONAL ACADEMY OF SCIENCES USA

MAKE ME A MATCH

"Me first, me first, me first," Helen Kim (MD '03) whispered as the Match Day proceedings got under way. Four deans stood at the front of the auditorium with a stack of white envelopes; the fourth-year students were about to find out where they would do their residencies. Finally, the first name was announced; it was Kim's. Moments later, back in her seat, sealed envelope in hand, she was shaking. In the days leading up to the match, she had been calm, trying to stay positive and relaxed. Now Kim couldn't muster the concentration to notice she'd matched with her top choice. Her friends had to tell her—Children's Hospital of Pittsburgh. Children's gave her balloons and flowers and even held a reception for Kim and their three other soon-to-be residents from Pitt.

Nearby, Rica Bonomo (MD '03) was engrossed in the atmosphere of tearing paper and excited screams. To her, it was "THE MATCH" in big capital letters. Bonomo found the matching process stressful and, at times, frustrating. She couldn't assure friends and family that she would remain in Pittsburgh, she couldn't sign a lease, she just *didn't know.* That's why she felt RELIEF when she matched with her top choice, UPMC's anesthesia program. "I'm glad it's over," Bonomo said after a deep breath. A few days later, Bonomo was asked how she wanted her name to appear on her white coat. She spelled out her name, then added an "MD" at the end. "That was exciting," says Bonomo. *Wow,* she thought to herself. *She was going to be a doctor, it was going to be on her coat!* —*Star Zagofsky*



JIM BURKE



LUTENERO

Pull!

BY KATE DUNFEE

The "patient," Mike McLaughlin (Class of '05), strips off his T-shirt and lies down on the conference table. Physician Keith Conover removes his shoe to demonstrate one of the dozen ways he knows to correct a dislocated shoulder. He jams his right foot snugly into McLaughlin's armpit, uses his leg for leverage, and steadily pulls the student's arm. Five students cluster around at this evening meeting of Pitt's Wilderness Medicine Society (WMS).

Soon, it's Elisa Nigrini's turn to try a hands-on exercise. Like others here, Nigrini (Class of '05) started attending WMS meetings to meet others interested in combining their love of medicine and the outdoors. Through the group, students learn about topics such as cold and warm weather emergencies and high-altitude mountaineering. WMS members have hiked together in Pennsylvania's Laurel Highlands and at West Virginia's Seneca Rocks. Some WMS topics are not taught in the med school's curriculum; tonight, Nigrini is learning how to treat sprains and shoulder dislocations in situations where standard medical resources aren't available.

Nigrini mimics another of Conover's methods. She buries McLaughlin's elbow in her belly button and clenches his forearm to her chest. After establishing a firm stance, she lifts McLaughlin's arm upward, grunting. "Good," says Conover at the end of the drill. "That's about half the strength you'll need in a real emergency." A mountainous groan rises from the group; someone suggests a truck would do the job.

"One of the nice things about humans is that we're bilaterally symmetrical," says Conover, medical director of the regional Wilderness Emergency Medical Services Institute. "If something doesn't look right, just make it look like it's supposed to."

VERDILE AND EBERLEIN RECOGNIZED

In the '80s, Vincent Verdile was an emergency medicine resident at Pitt. One night, he overheard a nurse giving medical advice over the phone. "What did you just do?" he asked her afterward. "I just told that [caller] how to manage a headache," she said. "We do it all the time." That conversation led Verdile to do a study that changed the way emergency departments around the country respond to calls for medical advice. (Now, most either refuse to give phone advice or follow a specified protocol.) Verdile is now dean of the Albany Medical College. In May, the Medical Alumni Association (MAA) recognized him with the 2003 McEllroy Award, given annually to a distinguished physician who did residency training at Pitt. At the same ceremony, Timothy Eberlein (MD '77), chair of surgery at Washington University in St. Louis, received the Hench Award, the School of Medicine's highest alumni honor. Addressing the graduating class, Eberlein, director of the Siteman Cancer Center, counseled students to remember "the vulnerability and fear patients experience in front of their doctors." —*DH*



C.E. MITCHELL

Catherine Zeta-Jones, Move Over

At the 49th Scope and Scalpel production, *The Sopranolols,* seniors caricatured and sang about memorable profs (one such *Chicago*-inspired number is shown left) and looked back to the early days of med school: *Pronounce these words you've never heard/It's all a freakin' crock/But you'll look and sound and act and feel/Just like you are a doc.* Interspersed among the stage performances were student-made videos, like *Joe Med Student*, modeled after *Joe Millionaire.*

Appointments

She has begun to explain addiction at the molecular level, has 20 patents to her name, and her studies of neurotransmitter transporters continue to turn heads. Howard Hughes investigator Susan Amara comes from the Vollum Institute for Advanced Biomedical Research at Oregon Health & Science University to chair Pitt's Department of Neurobiology. (See profile, p. 12.)



Schuman

A new imaging technology may allow ophthalmologists to diagnose eye diseases earlier. Researchers can now see cross sections of the eye, just by holding light up to it. With the new technology—called ultra high-resolution optical coherence tomography—scientists can see nearly as much detail as if they were observing tissue samples under a microscope. (The device offers a resolution of two to three microns.) Joel Schuman, the new chair of the Department of Ophthalmology, helped to develop the experimental technology, which is now in a prototype stage. Before coming to Pitt, Schuman was at the New England Eye Center at Tufts University, where he and others invented the now widely used optical coherence tomography (the precursor to the ultra high-resolution version). At Pitt, Schuman will develop a new imaging center within the ophthalmology department. The MD will continue to study, at the molecular level, how fluid made in the eyeball normally drains and how glaucoma alters this process.



Kolls

Because of their damaged immune systems, HIV-infected children often cannot be successfully vaccinated against disease. "Those who would benefit the most from a vaccine don't have an immune system that will respond to vaccine technology," says Jay Kolls, who will become a professor of pediatrics at Pitt in September. Kolls has developed a novel vaccination strategy that doesn't rely on T cells, which are destroyed by HIV. He is creating a vaccine against *pneumocystis carinii*, a microorganism that is harmless in healthy people but often causes pneumonia in the immunocompromised. He is currently testing the vaccine in mice. A pediatric pulmonologist, Kolls comes to Pitt from Louisiana State University. The MD's research also examines how a strain of mice that is susceptible to lung infection differs genetically from normal mice. And he is elucidating, at the molecular level, how alcohol suppresses the immune system. *—DH & EL*

PERFECT PARTNERS, PERFECT CARE

Imagine a physician writes a prescription for insulin; a pharmacist prepares it; a nurse administers it. Then the patient goes into convulsions or worse, a coma. What went wrong? That's the kind of question asked by Carl Sirio, associate professor of critical care medicine, in conjunction with RAND, a national nonprofit institution conducting research in health and other areas. Sirio's study is one of 20 RAND–University of Pittsburgh Health Institute collaborations.

As part of the partnership, experts from RAND work with Sirio's research team. His study is housed in the School of Pharmacy and pursued in conjunction with the Pittsburgh Regional Healthcare Initiative. Thirty-eight hospitals in the Pittsburgh region participate in Sirio's study. Each shares data about medical errors and nosocomial infections at its facility. "We're working together as a region to understand what's causing these problems," says Donna Keyser, associate director of the RAND–University of Pittsburgh Health Institute. "We're the only region in the country that's doing this." As one part of the many-faceted study, Sirio's team will interview hospital administrators and observe healthcare delivery. They want to find out: How do hospital leaders make patient safety a priority at their institutions? What barriers do they encounter?

They have some high ambitions: "Perfect patient care," says Sirio, is the ultimate goal of his $5 million study. *–SZ*

A LITTLE PUSH THEY NEEDN'T GO IT ALONE

BY MEGAN E. SOFILKA



CAMI MESA

FROM LEFT: Mously Almoza, Leon McCrea, and Maurice Chaplin

Even though she'd made the Dean's List every semester, Mously (pronounced moos-lee) Almoza, then a senior psychology major at the University of Pittsburgh, was worried about an impending biochemistry exam. She was studying at Hillman Library and ran into med student Lelai Ricks (Class of '05), whom she'd met through Pitt's Premedical Organization for Minority Students (POMS). Ricks reassured the panicking undergrad; joined her and a few of her classmates; and, over the next three hours, helped them grasp some difficult scientific concepts. Later, Ricks offered the younger student a ride home, saying, "You ready to roll, Mous?"

Ricks and other Pitt med students lend a hand to POMS undergrads as they explore medicine as a career, take premed courses, and apply to medical school. The med students attend POMS meetings every Friday night and make themselves available as mentors and friends.

"We realize that you can't get into medical school alone. There always has to be that one constant person there to encourage you. It's easy to get discouraged, and we are there to give that little push," says Leon McCrea (Class of '04).

Ricks and McCrea are members of the Pitt chapter of the Student National Medical Association (SNMA), a group dedicated to, among other community initiatives, helping minorities and people from disadvantaged groups become doctors and other health professionals. Paula Davis, assistant dean of student affairs and director of minority programs at the medical school, applauds the association's efforts.

"Studies have shown that underrepresented individuals are more likely to seek out healthcare providers [of the same ethnicity] and that minority physicians are more likely to serve in minority communities," says Davis. Fourteen percent of students in last year's entering class at the School of Medicine were from underrepresented minority groups such as African Americans, Native Americans, and Mexican Americans.

About 10 of the med school's 50 or so SNMA members help out with the POMS group, though Ricks, McCrea, and Maurice Chaplin (Class of '05) are the most involved. The med students offer guidance at all stages of the undergrads' careers. In October 2002, after Almoza had sent off her med school applications, she was invited to interview at the University of Connecticut. Nervous, she called on McCrea and Ricks for help.

A few days later, at 8 a.m. on a Saturday, Almoza, wearing a brown suit and carrying a briefcase, went into a small classroom where McCrea sat at a conference table, waiting to grill her. "What are your major weaknesses?" he asked. "What's the most important issue in medicine today?"

When McCrea had finished questioning her, he sent her off to Ricks for a second round. Then she had two more mock interviews with other SNMA members. Afterward, the med students critiqued Almoza.

She'd never get into med school, they told her, if she continued to say that tardiness and time management were her major weaknesses. Instead, she needed to describe weaknesses that were really strengths.

The advice was extensive and thorough—the med students even commented on her bronze lipstick, which they thought was "too bright" to be professional.

In the end, Almoza was accepted into *eight* med schools. After talking with Chaplin about her options, she decided on the University of Pennsylvania. She is one of three former POMS members who will start med school this fall (POMS alumnus Alvin Jones will join Pitt's Class of '07).

To McCrea, the POMS grads are like "little brothers or sisters." "We take pride in them doing well," he says.

FOOTNOTE

For a meal under $7, it's hard to beat the Dr. Fu Special at Lu Lu's Noodles, a "pan-Asian diner" and student hangout on Craig Street. Named for the new Medical Alumni Association president and orthopod Freddie Fu (MD '77), the dish has two kinds of noodles, with chunks of chicken and green vegetables, served with a sweet plum sauce. Mighty tasty and filling—just the fuel needed to tackle rounds. One question: If it's the Dr. Fu Special, why aren't there any *bones* in the chicken?



It's as though he's found another bridge to the North Side, Chuanyue (Cary) Wu says, explaining the pathway for cellular communication he found. The protein (migfilin) shown right, which helps cells know whether to divide, live, or die, is part of that pathway.

CELLULAR TRAFFIC COPS

SIGNAL PATHWAY FOUND THAT'S RELEVANT TO NEARLY EVERY DISEASE STATE | BY DOTTIE HORN

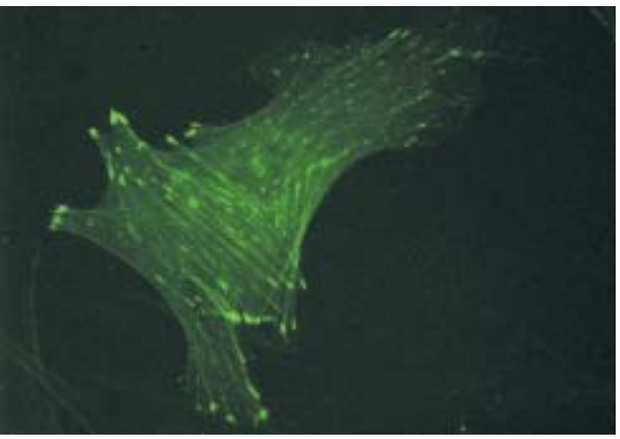
You accidentally cut your arm and begin to bleed. Cells rush to the spot and start to proliferate, stopping the flow of blood and eventually covering the wound over with new skin. But how did the cells know to go to the injured area and grow? It's almost as though a traffic cop directed them, helping them to function together in the crisis.

None of your cells lives in isolation. Each exists in constant communication with its environment. Sending vital signals to your cells—the so-called traffic cop—is the extracellular matrix, or ECM.

The ECM is made up of proteins secreted by cells and assumes different forms in different tissues. In skin, for example, the ECM forms a flat membrane beneath the bottom layer of skin—

a platform on which all the many layers of skin cells rest. In solid organs, like the liver, the ECM is like glue: It surrounds and lies between cells, holding them together in a mass. Scientists once thought that the ECM's function was primarily structural, because it physically organizes cells into cohered units. As it turns out, the ECM has another role, which is much more complex—and which is implicated in almost every disease imaginable.

In recent decades, researchers have found that the ECM and cells communicate back and forth—and that the ECM directs a cell to perform many of the cell's most basic functions. Whether a cell divides or doesn't divide, dies or continues living, is because of signals from the ECM. As an embryo grows, the ECM sends signals to each cell—saying things like, "You become a heart cell and move over there and divide."



The cell also sends messages back to the ECM. In effect, the ECM is an intermediary that allows cells to communicate with each other, to work in a coordinated fashion for the common good.

But when you're seriously ill, ECM-cell chatter can amount to cacophony. In cancerous cells, for example, the ECM's signal may be misinterpreted or go unheeded. Normal adult cells listen when the ECM says to stay put and not to travel. But despite a normal initial signal from the ECM, a cancer cell may take off and move to another part of the body. The cancer cell also does not respond if and when the ECM tells it to die.

In cancer, the two-way communication between the cell and the ECM becomes a negative feedback loop. As the cell becomes more deviant, it sends abnormal messages to the ECM, which then sends aberrant signals back to the cell as well as to nearby cells. As the cell and the ECM communicate back and forth, they both become more and more diseased.

One new strategy for treating cancer is to block key aspects of the ECM-cell communication. For example, if the ECM is telling the cancer cell to divide instead of die, why not simply cut off that signal? Without the signal, the cancer cell will eventually self-destruct.

To cut off such a signal, researchers would need to understand, at the detailed molecular level, how the ECM and cells communicate. Chuanyue (Cary) Wu, associate professor of pathology, and his lab are helping to delineate the intricacies of that communication. In a paper published on April 4 in *Cell,* they identified a new pathway through which signals travel between the ECM and the cell. (The pathway involves migfilin, a protein Wu discovered and named, and the proteins Mig-2 and filamin.) Wu likens the pathway to a bridge.

"From downtown Pittsburgh to the North Side there are five bridges. … It's almost like we've identified a new bridge which can connect downtown to the North Side," says Wu. "A lot of vehicles can move back and forth through this linkage."

Wu would like to identify the types of signals passing back and forth through the newly discovered pathway in future studies.

Understanding ECM-cell communication could be important for diseases other than cancer. Many kidney diseases, for example, are caused by fibrosis, an excessive and abnormal accumulation of ECM. Because the ECM controls such fundamental processes—like whether cells live, die, or reproduce—it is likely relevant to nearly every disease state, says Wu.

"Once we know the basic mechanisms controlling the communications, then we can develop a lot of new ways to treat those diseases," says Wu. "I always think that now is really the most exciting time because at this stage we can begin to understand [the communication] at the molecular level." ■

Trina Wood contributed to this article.

BRIDGES: CAMI MESA. MIGFILIN PROTEIN: COURTESY WU. CAKES: CORBIS.



HAVE YOUR LEPTIN AND CAKE, TOO?

CLUES TO WHY IT'S SO HARD TO LOSE WEIGHT

BY DOTTIE HORN

In 1994, the obesity research community held its breath: Had they found a cure for obesity? It was Jeff Friedman's tantalizing discovery that led to such hopes. For 10 years, the scientist at New York's Rockefeller University had studied ob/ob mice ("ob" stands for obesity),

a strain that eats voraciously and is obese, diabetic, and infertile. In 1994, Friedman discovered the mutation that leads to the mice's symptoms—they lack a hormone that was soon named leptin, after *leptos*, the ancient Greek word for lean. Researchers injected ob/ob mice with the newly discovered hormone; the animals ate less, lost weight, were no longer diabetic, and became fertile. Perhaps, obesity researchers thought, leptin could even lead to a cure for diabetes.

In 1996, Amgen spent $20 million on the patent for leptin. Soon after, scientists began raising red flags about the hormone's possibilities as an obesity cure. Unlike the ob/ob mice, obese humans did not lack leptin. Instead, researchers found, they had tons of it. In fact, the more obese one was, the more leptin one had. Despite these findings, Amgen began clinical trials: Would injections of leptin make people lose weight?

The answer was no. Only in extremely obese people did the hormone generate any weight loss at all—and the average loss was just six pounds.

Despite the disappointing results, researchers began to unravel the workings of the hormone. Leptin, they found, is secreted by fat tissue. When it reaches the brain, it suppresses hormones that stimulate people to eat. It also stimulates the release of hormones that inhibit appetite. In response to leptin, the brain sends messages to the body: Stop eating! Burn more calories by releasing more heat!

The more fat people have, the more leptin they have in their blood—so, on one level, it seemed that they should have less appetite and burn more calories than a person with less fat. But clearly that's not what happens. Somehow, in cases of obesity, the system for controlling how much food we eat breaks down.

"We have all these wonderful hormones such as leptin that are supposed to help us control appetite and body weight, but they don't work." says Allan Zhao, assistant professor of cell biology and physiology. He'd like to explain why, at the molecular level. He's already revealed what may be landmark findings on metabolism.

Researchers speculate that obese people's bodies become resistant to the effects of leptin. To study whether this is the case, Zhao used genetic manipulation to create a mouse model that is partially resistant to leptin. (The mouse has no receptors for leptin on its fat cells.) In Zhao's animals, the fat cells are totally immune to the effects of leptin, but the hormone affects cells elsewhere in the body, including the brain, as it would in normal mice.

He found that the partially leptin-resistant mouse has high levels of circulating leptin. Because the fat tissue cannot sense any leptin in the blood, it churns out more and more of the hormone. His mice eat the same amount as normal mice, but their body temperature is lower than normal (they burn fewer calories through heat release), and they gain weight—though they do not become as obese as the ob/ob mice. Because leptin affects the brain receptors of Zhao's mice as it would in normal mice, he surmised their *fat* tissue must be responsible for their decrease in body temperature. That proposition runs against convention, which says body temperature is controlled by the brain alone.

Zhao's mice are not diabetic, but they have resistance to insulin, which is a precursor to diabetes. If fed a high-fat diet, they become diabetic.

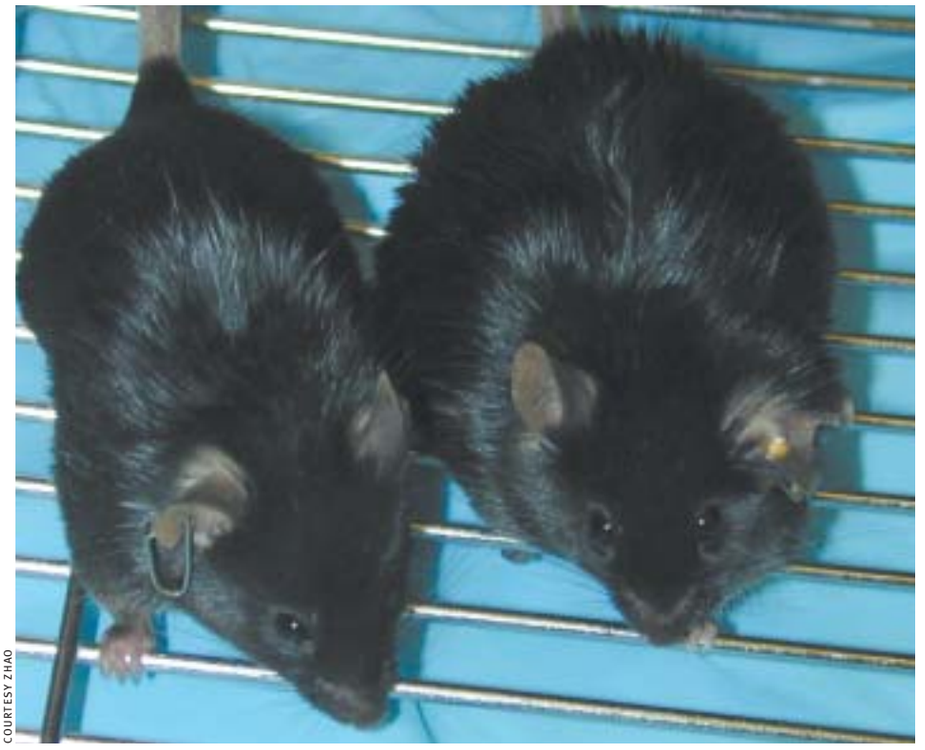
His mouse model lends support to the idea that leptin resistance is in fact associated with obesity. The model also shows that in cases of leptin resistance, fewer calories are burned through heat release—leading to weight gain despite normal food intake.

"Typically, we always blame obesity on overeating. Our model suggests that that's not necessarily true. You can still maintain the same food intake, but if you start having leptin resistance [in] fat tissue, you will still gain weight and become insulin resistant," says Zhao. Obesity researchers generally believe that obese people do eat more than lean people, so excess food intake and leptin resistance may both contribute to obesity.

In future studies, Zhao will study fat samples from human volunteers to see if leptin's actions on cells are reduced in obese people. Eventually, he hopes his work would lead to a drug to help leptin do its job, but he doesn't expect a pharmaceutical cure for obesity anytime soon.

"The more you appreciate this physiological system that helps us control food intake, the more you realize that probably our best hope is not to find the magic bullet, but to exercise and diet," he says. "Medical research can only do so much." ■

Jeff Friedman will be a featured speaker at Pitt's Science 2003 this September.



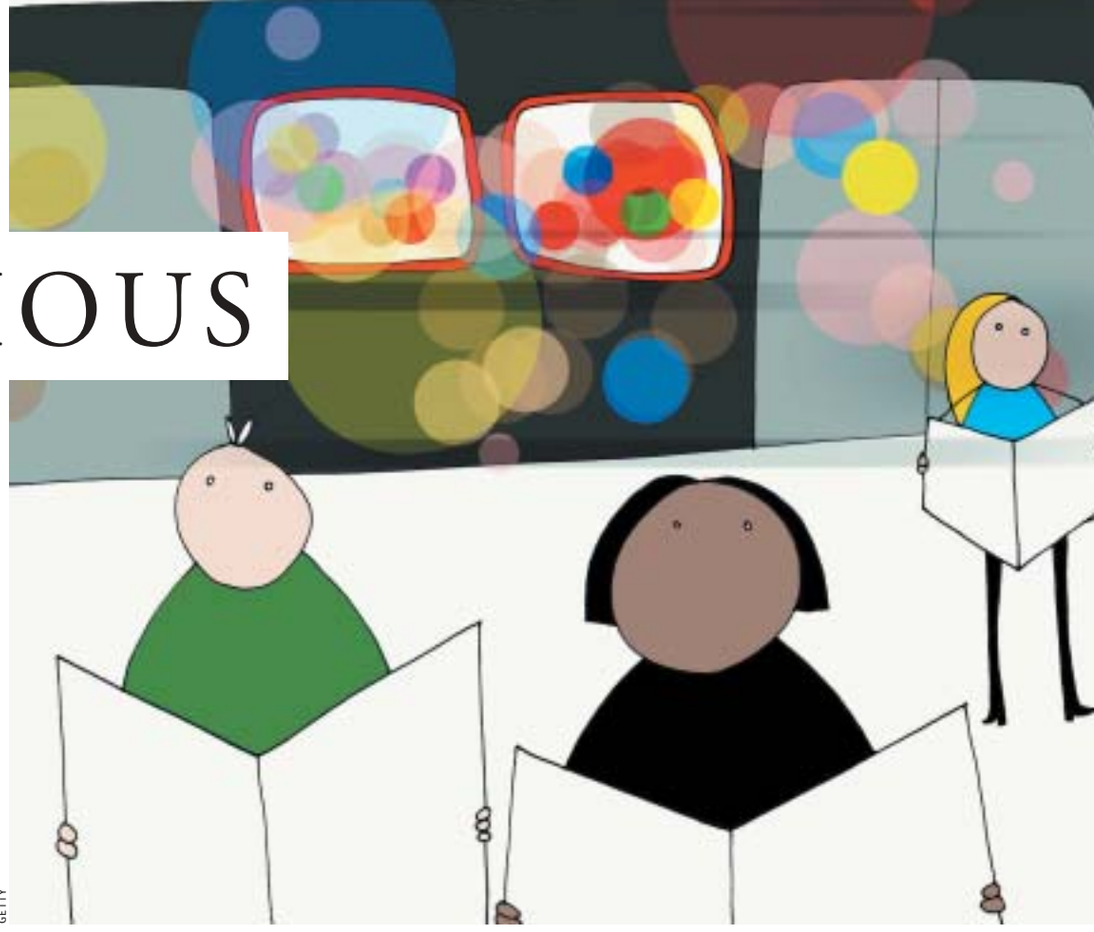
COURTESY ZHAO

These two mice ate the exact same diet—yet the animal on the right tips the scale at 1.5 ounces and his companion weighs only 1.1 ounces. Why the difference? The skinnier mouse burns more calories through heat release. His body temperature is a normal 98.6 degrees Fahrenheit—nearly two-and-a-half degrees warmer than the heftier mouse, whose temp is only 96.2 degrees. The mouse on the left is normal; Allan Zhao created the mutant on the right. Zhao's mouse is helping to show the world that fat tissue does more than just store energy.

IT'S CONTAGIOUS

A JOURNAL CLUB BY POPULAR DEMAND

BY CHUCK STARESINIC



GETTY

What are the odds that busy med students would sign up for extra work? What are the odds that they would not only sign up for extra work, but the program would be the academic equivalent to "sold out"?

Apparently, the odds are pretty good at Pitt.

Before the Journal Club for med students started in the fall of 2001, faculty organizers expected only a handful of students to join. Some 40 students signed up—so many that they had to split the group into two.

Then, for the 2002–03 academic year, the club expanded to include second-year students. Nobody camped out to get on the club list, but about 60 students participated this past academic year.

What makes the Journal Club so popular?

"Free food," quips Mark Gibbs while chewing a forkful of pasta salad at a recent meeting of second-year students. After swallowing, he admits the club provides a lot more than calories. Gibbs, who plans to work in a clinical setting, knows that physicians have to read and digest the literature "as soon as it's out there." Through the Journal Club, he is learning to read journal articles critically and to think about how physicians might apply what they glean to treating patients.

Across the conference table from Gibbs, Xinglei Shen finds the club equally nourishing to his interest in academic medicine and research. At club meetings, he and his classmates evaluate investigators' research techniques. "It's a good way to look at the process of going from research to medicine—how what we do in the lab gets into the medical textbooks and class lectures," he says.

According to its organizers, the club sheds light on the research practices that advance knowledge. It also prepares students for practicing medicine in a world in which rapid scientific advances quickly translate into treatment.

"We're not bringing students up to date on the literature. That's not what's going on," says Peter Drain, with a slightly conspiratorial air. Drain, an assistant professor of cell biology and physiology, is a founding codirector of the club along with associate professors of medicine Mary Choi and Amy Justice. "The club was designed to teach critical scientific thinking, to share an infectious enthusiasm for research, and to take young people from being students to being active participants in science and medicine," he says.

At the beginning of the term, the club's codirectors pair students with faculty mentors who display a certain "star quality." Some received glowing student evaluations as lecturers. Others are simply recognized by their colleagues as investigators whose excitement about science is contagious.

Mentors assign the articles—anything from a classic text to a more recent publication. Some articles explore clinical research. Some contain a daunting amount of science, or, as Mitchell Creinin, associate professor of obstetrics, gynecology, and reproductive sciences and current club codirector, puts it, "biochemistry that will make you pull your hair out." Mentors meet with their students informally and help them understand the article and prepare a presentation.

At the final meeting of the Journal Club in the spring, second-year student Charlotta Weaver stands and presents "Decline in Physical Activity in Black Girls and White Girls During Adolescence" (*New England Journal of Medicine,* Sept. 5, 2002), which was co-authored by her mentor, research assistant professor of family medicine Nancy Glynn.

After a lively discussion about how the study was designed and data were presented, Creinin presses the group to think about "the real meaning of this study."

Discussion turns to the factors that lead to inactivity in adolescent girls and how communities can foster healthy activity through organized sports and education. Creinin likes this direction, but he narrows the discussion again, as if the students are approaching a breakthrough and he refuses to let them walk away from it. He's looking for that moment when a student begins to, he explains later, "translate medical and social research into how you practice medicine in a community."

Creinin pointedly asks Weaver, "What do you do with this information?" She is quiet for a moment, then begins, "As a physician in my office with a patient, I would…"



How does cocaine give a rush? Susan Amara pretty much answered this question at the molecular level. Her lab's work has implications for drugs of abuse, neurodegenerative diseases, and the molecular basics of how we think and feel. Amara, a Howard Hughes investigator, joins Pitt's Department of Neurobiology as chair this academic year.

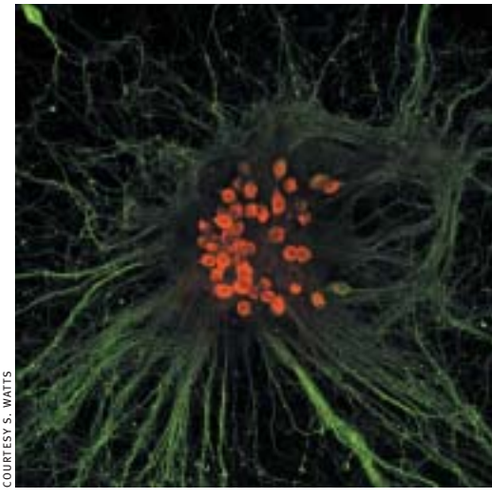
COCAINE HIJACKERS AND OTHER ADVENTURES IN NEUROSCIENCE | BY ROBIN MEJIA

ADDICTIVE RESEARCH

When journalist Jane Stevens visited the Bolivian Andes, she expected to fight the light-headedness and headaches that visitors get at such high altitudes. She didn't expect what the hotel staff had left in her room. Next to her bed, she found the traditional remedy for altitude sickness, coca tea.

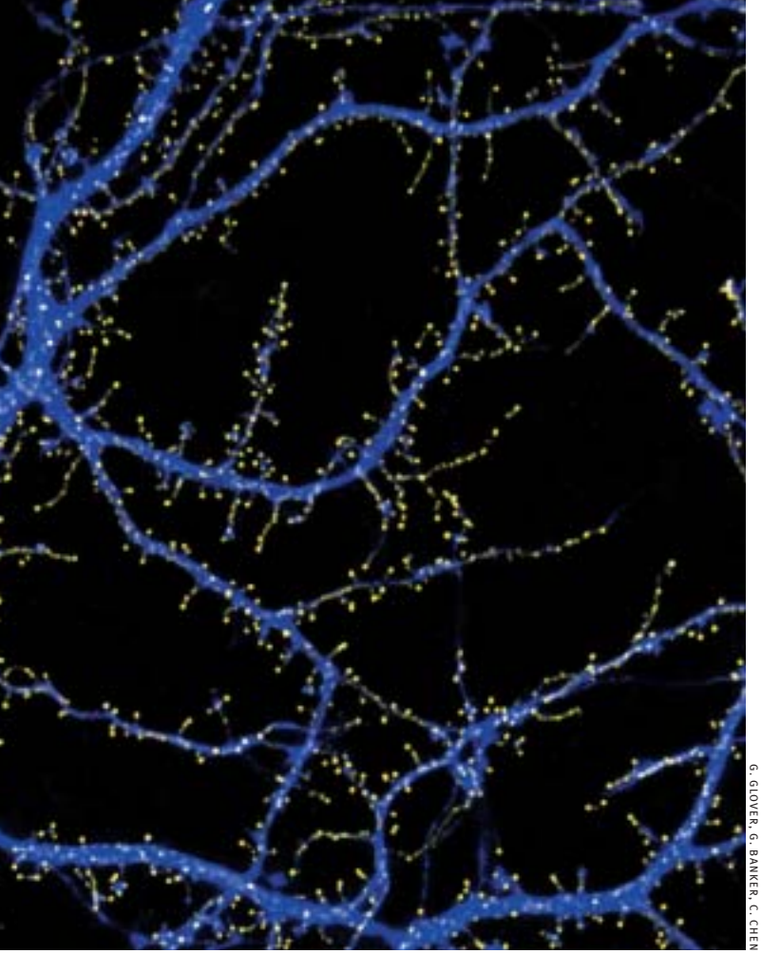
A common drink in Bolivia, the tea is made from dried leaves of the traditional coca plant. Cocaine is purified from a more potent strain of coca, one bred to increase its drug content. Coca tea helps visitors cope with thin air. The small amount of the drug in the tea helps the body get more oxygen. Native laborers chew coca leaves while they work. The tea worked so well for Stevens that when she ran into an American man who was clearly battling altitude sickness, she suggested he try it. He told her he couldn't—he was a DEA agent.

PORTRAIT | LÁSZLÓ BENCZE



COURTESY S. WATTS

Dopamine transporters (red) do more than anyone thought. They recently surprised Amara.



G. GLOVER, G. BANKER, C. CHEN

Glutamate transporters, which glow here on stained neuron dendrites, are key to a healthy brain.

The man told her that employees of the Drug Enforcement Administration are prohibited from drinking the mild traditional tea. Yet, cocaine itself was initially welcomed as a cure-all when it arrived in the United States. The stimulant was believed to improve brain function and cure impotence. Like opium, cocaine was a key ingredient in many over-the-counter medicines until the early 1900s. Sigmund Freud is one of the more famous early proponents of the drug. Thomas Edison also believed in cocaine's miraculous effects. France exported Vin Mariani, or coca wine, to these shores, and in 1886, John Pemberton introduced Coca Cola, named after the drug that gave the original formula its kick.

As cocaine use climbed in the late 1800s and early 1900s, the more negative effects of the drug started to mar its reputation. Doctors noticed the loss of appetite and inability to sleep that came with prolonged use, what we now recognize as symptoms of addiction. In 1914, cocaine sales were banned in the United States under the Harrison Act.

Still, no one knew exactly what cocaine did in the body. And it remained that way through much of the last century. Advances in pharmacological research helped scientists figure out what parts of the brain were excited when rats were dosed with the drug, but through the 1980s, no one knew exactly what it was that the cocaine molecules did to cause those effects.

Susan Amara, a Howard Hughes Medical Institute researcher, was intrigued by the question of how cocaine molecules created the myriad of effects we associate with the drug. Amara joins the University of Pittsburgh this academic year to chair the School of Medicine's Department of Neurobiology. She has built her career by applying molecular techniques to neurons so as to understand how nerve cells work and how they handle chemical signals.

Amara's research focuses on molecules called neurotransmitter transporters, critically important proteins that regulate chemical activity in the brain. These large molecules straddle a neuron's cell membrane, for the most part, scavenging compounds from the extracellular spaces back into the cell. They play crucial roles in maintaining a healthy environment for the brain and nervous system by regulating chemical levels in the fluid between cells.

Neurotransmitters, the brain's chemical messengers, allow nerve cells to communicate with one another. To send a message, a cell releases a batch of neurotransmitters. These molecules travel to the next cell, where they stimulate sensitive receptors. Some neurotransmitters are familiar to us, like serotonin and dopamine, which help modulate our moods. Antidepressants like Prozac are called "serotonin-specific re-uptake inhibitors" because they affect serotonin levels in the brain. Dopamine helps us experience pleasure—it makes necessary activities rewarding. Eating, for example, stimulates the dopamine system.

When they're working correctly, transporters ensure communications between neurons go smoothly by taking up any extra neurotransmitter molecules left floating around between cells. This way, neurotransmitters aren't wasted, and cells have more chemicals in their stash when they need to send another message. Likewise, extra neurotransmitters aren't left wandering around in the brain, accidentally hitting receptors and sending messages that weren't intended.

Some therapeutic drugs target transporters. Prozac slows a transporter's ability to take up serotonin, leaving more serotonin to hit the nerve cell's receptors. Many of what scientists call drugs of abuse, including cocaine, act on the dopamine system in the brain, essentially hijacking our natural reward system.

Thanks to Amara, scientists are learning more about what cocaine does in the brain. The cocaine molecule finds its way to the dopamine transporter and latches on. Then, instead of getting carried into the cell, like dopamine does, it sits on the outside, essentially plugging the system. Dopamine then builds up in the brain fluid and continues to stimulate neuron receptors, creating a rush on the brain's pleasure system.

Recently, Amara cloned a newly discovered cocaine-sensitive transporter in fruit flies, which she thinks may be an evolutionary ancestor of the dopamine and norepinephrine transporters in humans. (Norepinephrine is a neurotransmitter that physically arouses the body; when we face stress, it's released with adrenaline.) This discovery gives researchers a new animal model for behavioral studies of addiction. Scientists have already shown that flies react to cocaine in much the same way humans and rats do—they get hyper. But the fruit fly genome is better understood than that of most other animals, so it should be easier for scientists to alter the flies, for example, creating mutants that are more or less sensitive to the drug.

The National Institute on Drug Abuse gave Amara a MERIT Award for her work studying cocaine action. And in some ways, the cocaine research exemplifies the reasons Amara got into pharmacology. Though she does basic research—she describes herself as "very reductionist"—she says she tries to work on "questions that really have a lot of benefits." Perhaps that's why her research has resulted in 20 patents.

That practical aspect of pharmacology appealed to her from the very first time she was exposed to the field, on a high school field trip to a southern California pharmaceutical company. As a teenager, Amara was already proficient at concocting projects in her family's garden, where she dissected bugs and made plant extracts. (She'd asked if she could pull up the carpet in her bedroom so she could work inside, but her mother nixed the idea.) The field trip showed her that adults could make a living doing experiments full-time. But even more important, she saw that those experiments could actually help solve important problems. The scientists she met were involved in cancer research.

In 1987, Randy Blakely, a neuroscientist at Vanderbilt University, did his postdoctoral fellowship under Amara at Yale, where the two shared a 250-square-foot lab with four graduate students and a technician. They were on the all-too-common junior faculty/postdoc 8 a.m.-to-9 p.m. schedule. The arrangement could have been a disaster if tempers had flared, but Blakely says the interactions he had with his mentor were inspiring; her "creative spirit" was contagious.

Blakely had come to the lab to study a poorly understood receptor Amara had identified during her thesis work. After he'd been there a few months, another group showed that the frog eggs they were using in their project could be used to express a sugar transporter normally found in the gut. At that point, no one had yet cloned a neurotransmitter transporter from the brain. Blakely injected brain RNA into the frog eggs, to see what would happen. It looked like the frog eggs were synthesizing the transporters for all the major central nervous system neurotransmitters.

"We both realized it was a phenomenal opportunity," Blakely says. Amara agreed to put the existing project on hold to see if they could clone the norepinephrine transporter.

The diversion amounted to "a scientific flier experiment," says Blakely. They took a chance by heading off in a completely new direction. It was the kind of problem that appealed to someone like Amara, says Blakely, "a liberal thinker and a mentor who is willing to take chances on a young postdoc."

"She has total scientific taste," says Michael Geoff Rosenfeld, who was Amara's graduate adviser at the University of California, San Diego.

At the time Amara was in his lab, Rosenfeld and his wife were going to have a daughter. One morning, he came into the lab to find Amara looking cheerful. "Geoff, come over," he remembers her saying. She'd named all the frogs they were using for her thesis research. Rosenfeld walked over to the cage: there were all the name plaques, exactly the names he'd been thinking about for his girl. He quickly realized she'd stolen the list he'd been doodling on at his desk the day before.

When Rosenfeld lists the qualities that have helped Amara rise so quickly in the field, her intellect tops the list, but he also thinks her wit and personal style have been an asset. "She's so refreshingly unjaded," he notes. Throughout her career Amara has been known for bringing a fresh perspective to scientific questions.

By using molecular biology techniques to study brain function, Amara has been at the forefront of a transformation in the study of brain transporters. Through the 1980s, neuroscientists typically administered drugs and then measured their visible effects on the molecules. Amara's approach has been to isolate individual transporter systems and study their workings in minute detail.

"Her work on transporters has given us a series of clues [about] the way the brain is regulated moment to moment, minute to minute, and day to day," says Henry Lester, the Bren Professor of Biology at the California Institute of Technology in Pasadena. Lester explains that Amara's research has helped scientists study not only the structure of transporters, but how they work and how the success or failure of their functioning affects how we think and feel.

"We have to have ways of funding research that aren't tied to already knowing the outcome of the experiment and just taking it to the next step."

Amara discovered her interest in transporters soon after she finished her PhD. Her early successes in Rosenfeld's lab had already made her stand out, and within a year of graduation, she got her first faculty appointment, as a researcher at Yale. The school gave her three years to find projects in the area she wanted to pursue—linking microbiology to neuroscience.

Around the same time, the Howard Hughes Medical Institute knighted her as one of its assistant investigators, which gave her incredibly flexible research funding. Most funding agencies require very specific research proposals; HHMI is unique in that the organization picks people and lets them choose their projects. Yale and HHMI's faith in Amara paid off—she, Blakely, and graduate student Tad Pacholczyk promptly cloned the norepinephrine transporter, a first in the field.

"It was the sort of thing NIH would have laughed at" if she'd asked them to fund the endeavor, she says. But they succeeded, in part because of the fresh perspective they brought to the research, she believes.

"We've benefited greatly by looking at things in a different way. … When you're not biased by preconceived notions, you notice things," she says. "We have to have ways of funding research that aren't tied to already knowing the outcome of the experiment and just taking it to the next step."

At the same time she and Blakely were working on the norepinephrine transporter, a different team cloned another transporter. Both groups published papers within six months of each other.

"It suggested that because those two proteins resembled each other, they probably were from the same family," says Marc Caron, the James B. Duke Professor of Cell Biology at Duke University. A flurry of activity ensued, and within a few years, scientists had described almost two dozen brain transporters.

In the 1780s, Luigi Galvani of Bologna made dead frog legs twitch with static electricity. His followers called this phenomenon "animal electricity."

Since Galvani's day, a lot has changed in our understanding of electrical currents in animals. Amara's work has underscored that we've more to learn.

Her breakthrough came by studying glutamate, the most common neurotransmitter in the body. Glutamate is essential for survival, yet at high levels, it's a potent neurotoxin. It can excite most neurons in the brain and central nervous system, making it both critically important and potentially dangerous. Malfunctions in the glutamate system have been linked to degenerative diseases. (In fact, an Amara collaboration with Brazilian scientist Andreia Fontana has revealed that the venom of a spider, *Parawixia bistriata,* could be a key ingredient to cooking up a drug to reduce glutamate levels in the brain. They believe such a drug has promise for preventing brain damage, for example, after a stroke.)

Perhaps because glutamate is so important and ubiquitous, nerve cells have developed a large family of transporters—many of which Amara's lab cloned—to modulate its levels.

A few years ago, Amara showed that glutamate transporters do something no one realized: They act as gated ion channels, transmitting electrical currents under certain conditions. In fact, some transporters transmit electricity better than they transport glutamate. Last fall she demonstrated that dopamine transporters do the same thing. She found that low levels of dopamine make nerve cells fire more quickly.

"The importance of this is not yet fully realized," says Duke's Caron.

Blakely, who now has an endowed chair at Vanderbilt, is not surprised that Amara remains in the vanguard of neurobiology.

"She's like a rabbit's foot," he says. "You just want to stay close to her." ■



SORTING OUT THE PIECES THAT MAKE US TICK

BY JASON TOGYER

BIOLOGY RELOADED

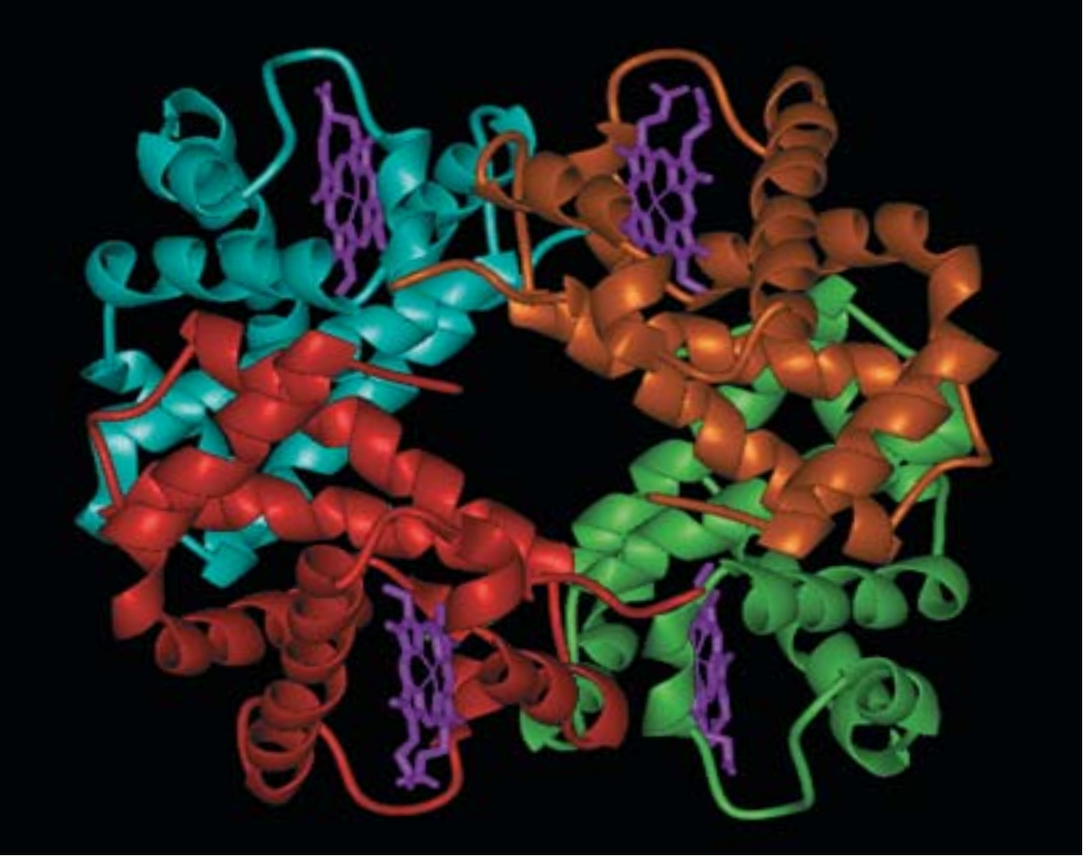
Imagine receiving a box containing 3 billion pairs of gears, springs, and levers. Inside are enough parts to build 24 working clocks and watches of various shapes and sizes. In the same box is a random selection of parts from windup toys and old typewriters. There are no blueprints to describe which parts fit together.

With enough experimentation, you might be able to construct several working machines. Some would keep time. The assemblages might even resemble the clocks from which the parts were taken. Still, even a skilled watchmaker would probably find the process frustrating and would explore many dead ends before creating something worthwhile.

This describes, roughly, the challenge presented to scientists by the human genome. The 24 clocks that can be assembled from the pile are the pairs of human chromosomes; the 3 billion pairs of parts are the nucleic acids—adenine, cytosine, guanine, and thymine (typically represented by the letters A, C, G, and T)—that come together to form DNA, the storehouse of information for encoding the tens of thousands of proteins responsible for most life functions.

Computational research team members at Pitt are ignoring what they hope are unnecessary biological data. They believe this approach will drastically accelerate our ability to cash in on the Human Genome Project, leading to new treatments for the enormous body of diseases and disorders caused by wayward proteins. FROM LEFT: **Hagai Meirovitch, Ivet Bahar, Takis Benos, and Dan Zuckerman.**

ILLUSTRATION | JOHN RITTER
PHOTOGRAPHY | C.E. MITCHELL



Last year, Bahar and postdoctoral fellows Dror Tobi and Chunyan Xu studied the movements of hemoglobin. They determined that relatively simple models of the protein could accurately and efficiently predict its movements. To do this they used "coarse-grained" structural information for the protein backbone, which is shown above in a ribbon diagram.

In April, 50 years after James Watson, Francis Crick, and Maurice Wilkins first described DNA's double-helix structure, researchers announced they'd completed sequencing the 3 billion pairs of nucleic acids in the human genome. With better than 99 percent accuracy, we now know the exact order of the building blocks of DNA.

That information alone has limited value, says Ivet Bahar, professor of molecular genetics and biochemistry in the University of Pittsburgh School of Medicine. When the sequencing process first began more than a decade ago, she notes, scientists thought they would eventually be able to go directly from the data they would glean to creation of new medical treatments.

"We soon realized that this gene-to-drug paradigm was not true," says Bahar, who heads the School of Medicine's recently created Center for Computational Biology and Bioinformatics. "It's not sufficient to know which genes exist or which are involved in a specific disease. We need to understand the machinery of the *proteins* encoded by these genes."

(Not to say mapping the human genome was unimportant. Pitt alumnus Lap-Chee Tsui, who in the late '80s helped discover the gene that causes cystic fibrosis, once told *The New York Times* that without a map of the genome, the work was like looking for a house in a city between New York and Los Angeles without a street address.)

Inside the cells of all living organisms, DNA interacts with probably 30,000 different kinds of proteins that carry out the biochemical reactions that keep cells alive, give them their unique characteristics, and allow them to reproduce. How a protein functions determines whether it can attach itself to DNA and other proteins, and what that attachment will look like. Some proteins don't attach, but serve as "signaling agents," triggering cascade reactions in other proteins in a cell.

When protein molecules, say, fold in the wrong place, cells go haywire. Many diseases are now believed to be caused by proteins that have the wrong structures. Some proteins trigger cascade reactions that cause cells to malfunction and multiply uncontrollably. We call that cancer.

The movements of protein molecules are vital to understanding genetic disorders and disease. If only we had drugs that could keep proteins from behaving in ways that cause malfunctions—then we could stop diseases before the first symptoms even appear, scientists believe.

"Each protein, to do its function, must undergo some motion at the molecular level," Bahar says. "It has to undergo some internal structural changes. These are like little molecular machines, and there are ways of increasing and decreasing the efficiency of these machines."

Given the three-dimensional nature of the interactions—all of these molecular machines whirring around—it makes sense to look at proteins not only by examining chemical reactions but mechanical movements as well. Yet conventional wisdom in research, until a few years ago, held that to understand the processes by which proteins function, we had to study activities solely at the atomic level.

That's like studying traffic patterns on a California freeway by analyzing the movements of every individual mechanical part in each individual car and truck—every piston and valve and bearing. The research would quickly be bogged down in details, some of which would be meaningful (the rotations per minute of the wheel bearings, for instance, which might give us the speed of the cars) and some of which would be worthless (the movements of the locks on the glove compartment doors).

What if we could look for patterns as groups of cars moved from lane to lane and from highway to off-ramp? Simultaneously, we might also look for anomalies—drivers who were speeding, ignoring traffic signs, and making left turns from the right lane.

To some extent, this describes the multilevel approach that Bahar has taken. She specializes in creating "coarse-grained" simulations of the ways that proteins interact. These computer models sacrifice detail on the atomic level in favor of more information about movements on the molecular level. Call it a "seeing the forest for the trees" approach.

"It was a brave start on her part in some ways, because she was taking a much different look at what people had done, and taking a look at much less detail than people had done before," says Robert Jernigan, former deputy chief of the experimental and computational biology lab at the National Cancer Institute in Bethesda, Md. He now directs the Laurence H. Baker Center for Bioinformatics and Biological Statistics at Iowa State University.

Jernigan says Bahar "ignores a lot of the details" that are not important at higher levels of protein functions.

Some details have to be ignored, because even the most powerful computers still get bogged down when trying to cal-

PROTEIN IMAGES: COURTESY THE CENTER FOR COMPUTATIONAL BIOLOGY AND BIOINFORMATICS

FORCEFUL INTERACTIONS

Half a century ago, a lab assistant at the University of Cambridge named Rosalind Franklin took the x-ray photographs of DNA strands that guided Francis Crick, Maurice Wilkins, and James Watson in deducing DNA's double-helix structure. Today, the method that Franklin used—called x-ray crystallography—is still the most efficient way to determine the 3-D structures of long molecules, including many proteins. Knowing the shapes of those molecules is vital to understanding how they work.

Yet x-ray crystallography has its limitations. As its name implies, crystallography requires the protein to be "crystallized"—"frozen" in an orderly fashion—and only a static picture of its structure can be obtained. However, in nature, proteins are dissolved in solution; and though they tend to prefer a well-defined structure, they are free to move. Pitt's Hagai Meirovitch demonstrates this by making two fists and placing them side-by-side, as if holding onto an imaginary bar.

"The protein chain has considerable freedom in space," he says, twisting and rotating his fists. "A large number of different 3-D structures can be formed by the flexible chain." That flexibility is essential to protein function.

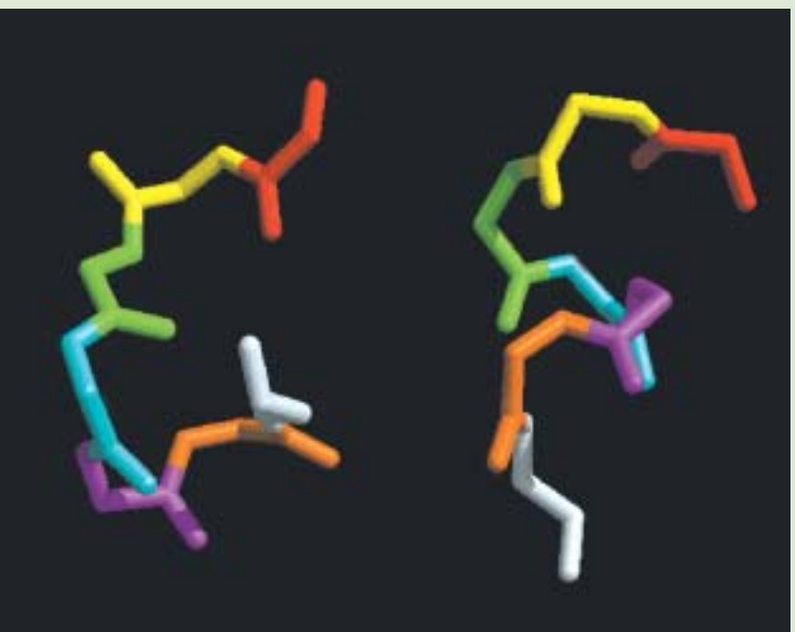
One thing researchers can do effectively is determine the sequence of amino acids in a protein. (For example, sequences of proteins that haven't even been determined experimentally are known from the genome project.) So, what if scientists could predict the structure and function of proteins based on their known sequences?

To do this, researchers would need a reliable mathematical description of the forces among all of the atoms involved—those of the protein and those in the surrounding water. They'd also need a way to simulate the movements of the molecules according to the laws of thermodynamics, taking into account tricky factors like entropy—the measure of order, or disorder, in a closed system.

Meirovitch has embraced this challenge. The professor of molecular genetics and biochemistry says there's much more work to do, yet his lab has created simplified models of protein-water interactions. In addition, he has developed computational methods for defining a protein's most stable structure. (A given protein's most stable structure also points scientists to its "active site," the location where certain chemical reactions occur most efficiently.)

His work has been helpful for studying segments of proteins called "surface loops." If the main protein body can be thought of as a few yards of bundled rope, imagine strands hanging off the sides on the outside. Those strands, or surface loops, are highly flexible and can act almost as feelers for the protein. (Sometimes they actually loop back to the molecule; sometimes they don't.) They play important roles in biological recognition processes such as antibody-antigen interactions.

Meirovitch says that tools like the ones his lab has developed will aid in the investigation of simple biological processes at the atomic level and the design of therapeutic drugs. "Stronger computers and improved computational techniques will enable [scientists] in the future to treat more complex problems," he notes. "Our mission is not just to develop methodologies but to apply them."



Meirovitch has developed simplified methods for determining stable protein and peptide structures. LEFT: The two most stable structures of a neural peptide known as deltorphin. The colors represent different amino acids.

culate the trajectories of tens of thousands of atoms, each changing direction thousands of times per second. "Computation is very, very time consuming," says Hagai Meirovitch, a professor of molecular genetics and biochemistry at Pitt, and one of three core investigators working with Bahar under the auspices of the Center for Computational Biology and Bioinformatics.

Because the human body is mostly water, reliable models of protein behavior and protein-DNA interactions must take into account the way the amino acids react to the water in which they're suspended, Meirovitch explains: "If you have 1,000 water molecules around the protein, each atom has an interaction with each of the 1,000 water molecules, plus the atoms inside the protein itself."

The volume of data that must then be processed means it's not unusual for computer simulations of molecules to run for *months* before useful results develop. And

Given the three-dimensional nature of the interactions, it makes sense to look at proteins not only by examining chemical reactions but mechanical movements as well.

the more data that is collected, the more complex those simulations become, says Kerstin Lindblad-Toh, a codirector of the genome sequencing and analysis program who led the mouse genome project at the Whitehead Institute's Center for Genome Research in Cambridge, Mass.

"We are clearly hitting issues with computing power," she says. Because computer technology and processing power continually improve, things will get better over time, Lindblad-Toh says, but science can't just wait for computers to evolve.

"It takes active thinking by the right people to make as simple a tool as possible so it takes the least amount of computing possible," Lindblad-Toh says. "We gain a lot by thinking about the most efficient way of doing things."

Computational efficiency is Bahar's goal, in the sense that she'd like scientists to have simpler, faster models of how DNA and proteins function. Understanding the chemical processes of the human body will allow "rational" design of drugs and vaccines, she says, rather than design by "trial and error." Since Bahar's arrival at Pitt in March 2001 from Bogazici University in Istanbul, she has recruited others, including

her fellow investigators at the center, to her line of thinking.

Bahar is unfailingly friendly, polite, and patient. With casual visitors, she seems somewhat reserved—colleagues who know her well, however, say that impression is misleading. Bahar's demeanor, they say, belies a mind that's constantly processing and an intellect that's intense and passionate. There's nothing mild about how Bahar approaches her work.

"Ivet is a real doer," says Ruth Nussinov, a professor of biochemistry in the Tel Aviv University School of Medicine and a principal investigator at the National Cancer Institute in Frederick, Md. She and Bahar met in 1994, when Bahar visited the NCI's Laboratory of Experimental and Computational Biology. "She is very energetic, very focused, and has always managed to accomplish a truly astonishing amount of work," says Nussinov. She points out the more than 150 journal articles that Bahar has published in the last 15 years.

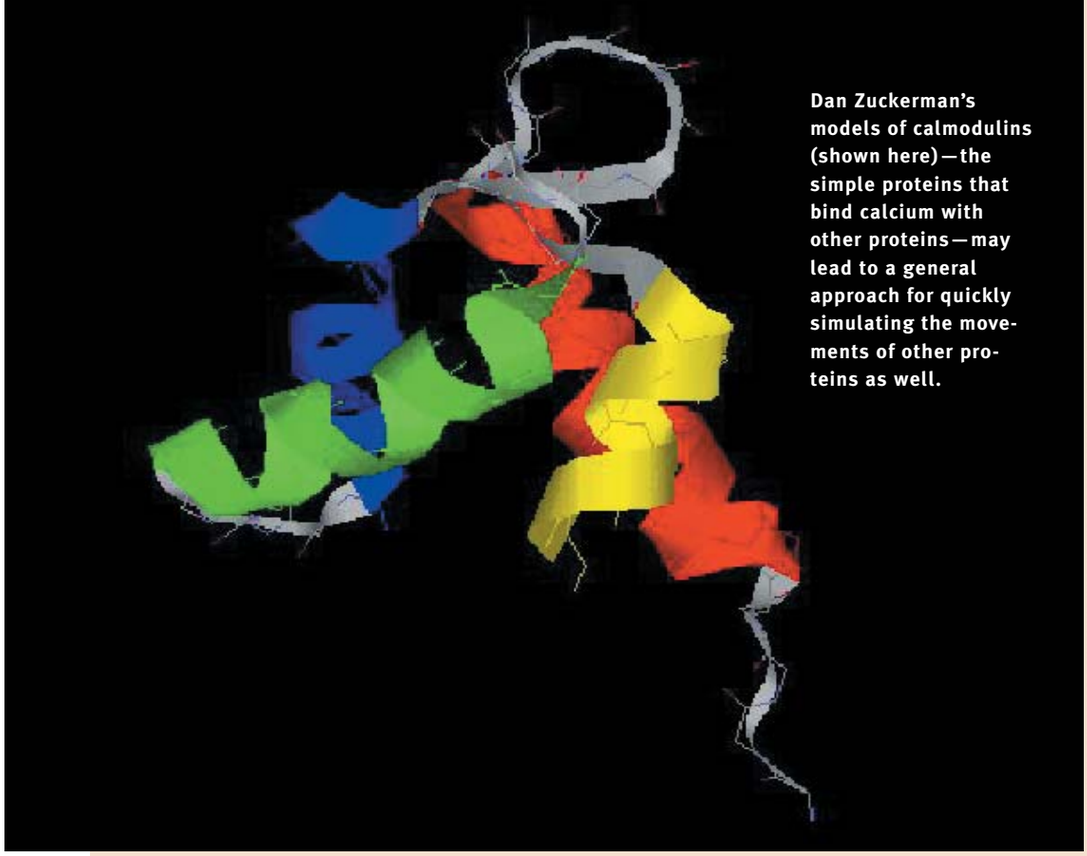
"I was always very impressed by her pace, and how quickly she [would] focus on a problem, [decide] how to go about it, do it, get results, and summarize them," Nussinov says. "If I remember right, every visit [by Bahar] to the [NCI] lab has resulted in at least two publications."

She has a way of putting her peers at ease and becoming deeply engaged in their work, says another NCI researcher, David Covell of the computational technologies laboratory in the screening technologies branch.

"She enjoys sitting down with people within her reach and very carefully going over all of the details of what they're doing," says Covell, who worked with Bahar on ways to model the flexibility of proteins. And although Bahar has advanced the study of coarse-grained models of protein behaviors, Covell calls Bahar's own behavior detail-oriented "in the extreme."

"Ivet goes to great lengths to ensure that you are treated hospitably," says Covell, who visited Bogazici University several years ago as a guest of Bahar and her husband. "The same attention to detail she puts into her science is the attention to detail she puts into her social interactions."

Bahar's research in recent years has touched on a wide variety of fields that all



Dan Zuckerman's models of calmodulins (shown here)—the simple proteins that bind calcium with other proteins—may lead to a general approach for quickly simulating the movements of other proteins as well.

PROTEIN IMAGE: COURTESY THE CENTER FOR COMPUTATIONAL BIOLOGY AND BIOINFORMATICS

FASTER, QUICKER, CHEAPER

For centuries, no one could figure out how a horse gallops; the movements happen too quickly for the human eye to discern. That's why so many early paintings show horses running with all four legs splayed out on the ground, like hobby horses. Then in 1872, California millionaire and racehorse owner Leland Stanford commissioned photographer Eadweard Muybridge to settle the debate once and for all. By arranging a series of remotely controlled cameras around a track, Muybridge was able to capture the intermediate movements of a horse's legs—and prove those early painters were incorrect. When a horse is running at full speed, all four hooves actually end up off the ground, but they never hit the ground splayed out hobby-horse-like.

Dan Zuckerman's work with protein molecules is on a substantially smaller scale than Muybridge's work with racehorses. But the principle is the same: To understand how bodies change from one state to another, we need to capture their intermediate stages of movement. The problem, Zuckerman notes, is that proteins can go through thousands of transitions every second. Modeling just one transition with conventional methods drains a tremendous amount of computing power.

"If studying these transitions requires hundreds of powerful computer processors, then the work is obviously limited to only a few scientists," Zuckerman says. "Given the number of important proteins that are being studied, the field can't advance very quickly."

On the other hand, if the model is able to run on a desktop computer, "then Joe Professor can do it," Zuckerman says. In other words, one would need the inspiration and know-how, but not access to large-scale computer processors.

This isn't just a hypothetical. In just two weeks, using the PC in his office, Zuckerman can generate more than 100 transitions in calmodulin, a fairly simple protein that binds calcium with a host of other proteins. Each of these transitions represents about one-tenth of a millisecond of calmodulin's ever-fluctuating motions.

Though calmodulin is "ubiquitous," says Zuckerman, he didn't set out to invent a method solely for analyzing it. He wants to create a general structural modeling approach for studying all sorts of proteins quickly. His solution to simplifying the simulations is to take a representative sample; instead of simulating the movement of every atom, for instance, Zuckerman's model might simulate every fifth or 10th atom.

"Maybe, if you throw away some of the data to get to the large-scale movements, you

are throwing away some interesting atoms," he says. But you can check the simulations against the available experimental information to see if the model's predictions are accurate. Certain very simple models can reproduce a surprising amount of data, says Zuckerman, who came to work with Ivet Bahar in September 2002 from a postdoctoral fellowship at Johns Hopkins University. "In the past, I had always worked on atomically detailed models," he says. Yet simulations of atomic models of proteins, which track the motions of tens of thousands of protein atoms, surrounded by thousands of water molecules, are stuck at extremely short time scales. A long series of simulations might have represented 10 nanoseconds in the life of a protein—not enough time to see anything, Zuckerman says: "Working here with Ivet has really opened my eyes to these simpler models."

That's like studying traffic patterns on a California freeway by analyzing the movements of every individual mechanical part in each individual car and truck—every piston and valve and bearing.

SIGNALS AMID THE NOISE

In the early 1990s, when the race to decode the human genome began, it cost about $10 to identify a single base pair. Back then, a technician could manually scan about 10,000 base pairs per day. At those rates, it would have taken a team of 20 technicians about 40 years and $30 billion to sequence the human genome.

Improved technology has lowered the cost to 5 cents per base pair; the leaders of the Human Genome Project estimate the final cost of sequencing the human genome at the bargain rate of $2.6 billion. And today's automated laboratory equipment can scan 10,000 base pairs per second. Not only are the new processes cheaper, they allow greater accuracy, because technicians can check and double-check sections of the genome.

To fully exploit this wealth of data, we need more efficient algorithms, says Pitt's Takis Benos. Many scientists are exploring how protein-coding and noncoding genes function; Benos is interested in how gene regulation is fine tuned. A change in a single base pair, for instance, could result in a gene being misexpressed, and that can translate to a serious disease. His laboratory is developing algorithms to scan the human genome and detect short but important sequences driving gene expression. They compare the human sequences with other species, like mice. "We expect that because the unimportant DNA changes quickly, this comparison will reveal the important parts," he says.

But finding this information is not easy. As Benos explains it, it's like sitting on the back porch late at night, tuning a shortwave radio. We patiently turn the dial, passing up squeals and rushes of static, until faint music or voices can be heard. "We're looking for faint signals amid the noise," Benos says. In genomes, he adds, "the signals that are important are relatively short, say six to 12 bases, and they are surrounded by long strings of genetic noise"—or base pairs that don't encode important information. That noise can generate a lot of false positives, notes Benos.

To cut down on these false positives, Benos is applying statistical methods to make a kind of spot check, taking a representative sample of genetic data. The formulas with which he is working dig through data from two or more genomes of different species, looking for similarities and matching patterns, then ranking the results to see if they might be important. In the case of our shortwave radio example, it would be like having two friends in neighboring towns tuning their radios randomly, then telling you about frequency ranges where they found what seem to be good programs. You would have a higher probability of finding something you liked this way than you would have without your friends' help.

In tuning out the genetic noise, another challenge for Benos: From the beginning of a gene in a genome, how far out does he keep looking for promising signals? "In a simple organism like yeast, 500 or 1,000 bases are usually sufficient," he says. "In a mouse or human, how far should we go looking? Five thousand? Ten thousand?"

fall under the general label of "computational biology." Her studies—and similar work being done elsewhere—could one day lead to better treatments for the enormous variety of disorders caused by protein misfolding and aggregations as well as for diseases caused by protein signaling and regulation mishaps (which are instrumental to the development of cancer). Yet Bahar's background isn't in biology or medicine. A chemical engineer by training, Bahar began her career studying polymers but found life sciences "more interesting than producing high technology chemicals for industry."

The engineer recognized that many of the methods, tools, and fundamental concepts from the world of synthetics could be applied to biological molecules.

"Her background is a great asset," says Nussinov, noting that Bahar's engineering training makes her well-suited for carrying out complicated mathematical calculations on biological molecules.

"In this respect, it's an infinitely better background than biology—and I know that for a fact, since my background is in biology," Nussinov says.

The principal researchers in the Center for Computational Biology and Bioinformatics share Bahar's varied interests and, like her, aren't traditional biologists. Meirovitch and Daniel Zuckerman, an assistant professor of environmental and occupational health in Pitt's Graduate School of Public Health (GSPH), examine problems of structural biology—determining the shapes of proteins and studying their motions and potential interactions. Zuckerman is a physicist; Meirovitch is a physical chemist. Takis Benos, an assistant professor of human genetics in GSPH, mines data—digging the most important facts out of mounds of unsorted information. His degrees are in mathematics as well as molecular biology.

The mix of disciplines Bahar has selected for her team is well-chosen, says Whitehead's Lindblad-Toh:

"We're going to need many different fields coming together to pull out this knowledge.

"We need physicians and biologists to ask, 'What is important to medicine for us to look at?' But we need computational biology to determine how." ■



Jim Withers tries to convince this young homeless woman to make an appointment at the clinic, but she seems a little confused and afraid of walking such a distance. "I walk that all the time," he assures her. (At right is Mike Sallows.)



A STREET DOCTOR OFFERS MORE THAN MEDICAL CARE

PHOTOGRAPHY BY MARTHA RIAL

TEXT BY MEGHAN HOLOHAN

"I'VE GOT NOTHING"

Every Monday, Jim Withers slips on his army-green backpack and walks the streets of Pittsburgh. He and Mike Sallows loop through the shiny PPG buildings or underneath the highway where cars passing overhead make a *thu-wap* sound. They climb around the south bank of the Allegheny River. They crawl through dark doorways into dilapidated factories.

There was a time when Withers (MD '84) and Sallows roamed the streets every night. Eleven years ago, Withers, who was treating patients at homeless shelters, realized there was a large population of people who were so alienated from society that they didn't even go to shelters or clinics. Sallows, a former transient turned outreach worker, had been looking for a physician to treat these people. He asked doctor after doctor for help, often getting the same answer: *Sounds great. Where can I send my check?* Withers asked, *What should I do?* And Operation Safety Net was born.



Pitt med student Kerry Sutherland talks with a man as Withers calls the hospital. Withers is trying to locate the man's friend, who has been absent from the street for days; both men have diabetes.







TOP: Withers examines this man's infected teeth, then refers him to a dentist who volunteers for Operation Safety Net. Many homeless people have serious dental problems.

BOTTOM: A memorial for "Little Eva." Eva Haniak, a 79-year-old woman who lived on the streets when her mental illness flared up, was bludgeoned to death in March.



In the Strip District, an OSN team, including from left, Eric Hong (Class of '06), Children's Hospital nurse Rebecca Wellinger, and osteopathic medicine student Jim Parry, examine a man's nose. They're checking to see if an abrasion is infected.







Withers and Art Leibowitz, an OSN volunteer who was once homeless, stand outside the van in the Hill District.

BOTTOM: Sallows, Hong, and Withers place their hands on a man reciting the 23rd Psalm.



Light from the new stadiums bounces off the Allegheny River, creating ripples of colors. Withers, Sallows, and Pitt med students Kerry Sutherland and Jessie Smith walk briskly toward the Roberto Clemente Bridge. A tall, lanky form appears from underneath. It's a man with disheveled hair. His arms flail out as he takes long strides. He's about to pass the Operation Safety Net (OSN) crew but stops.

"Where are you guys from?" he asks. "I've seen you before."

"We're from Operation Safety Net," Withers says.

"Yeah, I know you guys."

"How ya doin' tonight?" Sallows asks.

"Oh, I'm drunk. I've got nothing. I just lost my job. I'd be better off dead."

He speeds away. Withers and Sallows spin around to follow him. They catch up and talk with the man. Watching the episode from afar, the students wonder if Withers will "302" the man; 302 refers to the statute for involuntary mental health commitment. Withers and Sallows return about 10 minutes later. The man is upset about losing his job. After talking to him, they've ascertained that he is depressed but not suicidal.

The group heads for the bridge. Even though it is less than 20 degrees and the cold shelters have opened for the homeless, Withers is still doing rounds. OSN has identified at least 15 people who never take shelter. He wants to make sure they have enough socks, enough food, and a sleeping bag that withstands frigid temperatures.

Shelters and street clinics targeting the homeless are fairly prevalent, but in few if any other cities in this country do doctors actually go to the streets to treat people. Withers does. Along the way, he reminds the residents and med students who volunteer for OSN that they're treating much more than physical conditions.

"It's more important to know what person the disease has rather than what disease a person has," he likes to say.

Through the years, OSN has evolved from Withers and Sallows on rounds on the streets every night to more than 30 clinical volunteers in 16 teams. Each team consists of a formerly homeless person and a medical professional. The formerly homeless person serves as a guide for nurses, physicians, and medical students, introducing them to the culture of the streets.

Last year, Withers won the Robert Wood Johnson Community Health Leadership Award—the latest of many honors with which the Pitt alum and his colleagues have been recognized since 1992. OSN, now a Mercy Hospital program, continues to grow under Withers' guidance. He sees change as a natural part of an organization.

In 1997, Nell Davidson, a nurse who volunteers for OSN, began to address a problem she'd noticed. A lot of people living in Pittsburgh's Hill District didn't seem to be getting adequate medical care. She filled her blue pickup truck with medical supplies and drove into the neighborhood. Parked at a busy street corner, Davidson worked out of the back of her truck, treating residents who came by. It didn't take long before people gathered around the truck waiting for care. Today, taking the place of Davidson and her pickup, the well-staffed and equipped OSN van is in the Hill District every week.

The van is a sparkling RV that would make any road warrior retiree jealous. An exam room is in the back, where a bathroom and a bed would normally be. One day this winter, Withers observes a resident treating patients. Education is an important part of OSN, Withers says. He would like to create a fellowship "without walls." Medical students and residents only spend a short time with Withers, yet it can take a lot of time for a doctor to earn the trust of such alienated people. So a fellowship or residency would give new physicians the time to learn about and treat the complex problems many homeless have.

A tall man wearing a stocking cap limps to the back of the van and eases down onto a bench. He holds his arm at a funny angle, cradling it close to his body.

"How long has it hurt? Can you lift it?"

The resident asks the patient questions then solicits Withers' help.

Withers leans over the man, pressing his shoulder. After surmising the patient has a muscle abscess, he asks him to stay while he treats others. Later the van will take him to the hospital.

Abscesses normally require surgery, Withers explains. He suspects a lot of people who needed treatment for abscesses used to just "sit on them" before OSN had a presence here. "It's very rewarding," Withers says.

The patient asks if he can leave. He'll return in 15 minutes, he says, then steps out of the van. Crossing the street, the man walks past a pub with a crooked sign and bars covering the windows. This street is a main artery in the neighborhood, but there aren't any gas stations, pharmacies, or grocery stores in sight. Many of the homes are pocked with graffiti; plywood covers windows.

Withers treats a few other patients. An older man asks to see the doctor alone, so Withers guides him into the back, sliding a white door behind them. Ten minutes pass; Withers peaks his head out, leans over, and whispers to a nurse. Sighing, he leans his head on the door frame. A moment later, he straightens up; his blue eyes sparkle again as he smiles and returns to the exam room. ■

"Put your chest against this," she says, indicating the box holding the film. The x rays will enter me from behind, go through my chest, and hit the film contained within the holder. She hides herself behind a shielded screen within arm's reach of the control panel.

"Take a breath… now let it out." I do as I am told. "Take another… hold it." The technician takes the film cassettes into the darkroom to process them.

I hurriedly put my clothes back on, working my way back into my white coat while I wait the 90 seconds the processing takes. I still have a lot to do: lectures to prepare for a conference in a few days, rounds to make, residents to teach. And now this x ray, taking up more of my time. I'd already put off having it taken for several weeks. But here I am at last, hoping the x ray will reveal the cause of the recurrent sharp pain in my left chest. Maybe, I tell myself, it'll also explain that nagging cold and cough I had a few months ago. Perhaps I really had broken a rib when I coughed during one of my long training runs. As a matter of fact, I convince myself that a fractured rib would fully explain the pain, especially after weeks of aspirin didn't do anything except make me bleed excessively every time I cut myself shaving. The bleeding, I tell myself, was only because of the aspirin, which makes it harder for the blood to clot. None of this—the pain, the cough, the cold, the bleeding—none of it had completely stopped my running. But I know something is wrong, and that something is slowing me down.

Dave, a radiology resident here at the UC Davis Medical Center, had squinted sidelong at me in the near darkness of the processing room when I told him of the pain and asked for the x ray of my chest. But his brow furrowed, his gaze narrowed, and his jaw dropped when I told him that the pain had been sufficient to start to interfere with my running. Just as everyone at the medical center knows me as Dr. K., a nickname I've had since my own internship, I am equally marked as the physician who runs the year round, at night after work, carrying his beeper, in any weather. I am an acknowledged nut, running in the rain, singing on rounds, trading bad jokes with my patients, residents, and students.

Not only am I somewhat crazy, I'm tough, I keep reminding myself. It takes more than just a little pain to stop my running. Only four weeks ago, despite the pain in my chest, I did a 50-mile run and qualified for my ultimate goal, my personal Holy Grail: The Western States Endurance Run. All the thousands of miles I've run since I first started running as a teenager have been, unbeknownst to me, the physical and mental training for that 100-mile run over the Sierra Nevada Mountains, on trails over peaks into canyons, and across the icy American River. Now, after all those years, I am at last ready to face the challenge that will test my physical limits, perhaps allowing me to see a hidden part of myself. Nothing, not even the pain in my ribs or the fatigue in my legs, would be able to stop me from doing that run, I tell myself. Nothing.

Dave and I wait for the films to appear. A beeper goes off; as usual, it's mine. I pick up a nearby phone and tell the resident that I'll be up on the pediatric ward in just a few minutes, and we can see and discuss my patient together. The x-ray area is dark and quiet, and I savor the near silence, the hum of equipment, and the smell of developer fluid.

"Dr. K.," Dave revives me from my reverie, "your film is coming out of the processor. Want to take a look?"

"Dr. K.," he called, "you'll use lots of numbing medicine, won't you?"

He pulls the black pieces of film from the large, purring box. They are dark wings flapping in his hands as we cross to a view box up on the wall. Dave puts the x rays up against the fluorescent light; we both peer at them.

He is silent. I swallow hard and feel my throat suddenly become dry; my breath chokes in small bursts.

"Are you sure those are my films?"

"Donna, are these here Dr. K.'s x rays?" Dave asks hopefully.

"Only ones in there," is the reply from around the corner. They are mine and mine alone, the shadows before me flying out from the view box into my eyes, which stare with disbelief. I take a step back, then one forward, as if to erase what I see by refocusing the view. Then I look away, snatch a breath of air, and turn to Dave.

"Well, well, isn't this interesting."

"No," he says, "I don't think so."

My rib is fine. In fact, there's nothing wrong with that side of my chest, the area of the pain I've been having. But there, right there in the upper central part of my chest, is a large, fist-sized blotch of white, a mass, a something. It pushes my windpipe far to the right, kinking it. My spine, as if in religious devotion, genuflects with a soft curve pointing to my left, bowing toward the white mass filling the upper part of my chest.

My breath is now frozen in my throat, and my eyes glaze over as I attempt without success to smile through the fear that grips me. What the hell is this…this thing? What is going on with me? Then, quite suddenly, I realize into whom I have been transformed at the moment I saw the white shadow on my film. And although I can't possibly know it completely, my new persona is taking over as it melds itself unalterably into my being. I am no longer the doctor. I am the person with the disease.

My mother gets up from her chair before I can move. She is too accustomed to waiting on the family and is about to take my soup bowl when the phone rings. She picks it up, says hello, covers the mouthpiece, and turns to me.

"It's for you. It's Dr. Rosenow." She uses the formal term even though he can't hear her. She hands me the phone.

"Hello," I say into the phone.

"Hello, Geoff. Listen, I want you to come back in now. We need to get a sample of your bone marrow."

I am silent for a moment, then can only utter, "Now?"

"Yes. Come to my office, and I'll arrange it from there. We need to do it this afternoon." I hear myself say "okay" and hang up the phone even as I feel myself hurtle toward fear and panic. I know what a "bone marrow" is.

During my residency in pediatrics at Stanford, I spent several months on the hematology-oncology ward, where many children received chemotherapy. I gave a lot of the chemo. I also learned how to do "marrows," the medical shorthand for sticking a large needle through the thick outer layer of bone into the marrow and aspirating, or sucking out, a sample of cells into a syringe.

It was about my second week as an intern on heme-onc when I entered the small treat-

ment room to do my first bone marrow. The nurse and the resident who were there to help me were waiting with Joey, the 9-year-old boy fighting his losing battle with leukemia. He wore his customary knitted wool cap to cover his chemotherapeutically bald head. His usual grin was absent. He was an unwilling veteran of too many bone marrows, too many courses of chemotherapy, and a war he neither chose, desired, nor deserved.

The gurney on which Joey sat took up most of one side of the room. Joey's mother held his thin hand, the one without the IV, and rubbed his shoulder. For some reason, she gently pulled off Joey's hat, and his bald head aged him before me, the veins beneath the skin of his scalp showing a faint blue, his face a mixture of pallor and sallowness atop a fatigue derived from the chronicity of his illness. Joey and I'd quickly become friends soon after my arrival. I had seen him daily on rounds, had traded jokes with him, and had sat during late evenings with his parents, listening to their sorrow amid the dozens of families who each suffered alone and together in the terrible grip of cancer. I now felt that everything about the relationship I had with Joey was on the line.

Joey knew that I'd seen other marrows done, and he knew that I'd never actually done one. As the saying goes in medicine: "See one, do one, teach one." He offered himself, I think now, for my initiation with full understanding and willingness. He hated bone marrows, he told me, but he knew that they had to be done.

As I walked into the room, his gaze passed first to his mother as she said good-bye and went out of the room. She hated the procedure as much as her son did, and she could not stand to be in the room for any part of it. Joey then met my eyes, which tried not to belie my own fear and acknowledged inexperience.

"Dr. K.," he called, "you'll use lots of numbing medicine, won't you?"

"Sure, Joey. I promise I will. And I'll tell you everything I do, before I do it." That was the important part, my resident had said: don't lie. Always say what you're going to do before you do it. And always use enough of the "numbing medicine."

"Okay, Joey, bend your left leg and put it under your right one." I felt with my fingers the bone forming his small right hip. The anterior iliac crest, my target, was broad and easy to feel. The resident, there to supervise and teach, confirmed the location. It was all



I sit there hearing almost nothing except the sound in my head telling me that I hear nothing, that I am not there, that I am dying, that I am not dying, that I don't know what is happening to me.

business now. I opened the bone marrow tray and put on sterile gloves while the nurse poured the Betadine sterilizing solution into a cup. I picked up a gauze square from the tray, dipped it into the Betadine, and turned back to Joey.

"I'm going to clean off your hip, Joey. That's all I'm going to do, first. This'll be a little cold." I hoped he couldn't hear the flutter in my voice or feel the tremulous hand that cleaned his hip with one, then another, then yet a third Betadine-soaked gauze pad. The area was clean. I put a sterile towel with a hole in its center over the site, allowing me access to the bone. I loaded a syringe with nearly a teaspoon and a half of Xylocaine, the wonderful numbing medicine.

"Joey, I'm going to numb the skin. This will be a little bee sting." He said nothing but held his breath.

I put the needle just into the skin, just where I would want to get the marrow. I started to inject the Xylocaine. Joey gave a short gasp and started to cry as the Xylocaine went in with a burning sensation. He held perfectly still, giving me a good target.

"Okay, Joey. I'm sorry. But I want it to be numb. Okay? Joey?"

"Okay," he whimpered. The needle was still in his hip. I angled deeper, injecting the

medicine as I went. Joey was still whimpering when my needle hit something hard, the bone. I kept injecting, even as Joey cried out with the sudden extra burn of Xylocaine going into the covering of the bone. I stopped injecting and pulled the needle out.

"I'm done with that, Joey. You're all numb. I'll check and make sure. Can you feel this?" I asked, touching the skin with the point of the needle.

"No, I don't feel anything there."

"Great," I said, more for myself than for him. I made a small incision with a scalpel, right in the middle of the area, and turned back to the marrow tray. I picked up the large marrow needle, nearly an eighth of an inch in diameter. It looked and felt like an awkward, heavy, outmoded piece of equipment, like a discarded part of an old torture device, with a patina of dull brown, totally unlike the acceptable, shiny, thin, and delicate object a needle should be. If it had been an animal, it would have been an ox. Within its barrel fit a solid metal insert, called a trocar, which gave the entire device the strength to go through solid bone without breaking. I checked the fit of the two, taking the trocar out and replacing it within the needle. With the trocar inside it, the needle was solid.

I silently said a prayer. I wanted the needle to go in straight, not to slide alongside the bone. I wanted the needle to go in just far enough, not all the way through the bone and out the other side, not that that could happen, I tried to reassure myself.

"Joey, I'm going to put in the needle. You won't feel much except me pushing on you."

"I know" was the reply. And it was true. He knew far better than I did. And he knew how it really felt far better than I did.

I took the needle-with-trocar assembly and pushed the whole thing into the incision until I felt the bone. Then, with pressure as steady as I could muster, coupled with a slow rotation, I felt it go through the outer layer of bone until I felt a give. The end of the needle was sitting in the marrow. I pulled the trocar out of the needle, which stuck out of Joey's hip like some deadly projectile or a misplaced antenna. I took a large syringe, placed it on the needle, and turned it, locking it in place.

"Okay, Joey, this may hurt," I warned. I was about to aspirate a small amount of the marrow into the syringe. I had been told that it felt like a sucking deep in the bone. I had no idea what that meant, but Joey, who certainly knew, held his breath as I pulled up on the plunger of the syringe as hard as I could, holding the needle in place in the marrow. After what seemed like an eternity but was in actuality only a few seconds, I saw small bits of red tissue and blood, the aspirated marrow, dribble into the syringe. The sample was small, but the technician who took the syringe from my shaking hand told me it was adequate. I put the trocar back into place.

I somehow pull myself out of the chair and manage to get my jacket on despite my shaking hands. I am suddenly very cold.

"Joey, I'm taking out the needle… now," I said as I pulled out the weapon and covered the wound.

"You okay?" I asked. "We're done," I said, then realized that I was the only one who was done. Joey was the one who still had leukemia.

"Thanks, Dr. K.," Joey said. "You did okay. You gave me enough numbing medicine."

"Thank you, Joey. You were very good. I'll see you later today. After lunch." The gurney was being wheeled out to take Joey back to his bed.

"Okay. See you later."

Joey died less than three months later, his leukemia being stronger, smarter, and far meaner than all the drugs we threw into his tender body. It was to the end unfair: all the pain endured, all those drugs, all that suffering by someone so young, and for what?

Now, during lunch, I hear again Ed Rosenow's voice as he calls me for my own marrow examination. I swim into the cries of the children like Joey, whose marrow I'd taken in the past. I tell myself that I am feeling the cold Betadine, the hot Xylocaine, even though I've never felt either. The spoon falls from my hand into the soup.

"What was that about?" My mother mimics my own open-mouthed stare. The two of us breathe slowly.

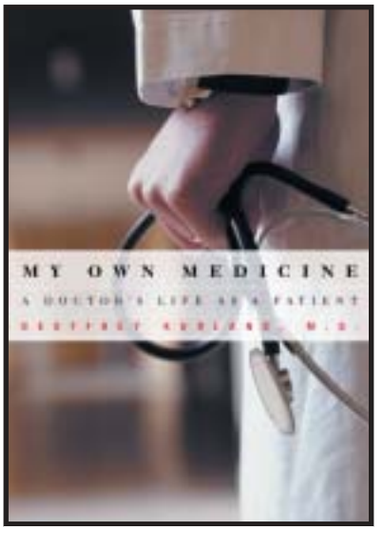
I tell her in two sentences. "Ed said there's something wrong with my blood count. I have to get back and have a bone marrow done this afternoon." I somehow pull myself out of the chair and manage to get my jacket on despite my shaking hands. I am suddenly very cold.

"Geoff, you have hairy cell leukemia." He may be saying more. In fact, I know he is saying more. But I sit there in a locked expression, hearing almost nothing except the sound in my head telling me that I hear nothing, that I am not there, that I am dying, that I am not dying, that I don't know what is happening to me. And somehow part of me sees Ed Rosenow and feels in some way sorry for him, for being the messenger of such terrifying news. And after what seems hours, during which I have left the room, talked with my parents, tried to comfort Karin, watched myself die, then start to live again, I find myself with the same locked expression, sitting on the couch, Ed calmly speaking to me:

"…you to meet Tom Habermann, who is a hematologist and knows a lot about hairy cell leukemia. We'll go to his office now; it's down on West Fifteen."

I will myself to get up and follow Ed to the elevator.

At Tom's office, only three floors down, Ed introduces us as he might introduce fellow physicians to each other. But I know (and Tom knows) who is the doctor and who is the patient. Tom had been filled in earlier by Ed, who soon excuses himself to get back to work. I am reminded of the time, seemingly long ago, when I'd been on my college track team, receiving, then passing the baton in a relay race. Now, I am the baton, and Tom Habermann has me for the next mile or two, or perhaps, if things go well or if they don't go well, longer. I only hope he's ready to run. ■



Kurland's memoir was released in 2002.

MATCH RESULTS
CLASS OF 2003



JIM BURKE

ANESTHESIOLOGY
Bonomo, Rica
University of Pittsburgh Medical Center
Chalifoux, Thomas
University of Pittsburgh Medical Center
Chong, Elaine
University of Washington Affiliated Hospitals
DeAngelis, Mario
University of Pittsburgh Medical Center
Edinger, James
University of Pittsburgh Medical Center
Majesko, Alyssa
University of Pittsburgh Medical Center
Montoya, Mario
University of Pittsburgh Medical Center
Onwere, Joyce
Mayo Graduate School of Medicine, Minn.
Tan, Andrea
University of Pittsburgh Medical Center
Taneja, Monica
Hosp. of the University of Pennsylvania
Thunberg, Christopher
Duke University Medical Center, N.C.

EMERGENCY MEDICINE
Apollon, Rebecca
Baystate Medical Center, Mass.
Dostal, Kerstin
McGaw Medical Center, Northwestern University, Ill.
Kennah, Adam
Emory University School of Medicine, Ga.
Kluetz, Paul
University of Maryland Medical Center
LaRocco, Brian
Christiana Care, Del.
Montoya, Anthony
University of Massachusetts Medical School
Powe, Darrell
University of Chicago Hospitals, Ill.
Vogrin, Tracy
University of Pittsburgh Medical Center

FAMILY PRACTICE
Dorsten, Michelle
Miami Valley Hospital, Ohio
Foulk, Brian
UPMC St. Margaret
Gamaluddin, Shereen
Lancaster General Hospital, Pa.
Hollis, Angela
Washington Hospital, Pa.
Kashlan, Melissa
Washington Hospital, Pa.
Orife, Ediri
Washington Hospital, Pa.
Sprando, Christopher
UPMC St. Margaret
Zawora, Michele
Lancaster General Hospital, Pa.

INTERNAL MEDICINE
Dixit, Sanjay
Ohio State University Medical Center
Grove, Meghan
University of Pittsburgh Medical Center
Joshi, Sheela
New York Presbyterian Hospital–Columbia
Kuk, Richard
Penn State Milton S. Hershey Medical Center
Lee, Jae
University of Southern California
Miller, Susan
Emory University School of Medicine, Ga.
Nagendra, Shweta
University Hospitals of Cleveland, Ohio
Nguyen, Hoang-hai
Virginia Commonwealth University Health System
Ratcliffe, Temple
SAUSHEC-Lackland AFB, Texas
Saylor, Philip
University of California, San Diego Medical Center
Shah, Keyur
University of Maryland Medical Center
Siu, Sonia
Thomas Jefferson University, Pa.
Sung, Yon
Brown University, R.I.
Tsai, Sing-I
UPMC Shadyside
Weston, Patrick
Duke University Medical Center, N.C.

INTERNAL MEDICINE – PRIMARY
Blakeman, Melissa
George Washington University, D.C.
DeSouza, Melanie
George Washington University, D.C.
Herrle, Scott
University of Pittsburgh Medical Center
Perlmutter, Dana
University of Colorado School of Medicine

MAXILLOFACIAL SURGERY
Facy, Rebecca
University of Pittsburgh Medical Center
Johnson, Scott
University of Pittsburgh Medical Center

MEDICINE – PSYCHIATRY
Omotade, Aderonke
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University of Pittsburgh Medical Center

NEUROLOGY
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Lu, Angela
University of Pittsburgh Medical Center
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University of California, Davis
Sorokorensky, Irene
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OBSTETRICS/GYNECOLOGY
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Brigham & Women's Hospital, Mass.
Cobb, Kristen
Penn State Milton S. Hershey Medical Center
Conway, Deirdre
New York University School of Medicine
Narcisse, Yanouchka
Western Pennsylvania Hospital
Parker, Sara
Drexel U COM, Pa.
Ramsey, Shavonne
Ohio State University
Woo, Kirstin
University of California, San Francisco

OPHTHALMOLOGY
Farhi, Parisa
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Ghajarnia, Mehdi
University of Pittsburgh Medical Center
Ryan, Timothea
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Wincko, Jeffrey
Ohio State University

ORTHOPAEDIC SURGERY
Brunton, Lance
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Coates, Kevin
SAUSHEC–Brooke Army Medical Center, Ft. Sam Houston, Texas
Larson, James
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Yagnik, Gautam
Hosp. of the University of Pennsylvania

OTOLARYNGOLOGY
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Temple University School of Medicine, Pa.
Cosetti, Maura
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Groblewski, Jan
Georgetown University Hospital, D.C.
Hackman, Trevor
University of Pittsburgh Medical Center
Mangiardi, Jason
SUNY-Brooklyn/Long Island Center, N.Y.
Nayak, Jayakar
University of Pittsburgh Medical Center
Pavlovich, Justin
Cleveland Clinic Foundation, Ohio
Sequeira, Roger
Indiana University School of Medicine

PATHOLOGY
Clark, Beth
University of Pittsburgh Medical Center
Clark, Kenneth
University of Pittsburgh Medical Center

PEDIATRICS
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University Hospitals of Cleveland, Ohio
Carlson, Misty
Oregon Health & Science University
Gilchrist, Amber
Thomas Jefferson University/AlantiCare duPont Hospital for Children, Pa.
Glass, Kristen
Children's Hospital of Pittsburgh
Johnston, Lindsay
Children's Hospital of Pittsburgh
Kim, Helen
Children's Hospital of Pittsburgh
Lesser, Daniel
Children's Hospital, Los Angeles, Calif.
Lipstein, Ellen
University of Washington Affil. Hospitals
Lockett, Lawrence
St. Christopher's Hospital for Children, Pa.
McAninch, Brett
UVM/Fletcher Allen, Vt.
Rakitt, Tina
University of Pittsburgh Medical Center
Robledo, Lisette
Children's Memorial Hospital, Ill.
Ruiz, Angelica
University of California, San Francisco–Fresno
Sullivan, Kevin
University of Washington Affil. Hospitals
Trucco, Sara
Stanford University Programs, Calif.
Uspal, Neil
Children's National Medical Center, D.C.

PHYSICAL MEDICINE AND REHABILITATION
Boone, Shelley
Ohio State University Medical Center
Gordon, Assaf
New York University School of Medicine

PUBLIC HEALTH (PURSUING MPH)
Jou, Roger
University of Pittsburgh GSPH
Robinson, Jamar
University of Pittsburgh GSPH

PSYCHIATRY
Strandberg, Gayle
University of Pittsburgh Medical Center
Sukonick, Danielle
Stanford University Programs, Calif.
Vora, Illa
University of California, San Diego Medical Center

RADIOLOGY DIAGNOSTIC
Chaudry, Adil
University of Rochester/Strong Memorial, N.Y.
Novitskaya, Dina
University of Pittsburgh Medical Center
Restauri, Nicole
University of Pittsburgh Medical Center
Yeretsian, Rita
New York University School of Medicine

RESEARCH
Duffy, Jamira
Fellowship/University of Pittsburgh
Song, Angela
Fellowship/University of Pittsburgh
Udoh, Emmanuel
Fellowship/University of Pittsburgh

SURGERY – GENERAL
Bomberger, Chloe
Naval Medical Center, San Diego, Calif.
Chung, Joseph
University of Iowa Hospitals and Clinics
Dumouchel, Justin
Dartmouth–Hitchcock Medical Center, N.H.
Gribar, Steven
University of Pittsburgh Medical Center
Holt, Douglas
Beth Israel Deaconess Medical Center, Mass.
Kaye, Jonathan
North Shore–LIJ Health System, N.Y.
Pandya, Kevin
University of Minnesota Medical School
Rana, Abbas
New York Presbyterian Hospital–Columbia
Rozmiarek, Andrew
University of New Mexico School of Medicine
Singhal, Dhruv
Brigham & Women's Hospital, Mass.
Syres, Kimberly
National Naval Medical Center, Md.

SURGERY – PRELIMINARY
Castilla, Suzanne
Mercy Hospital of Pittsburgh
Houda, Joseph
Mercy Hospital of Pittsburgh
Stanitski, Kate
Boston University Medical Center, Mass.

TRANSITIONAL
Pepperney, Amy
Western Pennsylvania Hospital
Sobehart, Robert
Naval Medical Center, San Diego, Calif.

UROLOGY
Hayn, Matthew
University of Pittsburgh Medical Center
Tarin, Tatum
Stanford University Programs, Calif.



Life, death, and AIDS in Southern Africa.

LESOTHO DIARY

AN AFRICAN COMING-OF-AGE STORY | BY JESSICA MESMAN

February 17, 2003, Jan Groblewski writes in his journal—
The storms came to Maseru again this afternoon.

At Maseru's Queen Elizabeth II Hospital, work continues when the power goes down with a thunderclap that shakes the building. Work continues when the diesel fuel that powers the generators is stolen. Surgeons close an above-the-knee amputation with only the tiny cone of light from a laryngoscope for illumination. From the doorway of the pediatrics ward, medical students watch as the morticians roll a body into the driving rain, using something like a wheelbarrow. They lay the cargo, loosely wrapped in a sheet, in the open bed of a Nissan pickup.

The students—Groblewski, Assaf Gordon, and Daniel Lesser, all of the University of Pittsburgh School of Medicine's Class of 2003—are two weeks into a monthlong rotation in Maseru, the small capital city of Lesotho (pronounced le-soo-too), which is about the size of Maryland. It's hot and





LEFT: Jan Groblewski, Assaf Gordon, and Daniel Lesser at Queen Elizabeth II. RIGHT: Male surgical ward.

PHOTOGRAPHY COURTESY GROBLEWSKI

wet in the summer, caged in by the mountains and South Africa. The students are getting used to dead patients—at least two or three full-size bodies, and often, the smaller kind, being wheeled away each day. On his first day, Lesser saw two babies die—the first and the second of his short medical career. When he arrived at his post, the doctors abandoned an infant resuscitation to greet him.

"Abandoned" implies neglect, but these doctors are not careless, reckless, or insensitive. Dr. Toba (that's what everyone calls the Nigerian orthopaedic surgeon with a commanding presence and five-syllable name) explains the triage-like mentality to Gordon: "In the West, you fight for every life; in Africa, you have to improvise." Resources are devoted to those who stand a better chance.

At QE II, as they call the hospital, there is no code, no fevered attempt at resuscitation. Patients die side by side, in full view of one another. They die without comfort and often without notice—and they don't always go quietly. Corpses lay in wards for hours, sometimes overnight, before being taken to the morgue. *Death in Lesotho is completely different than it is in America*, Groblewski writes. It is not a private matter. It is at once a given and forgotten, regarded more matter-of-factly than life is. It is something the students think about all the time.

February 23, 2003
HIV is here. It may not be talked about. It may not make the papers. But it is definitely here.

In the mountains, where most Basotho live in villages of round, thatch-roofed huts, HIV is a mystery, a curse of "bad blood" killing the young and strong. In Maseru, banners printed in English urge the use of condoms; but with no education programs in place for villagers, condoms are merely another kind of charm, one that might be left next to a bed for protection during sex. Other folk remedies are nightmarish: Drink the blood of an albino. Rape a child under the age of 5. The students hope these are legends, or at least antiquated beliefs, but while Lesser works in pediatrics at QE II, at least one child, a boy, is presumed a victim of HIV rape. Many more check in with limbs turned gangrenous after being punctured in attempts to drain "bad blood." Traditional healing remedies do little but delay visits to the hospital to the point where, often, the only option is amputation.

And there's the silence. Doctors say "Immuno Suppression" or "NS," never "HIV" or "AIDS." *When I suspect that a patient may be ill secondary to HIV, I whisper,* writes Groblewski, *because I am worried that I am breaking the unspoken rules.* None of the patients Gordon sees are on anti-HIV medications. Antibiotics and antifungals are provided by the government; antiretrovirals are not—too expensive. Even if the medications were available, there are no resources to test CD4 counts or viral loads, making meaningful long-term care impossible.

QE II has plenty of well-trained physicians. But without sufficient funding, they are unable to use what they know to combat HIV, so pervasive and relentless here. And without a widespread education program offered in the native tongue, Sesotho—most villagers can't speak or understand English—the cultural taboo of HIV remains firmly in place. So instead of treating HIV, doctors treat symptoms. When patients die of AIDS, the doctors and the families and the charts say pneumonia, meningitis, or "other."

This disturbs and frustrates the students, who will not accept the opinion held by some that it is too late for Lesotho. What they witness only reaffirms their conviction that HIV education is vital.

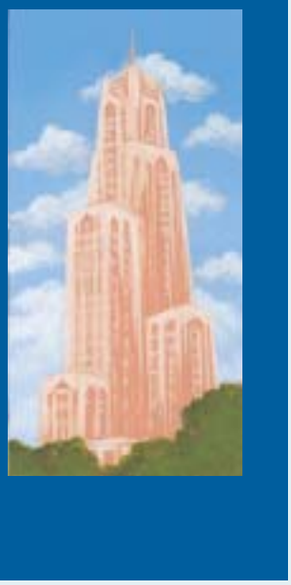
"I saw the tragic effects that ignorance and disease are having on a whole population," insists Lesser.

When the students chose Lesotho as the site of their senior year international elective, they'd hoped to offer the community the benefit of their experiences teaching HIV prevention to Pittsburgh area teens—the three of them served as coordinators for a local HIV education program their sophomore year. But according to the staff at QE II, what's really needed is not an AIDS education program or even more doctors, but the basics: money and supplies. The hospital gets by on mostly outdated medical equipment donated piecemeal over the years. The students' most valuable contributions are their suitcases full of latex gloves, new scrubs, syringes, and lab equipment. When they turn over these gifts, the nurse nods with approval and says, "Yes, this is exactly what we need."

March 4, 2003
It is getting harder to be so far away… to sit back and relax, adopt the laid-back Lesotho mentality, and realize that no matter how chaotic this all seems, you will eventually get where you need to go.

The students learn not to be surprised by surprises—to grab for the laryngoscope when the lights go out. And yet they can't help but be amazed, because beyond the death and disrepair of QE II there is so much strength and healing here, too. Their journals—written and taped—are catalogues of dichotomy, serendipity, and magic: scoring the only goal for what turns out to be a soccer squad staffed by former national team players; running a marathon with the country's Olympic hopefuls; attending a wedding where a princess and the prime minister eat and dance with the villagers.

They are moved. "The beauty of Lesotho is in the mountains," says Groblewski; generations of Basuto boys have gone there for rites of passage. When the students try to sleep in a village hut on an overnight horse trek, a group of about 20 teens emerges from the traditional six months of seclusion, stopping in each of their home villages along the way to perform a celebratory chant. Their rhythmic chorus pulses through the mountains, waking the students to flames from village fire pits reaching into the night sky, lighting the way for boys returning home as men. ■



CLASS NOTES

'50s

Robert Wilkins' (MD '59) last official act after 20 years as chief of neurosurgery at Duke University Medical Center in Durham, N.C., was to place his pager in front of a rear wheel of a limousine, which then ran over it. The pager was not mourned. Even without it, Wilkins remains in contact with residents at Duke, where he teaches on Saturday mornings. Wilkins now lives in Fearrington Village, in North Carolina, a community modeled after an old English village that's home to a herd of Belted Galloway cattle (they're nicknamed "Oreo cookie cows" for their black fore- and hind- quarters and white middles). One project keeping Wilkins busy is transferring 45 years of family slides onto compact discs. After scanning more than 4,900 pictures, he recently reached 1995. He "hopes to reach the 21st century" very soon.

'60s

Joel Haas (MD '67, Pathology Intern '67–'68, Pathology Resident '68–'69, Pediatric Pathology Resident '69–'71) chairs the Department of Pathology at the Children's Hospital of Denver. Haas was drawn to pediatrics because of the resiliency of children. While at Pitt, Haas worked in the lab at Children's Hospital of Pittsburgh at night, in exchange for free meals in the cafeteria.

'70s

After Sept. 11, 2001, when **Harry Poling** (MD '71) and his family visited the damaged Pentagon building—not far from their home in northern Virginia—Poling felt the need to serve his country. After 10 years as medical director of the Surgi-Center at Winchester Medical Center, the anesthesiologist also wanted a change of pace. ("I have a short attention span," he says, laughing. "That's one reason I'm an anesthesiologist.") The 56-year-old Poling enlisted in the air force; within months, he was in Montgomery, Ala., for officer training, learning regulations and traditions, including the lyrics to the air force song (the class was scolded when they couldn't sing it correctly). After being sworn in, the newly minted Major Poling retired from his civilian job and moved to Eglin Air Force Base in Fort Walton Beach, Fla.

Russell Munson (MD '79) launched his own family practice in Chester, Conn., shortly after finishing his residency. Later, he became an adjunct professor at Yale University School of Nursing, where he designed a training program for his office, similar to a medical internship, for nurse practitioners. In 2002, Munson gave up his clinical practice to become medical director of Anthem Blue Cross and Blue Shield in North Haven, Conn. Among other duties, Munson conducts medical technology reviews, investigating procedures which the insurance company doesn't currently cover to see if the therapies are safe.

RESIDENTS AND FELLOWS

Karen Green (Obstetrics and Gynecology Resident '72–'75) is chair of the division of maternal fetal medicine at the University of Massachusetts Medical Center in Worcester, where she specializes in high-risk pregnancies. For the past 12 years, she has worked on a multicenter study evaluating treatments for HIV-positive women. Improved treatments for HIV have lessened the chance that women will transmit the disease to their newborns, yet some women resist HIV screening, Green says. Many are frightened they are HIV-positive, so they don't get tested, unwittingly passing the disease onto their children.

'80s

Before being admitted to the School of Medicine, **Arthur Smerling** (MD '80) was interviewed by Joel Merenstein, who proved to be both a kind interviewer and a kind instructor. Merenstein taught Smerling the importance of a good bedside manner and of evaluating a patient as a whole person. Now director of pediatric cardiac critical care at Children's Hospital of New York–Presbyterian, Smerling, an anesthesiologist, puts Merenstein's lessons into action.

Larry Burk (MD '81) has helped bring alternative medicine to the Duke University Medical Center. He does acupuncture for and imagery with patients suffering from chronic pain. This approach helps patients whose shoulders have been frozen in place for many weeks release tension and recover more rapidly. Burk became interested in acupuncture when he witnessed the positive results that alternative treatments had on his father when he had cancer. As a diagnostic radiologist

IVAN SHULMAN | MAESTRO



During his internship and residency, Ivan Shulman built his own harpsichord—though his colleagues teased him that it looked like a coffin.

Shulman (MD '72) had spent his childhood surrounded by music, both in Pittsburgh and in his native New York, where his father, Harry Shulman, played oboe for the famed NBC Symphony Orchestra of Arturo Toscanini. Like his dad, Shulman took up the oboe. He studied music in college, but fearing the life of a musician was too unstable, Shulman decided to go into medicine instead. "If you have medicine, you can always have music, but it's not the other way around," he says.

A series of happy accidents led Shulman to become music director of the Los Angeles Doctors Symphony Orchestra (LADSO). Shulman began to

at Duke and director of education at the Duke Center for Integrative Medicine, Burk employs alternative treatments whenever practical. When his patients need an MRI scan, Burk uses hypnosis to guide them through a mental walk in the park, rather than administering a tranquilizer. When the scan is over, they don't require time in a recovery room, and Burk says many are proud to have overcome their fear of the procedure without medication.

As an undergrad at the University of Pittsburgh, **Frank Anania** (MD '88) was one of nearly 200 students in his Introduction to Molecular Biology class. As he walked into class one day, Albert Chung, his prof, pulled Anania aside to talk to the young student about research opportunities. Anania was shocked that Chung had noticed him. He couldn't imagine how a teacher could keep track of hundreds of faces and names. Anania ended up spending the summer working in Chung's lab, trying to isolate tumor cells. The endeavor helped him realize that he should pursue a research career. An assistant professor of medicine and the director of the hepatology section at the University of Maryland Medical Center in Baltimore, Anania recently received a National Institutes of Health grant to study the role leptin plays in liver disease. Leptin controls a person's appetite; Anania suspects it also affects stellate cells in the liver, causing scarring which occurs when a person suffers from chronic liver disease or cirrhosis. He will be heading to Emory University in the fall to continue his work there.

RESIDENTS AND FELLOWS

Deborah Armstrong (Internal Medicine Resident '85–'87, Chief Internal Medicine Resident '87–'88) is an assistant professor of oncology at the Kimmel Comprehensive Cancer Center at Johns Hopkins University School of Medicine. As part of the Gynecologic Oncology Group, Armstrong conducts several nationwide studies on the effectiveness of targeted cancer therapies. Unlike chemotherapy, which patients cannot undergo for extended periods of time, the study's noncytotoxic agents don't kill cells and have low levels of toxicity, allowing treatment to continue indefinitely. The experimental therapies, now in Phase II trials, prevented cancers from spreading even when they couldn't be cured or reduced. "You keep the cancer in check and basically let the patient live [with it] as opposed to going in with the big guns to cure it," she says.

Guy Petruzzelli (Otolaryngology Intern and Resident '87–'92, Advanced Head and Neck Oncology and Cranial Base Surgery Fellow '92–'93) recently became chair of the Department of Otolaryngology at Loyola University Medical Center in Maywood, Ill. His "great role models" at Pitt—Eugene Myers, Jonas Johnson, and Carl Snyderman—nurtured his interest in head and neck research and surgery. Today, he is implementing ideas these mentors were developing a decade ago, including certain targeted therapies. Petruzzelli uses specifically engineered antibodies to single out cytokines produced by cancerous cells. Cytokines trick the body into depressing the immune system and growing blood vessels for life support. The antibodies latch onto the cytokines and destroy them without harming the rest of the body. Petruzzelli hopes the otolaryngology program at Loyola someday rivals Pitt's.

'90s

RESIDENTS AND FELLOWS

Cecelia Boardman (Obstetrics, Gynecology, and Reproductive Sciences Intern and Resident '92 –'96, Fellow '96–'97) first met N. Douglas Boardman III (Orthopedic Surgery Intern and Resident '92–'98) at an orientation tour during their first week at the University of Pennsylvania. By the end of their third year of medical school, they were married. Now, both work at Virginia Commonwealth University School of Medicine, where Cecelia Boardman is the acting director of gynecologic oncology. Often she treats women who are dying from ovarian cancer because the disease was detected too late. Boardman is trying to develop a way to detect ovarian cancer early in its development from a few drops of blood.



1989 Hippocratean

Marc Safran (Orthopaedic Surgery Fellow '93–'94) was recently appointed director of sports medicine at the University of California, San Francisco. His goals are research, teaching, and superior athlete care (and, he says, to be "the Freddie Fu of the West Coast"). After researching knee cartilage replacement treatments (now in Phase I trials) and surveying common injuries in wheelchair tennis players, Safran instituted a program in which physicians volunteer at more than 20 public high schools. Before Safran's program, a different paramedic usually oversaw each game. Now, doctors who are sports medicine experts provide more specialized and consistent care, rather than paramedics, who are better suited to treating traumatic injuries. The physicians monitor football games, training sessions, and a free drop-in clinic for sports-related injuries. *—MH, SZ, and JM*



It surprised alum Ivan Shulman when he was asked to direct the Los Angeles Doctors Symphony Orchestra.

play with the LADSO shortly after moving to L.A. 24 years ago. At the invitation of David Weiss, principal oboist of the Los Angeles Philharmonic, and a former member of the Pittsburgh Symphony, Shulman began to play oboe in the Philharmonic both at the Hollywood Bowl and the Music Center. He later joined the orchestra as both an oboist and physician on tour in Mexico, Japan, and Europe.

Then in 1990, the LADSO's conductor left unexpectedly. Though many members of the orchestra are MDs, Shulman assumed a nonphysician would become the next conductor—that's what usually happened. Instead, the orchestra insisted that Shulman conduct the first concert that year. That concert went so well that the LADSO convinced him to stay on as music director.

Each year, the LADSO performs benefit concerts, including some for breast cancer research. (Six members of the orchestra are breast cancer survivors; Shulman performed their surgeries.) A recent concert featured the American premiere of music written by Czech Jewish composer Erwin Schulhoff, who'd written the music while imprisoned in a Nazi concentration camp; he later died in the camps. "It was a very powerful experience," says Shulman. "The power of the music, even in those desperate times, that energy, rather inspires me. I want to take our orchestra where a community orchestra wouldn't normally go." *—MH*

THE WAY WE ARE: CLASS OF '88

BY JENNIFER MATSON

Keith Mankin (MD '88) says that his dad, **Henry Mankin** (MD '53), gave him two main pieces of advice when he decided to become a doctor. First, get out of medicine. Second, if you're going to stick around, then make every patient the most important person to you in the world while you're treating him or her. Mankin rejected the first piece of advice and embraced the second. A pediatric orthopaedic surgeon, Mankin tries to make spinal surgeries as comfortable as possible for his young patients. Often, donor blood is not suitable for transfusions in children, so two or three units of the child's own blood must be drawn. The process is depleting and painful. When Mankin was at Massachusetts General Hospital in Boston, he began researching epoetin, a drug commonly used to raise the red blood cell count of people with anemia during cancer treatments. Since

moving to the Raleigh Orthopaedic Clinic in North Carolina in December of 2000, Mankin has used epoetin to treat 40 of his patients, without needing to transfuse a single unit of blood.

Mankin isn't the only Class of '88 grad to change jobs recently. **Charles Perrotta** (MD '88) recently returned to Pittsburgh after five years in Kansas. Before that, as a child psychiatrist in the U.S. Army, he was stationed in Germany for five years. As part of a rapid response team for disasters and terrorist incidents, he was twice sent to Saudi Arabia, following bombings in Riyadh and Dhahran. Perrotta also worked with some of the Airborne Rangers whose experience in Somalia was depicted in the movie *Black Hawk Down.* Now, he's back in Western Pennsylvania, serving as medical director of the Merck Unit at Western Psychiatric Institute and Clinic and an assistant professor of psychiatry in the School of Medicine.

Maryanne Hugo (MD '88), an obstetrician and gynecologist at Magee-Womens Hospital, remembers spending her senior year of med school in England. Often, after completing her rounds at the hospital, she and classmate **Stephen Day** (MD '88) would go to the theater in London. In Pittsburgh, during reunion weekend, another theatrical experience awaited her and her classmates, this year's Scope and Scalpel production, the *Sopranolols.* Hugo helped organize the Class of '88's 15-year get-together at PNC Park with classmates **Carl Bruning**, **Sam Buffer**, **Vincent Mosesso**, and **Lynn Sydor**.



At the Class of '88 reunion—front row (left to right) Sam Buffer, John Yoder, Vincent Mosesso, and Joel Horowitz; back row (left to right) Keith Mankin, Karen Bash, Steven Novak, Lynn Sydor, Alan Klein, and Andrew Kaye.

GRACE S. GREGG
NOVEMBER 25, 1919–
APRIL 23, 2003



OWL 1943

Gregg with fellow Alpha Omega Alpha members in 1943

Grace S. Gregg (MD '43) examined her 9-year-old son's enlarged spleen, took his temperature, and demanded that he be tested for leukemia. The diagnosis was that he had mononucleosis, not cancer, but Gregg wasn't so sure. "She almost couldn't be convinced until I didn't die." John S. Gregg (MD '73), now a cardiologist at Mercy Hospital of Pittsburgh, says with a laugh: "I won that argument."

Although she may have been overanxious when it came to diagnosing the health of her own children, Grace Gregg was remembered by her colleagues as a precise and dedicated clinician. Gregg graduated from the University of Pittsburgh School of Medicine with honors in 1943; then as an intern and resident, Gregg helped to fill the void left by physicians serving in World War II.

In the 1950s, Gregg treated children with rheumatic fever and polio. She also researched cerebral palsy and neonatal diseases. Later she became director of the development clinic in Children's Hospital of Pittsburgh and medical director of the Merck Unit in the Western Psychiatric Institute and Clinic. Her son says that Grace Gregg often felt uncomfortable at parties chatting with women who wanted to talk only about their duties as housewives; she preferred to join the men and talk medicine.

Medicine was a common family bond. Gregg learned to love the field as a little girl when her father, a physician, let her tag along as he made his rounds. She married Frank J. Gregg (MD '33), who was a cardiologist, and two of her five children became physicians. —*JM*

IN MEMORIAM

'20s

WILLIAM B. MCLAUGHLIN (MD '27)
FEB. 5, 2003

'30s

JULIUS HERMAN (MD '39)
APRIL 29, 2003

'40s

RICHARD H. MCCORMICK (MD '40)
FEB. 21, 2003

WILSON B. PIZZI, SR. (MD '42)
FEB. 1, 2003

ROBERT F. KLEINSCHMIDT (MD '45)
MARCH 16, 2003

MARY FRANCES RICKETTS (MD '45)
APRIL 13, 2003

'50s

PETER J. MATURO (MD '50)
MARCH 14, 2003

MARY GARRITY ROUND (MD '50)
MAY 24, 2003

FACULTY

R. WALTER SCHLESINGER
JAN. 11, 2003

ANNA-MARY CARPENTER
FEB. 4, 2003

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JACQUELINE TULSKY: INSIDE AND OUT

BY ERICA LLOYD



CAREN ALPERT

Tulsky with San Quentin State Prison in the background

In a room just off the yard, where a basketball game is under way and a man does squats with the intensity of an Olympian in training, class convenes. The "peer educators" session here at California's San Quentin State Prison was designed for inmates who want to be part of a program to coach new prisoners about health matters. Billy Ford (not his real name), like some of the other men in the class, just wants to learn. He hopes to be released soon and is eager to know about the germs "out there." Ford has been incarcerated for 27 years but is up for release this summer, that is, if Governor Gray Davis doesn't snatch his chance away from him again, as he says.

The instructor, Jacqueline (Peterson) Tulsky (MD '88), briefs the class on the different varieties of hepatitis. After a couple of hours, it's time for a role-playing exercise. Tulsky will act out the part of a woman with hepatitis; the class members will assume the roles of doctors whose job it is to diagnose which type of hepatitis she has.

Tulsky "the patient" hints at an instance where she might have shared a needle.

"Doc, it's true, I like to party," she says, nodding her head and placing a few wayward wisps of blond hair behind her ear. Everyone laughs.

"Come on. It could be true," Tulsky protests, with a hint of her native South Dakota in her voice. The men are having trouble swallowing her dramatization, but Tulsky doesn't seem to mind. She coaches them through the rest of the exercise with ease.

Their instructor brings a polite hardiness to her work. Throughout her general medicine career, she has been drawn to treat hard-to-reach populations like the homeless, the addicted, and the incarcerated. Tulsky is an associate professor of medicine at the University of California, San Francisco; she works with HIV-positive patients at San Francisco General Hospital's methadone clinic. As part of a two-year Soros Advocacy Fellowship, awarded last fall, the Pitt alum is focusing on improving linkages among healthcare providers and programs that affect incarcerated or recently incarcerated adults. Her work is supported by the community-based organization Centerforce.

"Right now, there are 2 million people locked up in the United States," says Tulsky, adding that several million more are released each year. (According to Justice Department estimates, 11 million were admitted to prisons and jails this year.) Their healthcare problems become society's healthcare problems, she notes. Beyond the statistics, some red flags have been raised in her own work, like the woman who was released from prison to her family in a coma. She ended up at the hospital under Tulsky's care. Tulsky knew next to nothing about her medical history, and she had no idea whom to contact at the prison to find out more. All she had to go on was a consult from a neurologist in the town near the prison, and the consult was only a couple of pages long. Tulsky did learn that the woman had been an "unremarkable" inmate who'd started behaving erratically and then developed seizures. As it turned out, the woman had HIV, which hadn't been treated, and ended up with progressive multifocal leukoencephalopathy, an incurable neurological disorder associated with advanced AIDS. The woman died shortly after her arrival at the hospital.

"Maybe she didn't get [HIV] meds. Maybe she didn't want meds. There was nothing I could say when the family asked if [the prison] had taken care of her well. I had no information about whether they had or hadn't."

Cases like this one got Tulsky asking, *What's wrong with this system?* About 4 percent of the American population was at its mercy. How many cracks were there to fall through?

She knows some people put a lot of heart into making the system work. There's a physician at San Quentin, for example, who raced after a bus to make sure a released prisoner didn't leave without his antipsychotic medication.

A nurse at the L.A. County Jail told her about some of the challenges that are simply routine there. Normally, inmates at the jail get medications by waiting in a pill line. But if there's a lockdown, the inmates aren't allowed to leave their cells; and that can last for days, even weeks. During lockdowns, staff members trudge the meds cart up and down stairs to make sure diabetic prisoners and others in dire need get their medications.

Through her fellowship, Tulsky has learned that security precautions can mean prison doctors aren't allowed to use outside pagers and may not have Internet connections. At huge prisons like San Quentin, a physician might work a quarter of a mile away from a fax machine; when you're responsible for the care of thousands of prisoners, that can become a significant hassle.

Tulsky has high regard for the medical director at the San Francisco County Jail, who asserts that offering preventive measures, like mammograms and Pap smears, is part of the mission of the healthcare program at the jail.

"I'm very much a realist," says Tulsky. "I used to work with the homeless population. There's nothing I'm going to do or any group of doctors is going to do that's going to make these institutions go away.

"It's making the best of a bad opportunity." ■



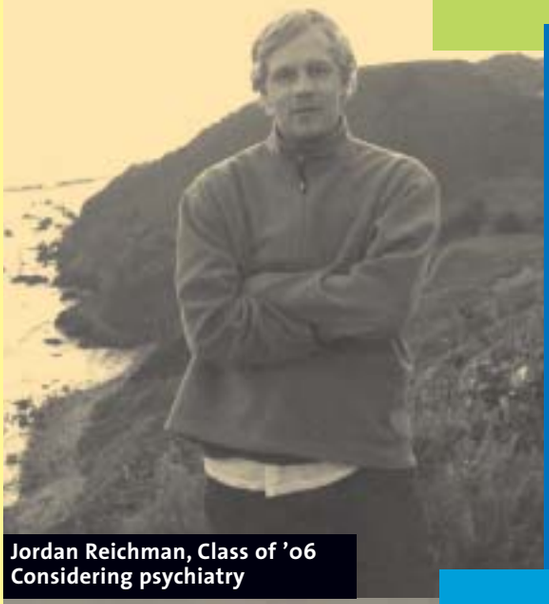
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Considering psychiatry

salad chef

Jeff Johnson, Class of '05
Considering sleep research/medicine



Minister



Jordan Reichman, Class of '06
Considering psychiatry

Oceanographer

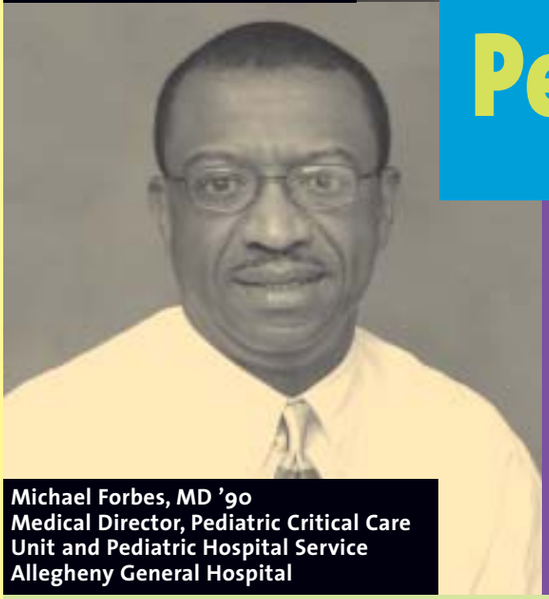
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Urban Redeveloper



Mark Zeidel
Chair, Department of Medicine
University of Pittsburgh

Percussionist



Michael Forbes, MD '90
Medical Director, Pediatric Critical Care Unit and Pediatric Hospital Service
Allegheny General Hospital

Sign Language Interpreter

So, how well do you know the chair of medicine? This summer, in our sometimes annual match, we explore past and dual lives. Try your hand at matching former and other vocations of these startlingly talented Pitt med people. We regret we weren't able to include many others we found, including a producer for *The Simpsons* and a beekeeper. (Answers are on the inside front cover.)

CALENDAR

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AUGUST 10
Lecture Rooms 5 and 6, Scaife Hall
3 p.m.
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Student Affairs Office
412-648-9040
student_affairs@medschool.pitt.edu

DR. RICHARD N. HARRIS MEMORIAL GOLF OUTING
SEPTEMBER 15
Edgewood Country Club
Churchill, Pennsylvania
1:30 p.m.
For information
John G. Kokales (MD '73)
412-647-4567
kokalesjg@msx.upmc.edu

CLASS OF '48 REUNION
SEPTEMBER 19–21
Hidden Valley Resort
Somerset, Pennsylvania
For information
Medical Alumni Association
412-648-9090 or 1-877-MED-ALUM
medalum@medschool.pitt.edu

HOMECOMING WEEKEND
OCTOBER 24–26
Pittsburgh Panthers vs.
Syracuse Orangemen
Saturday, October 25
For information
Medical Alumni Association
412-648-9090 or 1-877-MED-ALUM
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or visit www.alumni.pitt.edu

ROSS H. MUSGRAVE LECTURESHIP
NOVEMBER 7 AND 8
Speaker: Joseph McCarthy, MD
For information
Medical Alumni Association
412-648-9090 or 1-877-MED-ALUM
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Featuring Tony Bennett
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Concert at Heinz Hall, 7:30 p.m.
For information
UPCI Development Department
412-623-4700

MEDICAL ALUMNI WEEKEND
MAY 21–23, 2004
Classes Celebrating: TBA
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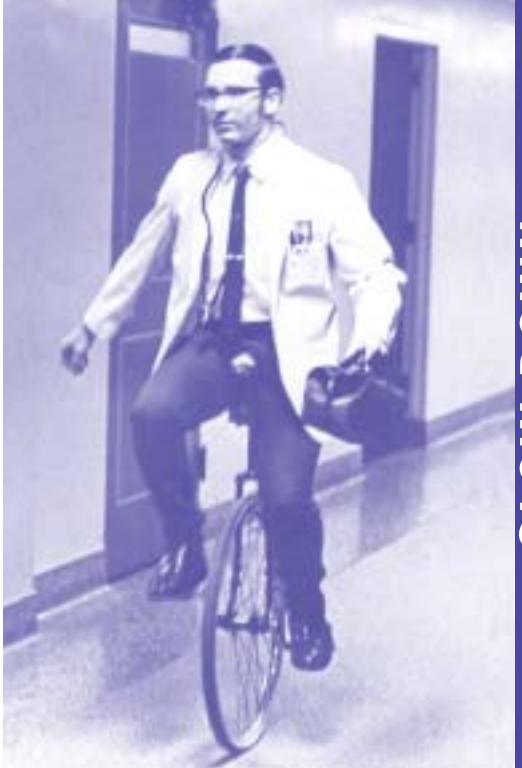
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