Explorations and revelations taking place at the medical school

This humanoid is failing fast.

JOHN RITTER

A GROWING SIM FAMILY

PAY NO MIND TO THE PROFESSOR BEHIND THE CURTAIN | BY RONAL MITCHELL

On the videotape is a Pitt med student (we'll call him Eric Marks) wearing indigo scrubs. He stands near a mannequin on a gurney. It's his first day in a four-week critical care medicine course.The life-size humanoid on the bed is SimMan, a computerized patient simulator. SimMan audibly breathes, his chest moves up and down, and he has a pulse, heart rhythms, and blood oxygen levels, among other features. Today, the mannequin is undergoing cardiac arrest—and Marks is called upon to lead a group of students responding to the crisis.

It's an urgent situation for SimMan, but instead of checking his vital signs, Marks stands motionless, asking the mannequin a series of questions: "Do you have a history of injuries to the chest? Can you climb a flight of stairs?" His bedside manner is terrific, yet SimMan, whose pulse is getting weaker and weaker, can barely summon the breath to reply. A person behind a curtain, much like the Wizard of Oz, speaks for SimMan; the voice is broadcast into the room where SimMan lies. Nine minutes into the exercise, Marks finally puts a blood pressure cuff on the mannequin and monitors the heart rate. Other students apply an oxygen mask—but they do it incorrectly, and it doesn't work. The steady blip of the heartbeat becomes irregular. The students try to insert a breathing tube but fail. The heart monitor displays an eerie flat line as it lets out a high-pitched beep.

Nervous chatter ensues throughout the room as Marks looks blankly at the equipment and his patient, wondering where he failed.

The hands-on exercise for Marks and his classmates is the stuff of a typical day at Pitt's Peter M. Winter Institute for Simulation Education and Research (WISER)—the largest civilian simulation center in the world. In 2002, WISER hosted 7,000 educational simulation experiences. Using SimMan, trainees can practice key skills—such as responding to a drug overdose, administering anesthesia, inserting a bronchoscope into a lung, or putting a central line into a neck vein without puncturing an artery or damaging the vocal cords. The center has 12 rooms set up for teaching, is home to 14 mannequins, and provides training to med students, residents, and fellows—it even offers refreshers so that faculty can brush up on skills.

Some of the mannequins are specialized. One, with splotches of fake red blood on his plastic body, has a broken foot, a snapped bone protruding from his leg, abdominal injuries, and a piece of barbed wire piercing his face—plus, he's in cardiac arrest. (His story: He suffered a myocardial infarction while mowing the lawn, fell down a hill, onto a fence, and the mower fell on top of him.) This memorable mannequin teaches students how to establish priorities: When someone comes into the emergency department with multiple traumatic injuries, how do you decide what to do first?

Although the mannequins can be used to mimic many different medical situations, the underlying goal of simulation education is always the same: Give trainees hands-on practice without posing any risk to patients. In most medical schools in the country, students learn clinical skills primarily through observation and by performing procedures on real patients under supervision, notes Tom Dongilli, WISER's director of operations. Pitt's facility gives students the opportunity to practice procedures first—and to get lots of practice. Before graduation, every Pitt med student spends 50 hours learning in WISER. The majority of students elect to take the fourth-year critical care medicine rotation, as Marks did—which means they spend an additional 40 hours learning in the facility.

The intensity of simulation education at Pitt is so unusual that every year about 4,000 visitors—many from other medical schools—tour the facility. (And that's not counting the 3,000 prospective med students who visit the center annually.)

Simulation research is also part of WISER's mission. In 1996 (before WISER was created), John Schaefer, now director of the institute, and René Gonzales, a former Pitt anesthesiologist, created and patented the simulator AirMan. Their invention was an improvement on previous simulators, and Laerdal Corporation, in Norway, licensed the patent, manufactured AirMan, then later upgraded AirMan into a yet more sophisticated model, the present-day state-of-the-art SimMan.

The Sim family is growing. In one of the rooms at WISER, a simulator prototype sits on a patient examination table; a small plastic chest is dismantled, with mechanical parts strewn about. It's SimBaby—a Laerdal creation. The pint-size mannequin will help medical trainees confront the challenges posed by an infant's physiology. For example, to insert a breathing tube into an infant, the neck and body must be positioned in a different way than when inserting a tube into an adult.

When SimBaby becomes available for sale later this year, it will have grand mal seizures, its lips and fingernails will turn blue to indicate lack of oxygen, and its pupils will dilate and contract. No other simulator can get sick in those ways. Every few weeks, Laerdal sends a new version of SimBaby to WISER for testing—the institute is helping to develop the mannequin into a more useful and sophisticated tool.

Four weeks after Marks' debut in critical care medicine, the med student tries again. He has received feedback from his instructor on his initial performance. His videotaped session with the mannequin (there are tiny cameras in each simulation suite) was accessible through the Internet for Marks to review. Now, he is back in action. SimMan is suffering, yet again, from cardiac arrest. This time, Marks takes charge of his team of students immediately. He has them get an IV going and an oxygen mask placed; he checks the pulse. When the heart stops, he tells his classmates to start CPR. He directs the use of a defibrillator. SimMan's heartbeat comes back, steady and strong. ■

KINDRED SPIRITS

CLOISTER FELLOWS DELVE INTO LIFE AT NIH | BY LOIS BARON

The communal dinners take place twice a week. It's dark outside by the time you sit down to eat the surprisingly good food off the buffet line. It feels cozy because you're with kindred spirits. The people here are as interested in science as you are. On Monday night, the speaker might be the man who invented the celebrated cancer drug Gleevec. On Thursday nights, it's two fellow students who are also doing research at the National Institutes of Health (NIH). You learn about tumor immunology, multiple sclerosis, how brain structure changes with addiction.

Ty Muhly (left) and Xinglei Shen

STEPH HOOTON/PICTOGRAM STUDIO

Wallis "Ty" Muhly and Xinglei Shen (both in the Class of '05) came to the red-brick, lush-green-grass NIH campus in Bethesda, Md., last summer as fellows in the one-year Howard Hughes Medical Institute–National Institutes of Health (HHMI-NIH) Research Scholars Program. And they're digging in to sample it all.

For the 2003–'04 academic year, 179 medical and dental students from around the country applied, and 42 won fellowships. (In addition to a stipend and subsidized housing, they also get a parking place—a privilege normally reserved for VIPs like institute directors.)

The HHMI-NIH scholars choose the lab in which they'll work. Options include those of more than 1,200 NIH researchers working on more than 2,500 research projects.

For Shen, the deciding factor was the chance to study the telomere—a cell structure that piqued his interest in high school. Telomeres are repeating sequences of DNA that appear at the ends of chromosomes. Because these sequences get shorter each time a cell divides, telomere length signals how close a cell is to senescence and no longer replicating.

The lab Shen works in is examining a hypothesis generated from the findings of Steve Rosenberg, an NIH researcher. Rosenberg successfully treated metastatic melanoma by taking a biopsy of a tumor, extracting immune cells (lymphocytes) embedded in the tissue, growing the cells in culture, and injecting large numbers of the cells back into the patient to proliferate and resist the cancer.

It stands to reason that the treatment might work better if it used immune cells that can divide many, many times—indicated by longer telomeres. So the lab explores whether patients who respond well to Rosenberg's therapy have immune cells that differ in telomere length from patients who don't.

It was important to Muhly to have a lot of interaction with his primary investigator, so he chose to work with Michael Iadarola. Not only did Muhly opt for an energetic PI who is around a lot, but also, with Iadarola, he found a research topic of great clinical import. The lab, part of the National Institute for Dental and Craniofacial Research, explores how neurons respond to painful stimuli. Muhly and his new colleagues want to learn which genes are turned on when animals are exposed to irritants. "If we can figure out how neurons respond to noxious stimuli, we might be able to design drugs that block the painful signal carried by the neuron before it reaches the brain," Muhly says. And doctors will likely treat more chronic pain as life spans extend, and the baby boomers march into advanced ages.

Like most of the HHMI-NIH fellows, Muhly (with his wife) and Shen live in the Cloisters, an old monastery tucked into a corner of the NIH campus. The shared living facility contributes to the communal atmosphere.

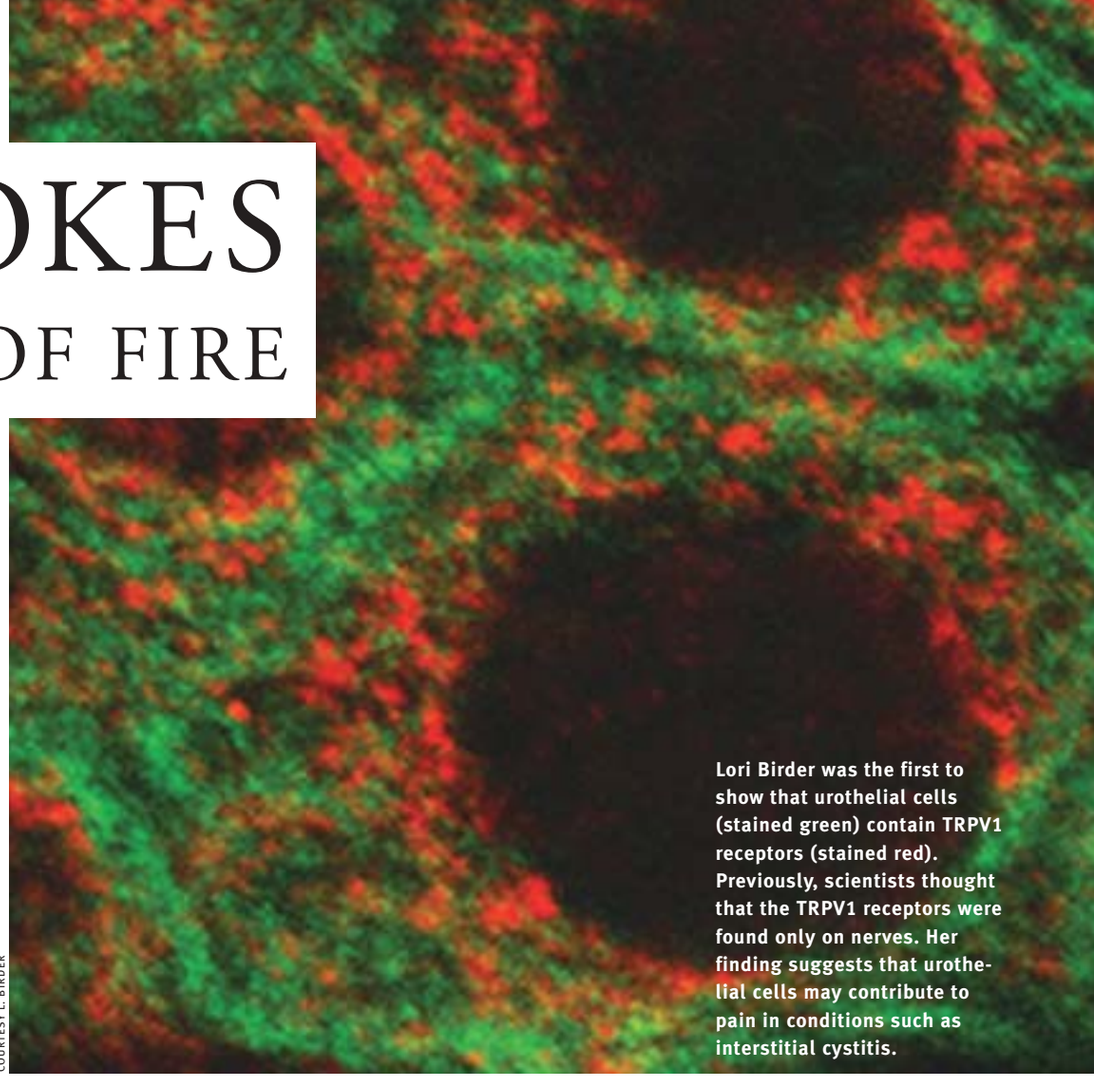
"Everyone here is very involved in science," Shen says. He never gets a blank look when he describes his work. "It's easy to talk with people who understand what I'm saying."

And at those biweekly dinners, Shen, 24, is astounded at how ably the fellows discuss NIH research. "We're so young, but we sound like real scientists," he says. ■

WHAT STOKES A BELLY OF FIRE

CELLS LINING BLADDER SIMILAR TO NERVES

BY KRISTIN OHLSON



COURTESY L. BIRDER

Lori Birder was the first to show that urothelial cells (stained green) contain TRPV1 receptors (stained red). Previously, scientists thought that the TRPV1 receptors were found only on nerves. Her finding suggests that urothelial cells may contribute to pain in conditions such as interstitial cystitis.

Some patients describe it as a belly full of broken glass, some as a fire deep in the abdomen. The 700,000 people in the United States who have interstitial cystitis feel pain and intense urgency to urinate even with only tiny amounts of urine in their bladders. They have to run to the bathroom frequently—up to 60 times a day in the worst cases, even at night. Under the stress of all this discomfort—and with no cure in sight—some patients become suicidal.

No one knows why people get interstitial cystitis, a chronic inflammation of the bladder. It has no identifiable bacterial cause. A few treatments can provide temporary relief, but no one knows how to cure the disease; it doesn't respond to antibiotics or other drugs that cure urinary tract infections.

Those studying the bladder typically hadn't given much thought to the urothelial cells as a source of the pain of interstitial cystitis. These large cells line the inside of the bladder and stretch and contract depending on how much urine is inside. They fit together so tightly that they protect the underlying layer of nerves and other more delicate tissues from toxic substances in the urine.

"People used to think of the urothelium as simply a barrier that protects the underlying tissue," says Lori Birder, assistant professor of medicine in the University of Pittsburgh School of Medicine. "People thought of it as a passive tissue that didn't have anything to do with sensation."

Birder changed this perception a few years ago when she discovered that these urothelial cells have some sensing behaviors that are similar to those of neurons. She had been conducting studies with capsaicin, the chemical that makes chili peppers hot. Capsaicin is used clinically for temporary pain control—it can desensitize nerves that carry pain signals. Some people with interstitial cystitis are treated by having their bladders filled with a solution containing capsaicin, which relieves some of their symptoms for a while. Birder studied the effect of capsaicin on strips of tissue from human bladders containing all the component parts—urothelial cells, nerves, and muscles. She assumed that only the nerves underlying the urothelium would be affected; she was wrong. The urothelial cells reacted to the chemical. In this and subsequent studies, Birder—who received a Young Investigators Award from the International Union of Pharmacology for this work—showed that the urothelial cell receptors released substances that a neuron would, like nitric oxide. As it turns out, the cells release transmitters and other mediators. And these actions can trigger an increase in neural activity, intensifying pain.

Her discovery suggests that, through messengers such as the transmitters and mediators, urothelial cells "talk" to the underlying nerves. "If there's an inflammation, the urothelial cells might 'talk' more, so that the person feels pain even if there is only a normal amount of urine in the bladder," says Birder. She suspects this happens when the bladder is inflamed or injured.

Eventually, Birder's work may give drug companies more options for the development of pain medications for people with interstitial cystitis. Drug companies are already working on compounds that target the bladder nerves, but it's possible that they may find different substances that target the urothelial receptors.

"In the last few years, a lot of new surprises have emerged regarding the role of these cells in bladder function," she says.

Birder continues to explore the nervelike properties of urothelial cells and to study the role the cells may play in interstitial cystitis. One finding: Cats with naturally occurring forms of interstitial cystitis have abnormalities in their urotheliums. Birder believes the urothelial cells may also be implicated in other conditions that can affect bladder function, such as diabetes and spinal cord injury. ■