

Devoted to noteworthy happenings

at the medical school

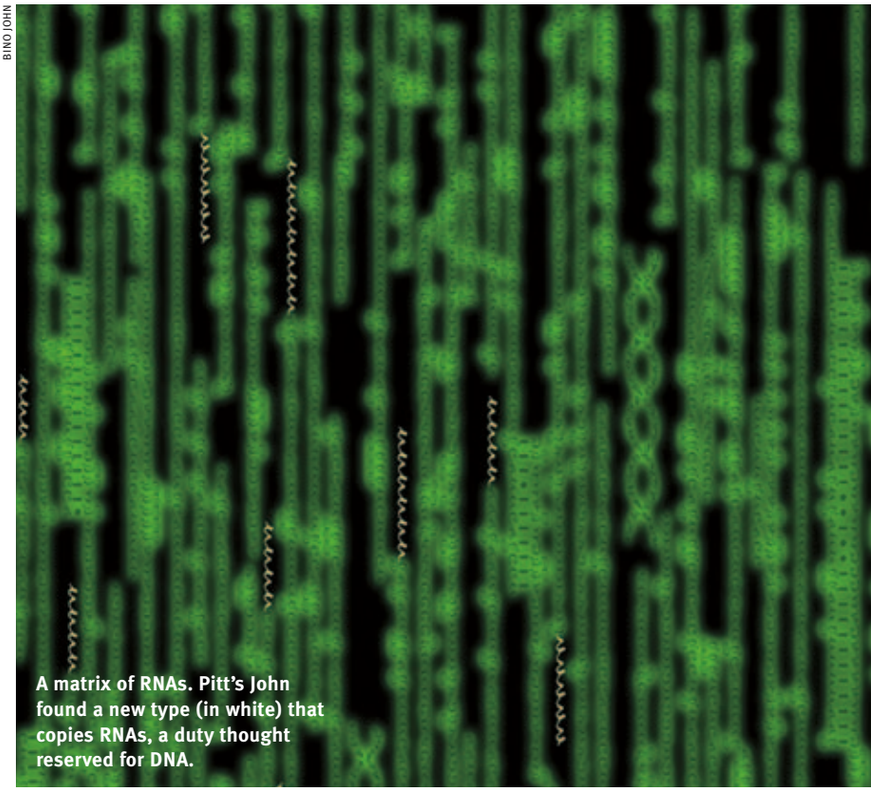
How Mammals Make RNA: Take 2

It's gospel in the scientific community that all RNA in human cells was copied from the DNA template. It's also wrong.

Along with collaborators at Helicos BioSciences Corporation and Integromics, the University of Pittsburgh's Bino John used single-molecule sequencing technology to confirm that mammalian cells can synthesize RNA by copying RNA molecules directly.

Some had suspected this was possible, but John's letter to *Nature* (July 29, 2010) is the first to confirm these suspicions. John, a PhD assistant professor of computational and systems biology, says that his findings show that single-molecule sequencing is vital for "accurate and comprehensive genetic profiling." The work also has implications for diagnosis, because scientists now have another place to look for causes of disease. —*Joe Miksch*

BINO JOHN



A matrix of RNAs. Pitt's John found a new type (in white) that copies RNAs, a duty thought reserved for DNA.

FOOTNOTE

You look tired. Why don't you rest your head on my spleen? Er, pillow. Um, actually, both, in this case. During Science 2010, Pitt's annual celebration of all things science-y, a display called "Translational Art: From Bench to Bed Top" featured a slew of soft pillows in designs inspired by hard science. The aforementioned pillow now shares space in the waiting area of Pitt's Center for Biologic Imaging with others, including one festooned with an image of a dendritic cell and a T-cell interacting; you could also cozy up to a plush white mouse wearing appliqué organs.

Aspirin for Cancer

Sometimes the simple things can be as valuable as the highest of high technology.

For years, doctors have known that nonsteroidal anti-inflammatory drugs (NSAIDs)—such as that old medicine-chest staple, aspirin—can lower the risk of colon cancer. The University of Pittsburgh's Lin Zhang, a PhD associate professor of pharmacology and chemical biology, thinks he finally knows why this is the case. In an article published in the *Proceedings of the National Academy of Sciences*, Zhang reports that NSAIDs target cancer stem cells that have accumulated mutations that may lead to cancer.

Zhang found that when their feed was augmented with NSAIDs, a line of mice predisposed to colon cancer experienced a marked increase in apoptosis—programmed cell death—in these cancer stem cells within one week.

Down the line, Zhang says, scientists can use this knowledge to develop agents that will further sensitize abnormal stem cells to NSAIDs while assessing the effectiveness of cancer-prevention drugs. —*JM*



CAMI MESA

A&Q

David K.C. Cooper: Surgery's Revolutionaries

David K.C. Cooper, who won the TTS-Roche Award for Excellence in Translational Science in 2010, was part of the team that did the U.K.'s first series of successful heart transplants in the 1970s; he also worked with Christiaan Barnard (who performed the first heart transplant in 1967) in Cape Town, South Africa. Now a University of Pittsburgh professor of surgery, Cooper has since put down his scalpel to pursue xenotransplantation research. He is working toward a future where genetically engineered pigs will supply needed corneas, hearts, and islets for transplant.

Cooper marveled at the bold and visionary surgeons, many of whom he knew, who made modern heart surgery possible. His hobby for the past 20 years was researching and writing his latest book, *Open Heart, The Radical Surgeons Who Revolutionized Medicine* (Kaplan, 2010).

Some of these men were establishment figures and some were mavericks. [For example], by putting patients in a hypothermic bath to drop their body temperatures for surgery, [Minnesota's] F. John Lewis gave himself six minutes instead of four to operate on the quiescent heart. He was the first person who was able to actually see what he was doing in the heart, rather than just operating blindly by inserting a finger. Yet he walked away from surgery soon after and developed computers for the ICU. He eventually became disenchanted with academic medicine and retired at 59. He took up residence in Southern California, where he kept busy developing physical fitness, studying mathematics, reading, and trying his hand as an artist and musician. He told me someday he'd like to sing and play piano in a bar, although he admitted he couldn't sing and playing the piano was "difficult enough." This is the man who initiated open heart surgery!

Able to push ahead despite high mortality rates. Christiaan Barnard told me, "Some weeks, we would operate on one patient every day, and by the end of the week we would have five dead patients." It took tremendous fortitude on the part of the surgeons to persevere against such a high mortality. They had to believe that what they were attempting would eventually prove successful.

His question for us. If there was a realistic chance that a pig heart would keep you alive for a number of years, sustaining a good quality of life, would you be prepared to have a pig heart as a transplant? *—Interview by Erica Lloyd*

Faculty Snapshots

It takes brains to be number one. A study published in the September 2010 *Journal of Neurosurgery* places Pitt's Department of Neurosurgery the overall leader, tied with the University of Virginia, in the academic impact of its publications. The journal counted the number of times a department's publications—113 American and Canadian residential neurosurgery departments were included in the survey—were cited in other academic neurosurgery papers. The journal counted citations from 2000 to 2009. Pitt's L. Dade Lunsford—Lars Leksell Professor of Neurological Surgery, Distinguished Professor of Neurological Surgery, and an MD—headed the department during many of those years. Robert Friedlander, an MD professor of neurological surgery and current chair of the department, says what makes the ranking impressive is that the study takes into account not only the volume of a department's work, but also its quality. "We have different colleagues at the highest levels all working with each other," says Friedlander. "It's a statement about the community as a whole."


Lunsford


Friedlander

George Michalopoulos is the recipient of the American Liver Foundation's Distinguished Scientific Achievement Award for 2010. The award honors scientists who undertake novel work, mentor other researchers, and attract substantial funding over the course of their careers. A professor in and chair of Pitt's Department of Pathology, Michalopoulos specializes in liver regeneration and was the first to identify hepatocyte growth factor and its receptor, c-Met. Michalopoulos, an MD/PhD, says it's an "acrobatic balance" to do his own work while mentoring others and managing the department. *—Kelsey Ballance*


Michalopoulos

No Time or Money

A whistle blows, and about 75 medical students leap out of their chairs and scatter, scrambling to be first in line to cash a check, make an appointment with social services, and get to work. They have a limited amount of time to fulfill a week's worth of obligations. A student waves his hands in frustration when he sees the line at the quick-loan store. Another sighs when she learns that food stamps won't kick in for two weeks. Rent is due at the end of the week, and there is very little money in the bank. On top of that, the bank won't cash her checks, she has no more transportation vouchers, and many of her neighbors' homes have been robbed recently.

This is a poverty simulation exercise, part of the Population Health Course, a class in the University of Pittsburgh School of Medicine's new second-year Patient, Physician, and Society block. Each student is assigned a role, and the exercise's four 15-minute blocks simulate one month in the life of a person in poverty.

"It's important for medical students to understand … that poverty will affect their work. The woman who is late to her appointment may have had to take three buses to get there and drop her child off at day care in between," says Hollis Day, an MD associate professor of medicine and medical director of the school's Advanced Clinical Education Center. "We're hoping the students develop empathy for people who … face barriers to health care."

After the exercise, students discuss the experience. Many detail how stressful it was to complete their tasks and that no one cared about their difficulties. Suzie Lee (Class of 2013) says, "I couldn't get anything done at all. I had no money or time to accomplish much. It was overwhelming. And eye opening." *—Maureen Passmore*



GETTY IMAGES

SELF-REPORTS IN QUESTION

There's an old saying among the ink-stained wretches of newspaper journalism: "If your mother says she loves you, check it out." Recent work done by Miguel Regueiro shows that the same sentiment can be applied to Crohn's disease patients who say they feel just fine after corrective surgery.

The Crohn's Disease Activity Index, which uses patient self-reporting to assess recurrence of the disease, might need to be replaced with more objective monitoring, such as endoscopy, suggests Regueiro.

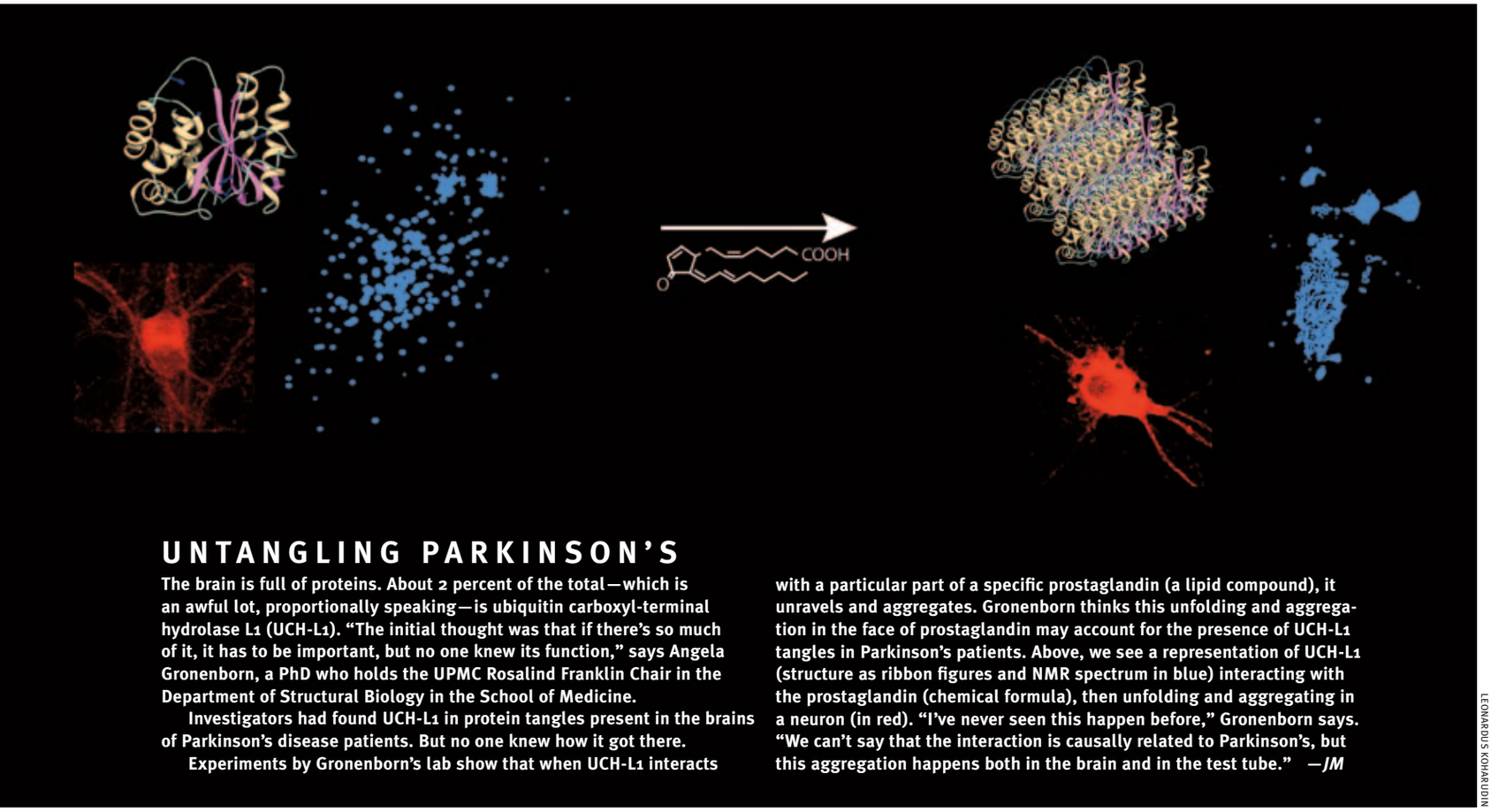
Regueiro is an MD associate professor of medicine and codirector of the Inflammatory Bowel Disease Center in the School of Medicine. He has found that even though many patients report they're symptom-free, sometimes even years after surgery, the disease may have returned and started wreaking havoc in their intestines. A delay in treatment, Regueiro says, may necessitate a second surgery. ***—JM***

POWER COUPLE JOINS PITT

The School of Medicine is set to welcome a heavyweight husband-and-wife team to Pittsburgh. Jeremy Berg, a PhD and current director of the National Institute of General Medical Sciences, will become Pitt's first associate senior vice chancellor for science strategy and planning for the schools of the health sciences in July. His wife, Wendie Berg, an MD/PhD, is a renowned expert in breast cancer screening and has led major, multicenter clinical trials to explore the efficacy of adding ultrasound and aspects of nuclear medicine as adjuncts to mammography in breast cancer screening. Formerly on the faculty at Johns Hopkins University and director of the breast imaging program at the University of Maryland, she is expected to arrive in Pittsburgh in March and will be a professor of radiology.

Wendie Berg says that Pittsburgh offered her opportunities she couldn't find elsewhere. "It's interesting and dynamic and well-positioned for the future," she says. "There's a can-do atmosphere, and it's clear that breast imaging is a top priority."

Jeremy Berg's research portfolio includes advancing the understanding of how zinc-containing proteins bind to DNA or RNA and regulate gene activity. In addition to serving as associate senior vice chancellor—as such he will help direct and expand the University's contributions to biomedical research—he will be a professor of computational and systems biology in the School of Medicine. *—JM*



LEONARDUS KOHARUDIN

UNTANGLING PARKINSON'S

The brain is full of proteins. About 2 percent of the total—which is an awful lot, proportionally speaking—is ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1). "The initial thought was that if there's so much of it, it has to be important, but no one knew its function," says Angela Gronenborn, a PhD who holds the UPMC Rosalind Franklin Chair in the Department of Structural Biology in the School of Medicine.

Investigators had found UCH-L1 in protein tangles present in the brains of Parkinson's disease patients. But no one knew how it got there.

Experiments by Gronenborn's lab show that when UCH-L1 interacts with a particular part of a specific prostaglandin (a lipid compound), it unravels and aggregates. Gronenborn thinks this unfolding and aggregation in the face of prostaglandin may account for the presence of UCH-L1 tangles in Parkinson's patients. Above, we see a representation of UCH-L1 (structure as ribbon figures and NMR spectrum in blue) interacting with the prostaglandin (chemical formula), then unfolding and aggregating in a neuron (in red). "I've never seen this happen before," Gronenborn says. "We can't say that the interaction is causally related to Parkinson's, but this aggregation happens both in the brain and in the test tube." *—JM*

Appointments

In September, Edward Chu was appointed chief of the Division of Hematology/Oncology in the School of Medicine and deputy director of the University of Pittsburgh Cancer Institute (UPCI). Chu is an internationally recognized MD in the biology and treatment of colorectal cancer. He says that UPCI attracted him because it is well-designed for translational research. Before his arrival at Pitt, Chu was a professor of medicine and pharmacology at Yale University and the chief of medical oncology and deputy director of the Yale Cancer Center. Chu is now planning a clinical trial to study how the Chinese herbal remedy Huang Qin Tang might boost the effectiveness of chemotherapy.


Chu


Lee

UPCI and Magee-Womens Research Institute recently joined forces to found the Women's Cancer Research Center, which will help breast and gynecological cancer researchers translate promising findings for use in the clinic. Pitt attracted Baylor College of Medicine breast cancer researchers Adrian Lee and Steffi Oesterreich, husband and wife PhDs, as center leaders. Lee codirects the center with Robert Edwards, an MD professor in and vice chair of the Department of Obstetrics, Gynecology, and Reproductive Sciences. Oesterreich, an expert in estrogen-receptor biology and action, is the director of education. Lee, whose own work focuses on growth factor pathways, says he expects the new center will have "a rapid and major impact on reducing the burden of [women's cancers]."


Oesterreich

The School of Medicine's new Department of Cardiothoracic Surgery has found its leader. James Luketich will be the founding chair. An MD and the Henry T. Bahnson Professor of Cardiothoracic Surgery, Luketich has pioneered minimally invasive surgical techniques for esophageal and lung operations. His other specialties include multidisciplinary management of several types of thoracic cancers and Barrett's esophagus. Luketich was formerly the director of Pitt's Heart, Lung, and Esophageal Surgery Institute.


Luketich

Although he has served as a professor at Harvard and then at Carnegie Mellon University, D. Lansing Taylor has spent the most recent part of his career as an entrepreneur. Taylor developed fluorescent light microscopy techniques to give scientists a new perspective on living organisms and ended up founding several biotechnology companies, including Cellomics, that produce equipment for drug discovery and systems biology. He is now the director of Pitt's Drug Discovery Institute and is Allegheny Foundation Professor of Computational and Systems Biology. Taylor aims to balance pure science with focused drug development and wants to encourage other promising scientists to embark on their own spin-off and licensing ventures. *—KB*


Taylor