PITT TO BUILD CELL-LINE BANK

Our cells are always tuning up and repairing the DNA they carry around. When they fail to attend to this maintenance, bad things can happen, like cancer and many other diseases. Now a team led by Pitt’s Robert Sobol will give researchers important tools for understanding these deficiencies.

Scientists have identified about 165 genes as “bona fide DNA-repair genes,” as Sobol, an assistant professor of pharmacology and chemical biology, puts it. “All tumors are going to be defective in one of these genes down the line,” notes Sobol, who is based at the Hillman Cancer Center.

The National Institutes of Health has earmarked $2.5 million for Sobol’s lab and Trevigen, a biotechnology startup, to be used to build a bank of cell lines depleted of DNA-repair genes. The partners will attempt to create a cell line for each gene and make the bank widely available to researchers. Sobol’s lab will weaken the abilities of DNA-repair genes with RNA interference “knockdown” technology, which limits a gene’s ability to express itself. “The research community will use these cell lines in more ways than we can probably imagine,” he says.

—Erica Lloyd

A Whole Millisecond?

A millisecond (i.e., a thousandth of a second) isn’t a lot of time—unless you are trying to map, say, the complex origami that folds amino acid chains into proteins. If that’s the case, the millions of calculations required to track such atomic-level choreography might stop you long before the millisecond mark. Fortunately, now, there’s Anton. This new supercomputer—named for 17th-century Dutchman Anton van Leeuwenhoek, one of the fathers of microscopy—will spend the next year at the Pittsburgh Supercomputing Center (PSC), on loan from its designer, New York–based D.E. Shaw Research.

Previously, even the most powerful computers could track only about a microsecond (a millionth of a second) of protein movement. “But the time scales of biologically interesting things typically start in the millisecond range and longer,” says Markus Dittrich, a senior scientific specialist at PSC. Anton’s hardware runs molecular dynamics exclusively, allowing it to keep tabs on the details of those interesting biological moments.

Anton will support projects submitted by scientists from across the United States, including faculty from the School of Medicine. Dittrich reports that, thanks to a $2.7 million grant from the National Institutes of Health, the center has set up a “pretty beefy” data storage unit and analysis cluster for Anton data. “There may be much more hidden in the data,” Dittrich says, for scientists to mine. —Keith Gillogly & Kelsey Ballance
In 2009, a little-known technology made headlines when it helped Pittsburgh Steeler Hines Ward—who’d been benched for weeks after spraining his MCL—back onto the field in time to play in Super Bowl XLIII. A small amount of Ward’s blood was drawn, centrifuged down to a concentrate known as platelet-rich plasma (PRP), and then injected into Ward’s injured knee. For two decades, PRP has been used by surgeons to speed healing, but this high-profile case got people thinking. Could PRP be used to boost athletic performance?

In May, Johnny Huard—the Henry J. Mankin Professor of Orthopaedic Surgery Research and director of the Stem Cell Research Center at Pitt—met with his fellow members of the International Olympic Committee in Lausanne, Switzerland, to discuss the ethics of PRP use in athletic medicine. The committee hopes to release a consensus paper with their recommendations this fall.

On the committee’s objectives
The paper will address several issues. There’s the basic science of PRP, the standard procedures for administering it, its uses in tissue repair, its potential adverse effects. And then the big questions: Could PRP be used to enhance athletic performance, and if so, would that be considered cheating? Also, how do we regulate against that—or even test for it—since these would be [one’s] own cells?

On his role
As a basic scientist, my role is to ask, “What is the mechanism of PRP action?” We really don’t know how it works. It’s been used in the clinic for years. Surgeons don’t need special permission to do it, since these are [the patient’s] own cells, and many surgeons say PRP is helping their patients recover faster. But there’s still a lot we don’t know about it. Just last year, the literature showed that it can induce arthritis.

His question for us
Should PRP be considered doping? With the committee, the jury is still out. Personally, I think it takes more than just strength and stamina to make a great athlete. There are also instinct and the mental aspect of the game. So it’s not like PRP is going to turn a bad athlete like me into a gold medalist. —Interview by Elaine Vitone

A&Q
Johnny Huard on PRP: Dope or nope?
**CLASS OF 2014 CHEAT SHEET**

A handful of newcomers to Pitt med—members of the Class of 2014—stood out among the typically diverse and talented new matriculants.

When Ben Rothrauff was a freshman at Northwestern University, he balanced the rigors of playing defensive back in Big Ten football with an 8 a.m. organic chemistry class. The result was a new appreciation for studying as well as an interest in orthopaedics—call all those injuries a kind of “field experience.”

Ian Joel started playing music at age 4, and by 13, he was composing. He went on to write the theme for Eve’s Blood, a made-for-TV vampire flick. Although Joel had planned on pursuing a career in music, he ultimately chose medicine for its potential “real, positive impact.”

Cynthia Grady’s family in her native North Carolina was often expanding—she had “eight or so” foster cousins. Her family established a human services organization that creates group homes and other programs for adolescents. Caring for others was part of a family tradition that Grady intends to honor in her medical career.

Jeremy Kauffman studied theology in college and originally planned on entering the ministry. After he graduated, he traveled to Peru with a Christian organization that offered social work and health care services to homeless children. The experience inspired him to pursue a career “to help people tangibly, as well,” he says. —KG

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**Hong Kong Partnership**

The University of Pittsburgh’s Rocky Tuan has led the School of Medicine into a partnership with the Chinese University of Hong Kong. The collaboration, he says, will allow the two biomedical research powerhouses to collaborate in unraveling the mysteries of stem cells, partner to seek grants, exchange faculty and students, and host annual conferences on stem cells and regeneration.

Professor Tuan is director of the Center for Cellular and Molecular Engineering in the Department of Orthopaedic Surgery in the School of Medicine and executive vice chair for orthopaedic research at the University.

He is also a native of Hong Kong. It happens that Tuan is a friend and former classmate of the director of the newly established School of Biomedical Sciences at the Chinese University of Hong Kong, one of the top schools in Asia. The two also worked together at the National Institutes of Health.

“We chatted before he took off [for Hong Kong], and I came to Pittsburgh,” Tuan says. “We thought, Wouldn’t it be nice to work together after we get settled?” They did, and a memorandum of understanding formalizing the ties between the two institutions was signed in the spring. —Joe Miksch

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**A DRUG REPURPOSED**

Among genetic diseases, alpha1-antitrypsin (AT) deficiency is fairly common—one in 3,000 live births. It leads to the accumulation of a misfolded protein (ATZ) and liver disease. AT deficiency is the cardinal genetic cause of liver transplantsations in children.

David Perlmutter, an MD and the Vira I. Heinz Professor and Chair of the Department of Pediatrics in the University of Pittsburgh School of Medicine, as well as physician-in-chief and scientific director of Children’s Hospital of Pittsburgh of UPMC, is hopeful that doctors will be able to combat AT deficiency and reduce the need for liver transplantation in AT-deficient children by teaching an old drug new tricks.

Carbamazepine, an antiseizure drug, seems to reverse the accumulation of ATZ and hepatic fibrosis, partially by enhancing autophagy, a cellular digestion and recycling pathway. A phase I clinical trial of carbamazepine as an anti-ATZ drug is about to begin. Perlmutter’s collaborators include Pitt’s Tunda Hidvegi, PhD assistant professor of pediatrics and lead author, and George Michalopoulos, MD/PhD professor and chair of the Department of Pathology. Their findings were published in the July 9 issue of Science. —JM
Name Dropping

In October, the University of Pittsburgh hosted a cavalcade of stars at Science 2010, its annual celebration and showcase of scientific achievement. This year the title was Transformations. Among the University’s out-of-town guests:

Ann Graybiel is a PhD and the Walter A. Rosenblith Professor of Neuroscience at the Massachusetts Institute of Technology. She gave the 2010 Mellon Lecture. Since the early 1970s, Graybiel has explored the architecture of the basal ganglia and the function of that brain region’s neurotransmitters. Graybiel was the first to establish a mechanism for directed neurochemical control of complex brain circuits. Her talk was titled, “Our Habitual Lives: How the Brain Makes and Breaks Habits.”

Mark Roth, a 2007 recipient of a MacArthur fellowship, delivered the Klaus Hofmann Lecture. He is a PhD cell biologist at the Fred Hutchinson Cancer Research Center in Seattle. Roth made his reputation as a researcher of suspended animation. His presentation focused on the prospect that a combination of inhaled or injected hydrogen sulfide and cooling of the body can induce a state of suspended animation that is helpful in stabilizing injured people en route to the hospital.

Stephen Elledge was the 2010 Dickson Prize in Medicine lecturer. Elledge, a PhD and the Gregor Mendel Professor of Genetics and Medicine at Harvard Medical School, won the 2005 Genetics Society of America Medal for outstanding contributions to the field of genetics. His address delved into the intricacies of DNA damage response. Elucidating this, Elledge says, will be key to treating a slew of diseases, including cancer. “Understanding how these pathways sense the DNA damage caused by cancer chemotherapies allows us to develop more potent chemotherapies and target them to the right kinds of cancer,” he said at the event. — JM

OLD MEDS

For 60 years, Frank Critchfield (MD ’47) has collected antique apothecary accoutrements, haunting auctions and stopping at every mom-and-pop pharmacy he passed in his travels across the United States and Europe. Last fall, Critchfield donated the whole lot to the School of Pharmacy’s Elmer H. Grimm Sr. Pharmacy Museum. His gift of nearly 80 items was appraised at more than $50,000 and includes apothecary jars, measuring tankers, medicine dispensers, a scale, and a brass mortar and pestle. Also featured are items from black bags of yore: several glass blood-letting collectors of unknown origin and two ivory “doctor’s ladies” from China dating as far back as the 17th century. In those days, it wasn’t proper for a Chinese woman to disrobe for her doc, the 92-year-old ob/gyn explains. So she’d use a nude figurine to point out where it hurt. How’s that for health care’s modest history? — EV