

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

At the Heart of the Disease

Fats accumulate on artery walls and harden into plaque—that's coronary artery disease. Immune cells then infiltrate the plaque, which explains why inflammation levels are elevated in patients with the disease. That's the traditional view. But which came first—the chicken or the egg? Accumulating research suggests that inflammation facilitates the buildup of fats on artery walls. Researchers at Pitt and other sites involved in the Women's Ischemia Syndrome Evaluation study have shed new light on this question. They measured levels of SAA, a protein that indicates inflammation, in women with chest pain and found that women who had higher SAA levels also experienced a higher incidence of heart attack, other cardiovascular events, and coronary artery disease. Though the data cannot prove which came first—the inflammation or the plaque—the strength of the link suggests that inflammation may play a role in the development of the disease, says Oscar Marroquin, assistant professor of medicine who is a coinvestigator in the study. ***—Dottie Horn***



FOOTNOTE

For all those who think that Scope and Scalpel is a frivolous diversion for medical students at Pitt: The great neuropathologist Santiago Ramón y Cajal said, "Of all men, physicians and playwrights alone possess the rare privilege of charging money for the pain they inflict on us." Apparently, Scope and Scalpel is good practice.

AMERICANS IN PARIS, INSERM IN PITTSBURGH

When one of the world's leading stem cell researchers, Frenchman Bruno Péault, broke the news to his boss, Christian Bréchot, that he'd been recruited to the University of Pittsburgh, he was surprised to find the news was met with enthusiasm. From the perspective of Bréchot, CEO of the French Institute of Health and Medical Research (INSERM), he wasn't losing a scientist, he was potentially gaining an international collaboration. Bréchot knew the Pittsburgh community well. Péault is now on the faculty at Children's Hospital of Pittsburgh and a professor of pediatrics and of cell biology and physiology at Pitt; he continues to be actively involved with an INSERM research unit. And he'll soon lead the first joint research unit between INSERM and a U.S. medical school; that unit will focus on stem cell research. Pitt and INSERM are also considering collaborations in psychiatry, transplantation immunology, hepatology, and computational biology. ***—Erica Lloyd***



CAMI MESA

A&Q

with Alik Widge on Politics—Gotta Have the Do Re Mi

Ask Alik Widge (shown above) for an interview, and be forewarned, this MD/PhD student has a question for you: Are *you* politically active? Widge currently holds the only spot for a medical student on the board of AMPAC, the political action committee of the American Medical Association. Since 1989, the bipartisan AMPAC has given nearly $20 million in contributions to political candidates and parties, making it one of the top 10 PACs in the country in terms of amount of money distributed, according to the Center for Responsive Politics. As a board member, Widge works to increase medical student involvement in the PAC and votes on each individual allocation of AMPAC funds. So far, he has completed two years at the University of Pittsburgh School of Medicine and is now in his third year of working toward a PhD in robotics at Carnegie Mellon University. This C-SPAN devotee aspires to hold political office one day.

On political involvement and cold, hard cash

You can have [a political candidate] who is the most ethical, brilliant person in the world, but they can't get elected unless they have [money] ... In 2002, the average House campaign was $898,000. ... What that means is that it's no longer enough just to go out and exercise your vote. If you are seriously going to be a citizen and participate in the process, you're also going to have to contribute to financially supporting candidates who are going to do the right thing for the patients of America.

On his perception of how politically interested medical students are around the country

That depends on how cynical I'm feeling on the day you ask me, honestly. There are days when I say, "Oh my God, nobody's interested. Everybody's just so bloody apathetic." ... There are other days when I feel really motivated and positive, and it's, "Oh, we've just got to talk to them, and they'll understand."

His question for the world

What are the issues that [our readers] really care about in terms of government, and who, of all the candidates out there, best reflects their views on that issue? If that candidate really does reflect their views on that issue, shouldn't they be doing something to help that person get elected? Can you really afford not to be [involved] if it's something you genuinely care about? —*Interview by Dottie Horn*

Faculty Snapshots

A new finding by **Robert Bowser**, a PhD associate professor of pathology, may lead to faster and easier diagnosis of patients with amyotrophic lateral sclerosis (ALS), a fatal disease that causes progressive degeneration of motor neurons. People with ALS gradually lose the ability to move and often to speak, although their cognitive function is, in many cases, unaffected. Currently, the disease is diagnosed only when all other possibilities have been eliminated, a process that can take months. Bowser has identified differences in the cerebrospinal fluid of patients with ALS that allow him to distinguish ALS patients from controls. Bowser's finding may lead not only to a diagnostic test for the disease, but also to new targets for drug development. Last year, Bowser received the Chancellor's Distinguished Public Service Award for his work as director of Pitt's ALS tissue bank and his service to local ALS patients.



Bowser

Within six hours of the onset of symptoms, stroke patients might be treated with the clot-busting drug known as TPA. After six hours, it's believed that the risks of using TPA outweigh the potential benefits. (If used too late, the drug can cause life-threatening brain hemorrhaging and swelling.) However, **Tudor Jovin**, an MD assistant professor of neurology and VA investigator, believes there is a better way to decide who receives TPA. Jovin studied 36 patients with blockage of the middle cerebral artery who all had xenon-enhanced CT scans within six hours of stroke onset. The scan quantifies how much of the brain is already dead and how much is threatened but potentially salvageable. Jovin discovered that the severity of the consequences of the blocked blood vessel varied from patient to patient regardless of how much time had passed since symptom onset. "Some patients at five or six hours had less ischemia—tissue dysfunction and damage from lack of blood flow—than other patients at two or three hours," says Jovin. His study suggests that analyzing xenon CT scans, or using imaging technology that provides similar information, may be the best method for determining who should receive TPA. His study was published in the October issue of *Stroke*.



Jovin

Thirty thousand term and near-term newborns each year develop a potentially life-threatening condition called hypoxic respiratory failure, in which the lungs cannot supply sufficient oxygen to the body. Recent research by **Derek Angus**, an MD professor of critical care medicine, demonstrated the cost-effectiveness of treating these infants with inhaled nitric oxide. The study was published in the December 8 issue of *Pediatrics*. —*DH*

Immunosuppressives: Less is More and None is Best

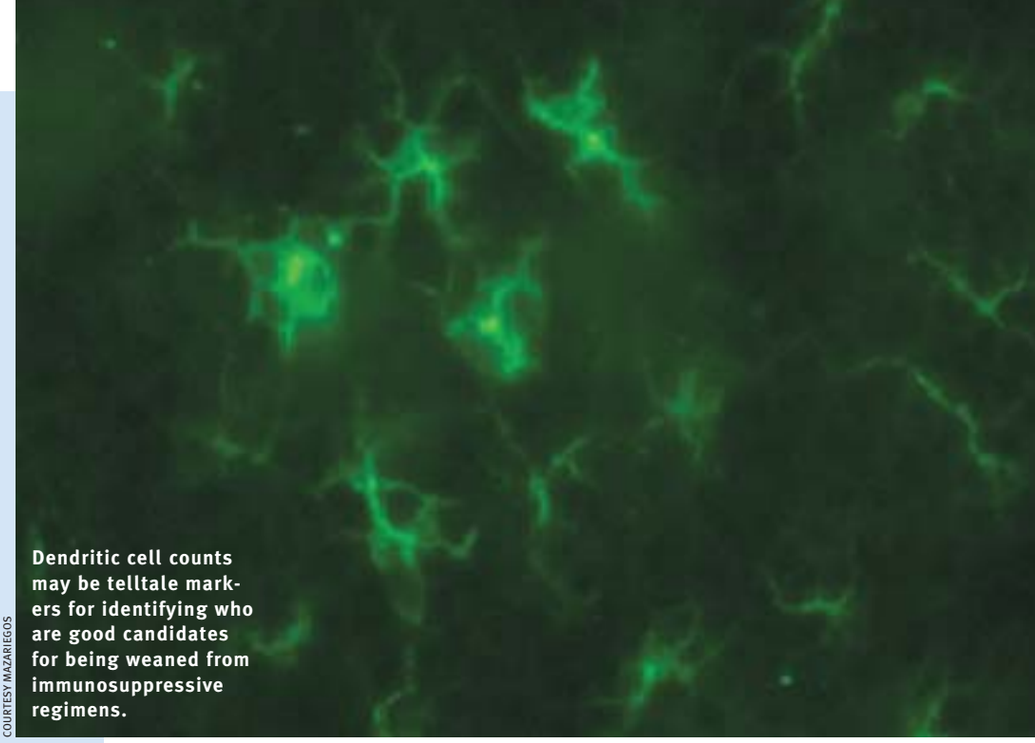
Fifty long-term survivors of liver transplants at the University of Pittsburgh are now completely free of immunosuppressive drugs—but that's less than 1 percent of the patients who have received liver transplants here. George Mazariegos, an MD associate professor of surgery, and other Pitt surgeons are working to make the percentage much higher.

Organ recipients typically receive steroids and an immunosuppressive drug; then, months after the transplant, doctors attempt to wean the patient off the steroids. At Pitt, since 2001, transplant surgeons have been using a steroid-free regimen whenever possible. Instead of steroids, patients are given an antibody treatment shortly before transplantation that weakens the immune system of the recipient without affecting the immune cells found in the donor organ. Following the transplant, patients are given lower-than-normal doses of an immunosuppressive drug. The hope is that the combination of antibody treatment and lower immunosuppression will allow the donor immune cells to gain a foothold and to establish a state of mutual tolerance with the recipient's immune cells—so that eventually the organ will be tolerated with little or no immunosuppression.

In adults who receive the steroid-free regimen and are doing well post-transplant, surgeons will try to wean the patient off immunosuppressive drugs three to six months following transplant. While not everyone can be successfully weaned, many patients are able to reduce the amount of drug they take.

Mazariegos is now trying to find blood markers that would enable physicians to distinguish which transplant recipients are good candidates for weaning. In a recent *American Journal of Transplantation* paper, he reported that increased type 2 dendritic cell counts seem to be linked to successful weaning.

Such findings may encourage other transplant centers to attempt to reduce immunosuppression. "One of the limitations that has discouraged other people from considering aggressive attempts at drug withdrawal is that it requires a lot of close follow-up," says Mazariegos. Pitt is currently the only center in the country that tries to wean patients from immunosuppressive drugs. *—DH*



COURTESY MAZARIEGOS

Dendritic cell counts may be telltale markers for identifying who are good candidates for being weaned from immunosuppressive regimens.

Inside a Tumor

Gliomas can be deadly brain tumors. Even with treatment, glioblastomas—the most common type of glioma—are usually fatal within a year of diagnosis. One strategy for fighting them is to develop drugs that inhibit the growth of new blood vessels that are necessary for the tumor to expand.

Last summer, Daniel Geynisman (Class of '06) studied gliomas while working in the shared lab of Kevin Walter and Eleanor Carson-Walter, who are both assistant professors of neurosurgery. The student showed that the plasmalemmal vesicle protein 1 (pv1) is more prevalent in the lining of blood vessels within gliomas than in normal brain blood vessel linings. The finding suggests that inhibiting pv1 could be a way to help stop new blood vessel growth.

Geynisman's work was supported by an American Brain Tumor Association fellowship; at the end of last summer, the association recognized him with the Lucien J. Rubinstein Memorial Award for completing the best research project among the fellowship winners. Besides kudos, he received $1,000. *—DH*

STROKES OF GENIUS

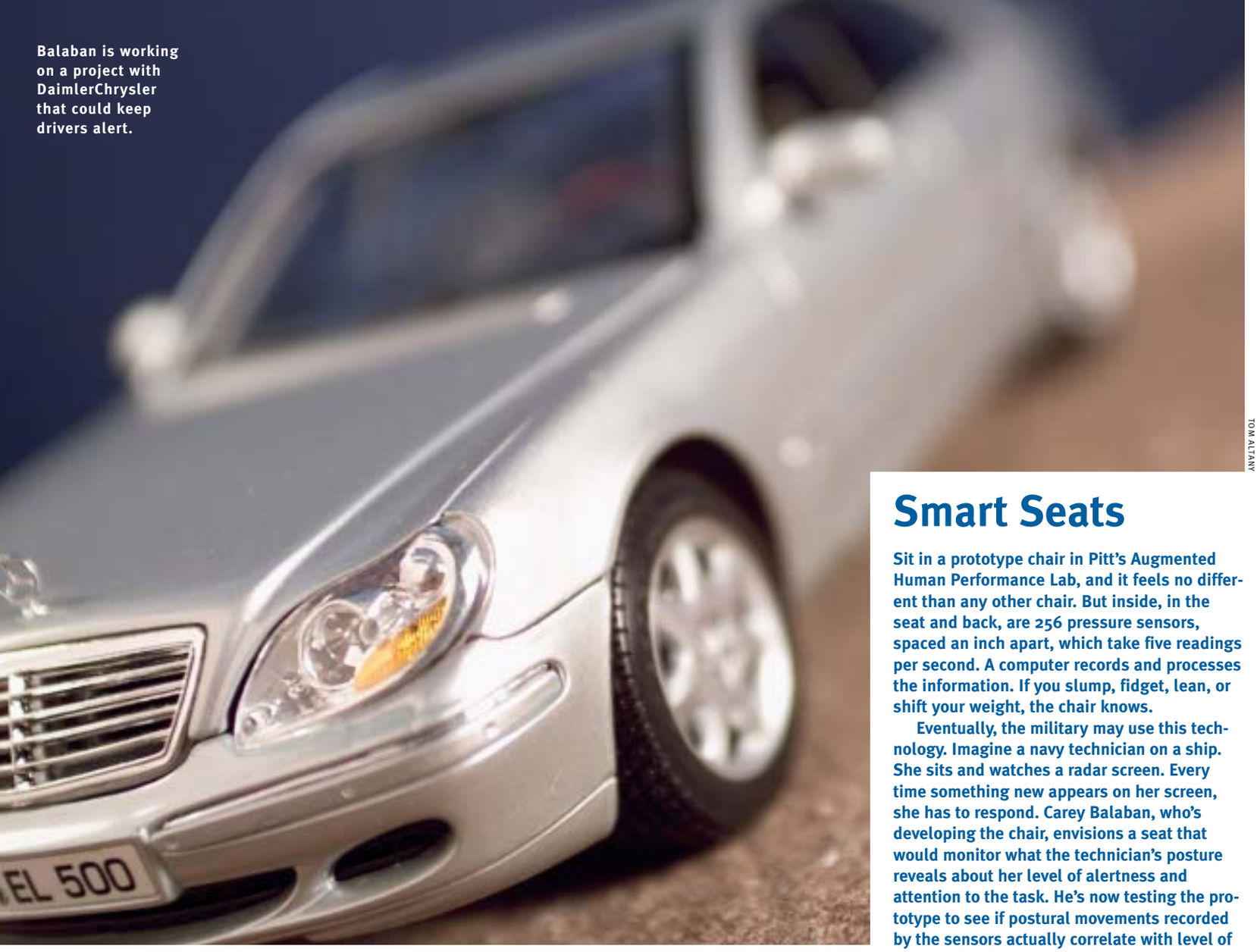
A new painting hangs in the lobby of the Biomedical Science Tower, showing Julius Youngner surrounded by the viruses that have compelled him to pursue his life's work. Youngner, now Distinguished Service Professor of Molecular Genetics and Biochemistry, worked with Jonas Salk from 1949 to 1955 as part of the Pitt team that created the killed polio virus vaccine. Youngner developed trypsinization, a cell culture technique now used in labs throughout the world, which made creation of the vaccine possible. Later in his career, Youngner unraveled mysteries of interferon and helped develop the FluAvert vaccine for horses. As artist Greg Kavalec created the portrait, the scientist posed for dozens of photographs, including close-ups of his eyes, clothes, and hands. "It's nice to see it hung while I'm still alive," he says.

—Dottie Horn and Sonya Kanti Patel



PORTRAITS PITTSBURGH/GREG KAVALEC

This portrait of Youngner now hangs on campus.



Balaban is working on a project with DaimlerChrysler that could keep drivers alert.

TOM ALTANY

Smart Seats

Sit in a prototype chair in Pitt's Augmented Human Performance Lab, and it feels no different than any other chair. But inside, in the seat and back, are 256 pressure sensors, spaced an inch apart, which take five readings per second. A computer records and processes the information. If you slump, fidget, lean, or shift your weight, the chair knows.

Eventually, the military may use this technology. Imagine a navy technician on a ship. She sits and watches a radar screen. Every time something new appears on her screen, she has to respond. Carey Balaban, who's developing the chair, envisions a seat that would monitor what the technician's posture reveals about her level of alertness and attention to the task. He's now testing the prototype to see if postural movements recorded by the sensors actually correlate with level of engagement in a task. Preliminary results suggest they do. In future studies, the PhD professor of otolaryngology will look at body movement and engagement in test subjects who sit in a prototype mounted on a moving platform that will simulate the motion onboard a ship.

His project is a Defense Advanced Research Projects Agency undertaking, but the technology has plenty of nondefense applications. Already, Balaban is working with DaimlerChrysler. He recently traveled to Germany to install a prototype chair in an experimental Mercedes-Benz sedan. The chair could become a safety feature in future cars. For example, drivers typically lean or shift their weight as they make a turn. If Balaban's pressure sensors don't pick up the appropriate body tilts as a driver turns, it could mean drowsiness or distraction, and a computer in the car could then intervene—perhaps with a verbal warning. Someday, the technology might even be used to help prevent long-distance truck drivers from becoming inattentive or from falling asleep at the wheel. ***—DH***

Appointments

Twenty million Americans now suffer from asthma. The incidence of the disease has doubled in the past 20 years. The medical community cannot definitively explain the reason for the increase. Some blame environmental pollutants. Others have found evidence to support the "hygiene hypothesis," which posits that the decreasing rates of infectious disease in developed countries may skew the immune system in a way that makes people more susceptible to asthma. Research by **Lawrence Kane**, who recently came to Pitt as an assistant professor of immunology, may help shed light on why asthma is on the rise. Kane researches Tim1, a little-studied molecule found on the surfaces of immune, and perhaps other, cells. Other research groups, using a mouse model, have found evidence that suggests Tim1 is linked to asthma. Kane joined the faculty last year after completing his postdoc at the University of California, San Francisco.



Kane

In the January issue of *Nature Immunology*, **Binfeng Lu**, assistant professor of immunology, reported on experiments in which he halted function of the Gadd45-beta gene in the T cells of mice. "We demonstrated that the gene is very important for the function of T cells and in their protective [action] against infection," says Lu, who recently came to Pitt via Yale University. Better understanding of the gene and its effects could help researchers design strategies to boost immunity, says Lu. *—SKP*



Lu

ON THE TRAIL OF A DREAM
PROGRAM FOSTERS WOMEN LEADERS

BY KRISTIN OHLSON



CAMI MESA

ELAM alumnae at Pitt include (from left) Carolyn Meltzer, Katherine Shear, Kathleen McIntyre-Seltman, Jill Siegfried, Katherine Wisner. Not shown: Ann Thompson.

Tina had a feeling of disbelief about her husband's death, though he had died four years earlier. She often experienced a reverie state, in which she remembered being with him. At other times, she avoided going places that would bring up memories of him. Although she had seen a counselor, she had not responded to traditional depression treatment.

After working with patients like Tina (a composite of cases), Katherine Shear, a University of Pittsburgh MD professor of psychiatry, developed a vision. She had already created a specialized therapy for patients who suffered from this kind of traumatic grief. She began thinking that she should create a center in the medical school to study grief, develop treatments, and train practitioners—the type of center that doesn't exist anywhere in the country.

Yet she wasn't sure where to begin. Then Shear was selected as one of 45 fellows in the prestigious Hedwig van Ameringen Executive Leadership in Academic Medicine (ELAM) Program for Women, sponsored by Drexel University in Philadelphia. Established in 1995, the program is designed to increase the number of women in leadership positions in medical and dental schools. Each fellow participates in eight months of networking, mentoring, leadership training, and skill building—and develops a project on her home campus during the fellowship. Three weeklong sessions bring the 45 ELAM fellows together as a group. Each week is intense, with many small group exercises and seminars.

For Shear, ELAM's benchmarking exercise—commonly used in corporate America—was especially helpful. The summer before ELAM, she gave questionnaires on her work performance to her supervisor, peers, and those who report to her. During her first ELAM week, she met with a counselor to review information compiled from the questionnaires. Together, they identified her strengths and weaknesses, and Shear made plans to capitalize on a strength she hadn't previously used and to compensate for a weakness. She found that people thought she was creative and a great problem solver. She was surprised to see how highly everyone rated her (a common reaction among ELAM fellows). "Women tend to rate themselves lower than other people rate us," she says. "It's a dangerous thing to do, to underestimate your own strengths." Women also tend to remain less visible than their male peers in academia, so ELAM asks its fellows to meet with influential people at their schools. In Shear's case, she met with the dean, associate deans, and chief legal officer.

Shear is the sixth faculty member from the School of Medicine to participate in ELAM. Other Pitt fellows have launched projects ranging from raising awareness of lung cancer to developing training programs.

Now, as her fellowship draws to a close, Shear is well on her way to achieving the grief center, which became her ELAM project. She's identifying personnel for the center and has submitted two grant proposals.

"My plans for organizing the center have become much more concrete," Shear says. "I have more ideas for who to involve and how to involve them. Without ELAM, I don't think I would … have had the same vision for the center." ■

FOOTNOTE

Researchers at Oxford University have identified a rare "foreign accent syndrome" in people who have suffered brain injuries or strokes. In 1941, the first case was reported in a Norwegian woman who suffered a shrapnel injury to the head, leaving her with a German accent. We'll let yinz know if a Pittsburgh accent turns up in any unusual places n'at.