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HIV Pathway Discovered

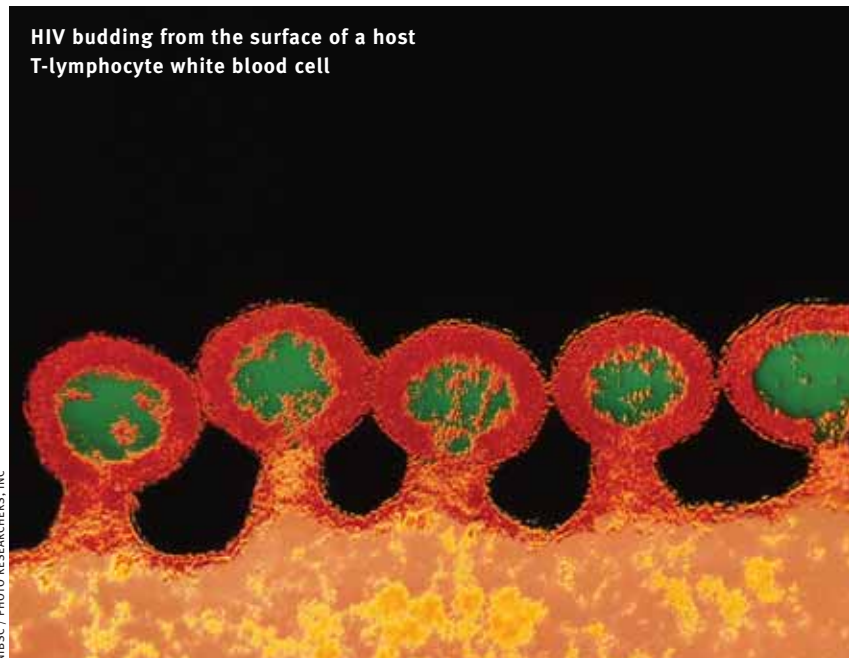
University of Pittsburgh researchers have discovered a previously unknown mechanism by which HIV spreads through the body.

Charles Rinaldo and Giovanna Rappocciolo unexpectedly came upon the mechanism when researching how the immune system responds to the herpesvirus that can cause Kaposi's sarcoma, a common cancer in AIDS patients.

Following a hunch, they learned that a B-cell surface molecule unlocks T cells and allows HIV entry. (B cells and T cells both can be thought of as surveillance patrols for the immune system.) T-cell infection subsided significantly when the scientists curtailed expression of the surface molecule in HIV-carrying B cells.

Rinaldo is a PhD professor and chair of the Department of Infectious Diseases and Microbiology in Pitt's Graduate School of Public Health; he has a joint appointment as professor of pathology in the School of Medicine. Rappocciolo is a PhD research assistant professor of infectious diseases and microbiology in GSPH.

This pathway is not the only manner in which HIV spreads, but Rinaldo imagines that therapies that disrupt it could help fight HIV. —*Joe Miksch*



HIV budding from the surface of a host T-lymphocyte white blood cell

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FLASHBACK

Ninety years ago, as the country prepared to enter World War I, 22 members of the School of Medicine faculty became the officer class of an army hospital unit. Thanks to \$75,000 in individual donations and support from the Pittsburgh chapter of the American Red Cross, they were particularly well-equipped. However, the unit's sergeant major was not impressed. To a superior officer, he remarked, "Sir, I'm afraid we can't ever make soldiers out of them there college boys."

MAGEE RESEARCHER LEADS INTERNATIONAL HIV EFFORT

Each year, 4 million people are infected by HIV. To try to curtail the disease here and abroad, the National Institutes of Health has restructured its clinical networks for HIV prevention and treatment. Magee-Womens Research Institute is one of six institutions that's been selected to lead the way. The NIH expects to spend \$285 million in the first year of the new leadership effort.

Sharon Hillier, a PhD professor of obstetrics, gynecology, and reproductive sciences and of molecular genetics and biochemistry, is the principal investigator for the Pittsburgh group. She will run an international research program looking into ways to stop transmission of the disease. Hillier and colleagues are evaluating HIV microbicides, which are applied topically and give women greater control over their health than condoms, whose use is usually a man's prerogative.

"In many parts of the world, a woman's single biggest risk factor for the acquisition of HIV is being married," Hillier says. "Currently, women have no way to protect themselves except condoms." —*JM*



CAMI MESA

A&Q

Personhood in a Brave New World

As scientists are able to shape how humans develop, Gerald Nora (above) wonders what it means—what it means in the big picture, that is. Putting things in the light of philosophy and history, he says, helps “keep the wonder, it keeps the lab from being routine.” Not that anything about his lab work sounds routine—Nora, as an MD/PhD student in the University of Pittsburgh/Carnegie Mellon University Medical Scientist Training Program, studies telomeres, those DNA extremities that may hold clues to aging and cancer. He is in the third year of his PhD work and has finished his psychiatry rotation.

We talked with Nora about why he was drawn to pursue an MA in bioethics as well. He spoke to us about issues of personhood and identity in the rapidly changing arena of genetics and biology.

Shaping identity

Our identities are tied up in our physical being: *I'm deaf. I'm depressed.* When science can change these features, we need to ask, “What am I changing with this treatment? How tightly bound are our personal identities with our genes?”

You alter a gene in an embryo after in-vitro fertilization, and then implant it. What sort of change did you [make] to its identity? If that child later on gets angry about whatever the alteration was [and says], “I didn’t want to be blond or tall. Why did you do this to me, Mom and Dad?” can that child actually sue? Was this a wrong? There have been some cases called wrongful birth cases in both the U.S. and France [where during] a prenatal diagnosis, the doctors didn’t catch something, and the patients had a child that was handicapped in some way. They said, “Well look, if we’d known about this [birth defect] we would have aborted the child.” They sued on the child’s behalf, saying that child should have never been born. He would have been better off dead. I think it’s going to get even more complicated as time goes on and as our capabilities expand.

How science will create new ethical dilemmas

What’s the line between curing a disease and augmenting a person? Is it ethical for the doctor to give [human growth hormone] even if there’s nothing really wrong with the kid?

His question for the world

How do we develop a moral reasoning, and a moral vocabulary, to adapt to these situations? Not only do we have to come up with an answer, but a reasonably logical one, because if we use bad reasoning, it can haunt us. —Interview by Reid R. Frazier

Faculty Snapshots

In the quarter-century plus that Margaretha Casselbrant has been at the University of Pittsburgh, she has pursued the causes and effects of otitis media, middle ear inflammation common in children.

The disease can affect hearing, speech, and balance. Casselbrant, an MD/PhD professor of otolaryngology, was recently appointed one of 18 members of the National Deafness and Other Communications Disorders Advisory Council. The council assesses grant applications and provides recommendations regarding the conduct and support of research related to hearing, speech, and balance for the National Institute on Deafness and Other Communication Disorders.

In her own lab, Casselbrant is seeking a genetic link for otitis media.



Casselbrant

In 1980, at Children’s Hospital of Pittsburgh, David Brent was responsible for determining which young people who’d attempted suicide needed psychiatric hospitalization. He was shocked at his inability to find much in the way of empirical guidelines. Brent, now a University of Pittsburgh professor of psychiatry, went on to make suicide-risk assessment and treatment in youth the focus of his career.



Brent

Brent, an MD, is the holder of the University of Pittsburgh’s endowed chair in suicide studies, academic chief of the Division of Child and Adolescent Psychiatry at the Western Psychiatric Institute and Clinic, and cofounder and director of the state-funded Services for Teens At Risk (STAR) Center. And now he has been awarded the Ruane Prize by the National Alliance for Research on Schizophrenia and Depression. The prize honors outstanding work pertaining to childhood mental illness. Brent is a leader in assessing the risk of teen suicide as it relates to mood disorder, substance abuse, impulsive aggression, parental suicide, and access to guns.



Billiar

Timothy Billiar, Pitt’s George V. Foster Professor of Surgery and chair of the Department of Surgery, was recently elected to the Institute of Medicine. The election puts the surgeon in the illustrious company of his mentor, Pitt’s Richard Simmons, Distinguished Service Professor of Surgery, and his nominators, Thomas Starzl, also a Distinguished Service Professor of Surgery, and Nobel laureate Ferid Murad, of the University of Texas Health Science Center at Houston, all of whom are in the institute.

Billiar is an accomplished trauma surgeon and researcher. In the latter capacity, he has deepened understanding of the role nitric oxide plays in the body’s response to septic shock. —JM

Can You Spare \$90K?

On a fine July day, Brett Michelotti (Class of '09) was in the kitchen at the Station Square amphitheater toiling over some ribs. A worker walking the floor near the buffet dining area—not far from the stage where country music performers Big & Rich were holding forth—noticed a lack of that barbecued delight. So, Michelotti loaded up the hotbox with a substantial ration of ribs, jumped onto a four-wheeler, and traversed 100-party-goer-packed meters—avoiding Major League Baseball Commissioner Bud Selig and former Pittsburgh Pirate Bobby Bonilla—to avert a meat emergency.

Michelotti and about 30 of his classmates were caterers for the thousands of guests at the Major League Baseball All-Star Game Gala. When he enrolled in med school, Michelotti probably didn't imagine ever being concerned with how much protein Bobby Bonilla had access to on a given night, but he had good reason for taking on that role last summer. The student workers donated at least half of the earnings from their 10-hour shifts to a campaign they're calling "90K from 2009."

The \$90,000 the class plans to raise by its commencement will support the Program for Health Care to Underserved Populations, which operates five free Pittsburgh-area clinics.

Thus far, the students have also raised money selling T-shirts, staffing concession booths at Steelers games, and soliciting friends and family. We hear they'll be hosting a wine tasting next. —JM

TO DONATE: www.giveto.pitt.edu
Specify, "University of Pittsburgh—90K from 2009."



CATHERINE LAZURE

ANESTHETICS AND ALZHEIMER'S LINK

Some elderly patients experience cognitive dysfunction and memory lapses after surgery under a general anesthetic. The University of Pittsburgh's Pravat K. Mandal recently uncovered the molecular mechanism that seems to be responsible.

Mandal's study, published in the Jan. 23 issue of *Biochemistry*, used nuclear magnetic resonance spectroscopy (NMR) to examine the connection between several commonly used anesthetics and amyloid beta-peptide. The peptide is known to accumulate and form plaques in the brains of patients with Alzheimer's disease. Scientists believe such plaques are responsible for the disease.

Mandal is a PhD assistant professor of psychiatry with a secondary appointment in bioengineering. He performed in vitro experiments in which he exposed the peptide to two inhaled anesthetics: halothane, which is no longer used in U.S. hospitals but is common elsewhere, and isoflurane, which is popular

in this country. Both anesthetics caused the peptide to clump into plaques. Advanced NMR, Mandal says, allowed his team of researchers to identify, at the atomic level, the specific binding region of the anesthetic to the peptide. "We now know the molecular mechanism ... responsible for the clumping," he says.

In addition, Mandal's lab studied two intravenous anesthetics, propofol and thiopental. Propofol only interacted with the peptide at very high concentrations. Thiopental did not interact at all. Mandal believes that the larger size of the propofol and thiopental molecules handicaps the anesthetics' ability to affect the peptide.

Mandal plans to perform animal experiments and hopes to study the anesthetic/peptide interaction in the human brain eventually. The research, he says, may lead to safer anesthetics and could contribute to the overall understanding of amyloid plaque formation. —JM



DEADLY MEDICINE

The contraption shown left is not an ice cube tray, and, yes, it's holding eyeballs. (They're glass.) Such tools used for studies of differences in "races" in Nazi Germany are on display at "Deadly Medicine: Creating the Master Race," at the Andy Warhol Museum until March 18. The exhibition explores how the misuse of medical and other research helped eugenics take hold in Germany. Susan Bachrach, the exhibition's curator at the United States Holocaust Memorial Museum, in D.C., lectured at Scaife Hall in December. On Feb. 20, the School of Medicine with the Memorial Museum will cohost a Pittsburgh summit examining how the study of the Holocaust can inform ethical dilemmas facing health professions today. "Science is never good nor evil, but it can be put to good or evil purposes," notes Arthur S. Levine, dean of the medical school and senior vice chancellor, health sciences.

Appointments

Jennifer Condon studies maternal-fetal signaling in the mouse to understand how it initiates labor. Condon, a PhD, joined the University of Pittsburgh School of Medicine faculty in October as an assistant professor in cell biology and physiology. She and her husband, **Jeyasuria Pancharatnam**, who is a PhD and research assistant professor, transferred here from the University of Texas Southwestern Medical Center at Dallas. Their recent work has shown that the fetal lung, when it is ready to breathe, produces a protein that causes fetal cells to migrate into the mother's uterus, signaling it to contract. The researchers hope to find the exact mechanisms of labor induction to prevent preterm labor.



Condon (right) and Pancharatnam

Kenton Zehr, a cardiac surgeon, wants Pitt's academic heart surgery program to become the busiest in the country. Zehr, newly appointed cardiac surgery division chief and professor of surgery at the School of Medicine, is working to expand Pitt's expertise in valve and aneurysm repairs. His own lab explores how to limit invasiveness and speed up

procedures in the O.R. Zehr, who came from the Mayo Clinic, believes the U.S. medical community and the world's physicians have much to teach one another. "We are going to be stormed by countries like China and India," he says, because their ideas are so interesting.



Zehr

Michael Becich and his research team have been international leaders in creating a system of patient-consent donations of serum, cells, and tissue, all of which are accompanied by detailed clinical descriptions. When using a breast cancer sample in research, you can imagine that it would help to know the type of cancer, whether the patient lived or died, whether she'd been treated, whether she had any genetic susceptibility to cancer, and other pertinent information. Becich, an MD/PhD, heads the new Department of Biomedical Informatics at Pitt. —Katie Hammer



Becich