Medicine@Yale

Advancing Biomedical Science, Education and Health Care

Volume 5, Issue 1 January/February 2009

Scientist is doubly honored for protein-folding breakthroughs

Last October marked a month to remember for the School of Medicine's Arthur L. Horwich, M.D., Sterling Professor of Genetics and Pediatrics. Over the course of two days, Horwich was elected to the Institute of Medicine (IOM) and named a winner of the 2008 Louisa Gross Horwitz Prize by Columbia University for his outstanding contributions in biology and biochemistry.

Arthur Horwich

Horwich, a Howard Hughes Medical Institute investigator, is one of the world's leading experts on the molecular mechanisms of protein folding, a process crucial to life. When proteins misfold, they can accumulate inside cells and cause illness. More than 20 diseases, including neurodegenerative disorders such as Alzheimer's disease, Huntington's disease and amyotrophic lateral sclerosis (Lou Gehrig's disease), have been linked to protein misfolding.

Horwich was one of 65 people chosen for their exceptional achievement in health and medicine for election to the IOM, an organization that is unique in its combined honorific and advisory roles. Established in 1970 by the National Academy of Sciences, the IOM is a national resource for independent, scientifically informed analysis and recommendations on human health issues.

First awarded in 1967, the Horwitz Prize is one of the top prizes in biomedical science; about half the Horwitz recipients have gone on to win a Nobel Prize. This year's award was shared by Horwich, Franz-Ulrich Hartl, M.D., DR.MED., of the Max Planck Institute of Biochemistry in Germany, an early collaborator on Horwich's research, and the late Rosalind Franklin, PH.D., honored posthumously for her X-ray crystallography work in the early 1950s, which was instrumental in the discovery of the structure of DNA.

Horwich was elected to the National Academy of Sciences in 2003, and has been a member of the medical school faculty since 1984. He holds undergraduate and medical degrees from Brown University and completed his residency in pediatrics at Yale-New Haven Hospital.

Yale Netcast
"Arthur Horwich: Protein Folding"

For faculty—past, present and future

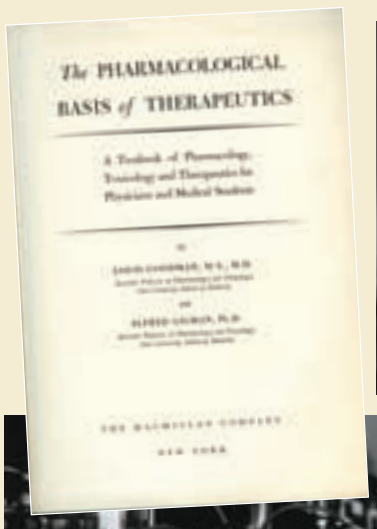
Pharmaceutical leader's newest gifts are a tribute to Yale's inspiring teachers

In 1879, 23-year-old Robert McNeil, who had recently graduated from the Philadelphia College of Pharmacy and Science, paid $167 for a fully outfitted drugstore that would soon bear his name. McNeil undoubtedly hoped that the store's soda fountain would prove as much a draw to the residents of Philadelphia's Kensington section as the medicines he planned to make and sell, but he could hardly have imagined that a drug stamped with the McNeil name would one day be the first choice for pain and fever relief in millions of homes and hospitals worldwide.

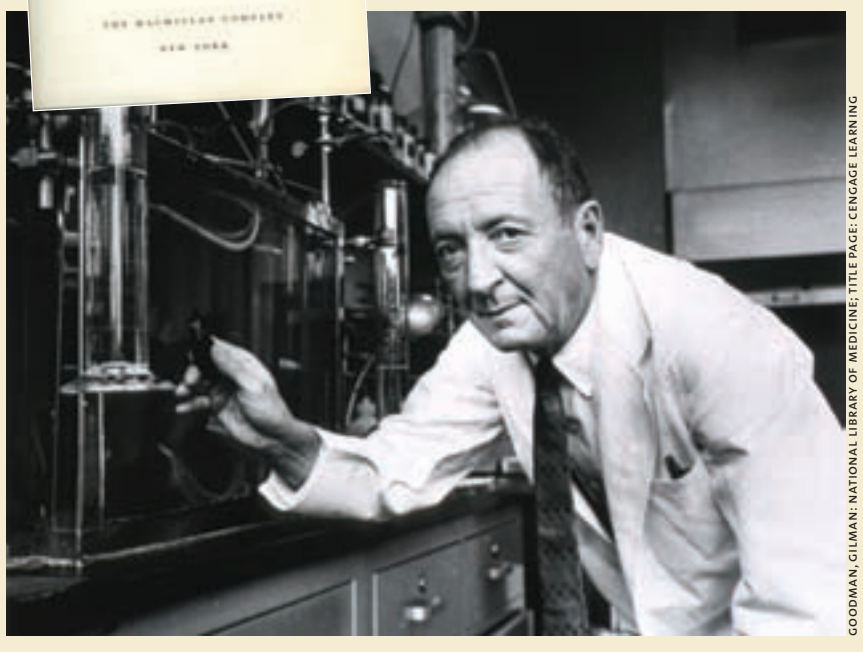
Today that drug, Tylenol, is a bona fide blockbuster, with combined annual sales of its various formulations totaling over $1 billion annually for McNeil-PPC and its parent company, Johnson & Johnson.

Directing the creation of Tylenol products in the early 1950s was Robert L. "Bob" McNeil Jr., grandson of that Philadelphia druggist and member of the Yale

Mentors, *page 6*



As assistant professors at the School of Medicine, Louis Goodman (left) and Alfred Gilman (below) wrote their landmark textbook (inset). Along with human nutrition expert George Cowgill, they have been honored by gifts from pharmaceutical executive Robert McNeil Jr.



GOODMAN, GILMAN: NATIONAL LIBRARY OF MEDICINE; TITLE PAGE: CENGAGE LEARNING

A brother's generosity and an uncle's skill live on in endowment

On a recent visit to the School of Medicine, Roy Polayes, of Hartsdale, N.Y., recalled the many weekends at his childhood home when his parents sat at the kitchen table sorting through paperwork. Polayes' father had a private surgery practice, for which his mother handled the billing. "They would sit around the table and discuss accounts receivable—which patients hadn't paid, and which ones couldn't pay," Polayes says. "Certainly my father had his own expenses and bills to pay, but more often than not he wound up making the decision that was best for the patient."

In keeping with that spirit of generosity, Roy's father, Irving M. Polayes, M.D., a New Haven plastic surgeon, dentist and voluntary faculty member in the Department of Surgery's Section of Plastic Surgery from 1965 to 1997, is one of two members of his family to be honored recently with a named professorship. The other, Roy's great-uncle, Silik H. Polayes, PH.D., earned his graduate degree from Yale in 1921 and worked as a pathologist in New York. The $2.5 million gift endowing the new Irving and Silik Polayes Professorship in Plastic Surgery in 2007 was made by

Polayes, *page 6*

Inside this issue

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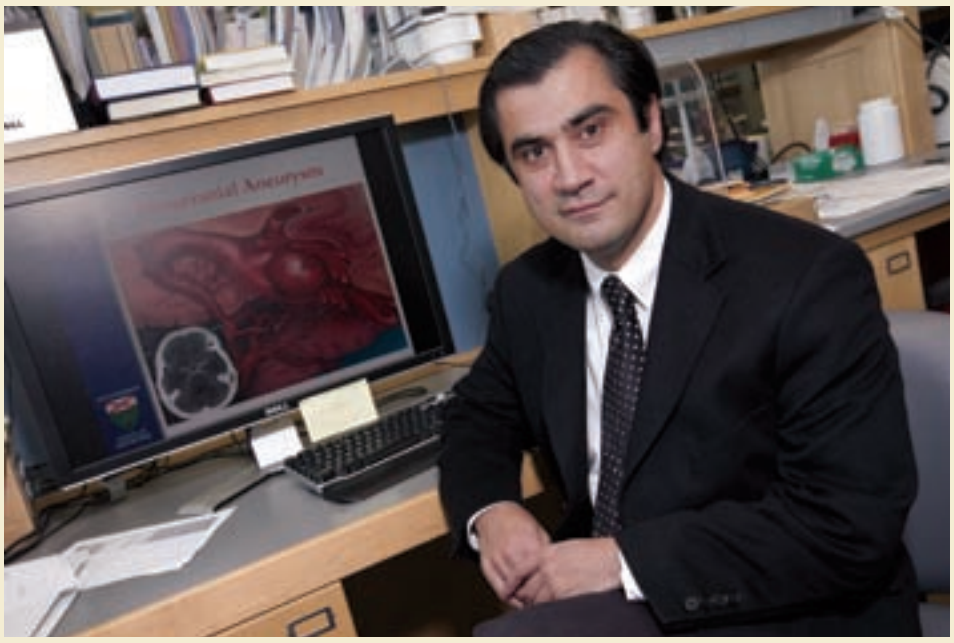

TERRY DAGRADI

Skilled in the surgical repair of brain aneurysms, Murat Günel is also leading genetic studies to identify those most at risk of developing these often-fatal vascular defects. Günel, co-director of the Yale Neurogenetics Program, says his work could help neurosurgeons find and repair aneurysms before hemorrhagic stroke causes disability or death.

Pushing the envelope

Neurosurgeon, geneticist sees a day when doctors can head off catastrophic stroke

In 2006, self-styled endurance artist David Blaine, equipped with a breathing tube, had himself sealed inside a transparent water-filled sphere in front of New York's Lincoln Center, where he planned to remain for seven days. The performance attracted thousands of gawking passersby and countless Internet voyeurs, but Murat Günel, M.D., the head of Blaine's medical team, observed the proceedings from a nearby tent, where he monitored Blaine's condition around the clock.

Günel, professor of neurosurgery and neurobiology at the School of Medicine and chief of the Section of Neurovascular Surgery, says that the bravado of Blaine's public persona belies his intellectual nature. "He explores life in a different manner than I do, but we are joined in a quest for life," Günel says. "He always pushes the envelope."

Günel tests some limits himself, combining a neurosurgical practice with an ambitious research program in human genetics. His main interest is intracranial aneurysms, weaknesses in the brain's blood vessels that can balloon, putting pressure on brain tissue, or rupture, causing hemorrhagic stroke.

The Turkish-born Günel's interest in the field was partly stimulated by the work of his compatriot, M. Gazi Yaşargil, M.D., a famed Turkish neurosurgeon who pioneered the use of surgical microscopes to treat aneurysms with clips that can prevent rupture.

However, most brain aneurysms, which affect 500,000 people worldwide each year, have no symptoms. Rupture is fatal in up to 40 percent of cases, and survivors usually have severe neurological damage. Over the years, Günel has seen the introduction of less invasive repair techniques and improvements in Intensive Care Unit procedures for those who have suffered a brain hemorrhage, but from the beginning of his residency at Yale in 1991, he has wanted to identify genes that put people at risk, so that neurosurgeons could someday intervene before aneurysms rupture.

Lifelines
Murat Günel

In 1993, Günel approached Richard P. Lifton, M.D., PH.D., chair and Sterling Professor of Genetics and a world-renowned figure in the genetics of human disease, about exploring the genetic basis of aneurysms. Lifton advised him that the field hadn't sufficiently developed to tackle so complex a problem, and suggested that Günel study cerebral cavernous malformations (CCMs), a less serious vascular irregularity in the brain that clearly runs in families. Over the last 15 years, Günel, Lifton and colleagues have zeroed in on genes that cause CCMs.

In collaboration with William C. Sessa, PH.D., professor of pharmacology and director of the medical school's Program in Vascular Biology and Transplantation, Günel and other Yale scientists are using this knowledge to conceive therapies that could enlist the body's own repair mechanisms to prevent the development of CCMs altogether.

In the last few years, technology advanced to the point that Günel and Lifton were finally able to launch a genomic study of intracranial aneurysms, an international venture that involved 10,000 research subjects in Finland, the Netherlands and Japan. In a paper in *Nature Genetics* in December, the team reported variations in three genetic regions associated with a greater risk of intracranial aneurysm and proposed a likely causative role for two specific genes. The study population has since grown to 15,000 people, and Günel says that more detailed genetic data on aneurysm risk should soon emerge from his research.

Most Yale neurosurgery residents wish to pursue research, so Günel is often asked how he balances his genetics work with his clinical practice. His answer? "I give both 100 percent." David Blaine would approve.

Student-run auction benefits charities in New Haven region

The 16th Annual Hunger & Homelessness Auction, a student-run event that combines entertainment with charitable giving, was held last November, raising $32,000 for several organizations in the New Haven area.

"This is about giving back," said auctioneer Wade Brubacher, a professional from Kansas and father of third-year medical student Jacob Brubacher, in his third appearance as auctioneer at the event. "You won't make money at it, but you'll feel good."

TERRY DAGRADI

John Binford of the medical school's Class of 2012 enters a bid at the auction for a quilt made by first-year students.

Since its inauguration as an afternoon event in 1993, the event has expanded to include a week of activities that include a football game between first- and second-year medical students, a performance of chamber music, a panel discussion on hunger and homelessness and film screenings.

The week ends with silent and live auctions in the School of Medicine's Harkness Ballroom and at Marigold's, a nearby dining hall.

Among the available items at the silent auction were works of art, services by students and faculty, dinners at homes and restaurants, quilts, jewelry, a mysterious item listed as "Mediterranean Dinner & Debauchery," concert tickets and homemade brownies.

Flu shots meet the ballot box in Yale public health expert's effort

Some voters completing one essential fall ritual by casting their ballots last Election Day could simultaneously take part in another—getting vaccinated against the flu.

Douglas Shenson, M.D., M.P.H., associate clinical professor at the Yale School of Public Health, organized the effort, which marks the first time that flu vaccination clinics were set up within or nearby select polling stations on a national scale. The "Vote & Vax" program operated 300 clinics in 42 states and the District of Columbia, including 11 clinics in Connecticut.

Individuals most at risk from influenza—those who are over 50 years old—are also the people most likely to vote, and Shenson hoped to provide these people with a convenient way to get vaccinated. "Vote & Vax is a public health strategy designed to better protect vulnerable Americans against influenza," Shenson says. "During national elections, polling places offer an extraordinary public health opportunity to reach very large numbers of older adults on a single day, early in the flu shot season."

The non-partisan program was funded by the Robert Wood Johnson Foundation and directed by the Connecticut-based SPARC (Sickness Prevention Achieved through Regional Collaboration), a nonprofit health agency that Shenson directs. The idea began in 2006 as a pilot program that reached some 13,000 people. Shenson said he wants to see the program continue in subsequent election cycles until it becomes a routine part of public health practice.

HAROLD SHAPIRO

Nurse Lesley Anderson gave vaccinations on Election Day in Milford, Conn.

Medicine@Yale

Peter Farley, *Managing Editor*

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Design: Jennifer Stockwell

Medicine@Yale is published six times each year by the Office of Institutional Planning and Communications, Yale School of Medicine, 300 George St., Suite 773, New Haven, CT 06511.
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Advances

Health and science news from Yale

NAT'L AQUARIUM, BALTIMORE

Electric eel inspires a shockingly good idea

A marvel of evolution, the electric eel packs a 600-volt punch to ward off attackers and stun its prey. Battery-like cells in the eel called electrocytes are studded with ion channels that precisely regulate sodium and potassium, but the exact configuration of these channels is unknown.

In the November 2008 issue of *Nature Nanotechnology*, Jian Xu, PH.D., postdoctoral associate in Yale's Department of Chemical Engineering, and David A. LaVan, PH.D., of the National Institute of Standards and Technology, describe a mathematical model of the electrocyte based on studies of the eel done in the 1950s. Surprisingly, they then found that eliminating all potassium channels from the model resulted in a cell that produced 28 percent more electricity than the eel's.

"Bio-batteries" based on this tweaked electrocyte could power prostheses such as retinal implants. "If it breaks," says Xu, "there are no toxins released into your system. It would be just like any other cell in your body."

Tiny disease detector is like a lab on a chip

The antigen-specific T-cells of the immune system are so called because they respond to particular infections. Antigens—protein fragments from viruses, bacteria or other microorganisms—are displayed to circulating T-cells on the surface of antigen-presenting cells. If a T-cell's receptors recognize and bind to an antigen, the T-cell is activated, prompting the rapid proliferation of additional T-cells that precisely target the same invader.

Monitoring this process is important for understanding the immune response in many contexts, including autoimmune diseases and cancer. However, current measurement techniques are time-consuming and labor-intensive and require sophisticated laboratory equipment.

In the October 2008 issue of *Nano Letters*, a team led by Tarek Fahmy, PH.D., assistant professor of biomedical engineering at Yale, describes a simple nanoscale measurement system that can detect the activation of as few as 200 antigen-specific T-cells in seconds.

The new device could power highly sensitive instruments that immediately determine which strain of flu, tuberculosis or *E. coli* a patient has, or detect the presence of minute amounts of residual disease after chemotherapy or antiviral treatment.

Hope sustains center's research on paralysis

Veterans join scientists to fight spinal cord injuries and neurological diseases

TERRY DAGRADI

(Front row, from left) Gene Crayton, senior vice president of the Paralyzed Veterans of America (PVA), Paul Tobin, president and CEO of the United Spinal Association, and Homer Townsend, PVA executive director, join (back row, from left) medical school Dean Robert Alpern, Stephen Waxman, Yale President Richard Levin, Joel Kupersmith, chief research and development officer of the Veterans Health Administration and West Haven, Conn. Mayor John Picard at the ribbon-cutting ceremony for the new research wing at the Center for Neuroscience and Regeneration Research.

When Stephen G. Waxman, M.D., PH.D., moved from Stanford's School of Medicine to Yale in 1986, he didn't pack light: he brought with him several scientists, including Jeffery D. Kocsis, PH.D., and Joel A. Black, PH.D., and a million dollars' worth of equipment.

On arrival, Waxman, now the Bridget Marie Flaherty Professor of Neurology, Neurobiology and Pharmacology, set up shop on the campus of the VA Connecticut Healthcare System in West Haven, Conn., where, with financial backing from groups of paralyzed veterans, including the Paralyzed Veterans of America (PVA), he established the Center for Neuroscience and Regeneration Research (CNRR).

Scientists at the CNRR, which marked its 20th anniversary last October with the opening of a new $3.8 million wing, are doing some of the foremost research on restoring function after spinal cord or brain injury. There, Waxman, CNRR director and longtime chair of the medical school's Department of Neurology, and associate directors Kocsis and Black lead a staff of thirty-odd Yale physiologists, pharmacologists and stem cell biologists working on cellular repair of the spinal cord and brain using transplanted cells and stem cells; molecular repair of demyelinated cells in disorders such as multiple sclerosis (MS); and understanding the basis of neuropathic pain, or long-term pain experienced after injury to the nervous system (or, in some cases, when there is no injury at all).

While scientifically diverse, the center's investigators are united by a common desire to reduce patients' discomfort and restore function to paralyzed limbs. "We know from earlier experiments that if we can coax just 15 percent of the axons in the motor tract of the injured spinal cord to conduct impulses, it will restore gait," Waxman says. "We won't be making somebody into a ballet dancer, but imagine telling somebody who's confined to a wheelchair that they could take ten labored steps—enough to get from their wheelchair into a car. Or giving somebody who has no function below the shoulders just enough function in their spinal cord so they can grasp and use a pencil."

The key to realizing such hopes for people like the 100 wheelchair-bound veterans who arrived to fete the CNRR's 20th year, Waxman says, is continued research. His group has found, for instance, that remissions occur in MS without the production of new myelin, an insulating sheath that coats nerve cell axons and is vital for the conduction of nervous signals in the brain and spinal cord. "We know axons can rebuild themselves in disorders like MS, and we know they produce new sodium channels, which act as batteries within their membranes so they can convey information, even though they have lost their myelin insulation," Waxman says. "Now, we want to be able to turn that process on and off at will."

While myelin may not always be necessary for improvements in nerve conduction, remyelination certainly does help. Kocsis's group is interested in remyelination therapies for spinal cord repair based on adult stem cells derived from bone marrow. Kocsis, professor of neurology and neurobiology, has found that such cells do not need to be implanted directly into the brain or other injured sites, but can be delivered intravenously and still lead to the production of new myelin and improved condition. In cases of non-penetrating, or closed, spinal cord injury, often caused by motor vehicle accidents or athletic mishaps, Waxman says, "It used to be thought they had cut the cord across. They usually haven't. Axons run up and down through the lesion in continuity, but they don't conduct because they've lost their myelin insulation. And we view that as a target of opportunity."

Will victims of paralysis someday be able to regain function? "You need luck as well as everything else," Waxman says. "If I was sure that a particular path would get you there, we would do it and get there. So we are taking multiple, parallel approaches. But I think that with hard work and a bit of luck, we may well get there."

MEDICINE tomorrow

Charitable gift annuities: a good choice for today's economy

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Out & about


1


2

TERRY DAGRADI (4)


3

September 13, 2008: Dramatic lighting and elegant décor transformed Yale's historic Commons for **A BLACK AND WHITE BALL**, the Discovery to Cure Gala sponsored by the Gynecologic Oncology Program of Yale Cancer Center (YCC). The gala benefitted YCC's efforts in the early detection and effective treatment of women's reproductive cancers. The event, which drew about 300 attendees, also featured a silent auction in the President's Room in Woolsey Hall and dancing. **1.** (From left) Gala co-chairs **Jacques Dickinson** and **Stephanie Ercegovic** with **Thomas J. Rutherford**, PH.D., M.D., associate professor of obstetrics, gynecology and reproductive sciences. **2.** Actor **Justin Long** (left) and comedian, author and member of the Yale College of 1994 **John Hodgman** (right), who play "a Mac" and "a PC" in the well-known advertisements produced by Apple Computer, were the evening's special guests. They joined (starting second from left) Rutherford; **Peter E. Schwartz**, M.D., the John Slade Ely Professor of Obstetrics, Gynecology and Reproductive Sciences; and **Arlene Schwartz**. **3.** Music was provided by **Flamingo**, an all-female swing band. **4.** (From left) **Richard L. Edelson**, M.D., the Aaron B. and Marguerite Lerner Professor of Dermatology and YCC director; **Hank and Nancy Bartels**; and Dean **Robert J. Alpern**, M.D.


4

November 13, 2008: **Robert and Beverly Bartner** paid a visit to the School of Medicine to celebrate the establishment of **THE BARTNER DISCOVERY SCHOLAR** in the Department of Pediatrics, which provides support to a promising young scientist whose research will make an impact on clinical practice. Associate Research Scientist **Julie E. Goodwin**, M.D., who studies kidney disease, is the first recipient of the award. (From left) **Alda Tufro**, M.D., PH.D., associate professor of pediatrics and section chief of pediatric nephrology; Beverly Bartner; Goodwin; Robert Bartner (seated); **Margaret K. Hostetter**, M.D., chair and Jean McLean Wallace Professor of Pediatrics; and **Robert J. Alpern**, M.D., dean and Ensign Professor of Medicine.

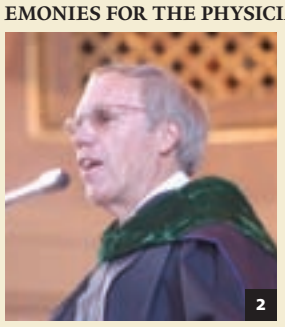

TERRY DAGRADI


RICHARD GREENHOUSE PHOTOGRAPHY

November 3, 2008: At its annual meeting, in San Antonio, Texas, the Association of American Medical Colleges (AAMC) awarded Assistant Professor of Medicine **Marcella Nunez-Smith**, M.D., M.H.S., **THE HERBERT W. NICKENS FACULTY FELLOWSHIP**, which recognizes an outstanding junior faculty member in academic medicine who leads efforts to remedy inequities in medical education and health care. Nunez-Smith, assistant director of the School of Medicine's Robert Wood Johnson Clinical Scholars Program, studies the impact of race and ethnicity on the professional experiences of health care providers. The fellowship is named in memory of Herbert W. Nickens, M.D., an African-American physician who worked to increase diversity in medicine and improve the health of minorities. Nickens, who completed a residency in psychiatry at Yale in the 1970s, served as vice president of the AAMC's Division of Community and Minority Programs from 1988 to 1999.


1

December 8, 2008: Yale's Woolsey Hall was the setting for **GRADUATION CEREMONIES FOR THE PHYSICIAN ASSOCIATE PROGRAM** of the School of Medicine.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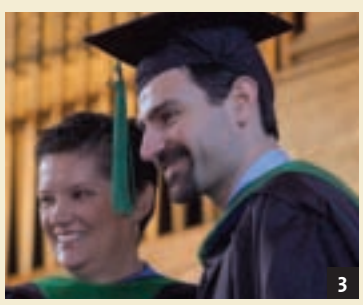
1. (From left) **Melissa Battista**, **Keri Bollman**, **Tami Brining** and **Karen Edwards** of the Class of 2008. **2.** The Commencement address was given by **Alfred M. Sadler Jr.**, M.D., who co-founded Yale's program in 1970. **3. Mary L. Warner**, M.S., dean of the Physician Associate program, presents **Adam Cohn** with the Dean's Award for Academic Achievement. Brining (**4**) and **Daniel Heacock** (**5**) are all smiles after receiving their diplomas.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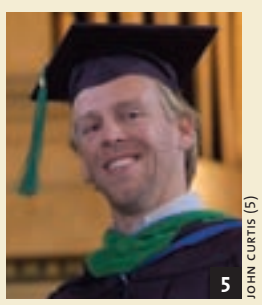
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JOHN CURTIS (5)

Advances

Health and science news from Yale

Blunted brain activity may spur obesity

When we bite into a favorite food, our pleasure is underscored by a rush of the neurotransmitter dopamine in the reward circuits of the brain. However, a new study shows that this reward response is blunted in obese individuals.

As reported in the October 17 issue of *Science*, Dana Small, PH.D., assistant professor of psychiatry, and collaborators gave women samples of a chocolate milkshake while measuring their brain activity. The neural response to the treat was significantly dampened in subjects with a higher body mass index, and especially diminished in subjects carrying a genetic variation associated with lower numbers of dopamine receptors. These latter subjects were also more likely to gain weight over the course of a year.

"Our study is exciting," says Small, "because it demonstrates an association between an abnormal response to food and future weight gain—and it shows that this relationship depends upon your genetic makeup."

Genetic risk adds to dangers of smoking

Though lung cancer is the leading cause of cancer deaths worldwide, scientists have identified few genetic risk factors for the disease. "Only 10 percent of smokers will develop lung cancer in their lifetime, and genetic testing to determine the population of smokers who are most predisposed to develop the disease is needed," says Joanne B. Weidhaas, M.D., PH.D., assistant professor of therapeutic radiology.

Weidhaas and Frank Slack, PH.D., associate professor of molecular, cellular and developmental biology at Yale, had previously shown that the microRNA *let-7*, a snippet of genetic material that puts the brakes on cell proliferation—a process that runs rampant in cancer—could significantly reduce lung cancer in mice.

In a study published in the October 15 issue of *Cancer Research*, Weidhaas, Slack and colleagues discovered a genetic variation in a *let-7* target gene that greatly reduces *let-7*'s protective effect.

The newly identified variation, which compromises *let-7*'s regulation of a cancer-associated gene called *KRAS*, was found in 5.8 percent of a sample of world populations, but in 20 percent of patients with non-small cell lung cancer (NSCLC); the researchers estimate that moderate smokers carrying the variation are 1.4 to 2.3 times as likely to develop NSCLC.

A Yale oncologist faces down pancreatic cancer

Multi-disciplinary teams, clinical trials of new drugs are weapons of choice


ROBERT A. LISAK

For medical oncologist Wasif Saif, helping patients with pancreatic cancer to live longer brings immense satisfaction.

The fourth-highest cause of cancer deaths in the United States, pancreatic cancer is one of the most dreaded diagnoses. With a five-year survival rate of only 5 percent, it is estimated that pancreatic cancer claimed the lives of more than 37,500 people in the United States in 2008.

Despite these alarming statistics, funding for pancreatic cancer research has lagged behind that for other cancers, prompting the National Cancer Institute (NCI) in 2000 to dub the disease the "orphan cancer." Since then, there has been a major boost in federal research funding, from $17. 5 million in 1999 to $73.5 million in 2007.

When M. Wasif Saif, M.D., M.B.B.S., was studying to be a doctor at King Edward Medical College in Lahore, Pakistan, he didn't plan to become an oncologist. But when a family member was diagnosed with cancer, he saw firsthand how malignancies can be a formidable foe. "I took this as a challenge," Saif remembers, "and decided to become an oncologist."

Saif, now associate professor of medicine, went on to a residency in internal medicine at the University of Connecticut School of Medicine and then completed a fellowship in medical oncology at the NCI. Since arriving at Yale in 1995, he has built an active clinical practice as a member of Yale Medical Group, and also serves as co-director of the Gastrointestinal Cancers Program at Yale Cancer Center (YCC), which provides specialized care for patients with pancreatic cancer.

Saif is a member of the Yale Pancreatic Disease Program, a team of Yale physicians in gastroenterology, genetics, pathology, diagnostic radiology, surgical oncology, medical oncology and radiation oncology. The YPDP offers comprehensive treatment for many pancreatic disorders, including cancer.

"Dr. Saif is one of the true rising stars in the field of gastrointestinal malignancies, and he has already developed a national and international reputation," says Edward Chu, M.D., deputy director and chief of medical oncology at YCC.

Saif sees the greatest potential for advancing the treatment

Pancreas, *page 6*

Enlisting virtual victims to test triage systems

Dominique Larrey, the chief surgeon of Napoleon's armies and a pioneer of military medicine, knew something of mass casualties. In the early 19th century, while accompanying Napoleon on his various campaigns, Larrey devised rules of triage (from the French *trier*, "to select" or "to sift") by which soldiers needing medical attention were sorted according to the severity of their injuries, regardless of rank.

Triage is still standard practice in mass-casualty emergencies, often in the form of the Simple Triage and Rapid Treatment (START) system, which assigns color codes to patients depending on their condition. For example, a victim might be color-coded as red, meaning he needs help immediately; yellow, meaning he will need help soon; green, meaning he has minor injuries; or black, meaning he cannot be helped with available resources.

Rules like these help rescuers choose a course of action in chaotic situations. Imagine being the first paramedic on the scene after a tanker truck has plowed into a bus. Traffic is snarled, cars are honking and people are screaming. Who needs attention most—the man on the concrete holding his bloodied knee or the woman on her back with closed eyes? What about the people inside the overturned bus? And what is that white vapor drifting from the truck's tank?

Yet although rules of triage exist to help rescuers, it is difficult to evaluate whether those rules actually save lives. Though the START system is decades old, says David C. Cone, M.D., associate professor of surgery and of epidemiology, "we have no idea if it works."

E-SEMBLE

Emergency medicine expert David Cone is using a virtual reality simulator in his research on triage systems.

Cone, director of the Division of Emergency Medical Services (EMS) in the medical school's Section of Emergency Medicine, studies how EMS should be deployed after chemical, biological and nuclear terrorist attacks, and he has run disaster simulations at Tweed-New Haven Airport complete with volunteers smeared with fake blood. But triage research is inherently difficult. For one thing, says Cone, "we don't even know what we want a mass-casualty triage system to do." Is the best system the one that's easiest to teach, the quickest to apply or the one that saves the greatest number of lives? The complexities mount when one considers that every disaster is unique, making it almost impossible to compare triage systems in the real world.

While studying in Italy for a master's degree in disaster management in 2004, Cone saw a virtual reality (VR) simulator used to train firefighters and realized that the software could be adapted for triage research. Developed by the Dutch company E-Semble, the simulator looks like the highly realistic video game *Grand Theft Auto*. Learners at a laptop "walk around" a vivid scene, assessing and triaging victims. Dangers and distractions, like toxic spills or television reporters, can be added to the scenario. The learners are timed and their actions exported into a database that can then be analyzed Working with emergency medicine resident John Serra, M.D., and supported by the Centers for Disease Control and Prevention and the Laerdal Foundation, Cone plans to teach paramedic students two different triage systems several months apart, then compare how they did with each system in identical VR scenarios.

"Once we get the software tuned, then we can design the larger studies," says Cone, who plans to use the tool to explore whether rules for triage are even necessary, or whether experienced rescuers are better off relying on their accumulated clinical wisdom.

One day, VR tools may allow triage researchers around the world to collaborate, exchange scenarios and compile "libraries" of standardized victims. Cone hopes his work with controlled VR environments will allow for real progress in triage research and ultimately save more lives during real disasters.

Pancreas *from page 5*

of gastrointestinal malignancies, particularly pancreatic cancer, in advancing clinical trials to test new drugs and treatment regimens, and he is enrolling patients in Phase I and II clinical trials at Yale. Information on these trials can be found at http://yaletrials.org. Saif is also working with a group of researchers to develop a pancreatic cancer screen in high-risk patients, such as those with mutations in the *BRCA1* and *BRCA2* genes that are involved in the development of breast and ovarian cancer; researchers believe such patients are also at greater risk for pancreatic cancer.

Pancreatic cancer continues to challenge physicians, and effective screening guidelines are still a long way off, but Saif believes the frustrations are worth it. "When I see the smiles on the faces of patients who are living longer because of our efforts," he says, "it is a great satisfaction."

Polayes *from page 1*

Irving's brother, Maurice B. Polayes, a Massachusetts-based engineer. "We were a very close family," says Maurice. "I think my brother accomplished a considerable amount in his specialty, and I felt that he and my uncle should be recognized."

SECTION OF PLASTIC SURGERY, YSM

Irving Polayes (left) and John Persing (right) in 1993.

The first surgeon to hold the new chair is John A. Persing, M.D., professor of surgery, chief of the section of plastic surgery and director of the Yale Craniofacial Program. Appointed to the chair in April 2007, Persing, like Polayes, specializes in treating children with facial and skull deformities.

The professorship will make it easier for Persing to continue his pro bono surgical work, which makes up some 35 to 40 percent of his practice at Yale's craniofacial clinic and has also taken him abroad to Brazil and Jordan.

"Polayes was a master craftsman of that area," says Persing. But he adds that his colleague, who died in 1999, was not merely skilled, he was an innovator. In addition to developing several surgical procedures, Polayes was among the first surgeons in the nation to train residents to repair facial injuries and congenital deformities like cleft palate. "He recognized there wasn't a good training program for people who wanted to do this work," Persing explains. "Thinking well ahead of everybody else, he developed a very extensive curriculum." The training system Polayes developed is still in use by the American Society of Maxillofacial Surgeons.

Roy Polayes thinks his father's interest in pediatric facial repair may have been sparked while he served as an emergency surgeon and found himself treating victims of automobile accidents, many of whom were children. "He felt almost called to help kids," he says, adding that he sees a reflection of his late father's caring manner in Persing's approach to medicine. Roy visited the clinic in October on behalf of his uncle Maurice, and he saw firsthand some of the many children under Persing's care. "I was so inspired by what I saw," he says. "I saw a lot of that very same benevolence at work. This is like my father's dream come to life."

Mentors *from page 1*

College Class of 1936. While earning his undergraduate degree at Yale, Bob had trekked across campus to the Department of Physiological Chemistry at the School of Medicine to take graduate-level courses under the wing of renowned researcher George R. Cowgill, PH.D., an authority on the human requirements for vitamin B_1 (now known as thiamin) and other aspects of human nutrition. He also came in contact with pharmacologists Louis S. Goodman, M.D. and Alfred Gilman, PH.D., who as assistant professors at the School of Medicine authored the magnum opus *The Pharmacological Basis of Therapeutics*—a classic textbook that, in its 12th revised edition, is still the universal reference book in the field.

McNeil, former chairman of the board of McNeil Laboratories, looks back fondly on his formative years in Sterling Hall of Medicine, and he has generously memorialized these Yale faculty members with recent gifts to the School of Medicine that total $8 million. The gifts will endow a George R. Cowgill Professorship, designated for a top School of Medicine educator with expertise in physiological chemistry, and a Yale Scholar endowment named in honor of Goodman and Gilman. The Yale Scholars program is a recent initiative of Dean Robert J. Alpern, M.D., which awards four years of research funding to the most promising new researchers recruited at the medical school.

CUSHING/WHITNEY MEDICAL LIBRARY

George Cowgill, seen in front of Sterling Hall of Medicine, was an authority on human nutrition, especially the requirements for vitamin B_1, or thiamin.

"I have wanted to help the medical school in any way I can. I'm especially excited about Yale's leadership in translational research, including its recognition with the Clinical and Translational Science Award," says McNeil, regarding the $57 million grant from the National Institutes of Health to the School of Medicine in 2006 aimed at accelerating the translation of discoveries in basic biomedical science into practical treatments for disease. "As an undergraduate, one of my outstanding teachers was Professor Cowgill at Yale School of Medicine, and I wanted to make certain that he would be remembered for the great scientist, mentor and teacher that he was. It was also important to me to make sure that the Goodman and Gilman textbook would be forever linked to the School of Medicine, where it was conceived and written."

McNeil's newest gifts are the latest of many donations to Yale University and the School of Medicine. His endowment in 2000 of the Robert L. McNeil Jr. Professorship in Translational Research, now held by psychiatrist John Krystal, M.D., an expert on schizophrenia and alcoholism, anticipated the medical school's current emphasis on translational research.

"Mr. McNeil is acknowledging a period of time in his life that he believes helped shape his career and nurtured his passion for medical science, and particularly clinical pharmacology" says David J. Leffell, M.D., deputy dean for clinical affairs and professor of dermatology, who has known McNeil for almost a decade. "Even back then, the School of Medicine was a resource for Yale College undergraduates," says Leffell, who did research at the medical school during his own undergraduate years at Yale and sees McNeil as a kindred spirit. "It created an environment that attracted the best and the brightest from Yale College and from other schools."

Over its first few decades the pharmacy founded by the McNeil patriarch built a citywide reputation as a provider of high-quality pharmaceuticals and eventually outgrew the original site, relocating to a nearby four-story building in 1900. Soon after, McNeil's son, Robert Lincoln McNeil, a graduate of the University of Pennsylvania's Wharton School, joined the firm, focusing on its growing manufacturing and drug development division. His efforts led to the incorporation of the business as McNeil Laboratories in 1933.

The company's shift to prescription drug manufacturing proved an ideal challenge for Robert L. McNeil Jr., who came on board as a research chemist in 1938 after receiving his Yale degree. One year later, his brother, Henry S. McNeil, a freshly minted Yale College graduate with a degree in applied economics, joined the company as well.

At that time, there was great interest among physicians and pharmaceutical companies alike in finding a compound that could equal the pain-relieving qualities of aspirin without its troublesome side effects, which include stomach irritation and thinning of the blood. By the early 1950s, under Robert L. McNeil Jr.'s guidance, McNeil Laboratories had a good candidate in hand in the form of acetaminophen, an analgesic that had been discovered in the 19th century but never developed, manufactured or marketed. After extensive testing to establish the drug's safety and efficacy, acetaminophen was released for sale by prescription only in 1955 as Children's Tylenol Elixir, the first commercially available aspirin-free pain reliever. In 1959, when the company was acquired by Johnson & Johnson, a tablet was approved for sale without a prescription. By the mid-1990s, Tylenol was the world's best-selling over-the-counter analgesic.

In 2005, at a meeting of the Chemical Heritage Foundation, Robert L. McNeil Jr. received the American Institute of Chemists' Gold Medal. This award, which has been given to Nobel Prize winners, is a unique tribute to a man who does not hold a graduate degree in the field. McNeil is also prominent as a patron of the arts, with a particular interest in American art and material culture. He has served on the boards of the Yale University Art Gallery (where the lecture hall bears his name), the National Portrait Gallery of the Smithsonian Institution and the Committee for the Preservation of the White House. He has also served as vice president of the Philadelphia Museum of Art. He is a fellow of the Athenaeum of Philadelphia and has been elected to membership in the American Philosophical Society.

COURTESY OF THE CHEMICAL HERITAGE FOUNDATION COLLECTIONS

Yale College graduate Robert McNeil Jr., who directed the development of Tylenol at McNeil Laboratories and eventually became chairman of the board, won the Gold Medal from the American Institute of Chemists in 2005.

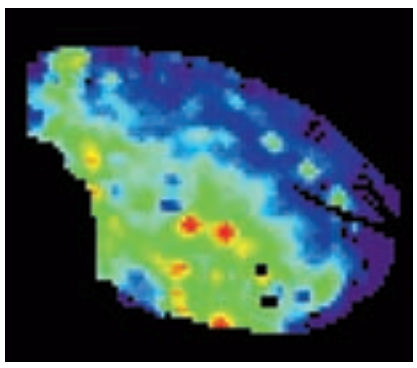
"Yale has many great traditions, but one of the finest is the quality of the students and faculty that have studied and worked at both the college and medical school," says Dean Alpern. "These gifts by Mr. McNeil represent one of the college's most accomplished students acknowledging the outstanding and inspiring faculty at the world-class Yale School of Medicine. It makes one feel proud to be associated with this great institution."

Grants and contracts awarded to Yale School of Medicine

March/April 2008

Federal

Amy Arnsten, NIH, *Molecular and Cellular Basis of Cognitive Aging in Prefrontal Cortical Networks*, 5 years, $9,114,359 • **Sanjay Basu**, Centers for Disease Control and Prevention (CDC), *Mathematically Modeling Transmission and Control of Extensively Drug Resistant (XDR) Tuberculosis*, 1 year, $37,338 • **Jeffrey Bender**, NIH, *Molecular Models of Estrogen-Induced Vascular Protection*, 4 years, $1,489,219 **Madhavi Bhoomagoud**, NIH, *Effect of Acidosis on Pancreatitis*, 2 years, $113,404 • **Daniel Biemesderfer**, NIH, *ADAM 10-Activated Signaling in Proximal Tubule*, 2 years, $398,063 **Robert Camp**, NIH, *Novel Methods to Localize Protein–Protein Interactions in Fixed Cells and Tissues*, 2 years, $409,472 • **Lawrence Cohen**, NIH, *Optical Studies of Neuron Activity and Organization*, 5 years, $1,406,132 • **Robert Constable**, NIH, *Upgrade of the Yale 3T Trio Imaging System*, 1 year, $500,000 • **Jonathan Dranoff**, NIH, *Regulation of Hepatic Stellate Cells by Extracellular Nucleotides*, 4 years, $1,406,486 • **Rachael Felberbaum**, NIH, *Sumo Regulation of mRNA Surveillance*, 2 years, $59,654 • **Biff Forbush**, NIH, *Function and High-Resolution Structure of an APC Superfamily Amino Acid Transporter*, 2 years, $454,969 **Nao Gamo**, NIH, *Role of cAMP and HCN Channels in Stress-Induced Prefrontal Dysfunction*, 3 years, $122,916 • **Thomas Gill**, NIH, *Research Training in Disability and Disabling Disorders*, 5 years, $903,900 • **Erol Gulcicek**, NIH, *LTQ Orbitrap Mass Spectrometer for Yale University Keck Laboratory*, 1 year, $500,000 **Mark Hochstrasser**, NIH, *Functions and Mechanisms of Deubiquitinating Enzymes*, 4 years, $1,410,256 • **Se-Te Huang**, NIH, *The Role of Decidual Innate Immunity in the Pathogenesis of Preeclampsia*, 5 years, $1,751,506 • **Paula Kavathas**, NIH, *Molecular Analysis of CD8 MHC Class I Interaction*, 5 years, $1,424,846 **Ami Klin**, NIH, *Mechanisms of Social Engagement in Autism Spectrum Disorders*, 5 years, $12,416,543 • **Robert LaMotte**, NIH, *Neurophysiology of Pain Adaptation and Hyperalgesia*, 4 years, $2,032,913 • **Haiqun Lin**, NIH, *Assessing Intervention Effectiveness in Longitudinal Trials of Antipsychotic Medicines*, 2 years, $390,206 • **Jennifer Long**, NIH, *Determining the Molecular Mechanisms of Vascular Sympathetic Innervation*, 3 years, $109,530 • **Mark Mamula**, NIH, *Post-Translational Modifications in Tolerance and Autoimmunity*, 5 years, $2,068,438 • **Robert Means**, NIH, *Modulation of DC-SIGN and DC-SIGNR by KSHV*, 5 years, $1,697,944 • **I. George Miller**, NIH, *Studies of Epstein-Barr Virus*, 5 years, $2,353,798 **Walther Mothes**, NIH, *Cell Biology of Retrovirus Replication*, 5 years, $957,794 • **Stephanie O'Malley** and **Ralitza Gueorguieva**, NIH, *Trajectories of Drinking and Compliance in the COMBINE Study*, 3 years, $572,299 • **Marina Picciotto**, NIH, *Anatomical Basis for Nicotine Addiction*, 5 years, $1,778,875 • **Jordan Pober**, NIH, *Proteins of the Endothelial Cell Surface*, 4 years, $1,846,876 • **George Richerson**, NIH, *Non-Vesicular GABA Release via GABA Transporter Reversal*, 4 years, $1,323,583 • **Ayano Satoh**, NIH, *The Role of Phosphorylation of a COPII Coat Protein, Sec31, in Molecular Export*, 2 years, $135,625 • **William Sessa**, NIH, *Phosphorylation and Endothelial Nitric Oxide Production*, 4 years, $1,654,583 • **Robert Sherwin**, NIH, *Diabetes Endocrinology Research Center*, 5 years, $8,339,144 • **Mark Shlomchik**, NIH, *Investigating Novel Memory B Cell-Specific Genes Using Fluorescent Reporter Mice*, 2 years, $454,917 • **Mario Strazzabosco**, NIH, *Epithelial Angiogenic Signaling in Polycystic Diseases of the Liver*, 5 years, $1,323,667 • **Nancy Suchman**, NIH, *Parenting Intervention and Assessment with Substance Abusing Mothers*, 5 years, $906,639 • **Mary Tinetti**, NIH, *Death as a Multi-Factorial Cumulative Health Event in Older Adults*, 2 years, $542,567 • **Christian Tschudi**, NIH, *Analysis of the* Trypanosoma brucei *Genome Using Tiling Arrays*, 2 years, $165,417 • **Agnes Vignery**, NIH, *XCT Research SA Plus pQCT Scanner*, 1 year, $129,275 • **Jiou Wang**, NIH, *Mechanism of SOD1-Linked ALS Studied in* C. elegans *and Mouse Models*, 2 years, $180,000 • **Ying Xia**, NIH, *Hypoxia and Neuronal Excitability: Cellular Mechanisms*, 5 years, $1,759,222 • **Yong Xiong**, NIH, *Structural Studies of HIV Vif and its Cellular Binding Partners*, 2 years, $441,140 • **Heping Zhang**, NIH, *Analysis of Genomic Data for Complex Traits*, 4 years, $1,327,549



LAWRENCE COHEN

With funding from the National Institutes of Health, Lawrence Cohen, professor of cellular and molecular physiology, is using optical techniques to map the activity of large populations of neurons. Here, the neural signature of the odorant cineole in the turtle olfactory bulb is shown, with red indicating the highest response and purple indicating no response.

Non-Federal

Ali Abu-Alfa, Roche Laboratories, Inc., *A Model of Compensated and Regulated Living Kidney Donation: Successes and Shortcomings*, 1 month, $2,000 • **Elizabeth Bradley**, Foundation for Professional Development, *Executive Management Program for Women in the Health Sector*, 1 year, $1,500 • **Peter Charpentier**, The Johns Hopkins University, *Experience Corps Trial: Improving Health of Older Populations through Generativity*, 3 months, $14,022 **Jonathan Choy**, International Society for Heart and Lung Transplantation, *Regulation of iNOS Expression in Human T Cells; Role of SDF-1*, 1 year, $40,000 • **Miguel Coca-Prados**, University of Arizona, *University of Arizona Eye Tissue Work*, 1 year, $7,500 • **Kelly Cosgrove**, Peter F. McManus Charitable Trust, *Regulatory Effects of Chronic Ethanol Consumption on the Nicotinic Acetylcholine Receptor (nAChR) in Brain Using [^{123}I]5-IA-85380 ([^{123}I]5-IA) and SPECT Imaging in Nonhuman Primates*, 1 year, $50,000 • **Joseph Craft**, Rheuminations, Inc., *Characterization of Pathogenic T Cells in Murine and Human Lupus*, 3 years, $360,000 **Marie Egan**, Cystic Fibrosis Foundation, *Bone Marrow Progenitor Cells: Potential Use in CF*, 2 years, $194,400 • **Matia Finn-Stevenson**, State of CT Dept. of Education, *Connecticut Family Resource Center Program Evaluation Study 2008–2009*, 15 months, $150,000 **Romina Fiorotto**, Cystic Fibrosis Foundation, *Experimental Cell Therapy of Cystic Fibrosis-Cholangiopathy*, 2 years, $86,400 • **Richard Flavell**, Juvenile Diabetes Research Foundation Int'l, *Memory CD8 T Cells in T1D and TGF-Beta*, 3 years, $495,000; Juvenile Diabetes Research Foundation Int'l, *JDRF Center for Developing Immune Therapies for Type 1 Diabetes*, 5 years, $7,660,655 • **Hoby Hetherington**, Albert Einstein College of Medicine, *MR Spectroscopy to Evaluate Liver Repopulation by Transplanted Hepatocytes*, 1 year, $9,000 • **Natalia Ivanova**, Edward Mallinckrodt, Jr. Foundation, *Genome-Wide Functional Analysis of Molecular Pathways that Control Pluripotency in Human Embryonic Stem Cells*, 1 year, $60,000 • **Leonard Kaczmarek**, FRAXA Research Foundation, *Regulation of FMRP-Slack Potassium Channel Interactions by Metabotrophic Glutamate*, 1 year, $60,000 • **Michael Krauthammer**, SAIC-Frederick, Inc., *Adoption of caTISSUE*, 9 months, $173,745 • **John Krystal**, Hartford Hospital, *Exposure, D-Cycloserine Enhancement, and Genetic Modulators in Panic Disorder*, 1 year, $92,505 • **Paul Lombroso**, American Health Assistance Foundation, *The Role of STEP in Alzheimer's Disease*, 3 years, $400,000 • **Sukanya Narasimhan**, L2 Diagnostics, LLC, *Tick Midgut Thrombin Inhibitor as a Vaccine Target*, 1 year, $95,990 • **George Richerson**, Children's Hospital, (Boston), *The Ventral Medulla and the Sudden Infant Death Syndrome*, 1 year, $1,703,675 • **Nancy Ruddle**, Nat'l Multiple Sclerosis Society, *MOG Expression in Lymphoid Organs: Regulation and Functional Consequences*, 3 years, $551,615 **Alessandro Santin**, Institute of Advanced Health, *New Therapeutic Strategies Based on Studies of Tumor Microenvironment and New Targets Identified Through Proteomic and Genomic Profile Analysis*, 1 year, $77,064; Institute of Advanced Health, *The Molecular Genetics of Neoplastic Pharmacoresistance and Oncogenesis*, 1 year, $179,251 • **Dominik Schenten**, Cancer Research Institute, *Exploring the Tissue-Specific Functions of Toll-Like Receptors in Adaptive Immunity*, 2 years, $85,000 **Rashu Seth**, Cancer Research Institute, *Targeting High-Fidelity and Error-Prone DNA Repair Pathways*, 3 years, $145,500 • **Matthew State**, Regents of the University of California, *A Genome Search for Autism Susceptibility Loci*, 9 months, $251,366 • **Carin Van Gelder**, New England Medical Center, *Early EMS and ED Use of GIK for ACS: The IMMEDIATE Trial*, 9 months, $217,322 • **Ligang Zhou**, Juvenile Diabetes Research Foundation Int'l, *Amygdala Modifies Counter-Regulatory Hormone Response to Hypoglycemia*, 2 years, $101,096

'Green' initiatives move medical school toward sustainability

In an era of worries about climate change and highly volatile energy prices, "sustainability" is on everyone's lips. The School of Medicine is doing its part, and sometimes all it takes are some hand-me-down jeans.

Denim discarded in the jean manufacturing process, which now helps insulate the C wing of Sterling Hall of Medicine (SHM), is one of many recycled materials that are lightening Yale's carbon footprint. The building's recently renovated lab casework, ceiling tiles and wall insulation also come from recycled material, such as wheat straw board and soy-based spray foam. In total, the sustainability campaign squeezes more light from the sun, diverts trash from landfills and conserves water and heat.

Yale's overall sustainability strategy began with the student-initiated Yale Green Plan in 1998. In 2002, the university's Advisory Committee on Environmental Management proposed a set of environmental principles, and in 2005 President Richard C. Levin committed the university to reducing greenhouse gases to 43 percent below 2005 levels by the year 2020.

Implementing sustainable laboratory renovations that could be benchmarked and measured by a national standard was not a simple process. Success is measured in this realm by the U.S. Green Building Council's Leadership in Energy and Environmental Design (LEED) standards, but the organization had not yet set standards for lab renovations. "LEED was designed for new buildings or full-building renovations but not laboratories nor smaller scaled renovations of the kind we do here at the medical school," says Virginia Chapman, director of construction and renovation for the School of Medicine's facilities office.

The work on the third floor of SHM's C wing created a yardstick in 2006 when it became what is believed to be the first laboratory renovation project in the nation to gain LEED gold certification for its sustainable features. Among those features, says Robert Skolozdra, an associate at the architectural firm Svigals & Partners, which designed the renovations, are sensors that switch lights on only when a person is in the room. "Daylight harvesting"—adding exterior and interior windows—maximizes available light. The project eased the strain on landfills by recycling 85 percent of construction and demolition debris. Lab faucets have reduced their output from 2 to 1.5 gallons per minute and dual-flush toilets and urinals have been installed; water use is down 35 percent overall.

TERRY DAGRADI

Virginia Chapman oversees construction and renovation projects at the School of Medicine with an eye toward recycling usable materials and conserving energy.

Adding such features to previously planned renovations costs more—they account for between 1 and 2 percent of the $8.2 million price tag of the Sterling renovations that were completed in 2006—but Yale can't afford not to go this route, says Chapman. "We're saving the university money as a by-product of reducing carbon emissions," she says. Using the lessons learned from the C wing, the SHM's I wing first floor renovation also received LEED gold certification. Still to come, Chapman adds, are renovations to the second and third floors of Sterling's I wing, the Brady Memorial Laboratory, the Hunter Building, the sixth and seventh floors of the Laboratory for Epidemiology and Public Health and the Laboratory for Surgery, Obstetrics and Gynecology, all of which will incorporate green features. The School of Medicine is also seeking LEED gold certification for the newly built research building at 10 Amistad St., which opened in 2007.

Head of medical school is honored by nephrology society

Dean lauded for leadership in medical education and research on the kidney

At its annual meeting last November, the American Society of Nephrology (ASN) awarded the 2008 John P. Peters Award to Robert J. Alpern, M.D., dean of the School of Medicine. The award honors "individuals who have made substantial research contributions to the discipline of nephrology and have sustained achievements in one or more domains of academic medicine including clinical care, education and leadership."

Alpern's career has combined research, teaching and administration in equal measure. He began his scientific work in 1979 at the University of California, San Francisco (UCSF), where he completed a postdoctoral fellowship in nephrology with Floyd C. Rector Jr., M.D., studying membrane transport, the means by which ions and molecules enter and leave cells, in the kidney. He continued this line of investigation, focusing on the regulation of kidney transport proteins.

ASN

(From left) Peter Aronson, the C.N.H. Long Professor of Medicine at Yale and past-president of the American Society of Nephrology (ASN), joined Donald Seldin, who holds the William Buchanan Chair in Internal Medicine at the University of Texas Southwestern Medical Center, to present the ASN's John P. Peters Award to Dean Robert Alpern. Seldin, a 1943 graduate of Yale School of Medicine, was a medical resident and fellow with John Peters.

Alpern has defined mechanisms of hydrogen and bicarbonate transport in the proximal tubule of the kidney, and he proved the existence of an electrogenic sodium-coupled bicarbonate transporter in mammals. More recently, his research has focused on the molecular mechanisms by which the sodium–hydrogen exchanger of the kidney's proximal tubule is regulated.

In 1987, Alpern was recruited from UCSF to serve as chief of nephrology at the University of Texas Southwestern Medical Center, where he later held the Ruth W. and Milton P. Levy Sr. Chair in Molecular Nephrology and the Atticus James Gill, M.D., Chair in Medical Science. In 1998, Alpern was appointed dean of Southwestern. Alpern became dean and Ensign Professor of Medicine at Yale in 2004.

A former president of the ASN, Alpern has served as associate editor of the *American Journal of Physiology: Renal* and *Hospital Practice: Physiology in Medicine*; as section editor of the renal and electrolyte section of the *Annual Review of Physiology* and the molecular cell biology and physiology of solute transport section of *Current Opinion in Nephrology and Hypertension*; as consulting editor of the *Journal of Clinical Investigation* and *Kidney International*, and on the editorial board of numerous other journals. He was elected to the American Society of Clinical Investigation, the Association of American Physicians and the Institute of Medicine, and has served on the Advisory Council of the National Institute of Diabetes and Digestive and Kidney Diseases. Alpern is co-editor of the latest edition of Seldin and Giebisch's *The Kidney: Physiology & Pathophysiology*, a top textbook in nephrology.

The Peters Award, established in 1983, is named for John P. Peters, M.D., one of the fathers of nephrology. Peters spent his entire career at Yale School of Medicine, where he was chief of the Metabolic Division of the Department of Medicine from 1922 to 1955. In addition to being a skilled clinician who was beloved by his patients, Peters was instrumental in the emergence of clinical chemistry as a quantitative field that could provide precise measurements of body fluids for the diagnosis and treatment of disease.

Yale biologist inducted into Connecticut Women's Hall of Fame

Joan Steitz

Two pioneering School of Medicine scientists were inducted into the Connecticut Women's Hall of Fame last October.

Joan A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry, was honored along with the late Patricia S. Goldman-Rakic, PH.D., who was inducted posthumously.

Steitz, a Howard Hughes Medical Institute investigator, is best known for her discovery and characterization of small nuclear ribonucleoproteins (snRNPs; pronounced "snurps"), intracellular complexes that play a key role in the splicing of pre-messenger RNA, the earliest product of DNA transcription. By excising non-coding regions from RNA and splicing together the resulting segments, snRNPs help to create the messenger RNA (mRNA) templates for the making of proteins.

Steitz's research has served to clarify how splicing expands the coding potential of human chromosomes, providing tools to advance the diagnosis and improve the prognosis of rheumatic diseases.

Steitz entered the PH.D. program at Harvard University in 1963 in biochemistry and molecular biology, and she was the first female graduate student to work under James D. Watson, PH.D., who had shared the Nobel Prize the previous year for his co-discovery of the structure of DNA. After completing postdoctoral work at the Medical Research Council Lab of Molecular Biology in Cambridge, England, she joined the Department of Molecular Biophysics and Biochemistry at Yale in 1970.

Steitz is a fellow of the American Academy of Microbiology and a member of the National Academy of Sciences, the Institute of Medicine, the American Academy of Arts and Sciences and the American Philosophical Society. She is also a fellow of the American Association for the Advancement of Science. She recently became the first of two women to share America's largest prize in medicine, the Albany Medical Center prize in medicine and biomedical research.

Goldman-Rakic, who was Eugene Higgins Professor of Neurobiology at the medical school, was a pre-eminent expert in the workings of the prefrontal cortex, seat of all higher-level cognitive functions. Her groundbreaking work led to the discovery of a link between the loss of the neurotransmitter dopamine and severe deficits in working memory, research that has contributed to understanding and treating diseases such as schizophrenia, Parkinson's, Alzheimer's and attention deficit hyperactivity disorder.

A member of the National Academy of Sciences and the recipient of numerous honorary degrees and awards, Goldman-Rakic died in 2003 at age 66.

Three psychiatric researchers are newest Murphy Professors

Three neuroscientists in the School of Medicine's Department of Psychiatry have been named to professorships funded by the late Charles B.G. Murphy, a 1928 alumnus of Yale College. Angus C. Nairn, PH.D., and Marina R. Picciotto, PH.D., have each been named Charles B.G. Murphy Professor of Psychiatry. Jane R. Taylor, PH.D., has been designated the Charles B.G. Murphy Associate Professor of Psychiatry.

Nairn is noted for his research on the molecular actions of the neurotransmitter dopamine in a brain region known as the basal ganglia. Dysfunction of the brain's dopamine systems have been implicated in movement disorders such as Huntington's disease and Parkinson's disease, as well as in schizophrenia, drug addiction and attention deficit hyperactivity disorder (ADHD). He has extensive expertise in enzymology, protein chemistry and the molecular biology of signal transduction, particularly with respect to the role of protein phosphorylation in the nervous system.

Angus Nairn

Marina Picciotto

Jane Taylor

Picciotto's research is focused on understanding addiction, depression and learning. She uses molecular, genetic and pharmacological approaches to link biochemical, cellular and anatomical levels of investigation to these complex behaviors. Picciotto's primary interest is the role of nicotinic acetylcholine receptors in brain development and function, with a special emphasis on behaviors related to nicotine addiction and smoking. Picciotto also studies galanin, a neuropeptide that protects against the development of addiction.

Taylor, a member of Yale's Interdisciplinary Research Consortium on Stress, Self-Control and Addiction, studies the brain's cortico-limbic-striatal circuits. Disturbances in this network may cause increased impulsivity and alterations in reward-related learning that can lead to drug addiction, and disruptions in these circuits have also been linked to depression, schizophrenia and ADHD. In her current work, Taylor is studying how dopamine-regulated intracellular signaling molecules and alterations in associated molecules within the prefrontal cortex, amygdala and nucleus accumbens contribute to motivation, learning and memory.

Charles B.G. Murphy established the Wood Kalb Foundation in 1953. Through three separate philanthropies, Murphy and his estate have given over $10 million to Yale, exclusively in the Department of Psychiatry and the School of Medicine. Following Murphy's passing, control of the foundation fell to his attorney and friend Ethan Allan Hitchcock of the Yale College Class of 1931, who had once been the roommate of Murphy's brother. In 1978, Hitchcock gave $1 million to the medical school to establish the Murphy professorships in psychiatry. In 1979, Hitchcock gave $100,000 in support of Yale Cancer Center.