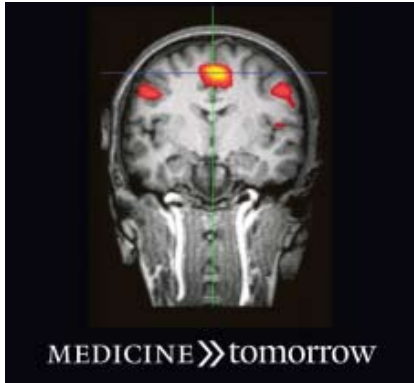


# Medicine@Yale

Advancing Biomedical Science, Education and Health Care

Volume 3, Issue 1 January/February 2007

## \$3 billion Yale campaign will benefit science and medicine



Nearly a decade after the close of its last major fundraising campaign, Yale has launched "Yale Tomorrow," a five-year drive to raise \$3 billion, a major portion of which will be directed toward science and medicine. At the public launch of the campaign in September, President Richard C. Levin announced that donors had already committed \$1.3 billion in gifts and pledges during the campaign's quiet phase, which began in mid-2004.

The campaign is organized around four major themes: "Yale College," "The Arts," "The Sciences" and "The World."

Within the sciences, under the rubric "Medicine Tomorrow," Yale will seek support for many research, educational and clinical programs, with the ultimate goal of finding new and better ways to diagnose and treat illness, says Dean Robert J. Alpern, M.D., Ensign Professor of Medicine.

According to Inge T. Reichenbach, Yale's vice president for development, the campaign's goals for the medical school are quite specific.

These goals include increased support for research, the establishment of new endowed professorships, increased financial aid for students, new buildings for research and clinical care, improved technology, educational innovation and support for the

**Campaign, page 6**

## Following in his father's footsteps

*Yale alumnus, investor makes unrestricted gift to School of Medicine*

Carrying on a philanthropic tradition begun by his late father, Adrian C. "Ace" Israel of the Yale Class of 1936, investor and Yale alumnus Thomas C. Israel has made a gift of \$5 million to the School of Medicine. Israel, who says his family has long had a deep interest in medical science, placed no restrictions on the new gift, saying that confidence in the medical school's leadership overruled any need to earmark the funds.

"If we trust the people and the institution we give money to, we should feel that they'll use good judgment as to how it's used," says Israel, a 1966 Yale graduate and chair of A.C. Israel Enterprises, a New York City-based firm that invests in private equity funds and makes direct private equity investments.

For Robert J. Alpern, M.D., the medical school's dean and Ensign Professor of Medicine, the warm feelings are mutual. "One of my great pleasures as dean has been the opportunity to come to know the Israel family closely," Alpern says. "Their enthusiastic support for Yale and the medical school continues a family legacy that has helped shape what we are and where we can go. I am



The Israel family—Wendy, Thomas, Barbara and (far right) Emily—has strong ties with the medical school and with Dean Robert J. Alpern (second from right).

especially appreciative that Tom and Barbara had the confidence in Yale and in me to place no restrictions on how this gift is used."

All told, Israel and his wife, Barbara, have donated more than \$7 million to the medical school, including a \$1 million commitment toward establishing a professorship in memory of Donald J. Cohen, M.D., a renowned child psychiatrist and director of the Yale Child Study Center (YCSC) who died in 2001.

These gifts complement a \$1.25 million donation made by Adrian Israel in 1986 to establish the School

of Medicine's Magnetic Resonance Research Center.

Both Thomas and Adrian Israel have also been active and longstanding supporters of the Yale School of Management (SOM), where the Adrian C. Israel Professorship of International Trade and Finance was established in 1976.

After Adrian's death, Thomas, who serves on the SOM's advisory board, combined money from his father's estate with his own 25th reunion gift to Yale to establish the International Finance Center at the

**Israel, page 6**

## New genes found in Crohn's disease, serious eye ailment

A decade ago, finding genes that contribute to human diseases was labor-intensive, time-consuming and prohibitively expensive. But today, cutting-edge research tools are changing all that, and two School of Medicine researchers are at the forefront of the revolution.

Last month, in the journal *Science*, Josephine J. Hoh, Ph.D., associate professor of epidemiology and ophthalmology, and Judy H. Cho, M.D., associate professor of medicine, reported that their research teams had homed in on genes involved in two genetically complex human disorders: age-related macular degeneration (AMD), the leading cause of vision loss and blindness in the elderly in the developed world, and Crohn's disease (CD), an inflammatory disorder of the gastrointestinal tract.

The key to the research strategy used by Hoh and Cho is the natural variability in the 3 billion "letters" in the human genome, the genetic instruction book that encodes all the proteins in the body. Compare the genomes of a large group of people and you'll find single-letter differ-

**Genes, page 6**



Josephine Hoh

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## Pediatric researcher is new ambassador for global health

Research!America, the nation's largest nonprofit educational and advocacy alliance for health research, has named Michael Cappello, M.D., professor of pediatrics, microbial pathogenesis and public health, an Ambassador in the Paul G. Rogers Society for Global Health Research.

Cappello, an expert on the molecular basis of hookworm infection (see *Advances*, p. 3), will join 26 other public health "scientist advocates" to foster a national discussion on the importance of research to improve global health. The ambassadors will



**Michael Cappello**

meet with opinion leaders and decision makers to convey the importance of global health research to Americans.

The Rogers Society, named for the former Florida congressman and chair emeritus of Research!America, was launched by the alliance this year with support from the Bill and Melinda Gates Foundation.

The society was formed to increase awareness of research on diseases that disproportionately affect the world's poorest nations and to make the case for greater U.S. investment in that research.

Research!America will provide advocacy leadership development to the inaugural group of ambassadors and will facilitate their public outreach and advocacy by arranging speaking engagements and a range of community-level activities to connect with policy makers, the media and the public nationwide.

### Medicine@Yale

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**A former captain in the Israeli army, Joseph "Yossi" Schlessinger is adding to our arsenal to combat cancer.**

## A scientist soldiers on

*Born on a battlefield, a fighter in real wars and the war against cancer*

When Joseph Schlessinger, PH.D., was born in Nazi-occupied Yugoslavia in 1945, gunfire cracked and shells exploded outside. His parents were Jewish partisans fighting the German invaders and local fascists. Three years later, with nearly all their relatives shot by the Germans or murdered in concentration camps, his family immigrated to Israel, only to land in the midst of the first of what would be many wars between the new Jewish nation and its Arab neighbors.

Sitting in his office in the Sterling Hall of Medicine recently, Schlessinger says, with some understatement, "Our life had a lot of dramatic events."

Just surviving such inauspicious, violent beginnings would seem an achievement. However, Schlessinger—known to friends as "Yossi"—not only lived, he went on to discern some of the most important mechanisms in the life cycle of the cell, discoveries that have led to effective new treatments for cancer.

Along the way, Schlessinger cofounded two biotechnology com-

panies and has served as an advisor to several others—work that led to Sutent, a drug approved by the U.S. Food and Drug Administration in January for advanced kidney cancer and for a stomach cancer known as gastrointestinal stromal tumor, or GIST. Sutent, now marketed by Pfizer, and other drugs based on Schlessinger's discoveries are being tested as treatments for more common renal cancers, as well as breast and other cancers.

Growing up in Israel, Schlessinger never lived far from a battlefield. He joined the Israeli army, becoming a captain, and fought in two wars and served in a third. But despite the disruptions of military reserve duty and call-up for wars,

### Lifelines

#### Joseph Schlessinger

Schlessinger never lost his childhood fascination with science.

"I was always interested in addressing fundamental questions," he says, and he had a productive career studying intracellular signaling and the role of growth factors circulating in the blood in the life cycle of the cell.

After moving to New York University in the early 1980s, Schlessinger and colleagues showed how epidermal growth factor (EGF) protein binds and activates cell-surface enzymes known as receptor tyrosine kinases (RTKs). This crucial

coupling launches a cascade of signals that eventually reach the cell nucleus and tell the cell either to divide and grow, or to ignore checkpoints that would normally cause it to die.

Schlessinger's lab then demonstrated that genetically aberrant EGF receptors and other RTKs can set off the rampant cell growth seen in cancer, including malignant brain tumors and other human cancers.

Schlessinger recognized that drugs that could inhibit RTKs might also control cancers, and the development of tyrosine kinase inhibitors like Sutent heralded the beginning of a new era of highly targeted cancer treatments.

Although he works closely with industry and has been offered presidencies of drug companies numerous times, Schlessinger, now the William H. Prusoff Professor and chair of the Department of Pharmacology, has chosen instead to continue his seven-day workweek at Yale. "I need the freedom of academia," he explains. "It's the freedom that makes me work."

He ascribes his drive to his tumultuous origins. "I have tremendous anxiety because of what happened to my parents," Schlessinger says. That anxiety, forged in war, has been an advantage at the lab bench. "You're only as good as your last work," he says. "You have to prove yourself again."

## Biologist cited for structural insights into action of antibiotics



**Thomas Steitz**

In a ceremony and commemorative symposium held at Keio University in Tokyo in November, Thomas A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry at Yale, was awarded the 11th Keio Medical Science Prize.

Steitz, also a Howard Hughes Medical Institute investigator, was honored for X-ray crystallography research that in 2000 led to publication of the structure of the large subunit of the ribosome, which is crucially

involved in translating instructions contained in messenger RNA (mRNA) into proteins.

Many antibiotics work by interfering with the translation of mRNA by the ribosome of bacteria, but some bacteria develop mutations that change the ribosome's structure and render the bacteria resistant to treatment. From their crystallographic work, Steitz and collaborators have identified the structural basis of antibiotic drug function and resistance, and he and several Yale colleagues founded Rib-X, a company developing new compounds to combat drug-resistant bacteria.

The Keio award, the only prize of its kind awarded by a Japanese university, recognizes outstanding research achievements in the medical or life sciences, and includes an honorarium of 20 million Japanese yen, or about \$173,000.

Steitz has been on the Yale faculty since 1970, arriving directly after completing postdoctoral training at Harvard University and at the Medical Research Council Laboratory in Cambridge, England.

The recipient of numerous awards, Steitz was appointed full professor in 1979 and named Sterling Professor in 2001.

## Advances

Health and science news from Yale



### In bacteria vs. worm, children are winners

If the bacterium *Bacillus thuringiensis* (Bt) did battle against the parasitic hookworm *Ancylostoma ceylanicum*, who would prevail? According to new research, the biggest victors may be the nearly 1 billion people infected by hookworms worldwide—especially children, who risk anemia, malnutrition and growth delay.

Bt-produced substances known as crystal proteins are commonly used on crops to control insects and worms. Michael Cappello, M.D., professor of pediatrics, microbial pathogenesis and public health, and colleagues at the University of California, San Diego, found that a Bt crystal protein known as Cry5B might also be an effective treatment for parasitic worm infections.

In the October 10 issue of the *Proceedings of the National Academy of Sciences*, Cappello and colleagues report that Cry5B inhibits hookworm growth in laboratory dishes and in infected hamsters. In the hamsters, Cry5B was as potent as a conventional anti-parasite medication in reversing weight loss and anemia, and no toxic effects were evident.

### Ruling the fate of a cellular blank slate

Stem cells make identical copies of themselves and can differentiate into many of the myriad cell types that form the body's tissues and organs. To maximize these cells' therapeutic versatility, they must be maintained in an undifferentiated state.

Some researchers have suggested that oxygen levels are low within the stem cell niche—the microenvironment within tissues that determines whether stem cells regenerate or differentiate. Seeking a method to preserve stem cells in their blank slate form, Zhong Yun, Ph.D., assistant professor of therapeutic radiology, and colleagues took a cue from nature, mimicking those low-oxygen conditions for cells in the lab.

As reported in the October 13 issue of *The Journal of Biological Chemistry*, under these conditions stem cell-like fat precursor cells remained in an undifferentiated state. And when the team upped the oxygen level, the precursor cells could again be converted into fat cells.

"Once we know how the microenvironment regulates the functions of stem and progenitor cells," says Yun, "we can potentially protect them from premature differentiation or find ways to mobilize these cells for tissue repair and regeneration."

# A crystal-clear look at a puzzling protein

## An enzyme's structure may provide new clues on Alzheimer's disease

Biologists and chefs alike know that oil and water don't mix. So several years ago, when researchers first discovered intramembrane proteases—a class of hydrophilic ("water-loving") enzymes that inexplicably appeared to function smack in the middle of the oily membrane that surrounds cells—many scientists were perplexed. Some were downright skeptical.

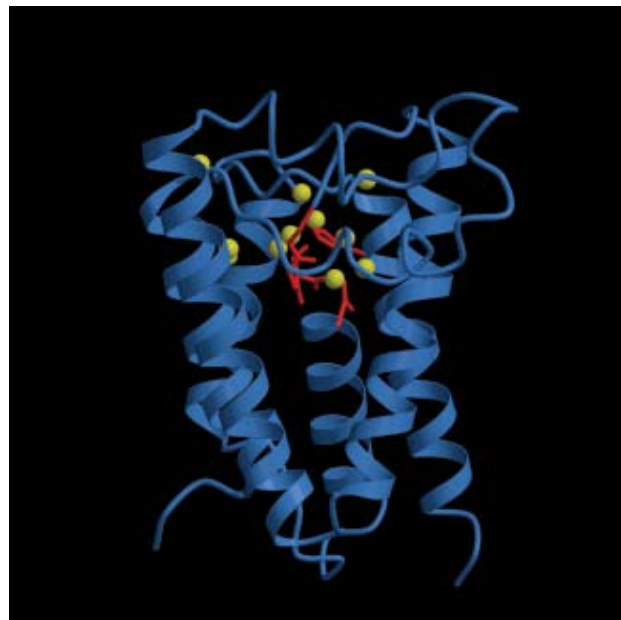
By publishing the first-ever crystal structure of one such enzyme, Ya Ha, Ph.D., assistant professor of pharmacology, and colleagues may have revealed the intramembrane proteases' recipe for success.

In addition to providing a solution to a slippery biological mystery, Ha's work could shed light on the mechanisms underlying Alzheimer's disease.

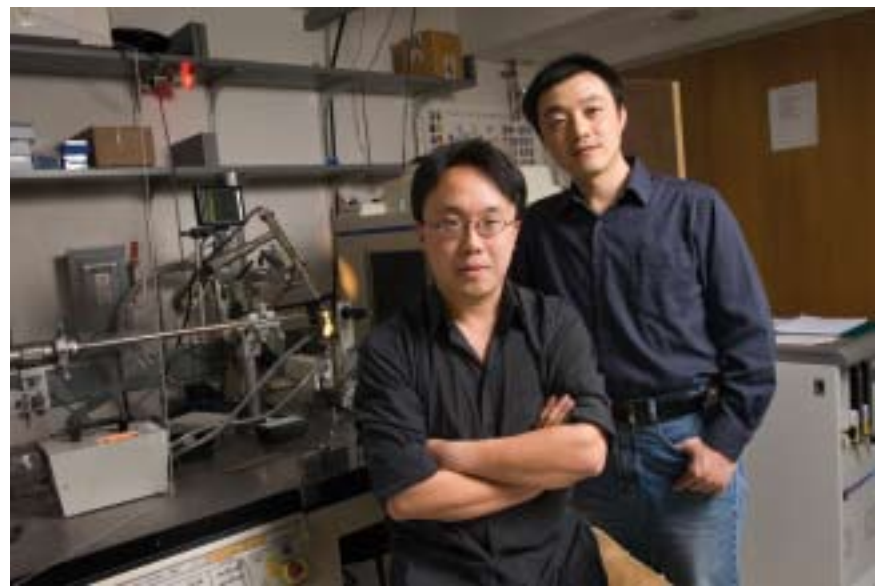
Chewing up proteins, a process known as proteolysis, is the job of proteases. But protein-splitting reactions require water, a substance that is normally excluded from the greasy interior of cell membranes.

In 1997, Nobel laureates Joseph L. Goldstein, Ph.D., and Michael S. Brown, Ph.D., published intriguing data in *Cell* suggesting that a protease involved in regulating cholesterol somehow did its work within the cell membrane. Goldstein and Brown acknowledged that this protease must be "unusual," but they proposed that gamma-secretase, the enzyme that cleaves amyloid protein into the toxic fragments seen in the brains of Alzheimer's patients, might operate in the same manner.

When structural biologist Ha came to the School of Medicine from Harvard University five years ago, he first set his sights on gamma-secretase to try to crack the paradox of intramembrane proteases. Ha was convinced that obtaining structural information through X-ray crystallography was the key to understanding how these controversial enzymes worked.



In an image from the laboratory of structural biologist Ya Ha, water molecules (yellow) are seen within the active site (red) of the membrane-spanning domains (blue) of rhomboid protease.



Structural biologists Ya Ha (seated) and Yongcheng Wang worked with Yingjiu Zhang to unlock a quirky enzyme's secrets.

But despite the Ha research team's best efforts, gamma-secretase could not be coaxed into forming crystals, the first step in determining a protein's molecular structure. Without a crystal, there was little chance of grant support from the National Institutes of Health, so Ha scraped together funds from the Department of Pharmacology and private foundations to continue his work.

When a family of bacterial enzymes with similar activity known as rhomboid proteins was discovered, Ha seized on those as an alternative. From there, he and postdocs Yongcheng Wang, Ph.D., and Yingjiu Zhang, Ph.D., worked for four more years before they successfully formed a rhomboid protein crystal and obtained the first X-ray data.

At last, they saw how an intramembrane enzyme is built: in the middle of a sea of fat, the rhomboid protease creates a protective bubble to shelter water molecules in its active site. The protein is serpentine, crisscrossing the cell membrane six times. Five of these segments bundle together to create a water-filled chamber within the membrane.

Ha says his lab's first picture of the rhomboid protease is merely a snapshot. A small dent in the protein facing outward from the cell might be an entryway for water molecules, and

a protein flap just outside the central chamber could be a gate that controls the entry of proteins to be cleaved. He wants to capture more views of the protein to find out how this gate might work and how the enzyme's activity is regulated.

However improbable this enzyme's mechanics, they are medically important. The rhomboid proteases are part of the family that includes human gamma-secretase, which cleaves a large transmembrane protein in the brain to release the amyloid fragments thought to cause Alzheimer's disease.

"Compounds that inhibit the production of toxic amyloid peptides are now believed to be one of the most promising approaches to the development of drugs for Alzheimer's disease," says Vincent T. Marchesi, M.D., Ph.D., Anthony N. Brady Professor of Pathology and an expert on both membrane protein structure and Alzheimer's disease. "Ha's findings are an important contribution to this effort."

Ha says that the rhomboid protease is a good model system for intramembrane proteases in general, but he confesses that he still has his eye on gamma-secretase. "I would love to see it," he says.

While the two enzymes are not related by their protein sequence or by evolution, Ha believes that they share common features because they face the same challenge of mixing water with oil. "Once you have a few structures, you'll see a pattern start to emerge," Ha explains. "That will give us a better understanding of how inhibitors might work, and then maybe we can design better inhibitors, and maybe those inhibitors can be used as drugs."

Now that a protein structure that proves that intramembrane proteolysis is possible is in hand, Ha says, "the doubters can be satisfied." And other researchers, doubters or not, are certainly taking note: the Ha lab's paper was published in the online version of the journal *Nature* at 1 p.m. on October 11; four hours later, scientists were ringing Ha's phone requesting his raw data to apply to their own studies.

## Out & about



August 27: Over 300 cyclists gathered in Fairfield, Conn., for the **SECOND ANNUAL CONNECTICUT CHALLENGE**, a noncompetitive bike ride ([www.ctchallenge.org](http://www.ctchallenge.org)) benefiting programs for cancer survivors at the Yale Cancer Center (YCC). Sponsored riders at this year's event rode 25, 50 or 100 miles, raising \$500,000 for the YCC.

**1.** Riders line up at the start of the event. **2.** Connecticut Challenge cofounder **Jeff Keith**, of Westport, Conn., with **Richard L. Edelson, M.D.**, professor of dermatology and director of the YCC. **3.** From left: **Aaron and Elizabeth Roberts** joined their father, **Kenneth B. Roberts, M.D.**, associate professor of therapeutic radiology, for the ride. **4.** Yale Cycling Team members (from left) **Curtis Eastin**, **Stephen Kriss**, **Anna Milkowski**, **Chris Ritacco**, **Jacob S. Hacker, PH.D.**, professor of political science, **Bruce McGalliard** (a friend of the team), **David A. McCormick, PH.D.**, professor of neurobiology, and **Steven Felix** took part in the Challenge.



September 20: The **ST. BALDRICK'S FOUNDATION**, founded on St. Patrick's Day in 1999 by three Irish-American executives, has raised over \$20 million for childhood cancer research by holding head-shaving events that encourage solidarity with children undergoing chemotherapy treatments. During a visit to the School of Medicine, the foundation

presented St. Baldrick's supporter **Jack Van Hoff, M.D.**, associate professor of pediatrics, with a check for \$25,000 to fund pediatric oncology research. **1.** From left: **Cheryl Davidson**, **Nina Kadan-Lottick, M.D.**, assistant professor of pediatrics, Van Hoff, **Kathleen Ruddy**, St. Baldrick's executive director, **Joli Lyn Gross** and **Peter Maloney**. **2.** The "shavee" team from St. Augustine's Church in Seymour, Conn., included (from left) **Dan Wasilewski**, **Cindy Hannon**, **Fr. Brian Jeffries** and **Linda Bojarczyk**.



September 20: A sold-out **EVENING WITH JUDY COLLINS** was held at Yale's Sprague Hall to benefit Women's Health Research at Yale (WHRY). **1.** From left: The singer was escorted to a pre-concert reception in the President's Room in Woodbridge Hall by **Linda Koch Lorimer, J.D.**, vice president and secretary of Yale University, and **Carolyn M. Mazure, PH.D.**, professor of psychiatry, associate dean for faculty affairs and WHRY director. **2.** From left: **Richard C. Levin**, president of Yale University and his wife, **Jane Levin**, join Collins at the reception.



October 4: A dinner to support the **CHILDREN'S HEALTH COUNCIL (CHC)**, a volunteer leadership group dedicated to raising funds to support research in the medical school's Department of Pediatrics, was sponsored by **David H. Dreyfuss**, principal of Dreyfuss Integrated Communications Group and a CHC founding member, and his wife, **Lauren**

**Tarshis**. The event was held at the Birchwood Country Club in Westport, Conn. **1.** From left: **Jonathan Lach**, **Albert Hallac** and Dreyfuss. **2.** Tarshis and **Margaret K. Hostetter, M.D.**, chair and Jean McLean Wallace Professor of Pediatrics. **3.** **Andrew and Jennifer Kanter**. **4.** Standing, from left: **Harold D. Bornstein Jr., M.D.**, and **Maureen L. Bornstein**. Seated, from left: **Carol Hallac**, **Dave Evans** and **Albert Hallac**. **5.** Standing, from left: **Leo Dreyfuss**, **Andrew Tarshis**, **Robert Biondi, M.D.**, associate clinical professor of pediatrics, and **Pat Thornton**. Seated, from left: **Karen Tarshis**, **Penny Kaestli** and **Marie E. Egan, M.D.**, associate professor of pediatrics and cellular and molecular physiology.

## Advances

Health and science news from Yale

### How the stressed become depressed

Some individuals persevere in hardship; others crumple like paper dolls. Mental fortitude in the face



of stress has been linked to variations in a gene that regulates the neurotransmitter serotonin:

individuals with a short version of the gene have a greater propensity to fall into depression under stress, while those with the longer version are more resilient.

To gain a glimpse of how these genetic differences might interact with stress to produce depression, R. Todd Constable, Ph.D., professor of diagnostic radiology and biomedical engineering, and colleagues in New York and Germany used brain imaging while individuals carrying short or long forms of the gene looked at images of faces.

Other work had suggested that short-gene carriers who had experienced life stress would show an elevated response to sad or fearful faces in brain areas involved in depression and coping.

But in the October 24 issue of *Proceedings of the National Academy of Sciences*, Constable and colleagues reported less activation in short-gene carriers under these conditions and greater activation at rest. This pattern may reflect “a chronic state of vigilance, threat, or rumination” in short-gene carriers that makes them more vulnerable to depression under stress.

### The immune system in a sticky situation

Neutrophils, critical cells of the early immune response, travel quickly through the bloodstream to sites of infection to engulf and kill bacteria. If genetic defects slow down this neutrophil migration, more severe infections may result.

School of Medicine researchers have now identified a key gene that regulates neutrophil movement through the body, which may clarify why some individuals are more susceptible to infection and inflammation.

A team led by Richard A. Flavell, Ph.D., Sterling Professor and chair of Immunobiology and Howard Hughes investigator, reports in the October 6 issue of *Science* that mice lacking the gene *Myo1f* have neutrophils that adhere more readily to their surroundings and are therefore markedly slower in reaching sites of infection.

*Myo1f*, not previously known to play a role in immunity, limits the number of proteins known as integrins on the cell surface. In the gene's absence, more integrins are released, making neutrophils more sluggish. “Without *Myo1f*, immune cells get too sticky and cannot move fast,” says first author Sangwon V. Kim, Ph.D., now at Memorial Sloan-Kettering Cancer Center. “So the host becomes vulnerable to acute infection.”

## A robot arrives in the operating room

### Da Vinci System adds precision, clearer vision to surgical procedures

Operating room nurse Elizabeth Lasorso, R.N., did a double take when she walked into the operating room in late August and saw four robotic arms looming over a patient undergoing a radical prostatectomy. “I saw those arms just moving away, and nobody touching them,” she recalls, “and I thought, ‘Wow!’”

Seated across the room was Associate Professor of Surgery John W. Colberg, M.D., his face pressed to a screen, his hands inserted in gloved controls and his feet on pedals that manipulated the arms of Yale-New Haven Hospital's newly acquired da Vinci Surgical System. To remove the patient's prostate gland, Colberg controlled three of the da Vinci System's arms for cutting and suturing; the fourth held a tiny binocular camera inserted into the patient's pelvis.

“The experience was phenomenal,” says Colberg, the first physician to use the new \$1.8 million device manufactured by Intuitive Surgical of Sunnyvale, Calif. Since then he has performed more than a dozen urological procedures using the da Vinci System.

As with other minimally invasive surgical procedures, robot-assisted surgery has distinct advantages, Colberg says. In the minimally invasive prostatectomy developed in the early 1990s using laparoscopic techniques, incisions are smaller than in open surgery and patients recover more

quickly. According to Colberg the robotic version is even better, causing “virtually no bleeding.”

The da Vinci device increases the surgeon's dexterity and improves the ability to see. The magnification of the operating field provided by the da Vinci System's camera is four to eight times greater than that provided by a standard surgeon's loupe, the viewfinder on the robotic console provides surgeons with a three-dimensional view. The equipment's “wristed” robotic arms can rotate 360 degrees, far greater than the human arm, which is limited by the shoulder joint to about 270 degrees. And robotic “hands” never shake.

Physicians train by observing three surgeries, practicing for two days and then doing cases proctored

by a physician credentialed in robot-assisted surgery. Colberg says that his patients have sought out the robotic procedure after hearing about it from their physicians, from friends or on the Internet.

Although the first robot-assisted prostatectomy was performed just six years ago and there are only about 400 such machines nationwide, Colberg says that 32,000 of the 80,000 radical prostatectomies performed in the United States in the next year will be robot-assisted.

Robert Udelsman, M.D., M.B.A., M.S.B., chair of the Department of Surgery and Lampman Professor of Surgery, calls the da Vinci System a major innovation: “The optics and the coordination that the surgeon gets with his hands are unbelievable.”



The da Vinci Surgical System, seen here in a photo from Intuitive Surgical, gives surgeons precise control over robotic arms (background) for minimally invasive procedures and a clear view of the operating field.

## State makes first stem-cell grants to Yale

Yale fared well in the first group of grants awarded in November by the state of Connecticut from a \$100 million fund established last year to promote stem cell research. Yale scientists received \$7.7 million of the \$19.8 million allocated by the State of Connecticut Stem Cell Research Advisory Committee for 21 research projects; \$12 million went to inves-



Michael Snyder will use his grant from the state of Connecticut to explore how stem cells become nerve cells.

tigators at the University of Connecticut and \$900,000 to scientists at Wesleyan University.

“After careful consideration and review by both an international panel of experts and by this committee, we are confident that Connecticut is investing in stem cell research projects that will yield significant scientific findings in the long term,” said J. Robert Galvin, M.D., M.P.H., committee chair and Department of Public Health Commissioner.

Five other states—California, New Jersey, Maryland, Missouri and Illinois—have decided to fund stem cell research.

Michael P. Snyder, Ph.D., professor of molecular, cellular and developmental biology, received the largest state grant, \$3.8 million to investigate how human embryonic stem cells (hESCs) differentiate into nerve cells.

Haifan Lin, Ph.D., director of the Yale Stem Cell Program (YSCP), received \$2.5 million to support a new core facility that will accommodate federal funding restrictions on hESC research. Diane S. Krause, M.D., Ph.D., associate professor of laboratory medicine and pathology and co-director of the YSCP, received

\$856,654 to study a leukemia gene using hESCs.

Other Yale researchers who received funding include Yingqun Joan Huang, M.D., Ph.D., an assistant professor of obstetrics, gynecology and reproductive sciences who received \$200,000 to study the Fragile X mutation, a leading cause of mental retardation, in early human neural development; Eleni A. Markakis, Ph.D., assistant professor of psychiatry, who was awarded \$184,407 to direct the isolation of neuronal stem cells from hESCs; and Erik Shapiro, Ph.D., assistant professor of diagnostic radiology, who received \$199,975 for magnetic resonance imaging studies of the migration of neural progenitor cells.

“With this first allotment of money, Connecticut becomes a national leader in the area of stem cell research,” said Gov. M. Jodi Rell in a statement announcing the grants. “We have proven ourselves able to provide a place where such research can be done safely, ethically and effectively, in addition to providing investment dollars for the growth of the bioscience industry in Connecticut, and making an investment intended to improve the health of generations to come.”

## Israel from page 1

SOM, which was formally dedicated in 1999.

The Israel name is best known on the Yale campus in association with the Adrian C. "Ace" Israel Fitness Center, a spectacular 20,000-square-foot facility at the Payne Whitney Gymnasium built with funds that Thomas Israel directed from the portion set aside in his father's bequest to support Yale athletics.

Thomas and Barbara Israel's interest in the medical school has been reinforced by the recent educational experiences of their two daughters at the YCSC. In 2001, the Israels' oldest

daughter Emily won a Harris Fellowship in Child Development and Early Childhood Education to work at the YCSC after college, and she later did research there to earn a PH.D. in clinical psychology at the Albert Einstein College of Medicine in Bronx, N.Y.

As a Yale undergraduate, their youngest daughter Wendy took courses taught by YCSC faculty and taught at the Calvin Hill day care center in New Haven. She now teaches at a school for children with learning disabilities in White Plains, N.Y. Both Thomas and Emily Israel now serve as YCSC Associates.

In addition to his father, his daughter Wendy and himself, Yale alumni in Thomas's family include an uncle, a brother (now deceased) and a nephew.

Of his own undergraduate years as an American Studies major, Israel says that although he didn't fully realize it at the time, the Yale of the mid-1960s provided an unusually rich setting for a young man with a keen interest in our country's history and culture. John F. Kerry, future war hero, senator and presidential candidate, was Israel's classmate and a fellow member of the Yale soccer team

(a knee injury that sidelined Israel from the soccer and lacrosse teams dogs him to this day); George Pataki, who would become governor of New York and a leader of the Republican Party, entered Yale one year later; Israel's junior year saw the arrival of freshman George W. Bush, who would go on to make history as the 43rd president of the United States.

Israel sees his family's gifts as giving back to Yale for the most enduring rewards of his college days, "a wonderful education and a wonderful group of friends—friendships that are hard to duplicate."

## Campaign from page 1

cancer hospital addition to Yale-New Haven Hospital.

The drive comes at a time when the university has attracted international press coverage for the record growth in its endowment, which increased from \$5.8 billion in 1997, at the conclusion of the university's last fundraising campaign, to \$18 billion for the fiscal year ending June 30. During that same nine-year period, the medical school's endowment rose from \$446.6 million to \$1.5 billion. The university has an operating budget of \$1.67 billion for 2006–2007, of which \$676 million is expected to come from the endowment.

But the size of the endowment, second only to Harvard's \$29 billion nest egg, does not mean the university

has all the resources it needs to grow in new directions, according to campaign leaders.

Jancy L. Houck, M.A., who joined Yale as associate vice president for university development and director of medical school development and alumni affairs in September, explains that income from the current endowment was earmarked at the time of the original gift decades or more ago. "It takes new resources to do new things," says Houck, adding that the same is true with grant dollars from the federal government, foundations and corporations.

Although the \$57 million Clinical and Translational Science Award (CTSA) that the medical school received in October is the largest grant

ever received by the school, Houck says the award presents an opportunity to engage donors in conversations about the medical school's future.

"This support from the National Institutes of Health doesn't replace our need for philanthropy, because grants are very, very specific. You have to use the funding in the exact manner outlined in the proposal," says Houck. "The philanthropy that we seek will be for needs that are not covered by a big grant, where donors can really leverage their gift, knowing that there is a certain level of activity that is already funded."

The public campaign kicked off with a day of presentations by noted faculty and alumni—including medi-

cal school professors Irwin M. Braverman, M.D., Christopher K. Breuer, M.D., Carolyn M. Mazure, PH.D., Milissa A. McKee, M.D., R. Lawrence Moss, M.D., W. Mark Saltzman, PH.D., Bennett A. Shaywitz, M.D., Sally E. Shaywitz, M.D., and Tian Xu, PH.D.—followed by a multimedia program narrated by actor Sam Waterston, a 1962 Yale College alumnus, and a gala dinner in University Commons.

"To expand Yale beyond its current scale and scope, to build the Yale of tomorrow, we will need new financial resources," says Levin. "Above all, we need to complete the transformation of Yale from a local to a regional to a national to an international university."

## Genes from page 1

ences at about one in every 1,300 letters. In all, there are about 10 million sites sprinkled throughout the human genome where common variations occur. Most of these variations, which are known as single-nucleotide polymorphisms, or SNPs (pronounced "snips"), have no relevance to health. But some SNPs may influence one's risk of developing a particular disease.

Genetic variations lying close to one another on a chromosome are often inherited together in chunks. By looking for chunks of variations that are always found in people with a particular disease but rarely in healthy individuals, scientists can narrow the search for disease genes and eventually pinpoint their locations. To effectively scan the SNPs in the entire genomes of large groups of people, however, one must compare hundreds of thousands of variations, which would have been impossible until quite recently.

Last year, Hoh's research group was among the first to complete such a whole-genome analysis by combining the SNP information compiled in public databases with the power of microarrays—silicon or plastic chips that are coated with hundreds of thousands of precisely arranged microscopic fragments of DNA.

The chip the Hoh team used allowed them to rapidly compare the genomes of more than 100 people with or without AMD for 100,000 different SNPs. As reported in the April 15, 2005, issue of *Science*, the research-

ers pinpointed a single-letter variation strongly associated with the so-called "dry" form of AMD, a common form of the disease that causes vision loss but which rarely leads to complete blindness.

Using the same approach, Hoh and colleagues have now identified a variation associated with the "wet" form of AMD, a rarer but far more damaging form of the disorder in which a proliferation of leaky blood vessels causes irreversible damage to the retina. In the November 10, 2006, issue of *Science*, the team reports that people who had inherited a particular SNP from both parents near a gene called *HTRA1* are 11 times more likely to get AMD than those lacking the variant.

The disease-associated SNP discovered by Hoh's team seems to increase the expression of the gene, but she cautions that her results do not definitively establish that the variation itself causes AMD. The SNP may just lie close to some other disease-promoting genetic variation, she says, and it is still not clear how overexpression of *HTRA1* would cause the blood vessel growth characteristic of the disease. However, previous research has demonstrated that *HTRA1* protein is present in the eyes of patients with wet AMD.

"It's a long way, probably many years, to prove it," Hoh says, but she adds that every clue is valuable when tackling poorly understood disorders like AMD. Hoh says that we know very



**Judy Cho has discovered a potential new drug target to treat Crohn's disease.**

little about the biological pathways causing AMD and that identifying potential disease-promoting genes like *HTRA1* may lead to a greater understanding of those pathways.

Cho, the new director of the medical school's Inflammatory Bowel Disease (IBD) Center, chairs the steering committee of the National Institute of Diabetes and Digestive and Kidney Disorders IBD Genetics

Research Consortium, an alliance of seven academic centers in the United States and Canada that combines resources and genomic data to efficiently pursue disease genes.

In the October 26, 2006, online issue of *Science*, Cho and other consortium members published results from a study comparing DNA from 547 CD patients and 548 healthy people. The team used microarray technology that simultaneously examines more than 300,000 SNPs in the genome—80 percent of the known SNPs in populations of European ancestry, who are most susceptible to CD—and identified a variation in the healthy people that is absent in those with CD.

The SNP, in a gene known as *IL23R*, tamps down the expression of a receptor for interleukin-23 (IL-23), a protein that promotes

inflammation. Cho speculates the SNP protects healthy people from CD by interfering with the protein's function, and she suggests that developing drugs to block the IL-23 may provide a new therapy for CD.

"We knew this was an unbelievably hot finding," says Cho, who believes that whole-genome analyses will lead to important advances in treating previously intractable diseases.

# Magnetic resonance system will open new scientific vistas

*State-of-the art magnet will enhance studies of metabolism and epilepsy*

The School of Medicine has been awarded a \$2 million grant from the National Center for Research Resources (NCRR) for the purchase of a powerful new 7 Tesla (7T) magnetic resonance system. The 7T system, one of only about a dozen in the world, will be installed in the medical school's Anlyan Center this summer. The system will allow Yale researchers to perform ultra-high-resolution MR studies of epilepsy, diabetes, psychiatric diseases, cancer and learning disorders in humans.

The new equipment, obtained with funds from the NCRR's High-End Instrumentation Program, will be a shared resource for several investigators funded by the National Institutes of Health under the leadership of Douglas L. Rothman, PH.D., professor of diagnostic radiology and biomedical engineering.

According to Rothman, the equipment will be used primarily for magnetic resonance spectroscopy (MRS) studies of humans, which create profiles of the chemicals present in various tissues, or in different regions of the same tissue. The 7T system can chemically analyze areas of tissue as small as 3 cubic centimeters.

As a complement to the new imaging initiative, the medical school has recruited the research team of Hoby P. Hetherington, PH.D., and Julie W. Pan, M.D., PH.D., from Albert Einstein College of Medicine.

Moving to the School of Medicine is a scientific homecoming for Hetherington and Pan, who along with Rothman received their doctoral degrees in the laboratory of Robert G. Shulman, PH.D., Sterling Professor Emeritus of Molecular Biophysics and Biochemistry and a pioneer of MRS research.

Since 1998, first at Brookhaven National Laboratory and then at Einstein, Hetherington and Pan have collaborated with Yale's Dennis D. Spencer, M.D., the Harvey and Kate Cushing Professor of Neurosurgery. In MRS studies of Spencer's epilepsy patients, Hetherington and Pan have generated biochemical brain images that Spencer has used as a guide to seizure-prone areas of the brain during surgery. The researchers hope the 7T system will allow them to accurately predict which patients will go on to develop epilepsy following a first seizure.

Hetherington says that MRS is a particularly powerful technique for studying neurological diseases, because it can detect depletions of a brain-specific chemical that occurs not only in epilepsy, but also in neurodegenerative diseases like Alzheimer's disease and multiple sclerosis.

"It's very clear that there is better sensitivity for a number of pathologies, especially epilepsy, using spectroscopic imaging," he says. "But for almost any neurological disorder, there's an advantage. Alzheimer's is a prime example of where spectroscopy works well for early detection."

According to Pan, the high resolution of the 7T system changes the landscape of her research. "The 7T



Douglas Rothman in 2003, during the construction of a steel-lined room in the Magnetic Resonance Research Center, which will house the medical school's new 7 Tesla system.

system is critical because it allows us to draw conclusions at a volume size that makes sense. At 1.5 T, you have to make a measurement from the entire brain, but with 7T you can make a measurement on the order of a few cubic centimeters," she says. "Having a measurement of the whole brain is interesting, but it doesn't tell me anything specific. With a 7T system I can tell exactly where in the brain I want to look and be accurate about it."

The NCRR makes one-time awards to support the purchase of sophisticated instruments costing more than \$750,000 to advance biomedical research and increase knowledge of the underlying causes of human disease.

"The High-End Instrumentation Program provides numerous investigators access to essential equipment, often benefiting entire research communities and dramatically advancing

their research projects," says Barbara M. Alving, M.D., the NCRR's acting director. "These awards spur the kind of scientific discoveries necessary for the development of treatments for a broad spectrum of diseases."

The School of Medicine will contribute approximately half of the system's cost, as well as the cost of installation in the recently constructed 30,000-square-foot Magnetic Resonance Research Center in the Anlyan Center.

"The new 7T system will provide Yale scientists with the capability of imaging biochemistry and functional activity of the brain and limbs at unprecedented levels of spatial resolution," says Rothman. "The research will be unique among ultra-high-field MR systems in its focus on developing and applying MR biochemical imaging for the understanding, diagnosis and treatment of disease."

## Grants and contracts awarded to Yale School of Medicine May/June 2006

### Federal

**Morris Bell**, NIH, *Cognitive Training and Enhanced Supported Employment*, 5 years, \$2,138,756 • **Christopher Breuer**, NIH, *Development of Second-Generation Tissue-Engineered Vascular Grafts*, 5 years, \$673,650 • **Tania Burgert**, NIH, *Postprandial Glycemia in Association with Vascular Disease in Childhood Obesity*, 3 years, \$384,544 • **Elizabeth Claus**, NIH, *Meningioma: Risk Factors and Quality of Life*, 5 years, \$3,383,676 • **Mark Cullen**, NIH, *Disease, Disability and Death in an Aging Workforce*, 5 years, \$5,236,618 • **Pietro De Camilli**, NIH, *Molecular Mechanisms in Synaptic Vesicle Recycling*, 4 years, \$1,177,200 • **Robin de Graaf**, NIH, *Novel Technologies for Global Optimization of Magnetic Field Homogeneity*, 2 years, \$332,273 • **Enrique De La Cruz**, NSF, *Kinetic Mechanism of DEAD-box RNA Helicase ATPase*, 5 years, \$942,639 • **Donald Engelman**, NIH, *TM Interactions in Membrane Protein Folding and Function*, 4 years, \$1,754,952 • **Durland Fish**, NIH, *Spread of Lyme Borreliosis Bacteria in the U.S.*, 2 years, \$449,625 • **Sankar Ghosh**, NIH, *Regulation and NF- $\kappa$ B and I $\kappa$ B Proteins*, 5 years, \$2,065,833 • **Erol Gulcicek**, NIH, *Differential Gel Electrophoresis (DIGE) System for Yale University Keck Laboratory*, 1 year, \$405,284 • **Joan Kaufman**, NIH, *Genetic and Environment Modifiers of Child Depression*, 5 years, \$1,858,595 • **Brian Leaderer**, NIH, *Asthma Severity in Children and Fine Particle*

*Composition*, 5 years, \$2,819,762 • **Elias Lolis**, NIH, *Functional and Structural Studies of CD74 Activation*, 5 years, \$2,065,833 • **Xingguang Luo**, NIH, *Fine-Mapping the Risk Loci for Alcoholism in ADH Gene Cluster and ALDH2 Gene*, 5 years, \$732,816 • **Robert Malison**, NIH, *Drug Abuse, Sleep and Cognition*, 3 years, \$975,109 • **Ruslan Medzhitov**, NIH, *Cell Biology of TLR Signal Transduction*, 5 years, \$1,839,375 • **Gero Miesenboeck**, Office of Naval Research, *Computation in Neuronal Microcircuits*, 1 year, \$400,000 • **Michael Nathanson**, NIH, *Regulation of Liver by Nuclear Ca<sup>2+</sup> Signaling*, 5 years, \$5,954,074 • **Jullie Pan**, NIH, *Metabolic Neuroprotection: Creative Supplementation in Human Brain*, 2 years, \$518,936 • **Nancy Ruddle**, NIH, *Lymphotoxin and Lymphoid Neogenesis*, 1 year, \$82,437 • **Albert Sinusas**, NIH, *Hybrid Imaging of Angiogenesis and Arteriogenesis*, 4 years, \$1,652,083 • **Anthony Van den Pol**, NIH, *Cytomegalovirus in the Brain*, 5 years, \$2,043,750 • **Detlef Wencker**, NIH, *Studies of Myocyte Apoptosis in Congestive Heart Failure*, 5 years, \$790,862 • **Sandra Wolin**, NIH, *Biogenesis of Small RNAs*, 4 years, \$1,346,148 • **Tongzhang Zheng**, NIH, *Environment, Gene and Testicular Cancer Risk*, 5 years, \$5,079,796

### Non-Federal

**Elizabeth Claus**, Susan G. Komen Breast Cancer Foundation, *Ductal Carcinoma in situ*

*and BRCA1/2: Outcomes and Risk Prediction*, 2 years, \$249,823 • **Robert Constable**, Pfizer, Inc., *MR Methodologies and Further Analysis and Reporting of Data*, 2 months, \$25,181 • **Gail D'Onofrio**, Yale-New Haven Health System, *Disaster Preparedness and Emergency Response Education and Research*, 1 year, \$55,000 • **Deepak D'Souza**, Astra Zeneca, L.P., *Nicotinic Modulation of a Noncompetitive N-Methyl-D-Aspartate (NMDA) Receptor Antagonist-Induced Schizophrenia-Like Information Processing Deficits in Humans*, 1 year, \$496,454 • **Daniel Goldstein**, Roche Organ Transplantation Foundation, *Role of Innate B1 Lymphocytes in Neonatal Transplant Tolerance*, 2 years, \$162,920 • **Zhiwei Hu**, Susan G. Komen Breast Cancer Foundation, *Targeting the Neovascularity for Immunotherapy and Photodynamic Therapy of Breast Cancer*, 2 years, \$250,000 • **Sven-Eric Jordt**, Health Effects Institute, *Health Effects of Air Pollution*, 1 year, \$80,000 • **Amy Justice**, University of Kentucky, *Computer Alcohol Interventions for HIV+ Veterans*, 1 year, \$29,219 • **Arie Kaffman**, American Psychiatric Institute for Research and Education, *The Effects of Postnatal Maternal Care on Neurogenesis During Development and Their Implications for the Development of Vulnerability to Stress*, 1 year, \$45,000 • **John Krystal**, National Alliance for Research on Schizophrenia and Depression, *GABRA2 Modulation of NMDA Receptor Deficit-Related PFC Dysfunction*, 1 year, \$100,000 • **Elias Lolis**, University of Florida, *Viral-Based Chemokine Receptor Antagonist*,

1 year, \$85,515 • **Elias Lolis**, Avigen, Inc., *Stage 1: Preliminary Characterization of a MIF Inhibitor*, 1 year, \$25,501 • **Paul Lombroso**, National Alliance for Research on Schizophrenia and Depression, *Characterization of the STEP Knock-Out Mouse*, 1 year, \$99,360 • **Diane McMahon-Pratt**, University of Iowa, *Collaborative Development of a Vaccine Against Cutaneous and Visceral Leishmaniasis*, 5 years, \$156,176 • **Guillermo Mor**, Novogen Limited, *Assay of Induction Apoptosis by Phenoxodiol in Cancer Cells*, 1 year, \$89,920 • **Prakash Nadkarni**, Mount Sinai School of Medicine, *WTC Medical Monitoring Program Data and Preventive Medicine*, 3 years, \$506,698 • **Angus Nairn**, National Alliance for Research on Schizophrenia and Depression, *Neuroproteomic Analysis of the Actions of BDNF and Other Neurotrophic Factors*, 1 year, \$99,900 • **Jill Reiter**, Susan G. Komen Breast Cancer Foundation, *Prognostic Significance of Soluble EGFR Expression in Breast Cancer*, 2 years, \$250,000 • **Sara Rockwell**, PharmaMar USA, Inc., *Preliminary Studies of the Effects of Aplidine in Hypoxic Environments and in Combination with Radiation*, 1 year, \$67,035

## Awards & honors



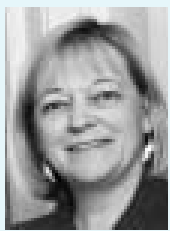
**Sidney J. Blatt, M.D.**, professor of psychiatry and psychology, has received the Mary S. Sigourney Award for lifetime contributions to psychoanalytic

theory, research and education. The award, which carries a cash prize of \$50,000, is considered the most distinguished international award for contributions to psychoanalysis.



**David C. Cone, M.D.**, associate professor of surgery and epidemiology, is president-elect of the National Association of EMS Physicians

(NAEMSP), a professional society with more than 1,200 members consisting primarily of emergency physicians who serve as the medical directors of EMS agencies and out-of-hospital care systems. Cone, who studies effects of emergency medical dispatch systems on EMS resources and mass casualty triage, begins his term as NAEMSP president in January.



**Linda C. Degutis, D.R.P.H., M.S.N.**, associate professor of surgery and public health, is president-elect of the American Public Health Association

(APHA). With more than 50,000 members, the APHA is the oldest and largest organization of public health professionals in the world. Degutis, who begins her term in the fall of 2007, does research on clinical and policy interventions related to injury and substance abuse, as well as disaster preparedness.



**Arthur L. Horwich, M.D.**, Eugene Higgins Professor of Genetics and professor of pediatrics, has been elected a Fellow of the American

Association for the Advancement of Science (AAAS). The AAAS named 449 members Fellows this year, for "advancing science applications that are deemed scientifically or socially distinguished." Horwich studies a large ring-shaped molecular machine called a chaperonin that mediates protein folding within a large cavity.



**Annette M. Molinaro, Ph.D.**, assistant professor of public health, has been elected as a member of the International Statistical Institute (ISI). The

ISI's approximately 2,000 elected members are internationally recognized leaders in the field who have made distinguished contributions to the development or application of statistical methods. Molinaro specializes in statistical genetics and computational biology.

## Expert on blood pressure genes is honored

It has been a busy fall for Richard P. Lifton, M.D., Ph.D., chair and Sterling Professor of Genetics and Howard Hughes Medical Institute investigator. In October, Lifton received the 2006 Robert Tigerstedt Award at the 21st Scientific Meeting of the International Society of Hypertension (ISH) in Fukuoka, Japan. A month later, he delivered the first Donald Seldin Lecture at Scientific Sessions 2006, the annual national meeting of the American Heart Association (AHA), held this year in Chicago.

The Tigerstedt Award is named in honor of a Finnish scientist who discovered renin, a kidney enzyme involved in high blood pressure. The prize is the highest scientific award of the ISH, and is presented at each biennial meeting "to honor a scientist or physician for outstanding achievements in the field of hypertension."

Lifton was cited by the society for his identification of genetic mutations that govern human blood pressure by affecting how the kidneys handle salt. By investigating families from around the world, Lifton's research team has identified mutations in seven genes that raise blood pressure, and eight that lower blood pressure.

The AHA lectureship was established this year to honor Donald W. Seldin, M.D., William Buchanan Chair in Internal Medicine at UT Southwestern Medical Center in Dallas.

Seldin, a 1943 graduate of Yale School of Medicine, served as an assistant professor at Yale until 1951, when he left for UT Southwestern, then a fledgling medical school with rudimentary facilities.



Michael Alderman (left), president of the International Society of Hypertension, presented Richard Lifton with the Tigerstedt Award in Fukuoka, Japan.

Over the next 35 years, Seldin was a central figure in UT Southwestern's rise into the ranks of the world's most elite research institutions.

Along the way, Seldin made seminal scientific observations on salt and potassium transport in the kidney, and he has been a leader in understanding the relationships between renal and cardiovascular diseases. Fittingly, Lifton's lecture in Chicago was entitled "Molecular Genetics of Cardiovascular Risks: The Kidney as the Cause of Hypertension."

A member of the Yale faculty since 1993, Lifton is a member of the National Academy of Sciences and the Institute of Medicine.

He is the recipient of numerous awards for his research. These include the highest scientific awards of several other organizations, including the AHA, the American Society of Nephrology, the American Society of Hypertension and the Council for High Blood Pressure Research, as well as the Pasarow Foundation Award for Medical Research.

## Education innovator wins award for work on transforming schools

School reform leader James P. Comer, M.D., the Maurice Falk Professor of Child Psychiatry at the Yale Child Study Center (YCSC), has won the 2007 University of Louisville Grawemeyer Award in Education. The award, which carries a \$200,000 prize, cites Comer as a champion of improving schools by applying knowledge from child development research.



James Comer has been a forceful advocate for schooling "the whole child."

Comer is best known for the School Development Program (SDP), founded at the YCSC in 1968. The SDP promotes optimal emotional, behavioral and academic development in schoolchildren through school governance teams that give all parties—teachers, administrators, parents, students, janitorial and cafeteria workers, and school psychologists—a voice in how their schools are operated and a stake in the educational outcome.

The SDP model has been applied in over 1,000 schools in the United States, South Africa, England, Ireland and the Caribbean, and research has shown that it improves children's performance in low-achieving schools.

Comer, author of the 2004 book *Leave No Child Behind: Preparing Today's Youth for Tomorrow's World*, joined the Yale faculty in 1968. He has received numerous awards, including the Smithsonian Institution's John P. McGovern Behavioral Science Award, the Heinz Award in the Human Condition, the Harold W. McGraw Jr. Prize in Education, and the Charles A. Dana Award for Pioneering Achievement in Education. He has also received a special presidential commen-

datation from the American Psychiatric Association and was named to *Education Week* magazine's list of 100 people who helped shape American education in the 20th century.

*The School Development Program, developed at Yale's Child Study Center, has improved children's performance in over 1,000 low-achieving schools all over the world.*

The Grawemeyer Awards, which are also given in music composition, religion, psychology and other fields, were established in 1984 by H. Charles Grawemeyer, an alumnus of the University of Louisville who made his fortune as an industrialist and entrepreneur. The awards are distinguished by Grawemeyer's belief that lay people as well as experts should judge candidates' contributions, and his conviction that sweeping, influential ideas are as important as personal accomplishment.