

# Medicine@Yale

Advancing Biomedical Science, Education and Health Care

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## \$23 million grant enables fresh look at stress and addiction



Rajita Sinha will direct a consortium of 16 scientists to better understand the links between stress, self-control and addiction.

People are much more likely to stick their hand in a cookie jar, smoke a cigarette, or gulp cocktails when they're overworked, ensnared in family conflict, or having trouble balancing the inordinate number of responsibilities thrown at them. According to Rajita Sinha, PH.D., professor of psychiatry, stress has been clearly linked to disease outcomes, but the complex effects of stress on self-control and addictive behaviors have not been

fully elucidated. Now, an interdisciplinary team of 16 Yale researchers and collaborators, led by Sinha, has won a \$23.4 million grant from the National Institutes of Health to study how and why stress fuels addictions.

The research group—known as the Interdisciplinary Research Consortium on Stress, Self-Control and Addiction—includes psychiatrists, neuroscientists, social psychologists and communications and policy

experts working on 14 projects aimed at finding new ways to combat the powerful cravings that make treating food and drug addictions so difficult. The Yale team is one of only nine nationwide to receive the grants, from a pool of more than 100 applicants.

"Stress is the kind of topic that really begs for being studied in an interdisciplinary way, because it affects every organ system in some way or another," says Sinha.

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## Giving back

*Top-notch surgery at Yale inspires a major gift to the School of Medicine*

Karen Pritzker and Michael Vlock of Branford, Conn., say the primary motivation behind their recent \$3 million gift to endow a School of Medicine professorship in pediatric surgery is gratitude. Two of their children have been treated over the years by surgeons at Yale-New Haven Children's Hospital (YNHCH), and in each instance, Pritzker and Vlock say, they received excellent medical advice and first-rate care.

The new professorship is named in honor of Karen Pritzker's father, Robert A. Pritzker, a Chicago-based executive and philanthropist who founded the Marmon Group, an international association of more than 100 manufacturing and service firms that is the 19th largest private company in the U.S. "My father has demonstrated an unwavering commitment to make the world a better place throughout his long business and philanthropic career," Karen Pritzker says. In May, R. Lawrence "Larry" Moss, M.D., professor of surgery and chief of surgery at YNHCH, was named the first Robert Pritzker Professor of Pediatric Surgery.

"This generous donation represents a quantum leap for Yale Pediatric Surgery," says Moss. "We ensure that children receive the care they need regardless of their family's ability to pay, so there are fewer resources to support innovation and discovery. This gift establishes a permanent source of funds to ensure that Yale Pediatric Surgery will always be able to invest in research that will result in continuing improvement in the surgical care of children."



R. Lawrence "Larry" Moss (left) is the first Robert Pritzker Professor of Pediatric Surgery, named in honor of the Chicago industrialist and philanthropist (above).

Robert Pritzker, a 1946 graduate in industrial engineering of the Illinois Institute of Technology (IIT) in Chicago, served as the chair of IIT's board of directors and gave a significant gift to establish the Pritzker Institute of Biomedical Science and Engineering at IIT. He also joined his father and his brothers to make a major gift to

the medical school at the University of Chicago, which was renamed the Pritzker School of Medicine in 1968. Pritzker is now CEO of Colson Associates Inc. and of six other companies that manufacture medical devices. He is past chairman of the board of trustees of The Field Museum of Natural History in Chicago, and a fellow of the American Institute for Medical and Biological Engineering.

The new Pritzker Professorship provides support for the clinical expertise that Pritzker and Vlock and thousands of other families rely on, but it will also advance Yale research on pediatric surgery that will improve children's health at YNHCH and beyond for years to come. Moss,

*Pritzker, page 7*

## Lightening the load for the physicians of the future

"I don't believe in giving for concrete," declares Sanford G. Bluestein, M.D., in as pithy a summation of his pragmatic approach to philanthropy as one could imagine. While recognizing the necessity of bricks and mortar for the School of Medicine, Bluestein, a 1946 alumnus, has unabashedly thrown his weight behind the school's flesh and blood—the people, both faculty and students, who imbue the classrooms and labs with life and meaning.

"In general, my goal is to continue to give at a regular rate to scholarships for young people," says Bluestein, and his latest gift to the medical school—\$500,000 that will add to a scholarship fund he established in 1996 on the occasion of his 50th reunion—is a case in point. "I've given to this scholarship fund regularly over the years," he says. "I intend as long as I live to keep doing that."

In all, Bluestein's steady contributions to the School of Medicine over more than 25 years exceed \$1 million, including support for the Department of Diagnostic Radiology, which also received support from his latest gift. In 1980 he endowed a fund in that department to support the Bluestein lecture, an annual presentation on biomedical imaging by a distinguished invited speaker.

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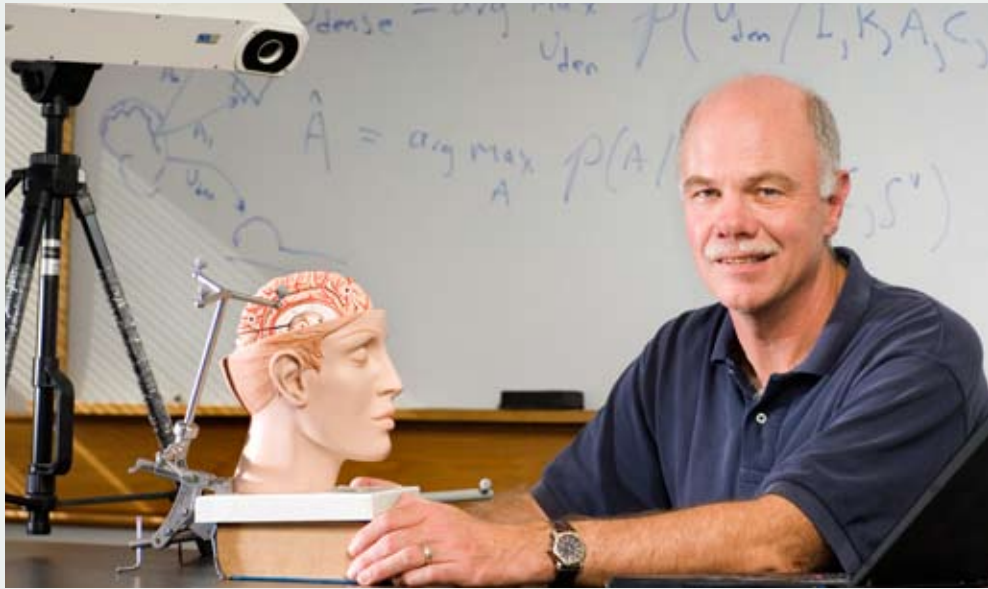
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James Duncan and colleagues are devising ways to extract the most clinically useful images from the mountains of data produced by biomedical imaging techniques such as MRI and echocardiography.

# Moving pictures

Expert on image analysis finds guideposts for doctors in the ever-changing body

Though James S. Duncan, PH.D., has ready access to the School of Medicine's state-of-the-art imaging technology, he still grapples with a problem faced by the tintype photographers of old—his preferred subjects just won't sit still.

No organ is more restless than the heart, and the constant movement of the muscle that forms its chambers only adds to the difficulty of interpreting the speckled, shadowy images produced by echocardiography. For more than 15 years, Duncan, vice-chair and Ebenezer K. Hunt Professor of Biomedical Engineering and professor of diagnostic radiology, has worked with cardiologist Albert J. Sinusas, M.D., professor of medicine and diagnostic radiology, to find better ways to extract information about the heart's health from these images. In 2006, their efforts received a major boost in the form of a five-year, \$7.2 million Bioengineering Research Partnership (BRP) grant from the National Heart, Lung and Blood Institute, the second BRP grant Duncan has received to support his research.

Along with ultrasound expert Matthew O'Donnell, PH.D., the Frank and Julie Jungers Dean of the University of Washington's College of Engineering, Duncan and Sinusas are devising computer algorithms

that automatically locate the heart wall in echocardiographic images despite the myriad shapes this tissue assumes over time as the heart beats. With image-based models of heart-wall thickness and elasticity such as those Duncan and colleagues are building at the bedside, cardiologists could precisely determine what structures have been damaged by a heart attack and how well patients are healing.

Duncan may inherit his technical bent from his father, who served in the Canadian Air Force and went on to work in the telephone industry in New York City. Duncan, born in the Bronx and still a diehard New York Yankees fan, was the first in

## Lifelines James Duncan

his family to graduate from college. He earned a master's degree in electrical engineering at the University of California, Los Angeles, and a PH.D. at the University of Southern California, both with the help of fellowships from the Hughes Aircraft Company. Duncan worked at Hughes for 10 years during his schooling, but found that he needed a change.

"I enjoyed the aerospace industry, but military-oriented projects weren't what I wanted to do as a career," Duncan says. "I even considered switching careers to medicine, but I decided that if I could take all that I had learned and turn it in a new direction, that would be a better course."

Duncan also collaborates with Dennis D. Spencer, M.D., the Harvey and Kate Cushing Professor of Neurosurgery, finding ways to guide surgeons through brain operations

such as those performed to treat epilepsy. Though the brain doesn't move as dramatically as the heart, its shape does markedly change during surgery, which alters the location of important anatomical landmarks. Christine DeLorenzo, PH.D., who just earned her graduate degree working with Duncan, found that by training two cameras on the surface of the brain during surgery and feeding the resulting stereo image into computers it is possible to create a mathematical model that provides an up-to-the-second, three-dimensional rendering of the brain as it shifts in the operative field.

By adding magnetic resonance spectroscopy, which detects biochemical changes in small regions of tissue, to the mix, Duncan foresees a day when neurosurgeons treating epilepsy will use "multimodality" imaging—anatomical, functional and biochemical—to accurately place tiny probes in patients' brains that detect the onset of a seizure and quickly deliver drugs to interrupt it.

Having once observed surgeries guided by images stuck to the operating room wall with masking tape and highlighted in colored pencil, Duncan says that today's technology presents an embarrassment of scientific riches.

"The whole idea of how you represent information as images, how you look across scales and modalities and problems, that's exploding," says Duncan. "It's a neat thing for those of us who do the analysis, but there's a lot out there. You need to grab on to certain pieces of it so you can get your arms around something you can really dig into."

# Dean for education is appointed Jockers Professor

Richard Belitsky, M.D., deputy dean for education and associate professor of psychiatry, has been named the Harold W. Jockers Associate Professor of Medical Education.

Since he joined the medical school faculty, Belitsky has focused on curriculum development at the School of Medicine, particularly with respect to training medical students in the biopsychosocial model of medicine, teaching techniques for patient-centered medical interviewing, and teaching how to counsel patients to change unhealthy behaviors. He is also interested in the development of professional identity in medical education, with emphasis on the impact of power and authority on the developing identity of medical students.

Belitsky received his M.D. from the University of Florida School of Medicine in Gainesville. He came to Yale in 1979 as a resident in psychiatry and continued on as a fellow in forensic psychiatry and chief resident/instructor in the Department of Psychiatry. He joined the faculty as an assistant professor in 1983, when he also became unit chief of the Inpatient Services Division of the Connecticut Mental Health Center.

Belitsky has served as the director of graduate education in the Department of Psychiatry and as the department's director of education from 1997 to 2006, when he became the deputy dean for education for the medical school.

## Medicine@Yale

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Erol Fikrig

In June, Erol Fikrig, M.D., an expert in vector-borne diseases and a pioneer in the development of a Lyme disease vaccine, was named chief of the Section of Infectious Diseases in the Department of Internal Medicine. Fikrig's new post is the first such appointment by Jack A. Elias, M.D., chair and Waldemar Von

Zedtwitz Professor of Medicine, since he became leader of the department in October, 2006.

On October 12, Fikrig was named one of 15 new "patient-oriented" investigators in the Howard Hughes Medical Institute; investigators are chosen through rigorous national competitions.

Elias says that Fikrig is "one of the world's experts" on Lyme disease and West Nile virus. A professor of medicine and epidemiology and pub-

lic health, as chief Fikrig is expected to place a new emphasis on emerging infectious diseases, an effort that will add at least four new basic science, translational and clinical investigators to the 15-member section. As a Hughes investigator, he will conduct research in which information gathered at the bedside will be used to develop laboratory models to test new therapies, including vaccines against diseases transmitted by mosquitoes and ticks.





Breaking away  
from child abuse?

When an infant breaks a bone, it's often not an accident. In fact, doctors cite abuse in more than a third of bone fractures in babies under a year old. But according to a new Yale study, that number may be on the decline.

John M. Leventhal, M.D., professor of pediatrics, and colleagues analyzed 24 years of data on fractures in children under 3 years old at Yale-New Haven Hospital. As reported in the March issue of *Child Abuse & Neglect: The International Journal*, the likelihood of a fracture being rated by the hospital as abuse fell substantially from 1979 to 2002, to just over 10 percent.

"We're encouraged by this," says Leventhal, even though his team's results seem to be at odds with an increased number of calls to child protective services seen over the past decades, both in Connecticut and nationally. Leventhal proposes that these calls may bring lower-risk families and mild abusive injuries to the attention of authorities, leading to early intervention and a decrease in serious injuries like fractures and burns.

For cardiac surgery,  
your brain on ice

We need blood to live, but blood makes life difficult for heart surgeons by obscuring the operating field. At a certain point in surgery on the aorta, the body's largest artery, surgeons must shut down the cardiopulmonary bypass machine, stopping blood flow entirely and cutting the oxygen supply to the fuel-hungry brain.

To prevent brain damage, the patient's head is carefully packed in ice and the body cooled until its core temperature reaches about 19°C (66°F), which slows metabolism to a standstill. For added brain protection, some surgeons use perfusion, pumping blood into the cerebral arteries, but this clutters the workspace and creates possible complications.

In the September issue of *Annals of Thoracic Surgery*, a Yale team led by John A. Elefteriades, M.D., chief and William W.L. Glenn Professor of Cardiothoracic Surgery, shows that perfusion is unnecessary. The researchers studied the outcomes of 394 aortic arch operations performed at Yale without perfusion and found a stroke rate of only 4.8 percent, on par with the best results seen with perfusion.

But speed is key. Strokes occur more often during aortic operations lasting over 40 minutes, and the average patient at Yale spent only 31 minutes in suspended animation.

A joint effort to tackle obesity and diabetes

Campus-wide projects  
address cultural, biological  
roots of public-health crisis

According to the Centers for Disease Control and Prevention (CDC), approximately 65 percent of adults in the United States are either obese or overweight, and therefore run the risk of suffering from chronic health conditions such as type 2 diabetes, cardiovascular disease and high blood pressure. This expanding epidemic appears to involve cultural, genetic and physiological factors that range from an overabundance of super-portioned junk food to how the brain regulates appetite. Researchers across the Yale campus are covering all the bases to uncover what causes obesity and how to counter its devastating effects.

A look at the culture surrounding food may go a long way toward explaining the rise of obesity, according to Kelly D. Brownell, PH.D., professor of psychology and epidemiology. The fact that obesity has skyrocketed over the last 30 years in the U.S. and elsewhere in the developed world "just screams out environmental causes," Brownell says. Unhealthy foods not only come in larger portions than ever before, but these foods are aggressively marketed and far cheaper and easier to obtain than healthier foods. "You put those factors together," says Brownell, "and it's hard to believe that we could have anything other than a bad diet."

Named one of *Time's* 100 Most Influential People last year, and co-founder and director of Yale's Rudd Center for Food Policy and Obesity, Brownell is well poised to help change this picture. The Rudd Center deals in what he calls "strategic science," in which research results are intended to help guide public policy. Brownell has helped build visibility of the center in the media, the food industry and the government by providing expertise for such initiatives as the recent move by New York City to ban trans fats and require calorie-labeling in restaurants. The range of topics covered by researchers at the center ranges from the social stigma of being overweight or obese to the possibility that food may be addictive in some people; in July, a Rudd Center conference brought together basic and clinical scientists with public policy experts and government officials to explore the idea of food addiction.

At the Rudd Center, established with a \$7.5 million gift from California food and wine magnate Leslie Rudd, scientists are also targeting childhood obesity by focusing on food served in schools. In March, Brownell testified before Congress that schools provide an unsafe nutrition environment for children, citing the array of high-fat, high-calorie foods and beverages sold in schools. In Connecticut, research led by Marlene B. Schwartz, PH.D., director of research and school programs at the Rudd Center, was a valuable resource



Kelly Brownell, director of the Rudd Center for Food Policy and Obesity, is one of many Yale scientists trying to tackle the world's obesity epidemic by studying its cultural and biological roots.

for legislators regarding a bill that was enacted last July banning the sale of all beverages in schools except milk, water and pure fruit and vegetable juices.

But while the environment undoubtedly plays a major role in obesity, there are physiological factors that influence it as well. Research on adolescents led by Sonia Caprio, M.D., professor of pediatrics, has shown that the distribution of abdominal fat varies by ethnicity. African-Americans have less fat in and between internal organs than do Caucasians and Latinos, and they rarely develop fatty liver disease. Latinos, who have more visceral fat, tend to deposit fat in the liver, which can lead to inflammation and cirrhosis.

Caprio recently conducted a study that showed that the deposition of fat in muscle is also different among ethnic groups, and that it may relate to insulin resistance, in which the body's cells become resistant to the effects of insulin. Insulin helps transport glu-

cose into muscles and other tissues, and insulin resistance can lead to type 2 diabetes. Approximately 16 percent of children and adolescents are now overweight according to the CDC, putting them at risk for type 2 diabetes. Excess weight can also lead to impaired glucose tolerance (elevated blood glucose levels two hours after ingesting glucose), which can rapidly progress to diabetes in adolescents, so Caprio is also looking at how to treat this condition. She is heading research funded by the National Institutes of Health on the effectiveness of the drug rosiglitazone in correcting pre-diabetes. "Diabetes is coming on board at least two decades earlier than what we saw in the past," says Caprio, who stresses the importance of addressing obesity in adolescents in order to prevent the disease.

While Caprio is working on the relation of muscle fat to insulin resistance, Gerald I. Shulman, M.D., PH.D., professor of medicine and

Obesity, page 6

MEDICINE»tomorrow

Campaign update

Campaign goal: \$750 million

Results through 6/30/07: \$250,947,949

Results through 6/30/07 by gift designation

Facilities: \$1,947,655

Permanent endowment: \$68,712,101

Gifts, use unrestricted by donors: \$2,093,278

Gifts, use restricted by donors: \$178,194,915

Results through 6/30/07 by source

\$100,000,000

\$80,000,000

\$60,000,000

\$40,000,000

\$20,000,000

\$15,482,027

\$45,678,224

\$35,380,626

\$85,472,700

\$20,257,224

\$48,677,148

Yale School of Medicine Alumni

Other Yale Alumni

Friends and Grateful Patients

Private Foundations

Corporations

Organizations

Obesity and diabetes research are top priorities of The Campaign for Yale School of Medicine. For information about gift opportunities, visit [yaletomorrow.yale.edu/medicine](http://yaletomorrow.yale.edu/medicine) or contact Jancy Houck, associate vice president for development and director, medical development, at (203) 436-8560.

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Out & about

June 1, 2: 1. At the medical school's REUNION WEEKEND, the Class of 1957 gathered on the steps of Sterling Hall of Medicine, just as they did 50 years ago as students. 2. THE 150TH ANNIVERSARY OF THE GRADUATION OF CORTLANDT VAN RENSSELAER CREED, M.D. 1857, the first African-American student to graduate from Yale, was marked by 50 of Creed's descendants from across the nation. (Back row, left to right) Troy D. Lawson; Forrester A. Lee, M.D., professor of medicine and assistant dean of multicultural affairs; Dean Robert J. Alpern, M.D.; Leon V. Creed III, great-great-great grandson of Cortlandt Creed; Taryn M. Archer, great-great granddaughter; Leon V. Creed II, great-great grandson; Reginald W. Creed, great grandson. (Front row, left to right) Andrea Rematore, great-great granddaughter; Richard P. Langella, great-great grandson; Tracey N. Lawson, great-great granddaughter; Miranda Lawson, great-great-great granddaughter; Myra Lawson, great-great-great granddaughter. Not pictured, but also in attendance, were Georgette N. Mitchell, great granddaughter; and Gwendolyn M. Washington, great granddaughter. 3. In a time-honored ritual, cardiologist Lawrence S. Cohen, M.D., Ebenezer K. Hunt Professor Emeritus, joins the Clamdiggers Dixieland Band for a special command performance during the annual New England Clambake. 4. Francis M. Lobo, M.D. '91, president of the Association of Yale Alumni in Medicine (AYAM; left) and Dean Robert J. Alpern, M.D. (right), present Distinguished Alumni Service Awards to Howard A. Minners, M.D. '57, M.P.H., (second from left), and Peter N. Herbert, M.D. '67, professor of medicine and chief of staff at Yale-New Haven Hospital, at the AYAM's annual meeting.



June 28, 29: Members of the newly formed DEAN'S COUNCIL met at Sterling Hall of Medicine to discuss the future direction of the medical school. Back row, from left: Richard N. Foster, B.E. '63, M.S. '65, PH.D. '66, managing partner, Millbrook Management Group; William R. Handelman, B.A. '53, partner, Meyer Handelman Company; John D. Baxter, M.D. '66, professor of medicine in the Diabetes Center of the University of California, San Francisco; Howard A. Minners, M.D. '57, M.P.H. (see story at left); Edward E. Madden, B.A. '62, vice chairman, Fidelity Management Trust Company and Pyramis Global Advisors; Franklin H. Top Jr., B.S. '57, M.D. '61, senior vice president, MedImmune Ventures; Jeffrey A. Rosen, B.A. '69, deputy chairman, Lazard Freres & Co. (Front row, from left) Daniel D. Adams, president and CEO, Protein Sciences Corporation; Peggy Brim Bewkes, U.GRD. '73, former producer of ABC News' "20/20" program; Dean and Ensign Professor of Medicine Robert J. Alpern, M.D.; Thomas C. Israel, B.A. '66, chairman and CEO of Ingleside Investors; Charles E. Bradley III, B.S. '51, president, Stanwich Consulting Corp. Not pictured: James M. Allwin, B.A. '74, president, Aetos Capital; Harvey J. Berger, M.D. '77, chairman and CEO, ARIAD Pharmaceutical; David A. Messer, B.A. '83, president, Sempra Commodities; Richard S. Sackler, M.D., co-chairman, Purdue Pharma; and David W. Wallace, B.S. '48, chairman, Joint Corporation Committee on Cuban Claims.

Bluestein from page 1

Bluestein, a retired radiologist known to friends as "Sandy," received some unrequested help paying his own medical school tuition—from the United States Army. He enrolled at the School of Medicine during the war years, just as the Army "took over" his class, enlisting Bluestein and about 40 other students in the Army Specialized Training Program, or ASTP.

"We were paid for, and they told us what to do, which led to some pretty weird circumstances," he says. "We had to stand in formation every morning at 7 a.m. We had to attend things we didn't want to attend; when Tommy Dorsey appeared on campus we had to go whether we liked it or not, because it was 'good for the Army.'"

Thanks to the basketball skills Bluestein had honed as a point guard at Lafayette College, in Easton, Pa., some of these burdens were eventually lifted. A lieutenant in charge of the medical school's soldiers knew of Bluestein's hoops prowess and asked him to assemble a basketball team to join a league formed by the Army from some of the thousands of ASTP students then at Yale College.

"We had a small gymnasium at the medical school, and I knew we could put together a good team, because many of the students had played college basketball, as I had. I agreed to give him a team if he'd give us special dispensation. I extracted a bargain from him, but I also told him that our team would be good enough that if he bet on us he'd make a lot of money, which he did," Bluestein recalls. "So I became a favorite of his, and we got to live a little better than the other guys. For one thing, we didn't have get up and stand in formation at 7:00 in the morning anymore."

Despite this minor wartime triumph, tennis is Bluestein's real game. Though he hasn't played competitively in 2007—he decided to take "an aging year," he says—as recently as last year he was the top-ranked player in his age group in the metropolitan New York City area, and he plays for recreation several times a week.

Bluestein's other great love is the New York City Opera, where he has been on the board of directors since 1978. He is the oldest member of the executive committee, and his contributions to the opera have helped



Sanford Bluestein, who has been a top-ranked tennis player in the New York area, continues to replenish a scholarship fund for Yale medical students.

many aspiring singers establish their careers.

As a practicing radiologist in New Jersey for nearly 50 years, Bluestein was something of a pioneer, performing some of the first cancer treatments with radioactive cobalt in the 1950s. He also performed some of the earliest brain scans, using radioactive mer-

cury to diagnose tumors. "I started scanning before scanning was a word," he says, "and I did chemotherapy before there were oncologists."

Bluestein retired from practice in 1996 at age 75, and he now divides his time between Montclair, N.J., New York City, and Boca Raton, Fla. "I adored practicing, and I never looked on it as anything other than a privilege," he says. "I thought it was an honor to be a doctor, something special."

But the financial strains that accompany medical education present hardships for many who wish to follow Bluestein's footsteps into clinical practice. According to the medical school's Office of Education, the average debt of the 2007 School of Medicine students who graduated with financial obligations is more than \$115,000.

For Bluestein, scholarships are the solution. "That's what it's all about, as far as I'm concerned," he says. "We should be giving gifts, not loans, because these students are never going to be able to pay this back. I feel very strongly about scholarships, and every little bit helps."



## Advances

Health and science news from Yale



### Mom was right: eat your vegetables!

Kids aren't the only ones who should be nagged to pile more vegetables on their dinner plate. A new study shows that men who regularly ate broccoli, cauliflower, cabbage, Brussels sprouts and turnips were 40 percent less likely to develop aggressive prostate cancer that spread outside the prostate than those who consumed few of these veggies.

Lead author Victoria Kirsh, PH.D., a former doctoral student under the advisorship of Susan T. Mayne, PH.D., professor of epidemiology, says that chemicals found in these and other "cruciferous" plants (named for their cross-shaped flowers) help prevent cancer. "All these vegetables have compounds called glucosinolates that have been shown to protect cells from DNA damage in the lab, and thus may be anti-carcinogenic" explains Kirsh, now at Cancer Care Ontario in Toronto, Canada.

Kirsh says she would like to see the findings, published in the August 1 issue of *JNCI: Journal of the National Cancer Institute*, replicated in additional studies. In the meantime, though, it can't hurt to eat your broccoli.

### "Touch-me-not" tubes kill bacteria

Carbon nanotubes, infinitesimally tiny "pipes" thousands of times smaller than a human hair, show great promise for medical applications. However, there has been concern that the tubes might damage human cells.

A Yale research group led by Menachem Elimelech, PH.D., chair and Roberto C. Goizueta Professor of Environmental and Chemical Engineering, wanted to find out how nanotubes affect *E. coli* bacteria. Because metallic impurities might lie behind the tubes' supposed toxicity to human cells, the team thoroughly purified their nanotubes in the laboratory of Lisa D. Pfefferle, PH.D., professor of chemical engineering.

In the August 28 issue of *Langmuir*, the scientists report that just one hour of contact with purified nanotubes proved deadly to about 80 percent of *E. coli*. The authors believe that the tubes killed bacteria by piercing cell walls: the cells looked flattened, and genetic material was seen floating freely in solution. Thinner nanotubes killed bacteria more efficiently, much as sharper objects pierce balloons more easily.

Even antibiotic-resistant pathogens may succumb to nanotubes, which may make new antimicrobial surfaces possible.

# Growing spare parts for sick children's hearts

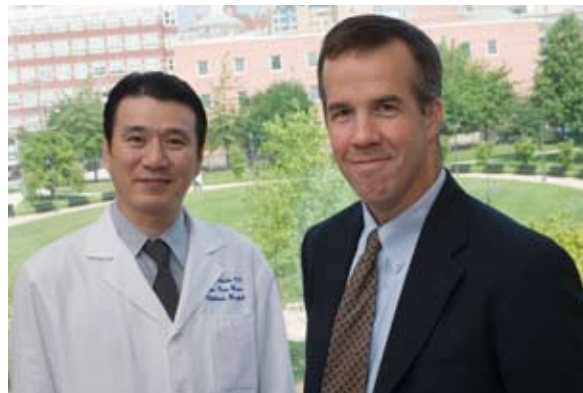
## Engineered blood vessels nearing clinical trials in congenital heart disease

Creating a living, growing organ from scratch sounds like the stuff of science fiction. But a pair of Yale physician-scientists are making it happen, coaxing cells to form artificial blood vessels that can be used to repair or replace faulty blood vessels in the body. Christopher K. Breuer, M.D., assistant professor of surgery and pediatrics, and Toshiharu Shinoka, M.D., PH.D., associate professor and director of pediatric cardiovascular surgery at Yale-New Haven Children's Hospital, have spearheaded this project, and they think their work can one day lead to the building of more complex organs.

"We figure if you start with blood vessels, that's going to be the first step in making just about anything," says Breuer. "Plus, there's an immediate need for vessels in vascular and cardiovascular surgery."

The blood vessels Breuer and Shinoka have created rely on stem cells harvested from a patient's own bone marrow, though the team hopes that by understanding how vessels form, they can soon create an "off-the-shelf" version that will not require harvesting cells. Either way, the engineered vessels are not prone to the immunological problems that affect transplanted tissue, such as inflammation or rejection. And they are living organs, an especially important characteristic in pediatric surgery because the vessels can grow as a child grows and can last a lifetime.

Typically, if a child is born with certain defects, such as a heart with two chambers instead of four, doctors first try to mold the child's own tissue into new vessels that can be used as grafts. "Whenever you use the child's own tissue, you get very good results," says Breuer. "But the problem is these children usually require multiple grafts and you never have enough tissue." The alternative has been to



Toshiharu Shinoka (left) and Christopher Breuer in the medical school's newly opened research building on Amistad Street, where they are building living blood vessels to treat children with congenital heart disorders.

use synthetic Gore-Tex grafts, which often have biocompatibility problems, leading to infections and blood clotting, or biological grafts from animals, which tend to calcify and need replacement as often as every few years.

To tackle these problems, Breuer and his colleagues designed a three-dimensional scaffolding in the tubular shape of a vein. The researchers coat this matrix with stem cells from bone marrow and sew it where needed, in place of a damaged or missing vessel. As blood begins to flow through the tube, the stem cells send out a signal that recruits all the right types of cells from elsewhere in the body to form a blood vessel around the scaffolding. As the vessel forms, the original matrix dissolves.

"The stuff we make the scaffolding out of is also what they make absorbable sutures out of," explains Breuer. "So we already know how the body reacts to this material, and that it's safe."

The resulting vessel, which can also be used to treat ischemic heart disease, or stroke, is almost indistinguishable from any other vessel in the body. It can grow over time and it constricts when treated with certain drugs. Additionally, the researchers showed that the elasticity of the engineered vessels matches that of the body's own vessels. "That is really important," says Breuer. "If you have blood flowing and it goes from this really stretchy tube to this really stiff tube, you tend to have problems; the grafts tend to narrow and cause blood clotting."

Over the past six years, Shinoka has used the process successfully in 47 children in Japan. No complications have arisen, he said, and no patients have needed replacement grafts. "They're fine," he said, "and they've avoided many medications that patients with traditional grafts need to take to prevent stenosis."

Shinoka and Breuer expect to hear soon about a U.S. Food and Drug Administration application they've filed to conduct clinical trials of their grafts at Yale, but they continue to pursue improvements in their techniques.

Breuer says that his next goal is to figure out what chemical from bone marrow is attracting cells to the scaffolding. He hopes to isolate that chemical and build it into the matrix so that the step of drawing bone marrow from each patient becomes unnecessary. "That would make this even simpler and increase the utility," he said. "We would have immediate off-the-shelf availability when a patient needed a graft."

And if he succeeds in that, Breuer and Shinoka plan to build a tissue-engineered heart valve. Over 80,000 heart valves are surgically replaced each year in the United States because they leak or don't open fully. And within 10 years of valve replacement, most patients need a second surgery. Breuer and Shinoka hope their valves would reduce post-operative problems. "It's significantly harder than making a blood vessel from a biomechanical standpoint," Breuer says, "but we've done the basic feasibility studies to show that you can do it."

## Student-run free clinic wins Ivy Award for community service

Working at HAVEN Free Clinic has given medical student Emma Barber, who serves as associate director, the chance to meet patients who are "some of the most grateful, humble, amazing people," she says. Open each Saturday, HAVEN (Health Care, Advocacy, Volunteerism, Education and Neighborhood) offers primary care, social services and free specialty referrals. Since the student-run center opened in November 2005, more than 200 patients have received free medical care.

Along with the gratitude of the patients, HAVEN received thanks this spring in the form of an Elm-Ivy Award, given to people and organizations that further partnership between New Haven and Yale. The awards were established in 1979 with the support of Fenmore Seton, a 1938 Yale Col-

lege alumnus, and his wife Phyllis, who established an endowment at the Community Foundation for Greater New Haven. Elm Awards are given to members of the New Haven community, and Ivy Awards are given to Yale staff, faculty and students.

HAVEN is based at the Fair Haven Community Health Center and is run by students in public health, nursing, medicine and the Physician Associate Program with assistance from undergraduates. The students work with attending physicians from the School of Medicine, the community and attending clinicians from the Fair Haven Community Health Center.

Although it was designed to provide temporary free care for patients while helping them obtain medical coverage, many patients—a large number of whom are undocumented



Medical students who launched a free clinic in the Fair Haven neighborhood of New Haven received an Ivy Award last spring for their efforts. (From left) Maggie Samuels-Kalow, Ryan Hebert, Mallika Mendu, Christopher Janson, Sara Crager and Andrew Simpson received the award from Yale President Richard Levin.

workers with no health insurance—see the clinic as their primary care provider. HAVEN offers free medications, Saturday hours and a friendly atmosphere, Barber says.



Some studies will use neuroimaging to illuminate how the brain changes when it's under stress. Others will explore the effectiveness of pharmacological agents to ease stress and improve self-control. Additionally, the consortium will organize large surveys and genetic studies to determine who is most likely to be vulnerable to stress. "We know that there are gene/environment interactions," explains Sinha. "So some people might be vulnerable even before stresses have hit them, based on their genotypes." One key research project will analyze how events early in life affect

the developing brain and how that shapes a person's ability to deal with stress later on, and its relationship to addictive behaviors. "There's growing evidence that early life stress shapes our responses to later stress," says Sinha. "So when we think about stress we really have to go back and think about childhood maltreatment and childhood exposure to stress." Carolyn W. Slayman, PH.D., the medical school's deputy dean for academic and scientific affairs, says the new grant is exciting not only because of the intriguing research projects it will fund (see "The Many

Sides of Stress and Addiction," below), but also because of its collaborative, interdisciplinary nature. "Yale already has a wonderful institutional tradition of low barriers across departments," says Slayman. "And this grant is going to be supporting a lot of research in a lot of different groups around the university. What one group finds will spur on others in the project to think in new ways about their own work." In all, the researchers expect more than 1,300 patients to be involved in the consortium's studies. However, through collaborations with community centers and an interactive

website, the researchers hope their work will reach many more people. To help put their research in the spotlight at Yale, the group will arrange an ongoing lecture series as well as an annual meeting on the topic of stress and addiction. "We're moving into a period of individualized medicine," says Sinha. "By providing specific information on new ways to improve one's sense of control in the face of stress, the hope is that people can learn how best to address the stress in their lives and make lifestyle choices that promote health."

## The many sides of stress and addiction



With a new \$23.4 million grant from the National Institutes of Health, 17 researchers will explore the multifaceted problems surrounding stress, self-control and addiction.

**George M. Anderson, PH.D.**  
Research scientist in the Child Study Center and laboratory medicine  
*"The Neuroendocrine, Pharmacology and Genetics (NPG) Core Resource will ensure optimal experimental design and assay utilization, will perform all analyses using rigorous quality control procedures, and will provide interpretive input to optimize use of genetic, drug level and biochemical measurements. In addition to performing assays and genotyping relevant to stress response system functioning, self-control and addictive behavior, the NPG Core is also mandated to develop new neurochemical, pharmacologic and endocrine measurements that will help advance this field of research."*

**Amy F.T. Arnsten, PH.D.**  
Professor of neurobiology and psychology  
**Mark F. Yeckel, PH.D.**  
Assistant professor of neurobiology  
*"Our project examines how stress affects cells in the prefrontal cortex, a part of the brain involved in the regulation of memory, attention and emotion. We will explore how waves of calcium released within these cells, under conditions that mimic stress, can open potassium channels that shut off cell firing, and how sustained stress can cause loss of gray matter in this higher brain region."*

**Roy Baumeister, PH.D.**  
Francis Eppes Eminent Scholar and professor of psychology, Florida State University  
**Dianne M. Tice, PH.D.**  
Professor of psychology, Florida State University  
*"Addictive behaviors, such as smoking, drinking and overeating are highly prevalent among young adults in the U.S. Losing self-control in stressful or highly arousing contexts plays an important role in perpetuating these behaviors. This project will*

*examine if increasing self-control via practice and training will reduce these maladaptive behaviors in college students. The findings will extend basic knowledge about self-control processes to identify effective ways to change addictive behaviors in the real-world setting of college life."*

**Hilary Blumberg, M.D.**  
Associate professor of psychiatry and diagnostic radiology  
**Linda C. Mayes, M.D.**  
Arnold Gesell Professor of Child Development in the Child Study Center and professor of pediatrics and psychology  
*"Adolescents, particularly those from stressful environments, are especially likely to engage in risky behaviors including drug use. These risky behaviors are due in part to the fact that brain systems involved in inhibiting behavior and understanding the consequences of actions are still maturing. This project will use cutting-edge brain scanning techniques to examine how stress can alter adolescent brain development to increase risk for addiction."*

**Daeyeol Lee, PH.D.**  
Associate professor of neurobiology  
*"When people are stressed-out they tend to want immediate rewards for their actions, and this can lead to impulsive behaviors. I think this may be linked to the function of the prefrontal cortex, an area of the brain involved in working memory and decision making. My lab will investigate this part of the brain to determine the effects of stress on decision-making at the cellular level."*

**Carolyn Mazure, PH.D.**  
Professor of psychiatry and psychology  
**Jacob K. Tebes, PH.D.**  
Associate professor of psychiatry and epidemiology  
*"The purpose of our grant is to implement educational initiatives that foster the process of conducting team science, and to generate outcomes*

*that advance a new interdisciplinary conceptualization of stress, self-control and addiction. We will integrate research across the consortium, develop mentoring programs and institutional review processes that overcome obstacles to career development in team science, and teach strategies for the rapid translation of research to the community and to policymakers."*

**Sherry McKee, PH.D.**  
Assistant professor of psychiatry  
*"Stress is often the reason why smokers are unable to quit smoking. Using a novel human self-administration paradigm examining how stress facilitates relapse behavior, we will test whether noradrenergic medications improve the ability to resist smoking. Noradrenergic agents, known to improve self-control, may attenuate the effect of stress on smoking relapse."*

**Alexander Neumeister, M.D.**  
Associate professor of psychiatry  
*"Addiction is one of the very complex and challenging problems facing Americans today. We will be using brain imaging techniques to understand the brain mechanisms underlying addictions, such as alcoholism and overeating. Specifically, we will look at how norepinephrine, a hormone, is involved in mediating addiction, with the ultimate goal of preventing and treating addiction."*

**Daniele Piomelli, PH.D.**  
Louise Turner Arnold Chair in the Neurosciences, professor of pharmacology and biological chemistry at University of California, Irvine  
*"Exposure to stress during childhood and adolescence increases the risk of developing drug abuse later in life, but the bases for this association are unclear. Previous work has shown that endocannabinoids, marijuana-like substances produced by the brain, help animals to cope with stress. We will ask whether alteration in the activity of these substances might explain the ability of early-life stress to change adult behavior."*

**Marc N. Potenza, M.D., PH.D.**  
Associate professor of psychiatry  
*"Obesity and tobacco smoking represent two of the most substantial causes of morbidity and mortality in the United States. Stress and diminished self-control are two important factors associated with these conditions. However, no studies have systematically examined the brain activations related to them. In our project, we will use functional magnetic resonance imaging to investigate brain activations related to self-control, stress, and food and smoking cues."*

**Jody L. Sindelar, PH.D.**  
Professor of public health  
*"This study examines how family, work life, and other stresses affect smoking, misuse of alcohol, and overeating. We focus on the interplay among these multiple addictions in response to stress. We use social science methods and large data sets, and will develop and disseminate policy implications."*

**Jane R. Taylor, PH.D.**  
Associate professor of psychiatry  
**Ralph J. DiLeone, PH.D.**  
Assistant professor of psychiatry  
*"Stress promotes compulsive behavior and addictions, like overeating and smoking, because it makes people want more immediate rewards for their behaviors, and also gives them less control over their behaviors in the first place. We will be studying how stress hormones in the brain act at a molecular and neural level to affect compulsive behaviors in these ways."*

## Obesity from page 3

cellular and molecular physiology, and colleagues are examining fat on the cellular level. Their work has shown that intracellular fat that accumulates in liver and muscles can trigger insulin resistance. Obesity is one of the ways in which this type of fat builds up, and Shulman's lab is now trying to figure out ways of melting it away. Along with Kitt F. Petersen M.D., he has shown that even modest weight reductions of 12 to 14 pounds will dissolve the intracellular pool of fat in the liver and reverse hyperglycemia. "The answers to obesity are going to come from a fundamental understanding of the processes that determine why we eat and how we

burn calories," says Robert S. Sherwin, M.D., the C.N.H. Long Professor of Medicine. Insulin influences a sense of fullness, and Sherwin suspects that the brain, like other organs in the body, can become insulin-resistant. He is also studying how the brain senses glucose and how that process relates to eating and energy expenditure. He has shown that hypoglycemia causes rats to gain weight, not because they eat more, but because they appear to burn fewer calories. Other researchers at the medical school are focusing on the brain's role in energy expenditure and the behavioral aspects of eating. Studies in mice led by Tamas L. Horvath, D.V.M., PH.D., chair and professor of

comparative medicine and obstetrics, gynecology and reproductive sciences, and have neurobiology, have shown that estrogen regulates the brain's energy metabolism in much the same way as leptin, another hormone that has attracted a great deal of attention because of its role in controlling appetite. Horvath is studying how higher brain regions, such as the hippocampus and cortex, help regulate food intake. He's also looking at the other side of the coin by trying to decipher how obesity may lead to metabolic changes that alter cortical function, which could have implications for neurodegenerative disorders such as Alzheimer's disease.

Our bodies and brains evolved over millennia when food was scarce to become highly efficient at obtaining and absorbing nutrients, but in a modern environment in which it is increasingly easy and cheap for us to eat more than our fill, and harder to work it off in daily activities, it's little wonder that obesity is a growing problem. Fortunately, clinical investigations, psychological studies and basic biological research are all in place at Yale to attack obesity from every angle. "On this issue you cannot have the typical ivory tower approach," said Horvath. "You need to combine different views and see what comes out of that."



# Grants and contracts awarded to Yale School of Medicine

## January/February 2007

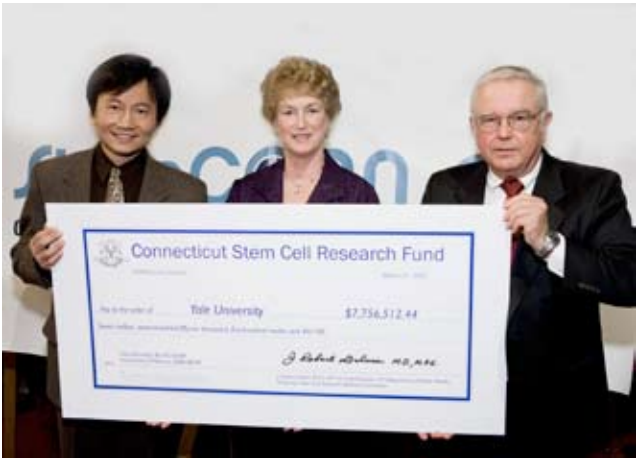
### Federal

**Roland Baron**, NIH, *From Adhesion to Bone Resorption: The Role of Dynamin in Osteoclasts*, 5 years, \$1,777,602 • **Alfred Bothwell**, NIH, *Revascularization of Islets to Treat Type 1 Diabetes*, 2 years, \$412,792 • **William Bradley**, NIH, *Adhesion-Dependent Inhibition of RhoA through Arg Tyrosine Kinase and p190RhoGAP*, 3 years, \$91,629 • **Suzanne Cassel**, NIH, *Role of Lung Inflammation in Th2 Priming*, 5 years, \$492,480 • **Junjie Chen**, NIH, *Analysis of 53BP1 Function in DNA Damage Signaling Pathway and Tumorigenesis*, 4 years, \$1,551,712 • **Kevin Collins**, NIH, *Heterotrimeric G-Protein Regulation of Neurotransmission in C. elegans*, 3 years, \$141,318 • **Michael Crair**, NIH, *Mechanisms of Visual Map Development*, 2.5 years, \$779,670 • **Isabelle Derre**, NIH, *RNAi Screen to Identify Host Factors Involved in Chlamydia Pathogenesis*, 2 years, \$412,792 • **Tore Eid**, NIH, *Temporal Lobe Epilepsy—Validation of a New Animal Model*, 2 years, \$397,259 • **Alison Galvani**, NSF, *Collaborative Research: Modeling and Behavioral Evaluation of Social Dynamics in Prevention Decisions*, 3 years, \$377,485 • **Charles Greer**, NIH, *Odorants, Receptors and Glomeruli*, 1.5 years, \$1,289,556 • **Lyndsay Harris**, Department of Defense, *Molecular Classifications of Response to Therapy in HER2 Positive, Early-Stage Breast Cancer*, 2.25 years, \$994,847 • **Raimund Herzog**, NIH, *Adaptations of CNS Metabolism to Hypoglycemia in Diabetes*, 2 years, \$116,072 • **Hoby Hetherington**, NIH, *MRS Measurements of GABA in Temporal Lobe Epilepsy*, 1.25 years, \$320,151 • **Tamas Horvath**, NIH, *Ghrelin in Hypothalamic Regulation of Energy Balance*, 4 years, \$1,289,357 • **James Howe**, NIH, *Single Channel Properties and Structure of Glutamate Receptors*, 4 years, \$1,446,394 • **Ruslan Medzhitov**, NIH, *TLRs in Host-Commensal Interactions*, 4 years, \$1,355,648 • **George Richerson**, NIH, *Developmental Defects in Serotonin Neurons and the Response to O<sub>2</sub> and CO<sub>2</sub>*, 5 years, \$1,657,482 • **Joseph Santos-Sacchi**, NIH, *Structural Correlates of Prestin Activity*, 3 years, \$1,053,470 • **Dieter Söhl**, NSF, *Expanding the Genetic Code with Phosphoserine*, 3 years, \$522,375 • **Scott Strobel**, NSF, *International: Undergraduate Rainforest Expedition and Laboratory*, 2 years, \$60,000 • **Zhaoxia Sun**, Department of Defense, *TSC1 and the Cilium in Zebrafish Kidney*, 2 years, \$221,100 • **Fayyaz Sutterwala**, NIH, *The Role of NALPs in Innate Immunity*, 4 years, \$504,280 • **David Willhite**, NIH, *Transsynaptic Tracing of Olfactory Bulb Input to the Olfactory Cortex*, 3 years, \$247,895

### Non-Federal

**Ali Abu-Alfa**, Abbott Laboratories Inc., *Educational Grant for Chronic Kidney Disease Center of Excellence*, 1 year, \$40,250 • **Maysa Abu-Khalaf**, Breast Cancer Alliance, Inc., *An Integrated Approach to Biomarker Validation in Patients with HER-2 Positive Metastatic Breast Cancer Treated with Rapamycin (Rapamune) to Overcome Resistance to the HER-2 Targeted*

*Therapy Trastuzumab*, 2 years, \$125,000 • **Karen Anderson**, Albert Einstein College of Medicine, *The Role of Viral and Cellular Proteins in Early Events of HIV-1 Replication*, 5 years, \$82,500 • **Michael Bloch**, American Academy of Child and Adolescent Psychiatry, *Clinical and Volumetric MRI Predictors of the Adult Outcome in Pediatric Obsessive-Compulsive Disorder*, 1 year, \$9,000 • **Hal Blumenfeld**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Impaired Consciousness in Epilepsy: Mechanisms and Consequences*, 5 years, \$595,791 • **Judson Brewer**, The Mind & Life Institute, *Mindful Training as Treatment and Mechanistic Probe for Drug Addiction*, 1 year, \$10,000 • **Stacy Castner**, Pfizer Inc, *Discovery Proposal for Nonhuman Primate Models Relevant to Schizophrenia*, 1 year, \$374,617 • **Katarzyna Chawarska**, Autism Speaks, *Computational Modeling of Visual Attention in Young Children with ASD*, 2 years, \$54,000 • **Michael Chen**, American Society of Maxillofacial Surgeons, *National Outcomes Studies in Craniofacial Surgery*, 1 year, \$6,680 • **Judy Cho**, Burroughs Wellcome Fund, *Characterization of Expression Patterns in Monocyte-Derived Cells in Inflammatory Bowel Disease*, 1 year, \$75,000 • **Dylan Clyne**, Robert Leet and Clara Guthrie Patterson Trust, *Neuronal Control of Courtship in Drosophila*, 2 years, \$104,000 • **James Comer**, Nellie Mae Education Foundation, *Nellie Mae Directors Grant*, 1 year, \$20,000 • **David Cone**, The Laerdal Foundation for Acute Medicine, *Virtual Reality for Disaster Triage Research*, 1 year, \$12,260 • **Michael Crair**, Rett Syndrome Research Foundation, *Examining the Role of MeCP2 in Regulating the Plasticity and Development of Synapses and Circuits in Mouse Somatosensory Barrel Cortex*, 3 years, \$100,000 • **Daryn David**, The International Psychoanalytical Association, *Investigating the Internal Working Model Concept*, 1 year, \$4,000 • **Nancy Dunbar**, Endocrine Fellows Foundation, *Characterization of Cystic Fibrosis Bone Disease Using Three Mouse Genetic Models*, 1 year, \$7,500 • **John Forrest**, Doris Duke Charitable Foundation, *International Clinical Research Fellowships (ICRF) in Africa Pilot Program*, 1.5 years, \$130,000 • **Gerald Friedland**, University of Connecticut, *Integrating HIV Prevention into Clinical Care for PLWHA in South Africa*, 5 years, \$217,999 • **Anna-Rachel Gallagher**, PKD Foundation for Research in Polycystic Kidney Disease, *Pathogenesis of Congenital Hepatic Fibrosis and Biliary Cyst Formation in ARPRD*, 1 year, \$75,000 • **Alan Garen**, Prostate Cancer Foundation, *Targeted Nanoparticles to Deliver the Icon Gene for Prostate Cancer Immunotherapy*, 1 year, \$100,000 • **Kim Good**, Arthritis Foundation of Australia, *Role of B7 Family Members in Enhanced Secondary Immune Responses*, 1 year, \$38,798 • **Carlos Grilo**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, *RCT for Obesity and Binge Eating in Monolingual Hispanic Persons*, 3 years, \$239,997 • **Bryan Hains**, Mike Utley Foundation, *Rescuing Motor Function after Spinal Cord Injury*, 1 year, \$47,833 • **Kevan Herold**, Juvenile Diabe-



In April, Haifan Lin (left), director of the Yale Stem Cell Center, accepted a check for \$7.7 million from the Connecticut Stem Cell Research fund from Connecticut Governor M. Jodi Rell (center) and J. Robert Galvin, commissioner of the Connecticut Department of Public Health.

tes Research Foundation Int'l, *Islet Growth in NOD Mice Tolerant to Autoimmune Diabetes*, 3 years, \$495,000; Juvenile Diabetes Research Foundation Int'l, *Mechanistic Studies and Identification of Biomarkers in Patients with T1DM*, 4 years, \$660,000 • **Melinda Irwin**, American Cancer Society, Inc., *Yale Exercise and Breast Cancer Survivorship Study: An Ancillary Study*, 2 years, \$202,000 • **Mustafa Khokha**, March of Dimes, *The BMP Antagonists, Noggin and Gremlin, are Required for Axial Skeleton Formation*, 2 years, \$150,000 • **Riku Kiviranta**, International Bone & Mineral Society, *The Roles of Delta FosB and MC-33, A Novel Zinc Finger Containing Protein, in Osteoblast and Adipocyte Differentiation*, 2 years, \$40,000 • **Anthony Koleske**, American Heart Association, *Regulation of Directed Cell Migration by Adhesive Cues*, 5 years, \$500,000 • **John Leventhal**, Salomon Family Foundation, Inc., *Bridging Mental Health Services for Sexually Abused Children and Their Families*, 2 years, \$148,162 • **Becca Levy**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Promoting Positive Age Self-Stereotypes: An Intervention*, 5 years, \$595,799 • **Ming Li**, Arthritis Foundation, *TGF-Beta Regulation of T Cell Responses in Collagen Induced Arthritis*, 6 months, \$75,000 • **Yilun Liu**, The Milo Gladstein Foundation, *Genome Instability and Tumorigenesis: The Roles of BLM and RecQ5 Helicases*, 1 year, \$75,000 • **Richard Matthey**, Pfizer Inc, *State Chest Conference*, 6 months, \$5,180 • **Qing Miao**, American Heart Association, *Role of Nogo-B Receptor in Regulating Endothelial Cell Functions*, 4 years, \$259,992 • **Gil Mor**, Wayne State University, *Services in Support of the Perinatology Research Branch*, 1 year, \$134,387 • **Shin Nagayama**, Robert Leet and Clara Guthrie Patterson Trust, *Individual Neuronal Contributions to the Function of a Cortical Network Module*, 2 years, \$96,000 • **Angus Nairn**, Rockefeller University, *Role of CK1 in Alzheimer Disease Etiology*, 1 year, \$49,171 • **Michael Pantalon**, National Alliance for Research on Schizophrenia and Depression, *Efficacy of Motivational Enhancement for Bipolar Postpartum Women*, 2 years, \$60,000

**Pasko Rakic**, Autism Speaks, *Effect of Non-Steroidal Anti-Inflammation Drugs on Neuronal Migration*, 2 years, \$101,000 • **Ann Rasmusson**, National Alliance for Research on Schizophrenia and Depression, *Neurobiological Predictors of Response to Cognitive Processing Therapy for PTSD in Women with and without Major Depression*, 2 years, \$59,891 • **Michael Robek**, Health Research Inc., *Inhibition of Virus Replication by Lambda Interferon*, 1 year, \$122,868 • **Rachel Roth**, PhRMA Foundation, *Regulation of Energy Expenditure and Lipid Metabolism by the Mitogen Activated Protein Kinase Phosphatase-1*, 2 years, \$40,000 • **David Rothstein**, Roche Organ Transplantation Foundation, *Mechanisms of Treg Generation by Tolerogenic Agents in Transplantation*, 3 years, \$242,266 • **Nancy Ruddle**, National Multiple Sclerosis Society, *Characterization of Pathogenic Myelin Oligodendrocyte Antibodies in Multiple Sclerosis*, 1 year, \$44,000 • **Gary Rudnick**, Autism Speaks, *The N-Terminus of Serotonin Transporter—A Role in Regulation*, 3 years, \$82,000 • **Masanori Sasaki**, Paralyzed Veterans of America, *Cortical Neuronal Protection in Spinal Cord Injury Following Transplantation of BDNF-hMSCs*, 2 years, \$149,040 • **Srijan Sen**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Investigation into the Interaction between Genes and Stress in the Etiology of Depression in Interns*, 2 years, \$88,039 • **Nenad Sestan**, Autism Speaks, *Role of Cell Adhesion Molecule in Cortical Minicolumn*, 2 years, \$99,000 • **Gerald Shadel**, National Organization for Hearing Research Foundation, *The Role of Dual-Function Transcription Factor/rRNA Methyltransferase in Modulating Mitochondrial Translation and Susceptibility*, 1 year, \$20,000 • **Edward Snyder**, Richard D. Frisbee III Foundation, *Richard D. Frisbee III Visiting Professorship*, 2 years, \$6,600 • **Zhaoxia Sun**, PKD Foundation for Research in Polycystic Kidney Disease, *Role of Pontin in Cilia Assembly and Cyst Formation in Zebrafish*, 2 years, \$150,000 • **Yufeng Zhou**, American Heart Association, *Determine the Structural Basis of hERG Channel Blockade at Atomic Resolution*, 4 months, \$65,000

### Pritzker from page 1

an expert on surgical problems in premature and newborn infants, is a forceful advocate for multicenter clinical trials of surgical procedures, many of which have not been subjected to the same level of scientific scrutiny as medicines. He is also leading his department's effort to use the latest genomic and proteomic tools to predict outcomes in surgery patients. In their first experience at YNHCH in 1997, Vlock and Pritzker sought medical opinions on their child's condition from many other hospitals, but ultimately discovered that, in addition to being close to their Branford, Conn., home, YNHCH had the people

and technology to make their child well. "We sent medical records to the finest hospitals around the world, and they all said you have the best team there at Yale, and what that team recommends is the best course of action," Pritzker recalls. Since an operation by Robert M. Weiss, M.D., now the Donald Guthrie Professor of Surgery, and a week-long hospital stay, their child has been healthy. Eight years later, the couple found themselves at YNHCH yet again, this time when a second child had a serious accident that resulted in a fractured liver, causing serious internal bleeding. "A team of first-rate doctors

and nurses had been assembled and were waiting at the hospital when we arrived," Pritzker says. On this occasion Milissa A. McKee, M.D., M.P.H., assistant professor of surgery and pediatrics, decided against traditional open surgery; instead, in a collaboration with Michael G. Tal, M.D., associate professor of diagnostic radiology, a small embolization catheter was inserted through an artery in the child's leg and brought to the injury site in the liver to control bleeding. Though this technique had only ever been attempted in adults, the child healed completely, and Pritzker

and Vlock say that McKee and Tal's decision to opt for a relatively non-invasive procedure was key to their child's quick recovery. "My father has taught me by example: one must give back to the people and institutions that have served you," Pritzker says. "We know Dr. Moss and those who succeed him in the chair will serve our community with distinction. Providing the opportunity for someone of Larry's skill and stature to build a program at Yale is a privilege, and will ensure that there are permanent resources available to our community for children's health."



# Transatlantic team probes kidney's role in hypertension

*Yale scientists join peers in Europe, Mexico in major new research effort*

Two School of Medicine scientists will join leading researchers in Switzerland, France and Mexico in a transatlantic collaboration aimed at pinpointing the kidney's role in high blood pressure. The new effort, known as the Transatlantic Network on Hypertension-Renal Salt Handling in the Control of Blood Pressure, is supported by a five-year, \$6 million grant from the Leducq Foundation, a Paris-based organization that supports international research collaborations in cardiovascular disease.

Hypertension affects more than 1 billion people worldwide and is one of the most important risk factors for cardiovascular diseases such as stroke and heart attack. The exact causes of hypertension remain unknown, but the kidney's management of salt levels in the body plays a major role.

Leading the team at Yale are Steven C. Hebert, M.D., chair and C.N.H. Long Professor of Cellular and Molecular Physiology, and Richard P. Lifton, M.D., PH.D., chair and Sterling Professor of Genetics and an investigator in the Howard Hughes Medical Institute.

"Breakthroughs in understanding and treating this complex and often devastating disease will come from collaborations among top scientists from around the world," Hebert said. "The grant from the Leducq Founda-

tion unites leaders in salt metabolism and hypertension from Europe and North America to understand the role of deranged salt handling by the kidney in causing and maintaining high blood pressure."

Hebert is the American coordinator of the project. His European counterpart, Bernard C. Rossier, M.D., of the University of Lausanne in Switzerland, will direct pharmacology and toxicology researchers at Lausanne and at Lausanne University Hospital. Also part of the network are researchers from the National Autonomous University of Mexico, under the direction of Gerardo Gamba, M.D., PH.D., and a team led by Xavier Jeunemaître, M.D., of L'Hôpital Européen Georges-Pompidou and the Collège de France in Paris.

The transatlantic team will study the metabolism of sodium, potassium and calcium and their influence on blood pressure. They will focus on the ion channels expressed in the kidney and on genetic factors that lead to a sensitivity or resistance to salt-related hypertension, with the goal of finding new therapeutic targets for the disease. In addition, the researchers will integrate their expertise in population genetics and animal models of hypertension, and they will combine approaches from molecular biology, proteomics and physiology.

The Leducq Foundation funding will enable the group to develop a network of PH.D. and postdoctoral researchers within the participating institutions; to develop a platform for



With a grant from the Paris-based Leducq Foundation, Richard Lifton (left) and Steven Hebert of the School of Medicine are part of a new international team studying how the kidney's management of salt levels in the body can lead to high blood pressure.

training, videoconferencing and real-time laboratory discussions using the Internet; and to create a centralized database that will allow easy access to shared tools, instruments, materials, and other resources.

Jean and Sylviane Leducq established the Leducq Foundation in 1996 to support cardiovascular disease research. Jean Leducq's grandparents owned the famed Le Grand Café in Paris, and his childhood meals were served by the family's cook, the legendary Auguste Escoffier. The Leducqs bequeathed Ehlers Estate, a Napa Valley, Calif., winery they had founded, to the foundation, which re-

ceives a portion of the proceeds from sales of Ehlers Estate wine. One of the foundation's goals is to promote collaboration between researchers in North America and Europe, and in 2004 it began to accept applications for its Transatlantic Networks of Excellence in Cardiovascular Research Program.

"The Leducq program," Lifton says, "uniquely allows us to bring together a 'dream team' of investigators around the world with diverse expertise in physiology, genetics, and clinical investigation to combine forces to tackle this important medical problem."

## Awards & honors



**Henry J. Binder, M.D.**, professor of medicine and cellular and molecular physiology, received the Distinguished Mentor Award from the American Gastroenterological Association, the premier professional organization in the field. The award recognizes his leadership in mentoring young physician-scientists and establishing Yale's Gastrointestinal Research Training Program, which has flourished for 35 years. Binder studies electrolyte transport in the large intestine and the mechanism and treatment of diarrheal diseases.



**Christopher K. Breuer, M.D.**, assistant professor of surgery and pediatrics, has been awarded a Doris Duke Clinical Scientist Development Award. These awards provide grants to junior physician-scientists to help them establish their own clinical research labs. Breuer aims to engineer living blood vessels and heart conduits that can grow along with a patient, which would be a boon to pediatric heart surgeons.



**Bernard G. Forget, M.D.**, professor of medicine and genetics, was named a fellow of the American Academy of Arts and Sciences. Members of the academy, an independent policy research center, are scholars at the top of their disciplines. Forget researches the mechanisms of gene expression during red blood cell differentiation, as well as the disorders that can result when this process goes awry.



**Barbara I. Kazmierczak, M.D., PH.D., M.S.**, associate professor of medicine and microbial pathogenesis, and **Yorgo E. Modis, PH.D.**, assistant professor of molecular biophysics and biochemistry, have received Investigators in Pathogenesis of Infectious Disease awards from the Burroughs Wellcome Fund. Each award provides



\$500,000 for multidisciplinary research. Kazmierczak studies how *Pseudomonas aeruginosa*, a bacterium that frequently causes hospital-acquired infection, is recognized by innate immune defenses.

Modis research explores how flaviviruses, such as West Nile and dengue virus, get into cells. Understanding this process could lead to vaccines for these currently untreatable emerging global health threats.



**Gil Mor, M.D.**, associate professor of obstetrics, gynecology and reproductive sciences, has received the J. Christian Herr Award from the American Society for Reproductive Immunology. This award is given annually to recognize a scientist who has made outstanding achievements in the field. Mor specializes in the immunology of reproductive organs, including implantation and tumor immunology. Recently Mor created a new diagnostic test for early detection of ovarian cancer, and developed new drugs to treat it.



**Craig R. Roy, PH.D.**, associate professor of microbial pathogenesis, won the 2007 Eli Lilly Award from the American Society for Microbiology (ASM). The award is the ASM's oldest and most prestigious prize, and the awardee delivers the Eli Lilly Award Lecture at the society's annual meeting.

Roy studies the bacterium *Legionella pneumophila*, the agent responsible for Legionnaire's disease, and how it interacts with cells it infects.



**Kim Woodrow, PH.D.**, a post-doctoral fellow in biomedical engineering, is one of the five American women recently honored by L'Oréal USA with their 2007 Fellowships for Women in Science. These competitive \$40,000 grants are given to encourage women scientists at the beginning of their careers. Woodrow is designing biodegradable nanoparticles that can direct themselves to specific targets in cells and deliver drugs to treat cancer and infectious diseases.



**Hongyu Zhao, PH.D.**, professor of public health and genetics, was elected a fellow of the Institute of Mathematical Statistics (IMS), an organization that fosters the development and dissemination of theory and applications of statistics and probability. The IMS honored Zhao for his "fundamental contributions to statistical genomics, genetic epidemiology, and computational biology."