

# Medicine@Yale

Advancing Biomedical Science, Education and Health Care

Volume 4, Issue 2 May/June 2008

## It's only rock 'n' roll, but it supports cancer research at Yale

A recent gift to support cancer research at Yale seems, at first blush, to follow a familiar pattern: It came from a man who, having parlayed his Ivy League education into a successful career, wanted to make a donation because of academic loyalties he forged long ago.

What sets the donation apart is that, in this case, Yale is the beneficiary of a windfall.

The donor, Cliff Burnstein, has no ties to the university (he went to the

University of Pennsylvania). And unlike many philanthropists, his fortune wasn't made in paneled boardrooms but in concert halls and recording studios.

Burnstein is the co-owner of QPrime, a talent agency that represents Grammy-winning, multi-platinum musical acts like Shania Twain, Metallica, and the Red Hot Chili Peppers. His \$1.5 million gift stems from a connection with Professor of Pathology and Laboratory



Jeffrey Sklar

Medicine Jeffrey L. Sklar, M.D., P.H.D., which began in middle school in Highland Park, Ill. The link between Burnstein and Sklar was one of association rather than abiding friendship—they were in the same classes but never bosom buddies—but Burnstein's eye for talent was keen even then.

“When you know somebody before there is any pretense,” Burnstein says, “in some ways you really know them the best. Jeff was the premier intellect of our class, and that was saying a lot.” Highland Park High School's Class of 1966 produced a bumper crop of achievers, including ABC investigative journalist Brian Ross; Penn State University President Graham Spanier, P.H.D.; producers/screenwriters Mark Victor and Michael Grais, co-authors **Rock**, page 6

## Smoothing the road

*To advance orthopaedics, couple bequeaths estate to the School of Medicine*

For someone who spent a lifetime in orthopaedics, mending hands, knees and hips damaged by age or trauma, Michael J. Cummings, M.D., a 1965 graduate of the School of Medicine, has adopted a rather bone-jarring hobby in retirement. He and his wife, Susan, a retired practitioner, educator and consultant in acute-care nursing, are enthusiastic participants in extreme off-road driving events arranged by AM General, the Indiana company that manufactures the military and civilian versions of the Hummer truck/SUV.

Cummings was smitten by the Hummer in 1993, when he saw television coverage of Arnold Schwarzenegger (who owned the first Hummer built for civilian use, and now drives a hydrogen-powered model) and wife Maria Shriver elegantly emerging in tuxedo and gown from a jet-black Hummer at the Academy Awards. “That was impressive,” he says.

In 1997, Cummings became a proud Hummer owner himself, and the following year he and Susan took the first of their annual off-road adventures, which Michael says offer



Dean Robert Alpern (left) joined Susan and Michael Cummings on a recent visit to the School of Medicine, where the Cummingses met on a blind date in the 1960s.

“great camaraderie and very difficult driving.” The couple have braved snowstorms at high elevation in the Rockies in Utah and Colorado, and once drove four and a half hours to traverse a mere quarter-mile of a boulder-strewn Virginia riverbed.

Now, to help ensure that the paths taken by the physicians and scientists of Yale's Department of Orthopaedics and Rehabilitation are a bit less hazardous than those the Cummingses have surveyed through many a mud-spattered windshield, the couple have bequeathed their entire estate to the School of Medicine.

The Cummingses met on a blind date at a church coffeehouse when Michael was in medical school and Susan was receiving clinical training at Yale-New Haven Hospital as a nursing student at the University of

Connecticut. Michael says his interest in orthopaedics was fueled by the late John Hartley Moore, M.D., a gifted clinical instructor with a practice in Stratford, Conn., whose teaching skills earned him the School of Medicine's Francis Gilman Blake Award in 1964.

Although Susan Cummings never officially attended the medical school, she still considers Yale to be an alma mater of sorts. “Quality faculty, clinical practice, research and education, are all necessary to positively impact health care,” she explains. “Even though I'm a graduate of the University of Connecticut, with a master's from the University of Washington, Yale is where I really learned about nursing and medicine, where the opportunities to engage in clinical practice were provided to me.”

**Road**, page 6

## Cartoonist's work on wartime trauma garners an award

In April, cartoonist Garry Trudeau, of “Doonesbury” fame, received the annual Mental Health Research Advocacy Award from the Department of Psychiatry for his portrayal of the physical and psychological challenges faced by soldiers returning from the



B.D.

wars in Iraq and Afghanistan. Trudeau, who holds undergraduate and master's degrees from Yale, was honored at the department's

Neuroscience 2008 symposium, “Stress, Resilience and Recovery.”

In a prolific series of strips, Trudeau has chronicled the wartime experiences of B.D., a venerable “Doonesbury” character who was modeled on Trudeau's classmate Brian Dowling, a legendary Yale quarterback in the late 1960s. The character made his debut in 1968 in the opening installment of “Bull Tales,” Trudeau's first published strip, which appeared in the *Yale Daily News* in the late 1960s. The strip's name changed to “Doonesbury” in 1970, when it was also syndicated in about two dozen other newspapers.

In an April 2004 strip, B.D. lost part of one leg—and his trademark football helmet—in an explosion;

**Doonesbury**, page 6

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Although David Leffell has a full plate of administrative duties, he is most at home in his dermatologic surgery office, where he performs Mohs surgery for skin cancer. Leffell is working to raise the profile of clinical medicine at the School of Medicine to be on par with Yale's world-class research and educational reputation.

## Making practice perfect

*Head of Yale's practices makes it his mission to serve patients' needs*

David J. Leffell, M.D., deputy dean for clinical affairs, CEO of the Yale Medical Group (YMG) and professor of dermatology, describes himself as “physician, academic, and administrator,” in that order. “If the dean needs to speak with me, but I have an appointment with a patient,” Leffell says, “he understands that the patient comes first.”

A surprising statement for an academic official, perhaps, but as an unflinching champion of first-rate patient care at the School of Medicine, an institution that has largely built its reputation on research and educational prowess, Leffell feels duty-bound to practice what he preaches—and he preaches about practice. “I am an advocate,” he says, “for the elevation of clinical practice to the same level of recognition as teaching and research.”

After graduating from Yale College in 1977, the Montréal-born Leffell returned to his hometown to attend medical school at McGill University, but never imagined he would specialize in dermatology. Then, during his residency in internal medicine at Memorial Sloan-Kettering Cancer Center in New York in the early 1980s, patients began arriving with purple skin lesions, the first wave of the AIDS epidemic. Leffell returned to Yale as a dermatology

resident attracted by the excitement developing around understanding the immunology of the skin. He spent a year as a postdoctoral fellow on a National Institutes of Health Training Grant, where he developed a patented laser device for measuring sun-induced skin aging. In 1987, he moved to the University of Michigan Medical School for training in Mohs surgery,

**Lifelines**  
**David J. Leffell**

a technique in which skin cancers are removed layer by layer and studied immediately under a microscope using a frozen section method. The Mohs surgeon creates a map of the specimen to allow removal of the entire tumor, providing the highest cure rate and minimizing scarring.

He soon was recruited back to Yale to develop a skin cancer program in the Department of Dermatology. Colleagues were skeptical that Leffell would find enough patients to make his Mohs training worthwhile. “There’s no skin cancer in Connecticut, you’re crazy. Go to Arizona, go to Florida,” Leffell recalls hearing in those days. However, the population of coastal Connecticut spends a lot of time outdoors, a prime risk factor for skin cancer. “Now our program is one of the busiest in the country,” Leffell, who heads YMG’s dermatologic surgery practice, says. “We treat about 4,000 cases per year, and also do significant clinical research.”

Leffell collaborates with several investigators across the medical school and was a member of the team that discovered the skin cancer gene PTCH in 1996.

As CEO of YMG, Leffell manages a practice with more than 800 physicians in over 100 specialties. “There’s no one-size-fits-all at Yale,” he says. “We have a very diverse faculty with many different interests and skill sets; there are many, many moving parts. Out of that soup we need to create an experience for our patients that’s seamless.” His own dermatologic surgery practice fares well on that front, scoring in the 99th percentile in nationwide surveys.

Leffell finds refuge from his many duties at his weekend house in Norfolk, Conn.; at the suggestion of his son, Alex, and daughter, Dahlia, he brought some country to the city in the form of eight chickens that the family keeps for fresh eggs. He is an avid sculptor, photographer and painter, and his photographs, many of Norfolk landscapes, adorn the walls of his offices. A much sought-after speaker and consultant, Leffell is the author of *Total Skin*, a layperson’s guide to dermatology and skin health.

Along with his wife, Cindy, Leffell recently made a \$100,000 gift to the medical school to endow an annual prize for clinical excellence. “It’s a complex environment at Yale; it can be challenging and frustrating. But at the end of the day when you stand back, you can see signs that you’ve made a difference.”

## Expert on myeloma, cancer vaccines to head hematology

Madhav V. Dhodapkar, M.D., an expert on multiple myeloma and monoclonal gammopathy of unknown significance (MGUS), the pre-malignant state from which myeloma



**Madhav Dhodapkar**

often develops, has been named chief of the Section of Hematology in the Department of Internal Medicine. Dhodapkar comes to Yale from Rockefeller University, where he headed the

Laboratory of Tumor Immunology and Immunotherapy since 2001.

Dhodapkar studies the effects of tumors on the immune systems of patients with multiple myeloma, and how the immune system permits the transition from MGUS to myeloma. His laboratory explores the use of dendritic cell vaccines and immunomodulatory drugs to bolster the immune system against tumor formation. As professor of medicine at Yale, he intends to expand his clinical research.

Jack A. Elias, M.D., chair and Waldemar Von Zedtwitz Professor of Medicine, says that Dhodapkar “is a world-renowned expert on the immunobiology of cancers, MGUS and multiple myeloma. He will add vibrant and visionary leadership to the Section of Hematology, the Department of Internal Medicine and Yale Cancer Center.”

Dhodapkar received his medical degree in 1987 from All India Institute of Medical Sciences in New Delhi, and completed his residency in internal medicine at St. Louis University Hospitals in Missouri.

### Medicine@Yale

Peter Farley, *Managing Editor*

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**Photographs:** Julie Brown, John Curtis, Terry Dagradi, AnnaMaria DiSanto, DK Images, Carl Lindskog, Michael Marsland, David Ottenstein, Judy Sirota Rosenthal, Harold Shapiro, Christopher Spock, Garry Trudeau, ChiChi Ubiña, Agnès Vignery, The Wiley Foundation

**Design:** Peter W. Johnson, Maura Gianakos

*Medicine@Yale* is published six times each year by the Office of Institutional Planning and Communications, Yale School of Medicine, 300 George St., Suite 773, New Haven, CT 06511.  
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Postal permit held by Yale University, 155 Whitney Avenue, New Haven, CT 06520

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## A match made in medical school: students find residencies

Each spring, fourth-year students at medical schools across the country eagerly anticipate Match Day, when students receive word of acceptance in residency training programs.

On the afternoon of March 20, word spread across the medical school campus that, for the second year in a row, the entire class had “matched,” meaning that every fourth-year student had been accepted as a resident at one of their chosen institutions, and no student would have to scramble to find an unfilled slot.

“This is the third year out of the last four where we’ve had a 100 percent match,” says Associate Dean of Student Affairs Nancy R. Angoff, M.D., M.P.H.

Four students will specialize in ophthalmology, four in dermatology and seven in anesthesiology. An unusually high number of students—nine—will begin residencies in psychiatry.

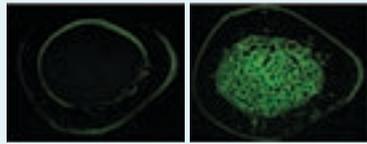
Ten students will head to the University of California—San Francisco, and 17 to the Boston area.



**Lindsay McGuire (back to camera) congratulates fellow student Sarah Frasure.**

## Advances

Health and science news from Yale



### A two-pronged tactic to grow new bone

School of Medicine researchers have devised a novel technique—removing bone marrow and injecting a hormone—that promotes rapid formation of new bone. “This could radically change the way patients are currently treated for weakened or fractured hips, vertebrae and acute traumatic long-bone fractures,” says senior author Agnès M. Vignery, D.D.S., Ph.D., associate professor of orthopaedics and rehabilitation. Existing therapy, which involves surgery and artificial materials, often leads to unsatisfactory outcomes.

As reported in the February issue of *Tissue Engineering: Part A*, Vignery’s team removed marrow from thigh bones in rats and then gave them daily injections of parathyroid hormone (PTH), which stimulates bone growth (see right panel of photo). The procedure created new bone tissue that appeared structurally and biologically normal, and endowed the bone with improved biomechanical properties at a rate that can’t be achieved by injecting hormones alone, Vignery says.

New research will determine whether the newly formed bone can be preserved and whether the technique is effective in other animals.

### Age no barrier for heart bypass surgery

Over the last 40 years, coronary artery bypass graft (CABG, pronounced “cabbage”) surgery has become commonplace; the National Center for Health Statistics estimates that 469,000 bypass procedures were performed on 261,000 patients in 2005.

According to a Yale study published in the December issue of *The American Journal of Cardiology*, even individuals in their 90s with heart disease may benefit from CABG surgery.

A research team led by Judith H. Lichtman, Ph.D., M.P.H., associate professor of epidemiology at Yale School of Public Health, studied outcomes of the procedure in 4,224 Medicare patients in their 90s who underwent the surgery from 1993 through 1999. The group found that age did not significantly lessen the procedure’s success.

Lichtman and senior author Harlan M. Krumholz, the Harold H. Hines, Jr. Professor of Medicine, note that women, while more likely to be discharged to nursing homes after the surgery, had better post-surgical survival rates than men. They also caution that additional research is needed to fully assess the suitability of CABG surgery for this elderly population.

## A scientific assault on brain diseases

### Program to unravel Alzheimer’s, Parkinson’s gears up for a tough battle

The School of Medicine is home to outstanding research programs in cell biology and neurobiology, and members of its faculty have made major contributions to our understanding of how nerve cells are organized and function in the brain. However, despite strong clinical programs in Alzheimer’s disease and other age-related disorders, up until a few years ago there was surprisingly little basic research at the medical school on the growing problem of neurodegenerative disease, and little effort to translate new insights into badly needed therapies.

To remedy that deficiency, the medical school called on two members of Yale’s Kavli Institute for Neuroscience, Stephen M. Strittmatter, M.D., Ph.D., the Vincent Coates Professor of Neurology, and Pietro De Camilli, M.D., the Higgins Trust Professor of Cell Biology and Howard Hughes Medical Institute Investigator, to create and direct a new Program in Cellular Neuroscience, Neurodegeneration and Repair (CNNR). The CNNR program, launched in 2006, has expanded the reach of cellular neuroscience at the School of Medicine from learning how healthy nerve cells work to understanding what goes wrong in disease.

During brain development, nerve cells send out long extensions, known as axons, that seek out and make contact with other nerve cells at specialized sites called synapses. In the normal adult brain, these connections form a network in which electrical signals are sent along axons to synapses, where they are converted to a chemical signal that passes the neural “message” on to other cells. Neurodegenerative diseases, stroke and spinal cord injuries cause damage to axons, synapses or both, and the complementary research interests of the CNNR program’s codirectors—Strittmatter is an expert on axon growth; De Camilli is a pioneering researcher in synapse formation and function—drive the center’s comprehensive approach to nervous system diseases.

Strittmatter’s research group has discovered that *NOGO*, a protein in the fatty myelin sheaths that insulate nerve cell axons prevents axons from seeking further connections in the adult brain. This helps to solidify neural circuits, but *NOGO* also blocks axon growth after spinal cord injury and stroke, keeping the brain from repairing itself. Strittmatter and his colleagues are exploring ways to block *NOGO*’s action to encourage the sprouting of axons and reconnection of nerve tracts before injury or disease cause permanent damage.

In many neurodegenerative diseases, a loss of synaptic connections between cells appears as one of the first signs of trouble. De Camilli has increased our understanding of



Primary and affiliated faculty in the medical school’s Program in Cellular Neuroscience, Neurodegeneration and Repair include (back row, from left) Anthony Koleske, Thomas Biederer, (middle row, from left) David McCormick, Sreeganga Chandra, Co-Director Stephen Strittmatter, (front row, from left) Susumu Tomita, Marina Picciotto, Co-Director Pietro De Camilli and David Zenisek.

how chemical neurotransmitters, which are packaged into spherical packets known as synaptic vesicles, are released into the synapse. Using biochemical and genetic techniques combined with light and electron microscopy, De Camilli is elucidating mechanisms underlying the formation and traffic of synaptic vesicles within axon terminals and unveiling how these mechanisms might be compromised in neurodegenerative diseases. The CNNR program’s first recruit, Assistant Professor of Neurology Sreeganga S. Chandra, Ph.D., is also a specialist on the synapse. Chandra is studying the synuclein family of synaptic proteins, one of which malfunctions in Parkinson’s disease.

The CNNR program has drawn in prominent scientists from other departments as affiliated faculty:

- **Cellular & Molecular Physiology:** Susumu Tomita, Ph.D., whose studies on the role of the excitatory neurotransmitter glutamate may produce new insights into Alzheimer’s and Parkinson’s diseases, and David Zenisek, Ph.D.,

who studies how vesicles transport and release neurotransmitters into the synapse, as well as how neurotransmitters are “recycled” by being gathered up from the synapse in newly formed vesicles;

- **Genetics:** Arthur Horwich, M.D., Ph.D., a widely recognized authority on protein folding who has recently turned his attention to the misfolded proteins that are characteristics of amyotrophic lateral sclerosis (ALS, or Lou Gehrig’s disease);
- **Molecular Biophysics and Biochemistry:** Thomas Biederer, Ph.D., who studies the development of synapses and how deficits in synapse formation may cause neurodegenerative diseases, and Anthony Koleske, Ph.D., who is seeking ways to prevent dendrite regression, an early hallmark of Alzheimer’s disease;
- **Neurobiology:** David A. McCormick, Ph.D., an expert on neural electrophysiological function from the cellular to the network level;

**Battle, page 5**

## MEDICINE » tomorrow

### The role of creativity in research

Solving the mysteries of Alzheimer’s, Parkinson’s and other neurodegenerative diseases will require creative, innovative ideas from the best minds in medical research. Creativity can’t be programmed to occur on a tight schedule or within a specific budget, yet that is precisely how most research grants are administered. Today’s tight budgets and risk-averse grant committees favor research awards that provide funds to build on what is already known—not what is novel or unexpected.

Private support for endowed professorships, like the Vincent Coates Professorship held by Stephen Strittmatter and the Higgins Trust Professorship held by Pietro De Camilli, provide researchers with secure, flexible funding to pursue new ideas ... to think creatively ... to discover new treatments.

This is the hope, and the promise, of the best biomedical research.

The Campaign for Yale School of Medicine seeks donors who are not satisfied with a conservative approach to research, who wish to participate in pushing the boundaries of knowledge. A commitment of \$3 million or more can create a named, endowed research professorship in neurodegeneration and neural repair or in any other area of donor interest.

For more information, visit [yaletomorrow.yale.edu/medicine](http://yaletomorrow.yale.edu/medicine) or contact Jancy Houck, associate vice president for development and director of medical development at (203) 436-8560.

# After heartbreak, a commitment to make a difference

## To honor a daughter, New Jersey couple builds a new fund for research

Few events are more tragic than the death of a child. When Steven and Carolyn Wortman of Livingston, N.J., lost their first child, Abby, in 2006 to necrotizing enterocolitis (NEC), an inflammatory disease of the gastrointestinal tract that affects roughly one in 20 premature babies, they grieved deeply, but they also resolved that they would keep Abby's memory alive by doing whatever they could to see that someday NEC would be understood and defeated.

Given how common NEC is in premature births, the Wortmans were surprised to find very little information on NEC research or advocacy groups devoted to the disorder. Steven Wortman, a small-cap mutual fund analyst who oversees small-cap mutual funds for Lord Abbett, a Jersey City, N.J.-based firm, surmises that the apparent lack of support for studies of NEC partly stems from parents' understandable desire for psychological closure when a child dies from the disease, and partly from the fact that these same parents are usually young, lacking the sort of financial resources to give the disease a high philanthropic profile.

"When you say that your daughter passed away from necrotizing enterocolitis, most people have no idea what you're talking about," he says. "Most

of the time young parents aren't in a position to give significant amounts of money, and it's also a disease where in many cases, parents have another child—not that they get over their loss, but they do try to 'move on' mentally." Carolyn D. Wortman, an accountant for Olympus Capital, a private equity firm in New York City, agrees. "People tend to become reclusive about it," she says.

One bright spot in a mostly bleak landscape of fruitless Internet searches was the work of the School of Medicine's R. Lawrence "Larry" Moss, M.D., the Robert Pritzker Professor of Pediatric Surgery and chief of pediatric surgery at Yale-New Haven Children's Hospital. "The outcome for this disease has improved almost zero in 30 years, but we're beginning to make some very positive baby steps in the right direction," says Moss.

In 2006, Moss and colleagues published the results of a six-year study comparing the effectiveness of surgical options for NEC in *The New England Journal of Medicine*—the first randomized, controlled, multi-center clinical trial in pediatric surgery ever conducted.

"That study sent us in a new and more sophisticated direction in our research, looking at biologic markers that may allow us to predict which babies are most at risk of the disease and at risk for a bad outcome," Moss says. "We're beginning to get a handle on this disease, and I think in our lifetime we're going to see significant



Steven and Carolyn Wortman, founders of the Abby Lauren Wortman Fund for research on necrotizing enterocolitis, with son Ryan at their New Jersey home.

improvement." The Wortmans have no personal affiliation with Yale, and Abby—who was born at 27 weeks, contracted NEC at three weeks old and died two weeks later—was never treated in New Haven. But after reading about Moss's work they contacted Yale and decided to raise funds to support his research.

"When we told our friends and family about our idea, they really responded to it," remembers Steven Wortman. "We had a lot of support, and it just kept growing. It definitely helped us heal, and gave us something to look forward to while we were in our grieving process, and it was a way to give our daughter's life some meaning."

So far, the Wortmans have raised \$46,000 for the Abby Lauren Wort-

man Fund. With an insider's eye, Steven says that his admiration for the "unparalleled" record of Yale's chief investment officer, David F. Swensen, PH.D., was added incentive to establish the endowment at the School of Medicine, which they hope will grow into an official endowment that will generate significant annual income to support NEC research at Yale.

"What our relationship with the Wortmans illustrates is that Yale has the opportunity, and one could argue, the responsibility to impact patients who will never come to this medical center," Moss says of the couple's gift. "What we're trying to do here is change the field—change the way we treat certain diseases, change the outcomes, change the way we look at premature babies, and develop new treatments that can be offered to affected patients."

As the Wortmans adjust their routines to care for their 10-month-old son, Ryan, born in June, 2007, Steven says that their fundraising efforts help to keep Abby on their minds. "We want to make some difference in studies," Steven says. "That obviously takes a lot of money, and this will take a long period of time. But we don't want this to be a flash in the pan. We want this to be sustained. It allows us to keep her memory fresh."

## Out & about

February 4: Former First Lady, senator from New York and presidential candidate **Hillary Clinton** made a **CAMPAIGN STOP** at the medical school's Child Study Center (CSC), taking questions from the audience on children's issues and health care policy. Clinton, who graduated from Yale Law School in 1973, volunteered at the CSC during her second year as a law student.



March 14: At a **CELEBRATION OF PROFESSORSHIPS ENDOWED BY DAVID W. AND JEAN McLEAN WALLACE** of Greenwich, Conn., four School of Medicine faculty members holding chairs endowed by the Wallaces joined the couple at the home of Yale President **Richard C. Levin**. Standing, from left: Levin; Jean McLean Wallace; **Ruslan M. Medzhitov**, PH.D., the David W.



Wallace Professor of Immunobiology; **Margaret K. Hostetter**, M.D., chair and Jean McLean Wallace Professor of Pediatrics; **James C. Tsai**, M.D., M.B.A., chair and Robert R. Young Professor of Ophthalmology and Visual Science; **Charles**

**J. Lockwood**, M.D., chair and Anita O'Keefe Young Professor of Obstetrics, Gynecology and Reproductive Sciences; **Robert J. Alpern**, M.D., dean and Ensign Professor of Medicine. Seated: David W. Wallace.

March 27: During a **VISIT BY FRANCIS S. COLLINS**, M.D., PH.D., director of the National Human Genome Research Institute, Collins attended the Department of Internal Medicine's grand rounds, speaking on "Medical Implications of High-Throughput Genomics," and later gave a lecture in the medical school's Anlyan Center on "Genomics, Medicine and Society." After the latter talk, Collins (left), who directed the Human Genome Project, exchanged ideas with **Fred S. Kantor**, M.D., the Paul B. Beeson Professor of Medicine.



April 4: The Department of Psychiatry presented its annual **MENTAL HEALTH RESEARCH ADVOCACY AWARD** to **Garry Trudeau**, the Pulitzer Prize-winning creator of the "Doonesbury" comic strip, for his strips highlighting post-traumatic

stress disorder among veterans of the Iraq and Afghanistan wars (see related story, p. 1). At the department's 2008 Neuroscience Symposium, "Stress, Resilience and Recovery" were (from left) **William H. Sledge**, M.D., interim chair and George D. and Esther S. Gross Professor of Psychiatry; **Al Atherton**, president of the Connecticut chapter of the National Alliance for the Mentally Ill; **Thomas A. Kirk Jr.**, PH.D., commissioner of the Connecticut Department of Mental Health and Addiction Services; Trudeau; **John H. Krystal**, M.D., the Robert L. McNeil, Jr. Professor of Clinical Pharmacology, deputy chair for research in the Department of Psychiatry and symposium co-director; and **Joan Kaufman**, PH.D., associate professor of psychiatry and director of the Child and Adolescent Research and Education (CARE) program in the Department of Psychiatry.

## Advances

Health and science news from Yale



### Taking a bite out of stroke

It may seem hard to believe that the rather menacing creature above, the Malayan pit viper, could be good for your health, but a Phase III research study of a compound found in the snake's venom could provide new hope for stroke victims.

Doctors at Yale-New Haven Hospital (YNHH) are administering ancrod (trade name Viprinex), a drug derived from pit viper venom, to eligible patients who enter the hospital with symptoms of acute ischemic stroke.

In such cases doctors typically administer a clot-breaking agent known as tissue plasminogen activator, or tPA, but it must be given no more than three hours after stroke symptoms appear to be effective. Anacro, which has a potent anticoagulant effect, may be effective up to six hours after symptoms begin. "If anacro is proven safe and effective," says Joseph Schindler, M.D., clinical director of the YNHH Stroke Center, "it will double the time frame during which stroke patients can be treated."

YNHH is the only Connecticut hospital participating in the trial, which is expected to last for one to two years.

### Sloppy gene repairs: a cause of lymphoma?

The blood and lymphatic systems transport the immune system's infection-fighting B cells throughout the body. During an immune response, random mutations are introduced in B cell genes by a process known as somatic hypermutation (SHM), which makes the cells more effective at fighting a variety of foreign invaders.

To keep harmful mutations at bay, B cells contain DNA repair enzymes that repair faulty genes created by SHM, but little is known about how effective these repair mechanisms are, or whether they might be related to the development of the cancerous B cells seen in lymphoma.

In the February 14 issue of *Nature*, a team led by David G. Schatz, Ph.D., professor of immunobiology and Howard Hughes Medical Institute investigator, found that almost 25 percent of B cell genes accumulated mutations, including genes that are strongly associated with human lymphomas.

"The implications of these findings are considerable," Schatz says. "It now seems likely that anything that compromises the function of these DNA repair processes could lead to widespread mutations and an increased risk of cancer."

## A 'reluctant honoree' receives his due at last

### Endowment in honor of surgeon enables students to treat disadvantaged

The late Gustaf E. Lindskog, M.D., who chaired the medical school's Department of Surgery from 1948 to 1966, deflected recognition at what seemed like every turning point in his career. A pioneer in thoracic surgery and a participant in the development of several important medical procedures that arose in the twentieth century, including chemotherapy and the clinical application of penicillin, Lindskog nonetheless remained an ever-reluctant honoree.

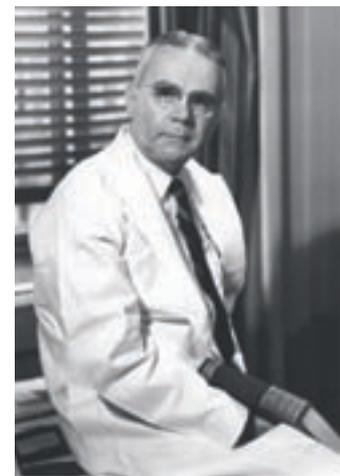
According to Andrew J. Graham, M.D., associate clinical professor of surgery, and John E. Fenn, M.D., clinical professor of surgery—both Lindskog trainees—when the idea of commissioning a portrait of Lindskog was tossed around, Lindskog not only issued a resounding no, but by way of explanation, trudged to a certain closet where portraits of esteemed medical school professors lay stashed away, hidden and unappreciated. Superficial honors were not his cup of tea. "We had to find something appropriate to keep his memory alive," says Graham, president of the Yale Surgical Society (YSS), a fellowship of graduates and faculty of Yale School of Medicine's surgical training program founded in 1994.

Fenn, in his roles as YSS treasurer and faculty advisor to first- and second-year students in the Yale Surgical Interest Group, conceived the idea of support to students at the School of Medicine to travel abroad to developing countries to perform much-needed surgery. Graham believed the initiative was something that would have appealed to Lindskog's sense of propriety and his longstanding interest in helping the disadvantaged. Lindskog's son, Carl W. Lindskog, of Woodbridge, Conn., heartily agreed, and the Lindskog International Travel Award was born.

The award affords medical students at Yale with an opportunity unlike any currently offered by any other medical school in the United States. Through the endowment, students receive stipends that make it possible for them to travel to other countries to provide medical services under the tutelage of their Yale professors and instructors.

### Battle from page 3

- **Pharmacology:** Ya Ha, Ph.D., who is solving the molecular structure of the neurotoxic amyloid beta peptide, a known culprit in Alzheimer's disease;
- **Psychiatry:** Angus Nairn, Ph.D., studies the neurotransmitter dopamine, which is disrupted in Huntington's and Parkinson's diseases. Marina Picciotto, Ph.D., works on nicotinic acetylcholine receptors, proteins involved in memory, which may reveal new drug targets for Alzheimer's.



(Left) Fourth-year medical student Matthew McRae holds a patient at Sappasithiprasong Hospital, in Ubon Ratchathani, Thailand. A winner of this year's Lindskog International Travel Award, named in honor of Gustaf Lindskog (right), McRae traveled to Thailand in February to provide surgical care to members of a needy community.

This year, the two winners of the prize were fourth-year medical students Matthew MacRae and Yuen-Jong Liu. Both traveled abroad in February, McRae to Ubon Ratchathani, Thailand, and Liu to San Pedro Sula, Honduras. For nine days MacRae and a team that included School of Medicine faculty members Deepak Narayan, M.D., M.B.B.S., associate professor of surgery, and Mark H. Weinstein, M.D., assistant clinical professor of surgery, treated cleft lips and palates, repaired congenital hand deformities, and managed the care of burns. Jong, part of a team led by Associate Professor of Surgery J. Grant Thomson, M.D., performed a wide variety of procedures, including carpal tunnel releases, skin grafts, bone settings, bone fusions, and conjoined finger releases.

Jong realized on arriving in San Pedro Sula that outdated hospital equipment and otherwise limited resources would require some creative thinking. "There was an intellectual challenge in trying to see what was the most you could get out of your limited supplies. We were a little bit less comfortable when sitting at the operating tables, but they all still functioned well," he explains. "We had to approach some of the cases differently.

For example, we didn't have C-arms, which we use for live radiological imaging. So we had to do more anatomical exploration or use more hands-on, more old-fashioned traditional techniques."

In contrast, the operating room facilities at Sappasithiprasong Hospital, where McRae and his team worked, were up to modern stan-

dards, McRae says. But the amount of unmet need there was palpable. "Children would be in bed, three rows of beds lined up, with their parents staying right next to the beds," he says. "It was an absolute jam of people, some of them there for over a week."

The flight of many of the hospital's surgeons from Ubon Ratchathani to Bangkok means that the hospital is severely understaffed, says McRae. Sappasithiprasong serves a population of 5 million, but only two plastic surgeons were on staff when McRae arrived in February.

"There was a huge number of trauma cases and they'd never be able to get to these kids," he says. "By operating on these kids and by making them look more normal, it allows them to integrate in society in a way that they just wouldn't be able to do without these operations. You'd bring these kids out and their parents would be there in tears, incredibly grateful. It was an amazing, heartwarming experience."

Although the award endowment is in its infancy, Fenn and Graham are optimistic about the Lindskog Award's future. It is a significant part of the total YSS endowment, and "as the endowment grows, we will be able to do more," says Graham.

For Fenn and Graham, the Lindskog Award not only offers Yale medical students an unparalleled opportunity, but also honors a man whose memory had lived on in the minds of his trainees but had gone publicly unrecognized.

"This is gratifying for me, personally, to see these students rewarded this way. It's also gratifying that we can honor Dr. Lindskog," says Fenn.

By linking with each other and with primary members of the CNRR program, these investigators will gain practical help from one another as well as a broader context for their work on neurodegenerative diseases. "While the main goal of the CNRR program is to advance knowledge about diseases," De Camilli points out, "studies of diseases will also help improve our understanding of normal nervous system function."

The medical school's Boyer Center for Molecular Medicine is the CNRR program's new home. Thanks to gen-

erous donors, core facilities for cell imaging, genomics and electrophysiology are in the works. With a plan to hire at least five more new faculty members, the program is ready to take off, according to Strittmatter.

"A few years ago, research on neurodegenerative disease at Yale was hit or miss, confined to corners of scattered departments, with no organization and fairly minor activity," Strittmatter says. "We have already changed that, and over the next few years, we plan to change it more."

“Susan and I decided that we’d like to leave some sort of legacy by funding a chair in medicine,” says Michael Cummings. “Even though I didn’t do my orthopaedic residency at Yale, I was fascinated by the idea of funding clinical people to do part-time research—doctors who would spend part of the week in the lab and the rest of their time in the operating room and seeing patients—as opposed to just having straight bench scientists. This really struck home for both of us, because orthopaedics is an area of medicine that needs people who can translate basic science into clinical applications for real patient scenarios.”

Robert J. Alpern, M.D., dean and Ensign Professor of Medicine, says that the Cummingses’ intentions align squarely with the School of Medicine’s goals. “Physician-scientists are crucial to the future of medicine, medical research and medical education. It is becoming more and more difficult, especially in procedure-intensive specialties such as orthopaedics, to be a master in both medical care and

research,” Alpern says. “Michael and Susan’s gift will provide much-needed support for such an individual, and we are grateful for their generosity and commitment to the medical school.”

Gary E. Friedlaender, M.D., chair and Wayne O. Southwick Professor of Orthopaedics and Rehabilitation, says that the Cummingses’ gift is thoughtful in both senses of the word. “What makes great donors is a combination of generosity and vision. Without both of those, a gift doesn’t reach its full potential. Michael and Susan Cummings are generous and visionary,” Friedlaender says. “Gifts like this allow us to pursue our missions—in the clinical arena, as well as in educational and research—with increased vigor.”

The department’s longstanding strength in biomechanics research has led to advances in the treatment and prevention of injuries. In the case of the spine, Friedlaender says, “our basic understanding of the mechanics has provided a basis for us and for others to expand on those observations and

make the world a safer place, both in how we can best take care of patients with spinal injuries and protect their neurologic function, and in terms of how we can redesign our environment to help prevent some of these injuries, whether by designing a new seat or headrest for a car, or a new piece of athletic equipment for the playing field.”

During the past 20 years, the biomechanics faculty has been complemented by a first-rate group of biologists who seek to understand how musculoskeletal tissues are assembled at the cellular and molecular levels, as well as how bones grow and repair themselves in health and disease. “The synergy between these two groups, the form and the function, the way things are put together at the cellular and molecular level and the way they function at the macro level” will directly improve well-being of patients, such as the large number of people over age 60 who have some degree of osteoporosis, says Friedlaender.

Joint replacement surgery is extremely well developed, Friedlaender

says, “but the time will come when we regenerate joints rather than replace them.” To do that, he explains, “we need to learn how to regenerate cartilage so you wind up with a ‘genuine GM part’ rather than a metal-and-plastic replacement. That’s going to involve tissue engineering: understanding how pluripotential stem cells recreate themselves into populations of cells that make up tissue-like cartilage and then maintain it for a lifetime.”

Friedlaender sees the clinical and research missions of his department as tightly intertwined and mutually reinforcing, and gifts like the Cummingses’ as crucial to continuing the department’s tradition of excellence. “Sometimes we turn to basic science and at other times we turn to clinical process, product or procedure development—a new operation, a new implant, an improved way of treating patients,” he says. “There’s not a single subspecialty of orthopaedics that’s not important, or that can’t be improved in terms of our ability to treat and prevent disorders and diseases.”



Music promoter Cliff Burnstein (center), co-owner of the QPrime agency, with (from left) QPrime partner Peter Mensch; singer-songwriter Nina Gordon; Lars Ulrich, drummer for the multi-platinum-selling rock band Metallica (both Gordon and Ulrich are QPrime clients); and Rick Rubin, celebrated producer and co-chair of Columbia Records.

of the “They’re heeere!” catchphrase from the 1982 film *Poltergeist*, and many others accomplished in academia, business, and the professions. “Everybody in the class said [of Sklar], ‘This is a guy who is going to make his mark,’” says Burnstein. “I don’t think anybody said that of me.”

Keeping tabs on each other through a mutual classmate who had become a psychoanalyst, Burnstein learned that Sklar was doing potentially groundbreaking research at Yale, but that research money was tight. “This is a very bad time for research,” says Sklar, also director of the medi-

cal school’s Molecular Diagnostics Program. “The lab made what I think is an important discovery, and I could not get funding to pursue it.”

Sklar says Burnstein “called me up out of the blue” last fall to get details on his research and what it would take to fund it. “I understood about 1 percent of it,” Burnstein says, but “he’s somebody that I trust. I knew him then. I reconnected with him in a way that made me feel that he was very vital and had tremendous amounts to contribute.”

Sklar says his research “challenges a fundamental tenet of cancer biology” because it describes how chromosomal abnormalities contribute to the development of the disease. Whereas the prevailing view holds that these abnormalities create on-

cogenic genes, Sklar’s lab found that they function more as mimics of a little-studied normal process—or as Hui Li, Ph.D., an associate research scientist who did the work with Sklar, puts it, “It’s a variation on the theme of cancers plagiarizing normal mechanisms in the cell, but in an exaggerated fashion. You could say that cancers are smart but they’re not original.”

Of his gift, which will support Sklar’s lab over five years, Burnstein says that he’s been fortunate and felt it was time to give back. “Jeff’s one of the highest-quality people I ever met in my life,” he says, “and I’m backing him.” And Sklar, though not a regular concertgoer, is urging everyone to see one of Burnstein’s bands. “They’ll be supporting medical research,” he says.

his physical rehabilitation, which included being fitted for a prosthetic leg, is collected in a book entitled *The Long Road Home*.

In 2006, B.D. was revealed to be suffering from post-traumatic stress disorder (PTSD), and his struggles with the disorder are depicted with Trudeau’s inimitable mix of humor, poignancy and indignation in a second book, *The War Within*.

Proceeds from sales of the books, which feature forewords by Republican presidential candidate John McCain and General Richard B. Myers, former chairman of the joint chiefs of staff, benefit Fisher House, a “home away from home” that provides temporary lodging in 38 facilities across the country to more than 10,000 military families in need.

In 1975, Trudeau was the first comic-strip artist to receive the Pulit-

## Doonesbury



zer Prize for editorial cartooning. He was elected to the American Academy of Arts and Sciences in 1993.

“The Mental Health Research Advocacy Award is given annually by the Department of Psychiatry to someone who has made an important contribution to the effort to advance

research designed to improve the lives of people with mental illness,” says Yale PTSD researcher John H. Krystal, M.D., Robert L. McNeil, Jr. Professor of Psychiatry. “Mr. Trudeau provides millions of Americans with a gut-level appreciation of the impact of PTSD on soldiers and their families as well

as the real opportunities for obtaining help with the readjustment process. In so doing, he is helping to raise awareness about the importance of PTSD as a national challenge, where investment in treatment and research could have an important and lasting impact.”

# Grants and contracts awarded to Yale School of Medicine

## July/August 2007

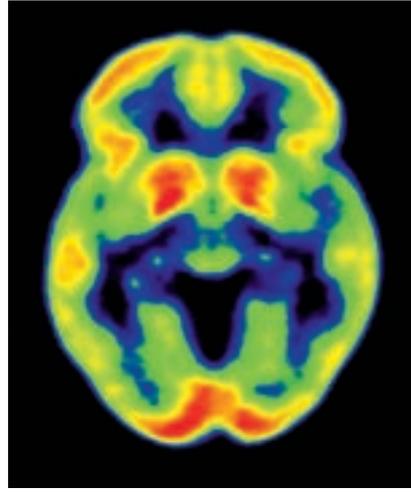
### Federal

**Hervé Agaisse**, NIH, *JAK/STAT Signaling in Drosophila Acute Phase Response*, 5 years, \$1,654,083 • **Morris Bell**, NIH, *Research Training in Functional Disability Interventions*, 5 years, \$1,188,507 • **Anton Bennett**, NIH, *Mechanisms of Metabolic Control by MKP-1*, 5 years, \$1,685,126 • **Clifford Bogue**, NIH, *The Development of Cardiovascular and Pulmonary Function*, 5 years, \$1,700,395 • **Elizabeth Bradley**, NIH, *For-Profit Hospice Ownership and End-of-Life Care*, 3 years, \$1,357,132 • **Richard Bucala**, NIH, *Mechanisms of Rheumatoid Synovial Fibroblast Activation*, 5 years, \$2,185,095 • **Susan Busch**, NIH, *Antidepressant Use and Suicide*, 3 years, \$845,277 • **David Calderwood**, NIH, *Identification of Beta1 Integrin*, 2 years, \$454,375 • **Richard Carson**, NIH, *Quantitative High-Resolution Human Brain PET Imaging*, 4 years, \$1,323,273 • **Steven Coca**, NIH, *Urinary Biomarkers for Acute Kidney Injury in Critical Illness*, 1 year, \$66,782 • **Robert Constable**, NIH, *Influence of Baseline Brain State on fMRI*, 5 years, \$1,755,279 • **Joseph Craft**, NIH, *Yale Rheumatic Diseases Research Core Center*, 5 years, \$3,210,030 • **Ralph DiLeone**, NIH, *Effects of MCH Receptor Signaling in the Nucleus Accumbens*, 4 years, \$1,042,825 • **David Donnelly**, NIH, *Mechanism of Perinatal-Hyperoxic Suppression of Chemoreceptor Function*, 5 years, \$1,912,500 • **Deepak D'Souza**, NIH, *Cannabinoids, Neural Synchrony and Information Processing*, 2 years, \$356,950 • **Richard Edelson**, NIH, *Yale Comprehensive Cancer Center*, 5 years, \$9,355,000 • **David Fiellin**, NIH, *Buprenorphine Maintenance vs. Detoxification in Prescription Opioid Dependence*, 5 years, \$3,000,971 • **Richard Flavell**, NIH, *Pathogenesis and Prevention of Autoimmune Diabetes*, 5 years, \$1,557,503 • **Bernard Forget**, NIH, *Blood Diseases*, 5 years, \$2,273,025 • **Patrick Gallagher**, NIH, *Molecular Biology of Erythrocyte Ankyrin*, 4 years, \$1,355,990 • **Antonio Giraldez**, NIH, *The Role of Micro RNAs in Vertebrate Development*, 5 years, \$1,554,838 • **Peter Glazer**, NIH, *DNA Repair in Cancer Biology and Therapy*, 5 years, \$8,376,289 • **Daniel Goldstein**, NIH, *Mechanisms to Augment Primary Immunity in Aging*, 5 years, \$1,715,262 • **Fred Gorelick**, NIH, *Training Program in Investigative Gastroenterology*, 5 years, \$851,009 • **Michele Goyette-Ewing**, Health Resources and Services Administration, *Graduate Psychology Education Program*, 3 years, \$327,221 • **Jiankan Guo**, NIH, *Role of Stem Cells in Renal Repair after Inducible Epithelial Ablation*, 5 years, \$718,200 • **Robert Heimer**, NIH, *Environmental Factors in HIV Transmission among Suburban IDUs*, 5 years, \$2,866,995 • **Josephine Hoh**, NIH, *CFH-Independent Risk Factors in Age-Related Macular Degeneration*, 2 years, \$626,916 • **Margaret Hostetter**, NIH, *Pediatric Physician-Scientist Program Award*, 5 years, \$11,267,626 • **Karl Insogna**, NIH, *Colony Stimulating Factor 1: Regulation and Role in Bone*, 4 years, \$1,323,000 • **Susan Kaech**, NIH, *Control of Terminal Differentiation of Effector and Memory T Cells by Blimp-1*, 2 years, \$454,438 • **Young-Shin Kim**, NIH, *Genetic Epidemiology of Autism Spectrum Disorder*, 5 years, \$781,663 • **John Krystal**, NIH, *Symposium on Neuroimaging in Alcoholism*, 1 year, \$62,667 • **Forrester Lee**, NIH, *Yale Biomedical Science Training and Enrichment Program*, 5 years, \$1,138,275 • **Stephen Malawista**, NIH, *Resolution of Gouty Inflammation*, 2 years, \$413,825 • **Robert Malison**, NIH, *Clinical Neuroscience Research Training in Psychiatry*, 5 years, \$1,202,615; NIH, *Patient-Oriented Research and Mentoring in the Translational Neurobiology/Genetics of Addiction*, 5 years, \$827,080 • **Mark Mamula**, NIH, *Molecular Mechanisms of Lymphocyte Interactions in Autoimmunity*, 5 years, \$1,600,247 • **Laura Manuelli**, NIH, *Experimental Creutzfeldt-Jakob Disease*, 1 year, \$583,558 • **Robin Masheb**, NIH, *Cognitive Behavioral Therapy and Dieting: Effects on Psychopathology and Weight in Binge Eating Disorder*, 2 years, \$398,527 • **Graeme Mason**, NIH, *Neuroimaging Sciences Training Program*, 5 years, \$1,202,772 • **Wajahat Mehal**, NIH, *Regulation of Hepatic Repair by Metabolites of the Uric Acid Pathway*, 5 years, \$1,356,075

**Perry Miller**, NIH, *Biomedical Informatics Research Training at Yale*, 5 years, \$5,726,858 • **Andrew Miranker**, NIH, *Predoctoral Program in Biophysics*, 5 years, \$1,042,899 • **Gil Mor**, NIH, *Apoptosis Regulators in Ovarian Cancer*, 5 years, \$1,571,380 • **Jon Morrow**, NIH, *Experimental and Human Pathobiology*, 5 years, \$1,313,645; NIH, *Membrane Skeletal Control in Hemolytic Disorders*, 5 years, \$1,860,750 • **Xenophon Papademetris**, NIH, *Image-Guided Deep-Brain Microscopy for Neurosurgical Intervention*, 3 years, \$1,088,103 • **Rebecca Papas**, NIH, *Alcohol and HIV in Kenya: Stage 1 Trial of a Peer-Led Alcohol Behavior Intervention*, 2 years, \$329,085 • **Anna Marie Pyle**, NIH, *Structure and Function of Group II Intron Ribozyme*, 4 years, \$1,147,885 • **Peter Rabinowitz**, NIOSH, *Daily Exposure Monitoring Intervention to Prevent Hearing Loss*, 4 years, \$1,653,750 • **Karin Reinisch**, NIH, *Assembly and Architecture of the Exocyst, a Membrane Tethering Complex*, 4 years, \$1,256,930 • **Harvey Risch**, NIH, *Case-Control Study of Pancreas Cancer in Shanghai, China*, 5 years, \$2,757,617 • **David Rothstein**, NIH, *Induction of Renal Allograft Tolerance in Monkeys with Anti-CD45RB-Based Therapy*, 5 years, \$3,442,667 • **Craig Roy**, NIH, *Genetic Analysis of Legionella Phagosome Trafficking*, 5 years, \$2,092,398 • **William Sessa**, NIH, *Institutional National Research Service Award*, 5 years, \$1,321,431 • **Richard Shiffman**, NIH, *Improving Guideline Development and Implementation*, 4 years, \$1,482,799 • **Mehmet Sofuoglu**, NIH, *Cocaine Withdrawal and Pharmacotherapy Response*, 4 years, \$1,497,505 • **Joan Steitz**, NIH, *Small RNP Mediators of Gene Expression*, 4 years, \$1,079,348 • **David Stern**, NIH, *Transformation by the NEU Oncogene Product and EGF*, 5 years, \$2,011,480 • **Daniel Stetson**, NIH, *Mechanisms and Consequences of Innate Immune Recognition of Nucleic Acids*, 1 year, \$89,996 • **Peter Tattersall**, NIH, *Molecular and Epidemiologic Characterization of a Pathogenic Human Bocavirus*, 2 years, \$454,500 • **Benjamin Toll**, NIH, *Promoting Tobacco and Cancer Control-Message Framing for Telephone Quitline Callers*, 2 years, \$347,014 • **Derek Toomre**, NIH, *Novel Delivery and Targeting of QDots to Track Single Molecules Inside Live Cells*, 5 years, \$1,033,802; NIH, *Novel TIRF Microscopy for Analyzing Trafficking and Signaling at the Cell Cortex*, 5 years, \$2,481,250 • **Phong Trang**, NIH, *Let-7 MicroRNA Therapy to Enhance Radiosensitivity in Lung Cancer Treatment*, 3 years, \$153,834 • **Anthony Van den Pol**, NIH, *Oncolytic Virus Targets Brain Tumors*, 5 years, \$1,571,220 • **Joshua Van Houten**, Dept. of the Army, *Does Increased Expression of the Plasma Membrane Calcium-ATPase Isoform 2 Confer Resistance to Apoptosis on Breast Cancer Cells?* 1 year, \$123,750 • **Robert Weiss**, NIH, *Encapsulated siRNAs for Treatment of Urological Disease*, 2 years, \$454,552 • **Tian Xu**, NIH, *Utilizing PB Transposon to Generate a Comprehensive Mouse Knockout Resource*, 2 years, \$1,050,000; NIH, *Deciphering the Genetic Basis of Tumor Progression and Metastasis in Flies*, 5 years, \$1,548,522 • **Fang Yi**, Dept. of Defense (U.S.), *Inhibiting the Folding and Maturation of ER and EGFRs Using Novel Hsp90 Inhibitors*, 1 year, \$125,126 • **Zhong Yun**, NIH, *Role of Hypoxia in the Maintenance and Homing of Hematopoietic Stem Cells*, 2 years, \$284,319; NIH, *Role of Hypoxia in the Regulation of Cancer Cell Differentiation*, 5 years, \$1,571,220 • **Hitten Zaveri**, NIH, *Third International Workshop on Seizure Prediction*, 1 year, \$23,000 • **Heping Zhang**, NIH, *Data Coordination Center for the Reproductive Medicine Network*, 5 years, \$12,373,375 • **Yawei Zhang**, NIH, *Quality of Life of Testicular Cancer Survivors*, 2 years, \$165,270

### Non-Federal

**Lisa Barry**, The Brookdale Foundation, *The Effect of Depression and Disability Burden and Subtypes over Time*, 2 years, \$140,487 • **Susan Baserga**, North Carolina State University, *Structural and Functional Analysis of Archaeal sRNPs*, 1 year, \$46,212 • **Steven Berkowitz**, Child Health and Development Institute of Connecticut, *Trauma-Focused Cognitive Behavioral Therapy Training*, 1 year, \$32,670 • **Zubin**



**A National Institutes of Health grant to Richard Carson funds research at the Yale PET Center. Here, the PET (positron emission tomography) technique reveals the average binding potential of serotonin 1B receptors in a transverse view of the brain in human control subjects. Highest binding is visible in the globus pallidus and the occipital cortex (red regions).**

**Bhagwagar**, American Psychiatric Association, *Glutamatergic Modulation of Mood in Bipolar Depression*, 1 year, \$45,000 • **Vineet Bhandari**, American Heart Association, *Angiogenic Agents in Alveolar Maturation*, 3 years, \$198,000 • **Clifford Bogue**, PKD Foundation for Research in Polycystic Kidney Disease, *Mechanisms of Polycystic Liver Disease in the Hhex Mutant Mice*, 1 year, \$75,000 • **Elizabeth Bradley**, Commonwealth Fund, *Diffusion of Hospital Strategies to Improve Care for Heart Attacks: How and Why do Organizations Learn?* 18 months, \$295,793 • **Ronald Braithwaite**, Robert Wood Johnson Foundation, *Tailoring Clinical Guidelines to Comorbidity*, 3 years, \$390,243 • **Christopher Breuer**, Doris Duke Charitable Foundation, *A Clinical Trial Evaluating the Safety and Efficacy of the Use of Tissue Engineered Vascular Grafts in Congenital Heart Surgery*, 3 years, \$405,000 • **Shi-Ying Cai**, American Liver Foundation, *Ursodeoxycholic Acid and Retinoic Acid Combinational Treatment for Primary Biliary Cirrhosis*, 2 years, \$200,000 • **Paul Cleary**, Robert Wood Johnson Foundation, *Internally Managed Project to Develop Public Health Systems Research*, 18 months, \$399,965 • **Kelly Cosgrove**, National Alliance for Research on Schizophrenia and Depression, *A Pilot Study to Assess the Sensitivity of a Novel 5-HT1B Receptor Ligand to Endogenous Serotonin*, 2 years, \$60,000 • **Irina Cottrill**, National Alliance for Research on Schizophrenia and Depression, *Effects of Nicotine Administration on Beta2-nAChR Occupancy in Smoking Patients with Schizophrenia*, 2 years, \$59,982 • **Meredith Crosby**, American Cancer Society, Inc., *Hypoxia-Induced DNA Repair Pathway Regulation*, 3 years, \$138,000 • **Mark Cullen**, State of CT Dept. of Labor, *Proposal for the Provision of Occupational Health Clinic*, 1 year, \$93,475 • **Linda DiBella**, Tuberos Sclerosis Alliance, *Investigating a Link Between the Cilium and the TSC/mTOR Pathway*, 3 years, \$150,000 • **Ralph DiLeone**, The University of Texas Southwestern Medical Center at Dallas, *Studies of Feeding Peptides in Animal Depression Models*, 1 year, \$69,696 • **Ronald Duman**, The University of Texas Southwestern Medical Center at Dallas, *Studies of cAMP Signaling and CREB in Nucleus Accumbens in Depression*, 1 year, \$47,897 • **Raymond Eid**, The National Marfan Foundation Inc., *The Role of IL-17A in Marfan Syndrome*, 1 year, \$50,000 • **Damien Ellens**, Howard Hughes Medical Institute, *Functional Neuroimaging, Neuro-Energetics and Electrophysiology in Spike-Wave Seizures in the WAG/Rij Rat, A Model of Human Absence Epilepsy*, 2 years, \$36,000 • **Andrew Epstein**, University of Pennsylvania, *Clinical Outcome-Based Assessment of Medical Education: Concept and Evaluation*, 1 year, \$43,890 • **Erol Fikrig**, Health Research Inc., *Role of Nod-Like Receptors in Rickettsial Infections*, 8 months, \$165,242 • **Richard Flavell**, American College of Rheumatology, *Regulation of T Cell Function in Collagen-Induced Arthritis by IL-10*, 2 years,

\$397,440; American Diabetes Association, Inc., *Mechanisms of Protection of Autoimmune Diabetes*, 4 years, \$180,000 • **Jason Fletcher**, The Board of Regents of the University of Wisconsin System, *Assessing the Effect of Increasing Housing Costs on Food Insecurity*, 18 months, \$40,000 • **Carlos Fragoso**, American College of Chest Physicians, *Establishing Chronic Obstructive Pulmonary Disease in Older Persons*, 2 years, \$100,000 • **David Geller**, Amgen Nephrology Institute, *Molecular Mechanisms of Hypertension in the Metabolic Syndrome*, 1 year, \$60,000 • **Thomas Gill**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Enhancing Independent Bathing in Community-Living Elders*, 3 years, \$240,000 • **Walter Gilliam**, State of CT Dept. of Children and Family Services, *Early Childhood Consultation Partnership Evaluation*, 3 years, \$419,988 • **Elaine Gilmore**, Dermatology Foundation, *Electrophysiologic Characterization of Voltage-Gated Sodium Channels in Keratinocytes*, 1 year, \$30,000 • **Jonathan Goldstein**, Allergan Sales, Inc., *Neuromuscular/EMG Fellowship Program*, 1 year, \$35,000 • **Baiba Grube**, Breast Cancer Alliance, Inc., *Interdisciplinary Breast Fellowship Grant*, 1 year, \$75,000 • **Handan Gunduz-Bruce**, National Alliance for Research on Schizophrenia and Depression, *Modeling Glial Dysfunction in Psychotic and Mood Disorders*, 2 years, \$60,000 • **Bryan Hains**, International Institute for Research in Paraplegia, *Rescuing Motor Function after Spinal Cord Injury*, 2 years, \$93,380 • **Tibor Hajszan**, National Alliance for Research on Schizophrenia and Depression, *Hippocampal Synaptic Remodeling in Postpartum Depression*, 2 years, \$60,000 • **Stephanie Hamill**, Jane Coffin Childs Memorial Fund for Medical Research, *Structural and Functional Studies of the RNA Quality-Control TRAMP4 Complex*, 3 years, \$139,750 • **Lyndsay Harris**, Veridex, LLC, *Yale Fellowship*, 1 year, \$10,000 • **Natalie Hayes**, Cystic Fibrosis Foundation, *Effects of Airway Clearance on Lung Function in Cystic Fibrosis*, 1 year, \$11,452 • **Tamas Horvath**, Foundation for Prader-Willi Research, *Synaptology in Prader-Willi Syndrome*, 1 year, \$50,000; Oregon Health Sciences University, *Maternal High Fat Diet and the Melanocortin System in the Offspring*, 4 years, \$165,375 • **Henry Huang**, GlaxoSmithKline Research and Development, Ltd., *PET Radiotracer Development for Dopamine Receptor*, 1 year, \$282,982 • **Yingqun Huang**, State of CT Dept. of Public Health, *Development of Novel Tumor-Specific siRNA Delivery System for Cancer Gene Therapy*, 20 months, \$177,223 • **Kashif Jafri**, American Heart Assoc. (Heritage Affiliate), *The Effect of Neuregulin/ErbB Signaling on Glucose Uptake in the Heart*, 1 year, \$22,000 • **Sven-Eric Jordt**, Sandler Program for Asthma Research, *Sensory Chemoreceptors in Asthma and Airway Hyperresponsiveness*, 3 years, \$450,000 • **Manisha Juthani-Mehta**, Infectious Disease Society of America, *Defining UTI in Nursing Home Residents*, 2 years, \$75,000 • **Leonard Kaczmarek**, American Heart Assoc. (Heritage Affiliate), *Properties and Regulation of Slack and Slick Channels*, 3 years, \$198,000 • **Nina Kadan-Lottick**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Survivors of Cancer in Adolescent and Young Adults*, 2 years, \$240,195 • **Susan Kaech**, Sandler Program for Asthma Research, *Identifying the Signals that Keep TH2 T Cells Alive During Chronic Asthma*, 3 years, \$450,000 • **Arie Kaffman**, National Alliance for Research on Schizophrenia and Depression, *Vulnerability to Stress Programmed by Postnatal Care Via Stable Alterations in Neurotrophic Factors Expression Levels*, 2 years, \$60,000 • **Insoo Kang**, American College of Rheumatology, *ACR/REF Rheumatology Fellowship Training Award*, 1 year, \$25,000 • **Anil Karihaloo**, American Society of Nephrology, *Role of VEGF During Early Embryonic Kidney Development*, 2 years, \$200,000 • **Maya Kasowski**, Howard Hughes Medical Institute, *High Resolution Mapping and Genome-Wide Expression Analysis of a Panel of Partial Trisomy 21 Patients*, 3 years, \$36,000 • **Barbara Kazmierczak**, Burroughs Wellcome Fund, *The Role of Injury in*

Grants, page 8

# Yale geneticist wins Wiley Prize for hypertension research

## Scientist is lauded for identifying many genes that control blood pressure

Richard P. Lifton, M.D., PH.D., chair and Sterling Professor of Genetics, an internationally known expert on the genetic basis of hypertension, has received the seventh annual Wiley Prize in Biomedical Sciences, which honors scientific contributions that demonstrate significant leadership and innovation. The prize is given by the Wiley Foundation, established in 2001 by John Wiley & Sons, a 200-year-old publisher of scientific, technical and medical books and online services.

Lifton, a Howard Hughes Medical Institute investigator, was recognized by the foundation for his discovery of genes that cause many forms of high and low blood pressure by affecting how the kidneys regulate the body's salt balance. The award, which includes a \$35,000 cash prize, was presented on April 4 at The Rockefeller University in New York City.

Günter Blobel, M.D., chair of the awards jury and winner of the Nobel



At an April 4 event marking Richard Lifton's winning of the 2008 Wiley Prize were (front row, from left) Joan Steitz; Lifton; Deborah Wiley, senior vice-president of John Wiley & Sons and chair of the Wiley Foundation; (back row, from left) Arthur Horwich, Kaye Pace, vice-president and executive publisher at John Wiley & Sons; Günter Blobel; Patrick Kelly, vice-president and director of journal publishing at John Wiley & Sons; Qais Al-Awqati; Elizabeth Cox, John Wiley & Sons editor; and Colette Bean, associate publisher at John Wiley & Sons.

Prize in physiology or medicine in 1999, cited the clinical relevance of Lifton's research. "Dr. Lifton's findings highlight the importance of dietary salt in the causation of hypertension, a major risk factor in cardiovascular disease, which is the leading cause of death worldwide," said Blobel, John D. Rockefeller, Jr. Professor and Howard Hughes Medical Institute investigator at Rockefeller University.

"Rick Lifton's research has demonstrated unequivocally the importance

of renal salt handling in the regulation of blood pressure," says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. "While hypertension can be due to over-constriction of blood vessels or abnormal salt handling by the kidney, Rick has found, in multiple genetic causes of high and low blood pressure, that the etiology resides in the kidney. These findings have settled a controversy that persisted for much of the 20th century."

Past Wiley Prize recipients include

Nobel Prize-winning scientists Andrew Z. Fire, PH.D., Craig C. Mello, PH.D., and H. Robert Horvitz, PH.D. Last year the School of Medicine's Arthur Horwich, M.D., was a joint recipient of the prize for his research detailing molecular machinery that guides proteins into their proper functional shape, work that is important in research on neurodegenerative disorders such as Alzheimer's and Parkinson's diseases and amyotrophic lateral sclerosis, or ALS.

## Grants from page 7

*Pseudomonas aeruginosa Pulmonary Infection*, 5 years, \$500,000 • **Tae Hoon Kim**, Rita Allen Foundation, *Genome-Wide Analysis of the Protein CTCF Function*, 3 years, \$150,000 • **Young-Shin Kim**, Autism Speaks, *Prospective Examination of Six-Year Cumulative Incidence of Autism Spectrum Disorders: A Total Population Study*, 2 years, \$120,000 • **Michael Kozal**, Boston University, *Cranberry and Prevention of UTI: A Comprehensive Approach*, 6 months, \$83,437 • **Harlan Krumholz**, Robert Wood Johnson Foundation, *RWJ Clinical Scholars Program CORE 2007–2008*, 1 year, \$507,420; Robert Wood Johnson Foundation, *RWJ Clinical Scholars Program, 2007–2009*, 2 years, \$1,024,261 • **Gary Kupfer**, Newman's Own Foundation, Inc., *Pediatric Oncology Research Program*, 1 year, \$25,000 • **Begona Lainez**, Arthritis Foundation, *Role of ICOS Ligand Expression in Murine Lupus*, 3 years, \$150,000 • **Ping Lam**, American Liver Foundation, *Molecular Determinants Controlling Bile Salt Export Pump Trafficking and Function*, 3 years, \$225,000 • **James Leckman**, Tourette Syndrome Association, Inc., *Transcranial Magnetic Stimulation for Adults with Severe Tourette Syndrome*, 1 year, \$74,149 • **Patty Lee**, American Heart Assoc. (Heritage Affiliate), *Protective Mechanisms of HO-1 and its Reaction Products during Ischemia-Reperfusion Lung Injury*, 3 years, \$198,000 • **Tene Lewis**, University of Pittsburgh, *Center for Aging and Population Health Visiting Scholar*, 2 months, \$24,701; American Heart Association, *Experiences of Discrimination and Endothelial Dysfunction in African-American Women*, 2 years, \$75,000 • **Chiang-Shan Li**, Alcoholic Beverage Medical Research Foundation, *Inhibitory Control and Alcohol Dependence*, 2 years, \$99,318 • **Yilun Liu**, American Foundation for Aging Research, *Defining the Biochemical Functions of Rothmund-Thomson Syndrome Helicase RecQ4*, 2 years, \$58,500 • **Simonne Longrich**, The Leukemia and Lymphoma Society, *Molecular Basis of BRCA2-Mediated Repair of Chromosome Damage*, 3 years, \$150,000 • **Ethan Marin**, National Kidney Foundation, *Increased Endothelial Nitric Oxide Synthase Activity by a Dominant Negative Caveolin*, 2 years, \$80,000 • **Andres Martin**, Medical University of South Carolina, *Patterns of Service Use and Costs Associated with Autism*, 1 year, \$27,911 • **Linda Mayes**, Gustavus and Louise Pfeiffer Research Foundation, *Electrophysiological Markers of Emerging Inhibitory Control, Stress-Reward Circuitry, and Risk for Addiction in Adolescents*, 2 years, \$149,150 • **John McArdle**, Cystic Fibrosis Foundation, *Cystic Fibrosis Center*, 1 year, \$23,700 • **Yorgo Modis**, Bur-

roughs Wellcome Fund, *Cell Entry and Innate Immune Recognition of Flaviviruses*, 5 years, \$500,000 • **Girish Neelakanta**, Arthritis Foundation, *Regulation of F194 ospA in the Development of Lyme Arthritis*, 3 years, \$150,000 • **William O'Connor**, National Multiple Sclerosis Society, *Molecular Mechanisms Underlying the IL-23 – IL-17 Immune Axis*, 3 years, \$150,800 • **Justin Paglino**, American Cancer Society, Inc., *Understanding and Enhancing the Oncoselectivity of Autonomous Parvoviruses*, 2 years, \$94,000 • **A. David Paltiel**, Stanford University, *Making Better Decisions: Policy Modeling for AIDS and Drug Abuse*, 9 months, \$121,158 • **Justin Peacock**, American Foundation for Aging Research, *Determine How Arg Regulates Cytoskeletal Rearrangements Resulting in General Changes in Cell Morphology, Adhesion, Contractility, and Motility*, 21 months, \$500 • **Elizabeth Peterson-Roth**, American Cancer Society, Inc., *The Role of Gap Junctions in Cell-Interdependent Cisplatin Killing*, 3 years, \$138,000 • **Christopher Pittenger**, Tourette Syndrome Association, Inc., *An Animal Model of Tourette Syndrome: Targeted Ablation of Striatal Fast-Spiking Interneurons*, 1 year, \$72,377; American Psychiatric Institute for Research and Education, *The Mechanisms of Habit: Studies of Striatum-Dependent Procedural Learning in Genetically Modified Mice*, 1 year, \$45,000; National Alliance for Research on Schizophrenia and Depression, *Mechanisms of Habit Learning: The Role of CREB-Regulated Genes in Long-Lasting Striatum-Dependent Procedural Memory*, 2 years, \$60,000 • **Jennifer Possick**, The Chest Foundation, *Serum Chitinase Activity and Chitotriosidase Mutations in Cigarette Smokers with and without COPD*, 1 year, \$10,000 • **Dake Qi**, American Heart Association, *Macrophage Migration Inhibitory Factor (MIF) in Ischemic Heart*, 2 years, \$80,000; Canadian Diabetes Association, *Macrophage Migration Inhibitory Factor (MIF) Induces Insulin Resistance and Affects Cardiac Injury During Acute Ischemia*, 3 years, \$14,151 • **Elizabeth Ralevski**, National Alliance for Research on Schizophrenia and Depression, *Mecamylamine for the Treatment of Patients with Depression and Alcohol Dependence*, 2 years, \$60,000 • **Brian Ramos**, American Psychological Association, *Diversity Program*, 1 year, \$38,976 • **Mohini Ranganathan**, National Alliance for Research on Schizophrenia and Depression, *Psychotomimetic Effects of Kappa Receptor Agonist Salvinorin A in Healthy Humans*, 2 years, \$60,000 • **David Rothstein**, Children's Hospital, (Boston), *The Role of TIM-1 – TIM-4 Pathway in Allograft Rejection and Tolerance*, 1 year, \$82,500 • **Samuel Sathyanesan**, University of Mississippi, *Vascular*

*and Cellular Pathology in Depression*, 1 year, \$21,158 • **Robert Schultz**, University of North Carolina at Chapel Hill, *A Longitudinal MRI Study of Infants at Risk for Autism*, 3 months, \$539,009 • **Srijan Sen**, American Psychiatric Association, *Minority Fellowship*, 1 year, \$32,571 • **Robert Sherwin**, American Diabetes Association, Inc., *The Role of RegII, a New Islet-derived Autoantigen in the Development of Type 1 Diabetes Mellitus*, 3 years, \$300,000 • **Anish Sheth**, American College of Gastroenterology, *The Effect of Symbiotic Therapy on the Hyperdynamic Circulatory State of Cirrhosis*, 18 months, \$10,000 • **Warren Shlomchik**, Burroughs Wellcome Fund, *Memory T Cells for Improved Immune Reconstitution and GVL in Allogeneic Hematopoietic Stem Cell Transplantation*, 5 years, \$750,000 • **Arthur Simen**, Obsessive Compulsive Foundation, Inc., *Genomic Copy Number Variation in Obsessive Compulsive Disorder*, 1 year, \$39,993 • **Carlo Spirlì**, American Liver Foundation, *Epithelial Angiogenic Signaling in Polycystic Diseases of the Liver*, 3 years, \$225,000 • **Vinod Srihari**, The Patrick and Catherine Weldon Donaghy Medical Research Foundation, *Specialized Treatment Early in Psychosis*, 3 years, \$239,502 • **Daniel Stetson**, Arthritis Foundation, *Nucleic Acid Recognition in Immunity and Autoimmunity*, 1 year, \$89,996 • **Hanna Stevens**, American Academy of Child and Adolescent Psychiatry, *Prenatal Stress and Effects on Inhibitory Neurons*, 1 year, \$9,000 • **Stephen Strittmatter**, Wings for Life Spinal Cord Research Foundation, *Ibuprofen Therapy to Improve Recovery from Chronic Rat Spinal Contusion*, 1 year, \$98,479 • **Matthew Strout**, The Leukemia and Lymphoma Society, *The Role of Small RNA Molecules in DNA Modification by Activation-Induced Cytidine Deaminase*, 3 years, \$150,000 • **James Swain**, National Alliance for Research on Schizophrenia and Depression, *Effects of Postpartum Depression on Adolescent Mothers – Interview, Videotape and fMRI Studies*, 2 years, \$59,772 • **Tamar Taddei**, American Association for the Study of Liver Diseases, *Pathophysiologic Mechanisms of the Hepatobiliary Phenotype of Gaucher Disease*, 2 years, \$150,000 • **Jane Taylor**, The University of Texas Southwestern Medical Center at Dallas, *Studies of Motivation for Food in Animal Depression Models*, 1 year, \$34,848 • **Jacob Tebes**, Child Health and Development Institute of Connecticut, *Statewide Evaluation of Children's Services*, 1 year, \$49,844 • **Susumu Tomita**, National Alliance for Research on Schizophrenia and Depression, *Regulation of Glutamate Receptors by TARPs: Regulation by Psychotomimetic Drugs*, 2 years, \$60,000 • **Masaaki Torii**, National Alli-

ance for Research on Schizophrenia and Depression, *Role of Eph/Ephrin Signaling on the Development of Neocortical Columns: Relevance to Psychiatric Disorders*, 2 years, \$60,000 • **Jonathan Touryan**, Robert Leet and Clara Guthrie Patterson Trust, *Neural Basis of Feature Attention in Area V4*, 2 years, \$92,000 • **James Tsai**, Research To Prevent Blindness, Inc., *Support of Pilot and Ongoing Research Programs*, 4 years, \$220,000 • **Edward Uchio**, Flight Attendant Medical Research Institute, *The Use of Spectral and Spatial Analysis to Improve the Utility of Urine Cytology in the Diagnosis of Transitional Cell Carcinoma (TCC) of the Bladder*, 3 years, \$325,500 • **Flora Vaccarino**, Autism Speaks, *Neurogenic Growth Factors in Autism*, 3 years, \$446,744 • **Christopher van Dyck**, Alzheimer's Association, *Amyloid Binding in Subjects at Risk for Alzheimer's Disease*, 3 years, \$239,967 • **Fred Volkmar**, Autism Speaks, *A Randomized Controlled Trial of Two Treatments for Verbal Communication*, 3 years, \$450,000 • **Charles Walker**, American Geriatrics Society, *Geriatrics for Specialty Residents (GSR) Yale Geriatric Urology Initiative*, 2 years, \$40,000 • **Joanne Weidhaas**, American Society for Therapeutic Radiology and Oncology, *Defining the Genetic Basis of the Radioresponse Using a C. elegans Tissue Model*, 1 year, \$125,000 • **Andrea Weinberger**, National Alliance for Research on Schizophrenia and Depression, *Cue Reactivity in Cigarette Smokers with and without Major Depression*, 2 years, \$60,000 • **Christopher Wendler**, American Heart Association, *The Role of Sphingosine-1-Phosphate Signaling during Cardiac Cushion Formation*, 3 years, \$198,000 • **Daniel Williams**, American Cancer Society, Inc., *The Role of Sro7p in the Maintenance of Cellular Polarity*, 3 years, \$138,000 • **Joseph Woolston**, The Children's Fund of Connecticut, *Moving Science to Practice in Children's Mental Health Services in Connecticut*, 18 months, \$125,000 • **Ying Xia**, American Heart Association, *Novel Insights into Neuroprotection from Hypoxic Dysfunction*, 3 years, \$198,000 • **James Yue**, Medtronic, Inc., *Medtronic Charitable Spine Fellowship*, 1 year, \$75,000; Synthes (USA), 2007–2008 *Spine Surgery Fellowship Program*, 1 year, \$75,000; Deputy Spine, Inc., 2007–2008 *Spine Surgery Fellowship Program*, 1 year, \$74,525 • **Richard Yun**, National Alliance for Research on Schizophrenia and Depression, *Fronto-Limbic Mechanisms of Vulnerability to Cognitive Stress in Depression*, 2 years, \$60,000 • **Yong Zhu**, Rensselaer Polytechnic Institute, *Light-Measuring Device for Correcting Circadian Disruption*, 9 months, \$49,500