

Medicine@Yale

Advancing Biomedical Science, Education and Health Care

Volume 4, Issue 1 March/April 2008

Slow readers, creative thinkers: gift will spur dyslexia studies

New center will explore links between reading problems, creativity

Sally E. Shaywitz, M.D., professor of pediatrics at the School of Medicine and an internationally recognized authority on dyslexia, has been named the first Audrey G. Ratner Professor in Learning Development. The professorship was established with a

\$3 million family gift honoring Ratner's lifelong interest in reading disorders.

In a 20-year research collaboration with her husband Bennett A. Shaywitz, M.D., professor of pediatrics and neurology, Sally Shaywitz has made major contributions to gauging the prevalence of reading disorders, defining the brain systems responsible for dyslexia. She has also formulated practical strategies for dyslexic



Audrey Ratner

individuals and for policy makers to lessen dyslexia's impact on educational and work success and on society at large. Shaywitz has summarized much of this work in *Overcoming Dyslexia*, a 2003 book written for the general public. Audrey Ratner, a former special reading teacher, is the

wife of Albert B. Ratner, co-chairman of Cleveland-based real estate developer Forest City Enterprises.

Now an interior design consultant, Ratner first became interested in reading difficulties as a teacher at Chicago's Francis W. Parker School, a day school founded in 1901 according to the progressive educational philosophies of John Dewey and Colonel Francis Wayland Parker. When Ratner arrived at the school, there was a

Dyslexia, page 6

Couple with a cause

\$10 million gift will drive research, trials of new skin cancer treatments

Roz Milstein and Jerry Meyer met in October 1971 in the Cross Campus Library at Yale. He was a fourth-year medical student. She was starting a doctorate in clinical psychology. Both were interested in community issues, and in making society a better place.

"We talked for five hours and found we shared a tremendous amount," Jerome H. Meyer, M.D., recalls. "But we never thought back then that New Haven would be our home."

Nonetheless, New Haven has remained at the core of their lives ever since that autumn evening. After marrying the following May, he began a residency in psychiatry and went on to practice in the city as a psychoanalyst. She finished her training and became a practicing psychologist, working with individuals and couples. They raised three children, who are now in their 20s and early 30s, and got involved in local education and arts organizations, helping to establish two of the city's major educational and cultural programs.

Now the Meyers are turning their attention to health care and medical research. With a gift of \$10 mil-



Jerry Meyer and Roz Milstein Meyer, who have set down firm roots in the New Haven area, are enthusiastic participants in the city's "industry of arts and ideas."

lion to the School of Medicine, they are helping to expand the school's research and treatment programs in melanoma, an often fatal skin cancer that has affected family members on both sides.

"Melanoma is one of the fastest growing and most deadly forms of cancer, and there are few options for people with advanced melanoma," says Roslyn Milstein Meyer, PH.D. "We'd like to see new treatments—effective treatments—developed, as well as new understanding of how cancer works."

To that end, their gift will establish the Milstein Meyer Center for Melanoma Research and Treatment, with the goal of developing new treatments for melanoma. One relatively new approach that has proved promising is immunotherapy, which aims to use

the immune system to treat disease, for example by training a patient's T-cells to attack tumor cells.

Roz Meyer, a trustee of Yale-New Haven Hospital, is also a patient advocate for Yale's NIH-funded Specialized Program of Research Excellence (or SPORE) in Skin Cancer. She's become excited by the work of Mario Sznol, M.D., associate professor of medicine, Ruth Halaban, PH.D., senior research scientist in dermatology, and their colleagues in a half-dozen departments, who are pursuing new ways of diagnosing, classifying and treating melanoma. Yale holds one of four SPORE Skin Cancer grants nationally.

According to Dean Robert J. Alpern, M.D., Ensign Professor of Medicine, Yale is ideally suited to attack melanoma. Yale has the top im-

Cause, page 6

New faculty prize will recognize superb patient care

The medical school has announced the creation of the David J. Leffell Prize for Clinical Excellence, an annual award that will be bestowed on the faculty member who best exemplifies clinical expertise, a commitment to teaching and the highest standards of care and compassion for patients.

The new award is made possible with a \$100,000 gift from David J. Leffell, M.D., deputy dean for clinical affairs and director of the Yale Medical Group (YMG), and his wife, Cindy, to mark the 30th anniversary of Leffell's graduation from Yale College in 1977.

The prize recipient will be selected by Dean Robert J. Alpern, M.D., based upon the recommendation of a panel comprised of five members of the YMG's Board of Governors. The panel will solicit nominations for the prize and recommend a recipient who represents the best in clinical medicine and who serves as a role model for faculty peers, residents, fellows and medical students. The first winner of the prize will be announced in May. The award will include a cash prize and permanent recognition in a medical school venue.



David Leffell

Excellence, page 8

Inside this issue

Lifelines

Pasko Rakic shows how a brain is built, p. 2

Have genome, will travel

Genetics researchers comb the world for cures, p. 3

Joint venture

Connecticut's first total ankle replacement, p. 5

A family's journey

Yale surgeon helps six family members fight cancer, p. 7

Champions for children

Advocates for universal preschool are honored, p. 8

Also

Advances, pp. 3, 5; *Out & About*, p. 4; *Grants and Contracts*, p. 7;

Medicine@Yale

300 George St., Suite 773
New Haven, CT 06511
www.medicineat Yale.org

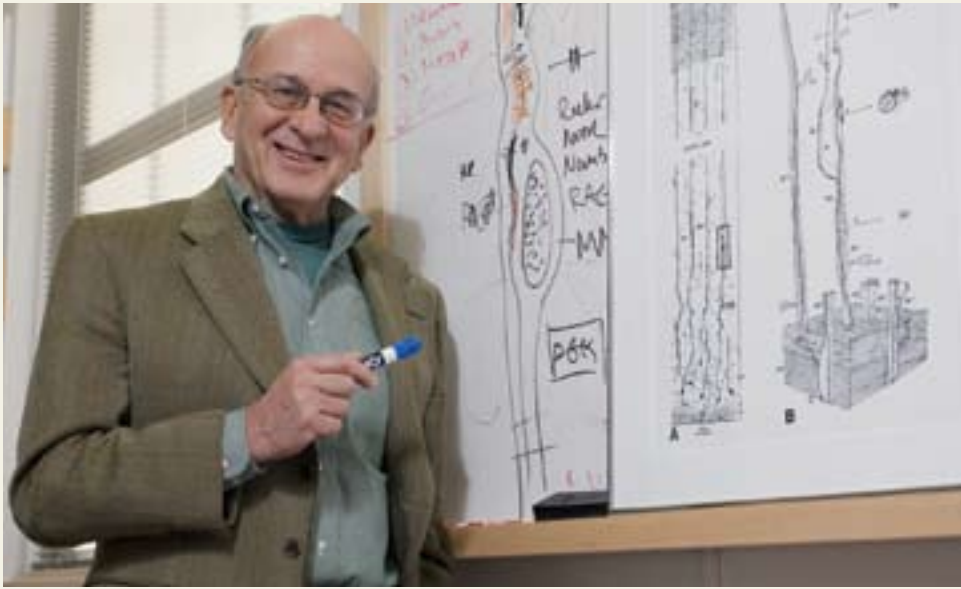
Want to find out more about medicine at Yale?

E-mail us at medicine@yale.edu or phone (203) 785-5824.

Non-Profit Org.
U. S. Postage

PAID

New Haven, CT
Permit No. 526



Pasko Rakic has spent a lifetime deciphering how neural stem cells in the embryonic brain arrange themselves during development into the highly ordered, densely interconnected and immensely complex circuitry of the adult cerebral cortex.

Cartographer of the brain

On a quest to decipher how a complex brain arises from a single cell

The cerebral cortex is comprised of distinct, orderly regions that subserve particular cognitive functions such as vision, hearing, movement and language. The function of every neuronal cell depends on its position and pattern of connectivity. How this complex neuronal map arises from a single fertilized cell during development is one of the most intriguing puzzles in science. "This map holds the secret of unique human mental abilities," says Pasko Rakic, M.D., PH.D., director of the Kavli Institute for Neuroscience at Yale, "and I have long wondered how it is made and reproduced from individual to individual."

A Croatian, born in the former Yugoslavia, Rakic's first forays into neurobiology began during his medical education, followed by graduate training in developmental biology and genetics at Belgrade University. He entered residency in neurosurgery but became restless, and in 1969 immigrated to the United States to join the Department of Neurosurgery at Harvard. However, an inclination toward basic science soon inspired him to transfer to Harvard's Department of Neuroscience. "I felt that I could help more by doing research," he says, "since so much was unknown." In 1978 Rakic was recruited to Yale School of Medicine by famed cell biologist and Nobel laureate George E. Palade, M.D., as professor of neurosci-

ence and the founding chair of the Department of Neurobiology, a position he continues to hold as Dorys McConnell Duberg Professor.

Rakic was fascinated by his initial experiments using DNA markers of cell division on slices of embryonic human brain, which showed that none of the billions of our cortical neurons are generated locally. Thus, unlike those in other organs, cortical cells must migrate to their final destinations from a proliferative zone in the embryonic cerebral brain that becomes increasingly distant from the cortex as the brain grows. Perhaps Rakic's greatest contribution is that he provided the first cellular and molecular explanations of how this migration could occur.

His studies of the remapping of the proliferative zone upon the expanding cerebral cortex in various species led him to publish a unifying hypothesis of cortical development and evolution in the journal *Science* in 1988 that has since been confirmed in his as well as other laboratories. Over the years he and his colleagues have identified genes and molecules involved in the regulation of the production and migration of cortical neurons. His 4-dimensional model of the developmental events that take place over time, from the initial divisions of neuronal stem cells through their migration and stratified settlement in radial cortical columns, is reproduced in virtually every neuroscience

textbook. Further, by manipulating neuronal migration using genetic and environmental factors, Rakic has discovered the hidden abnormalities of neuronal positioning that cannot be discerned by routine postmortem examination of the human brain, opening a new insight into the pathogenesis of a variety of the so-called idiopathic disorders of higher brain functions, such as childhood epilepsy, autism, developmental dyslexia and mental retardation.

Rakic is also known for his assertion that the adult human cerebral cortex does not generate new neurons—in other words, you get what you are born with. He postulated that the stability and longevity of the human neuronal population may be a biological necessity for the retention of long-term memory and learned behavior over the life span, since we rely heavily on acquired knowledge soaked up through schooling and experience. In other words, "it is actually an advantage that no new neurons are generated," he says, "lest the brain's slate be continually wiped clean."

Rakic's conclusion that cells subserving the most precious human mental functions are irreplaceable has repeatedly been corroborated, inspiring researchers to study how to best preserve the cortical neurons and their circuits, in which our life-long experience is stored.

Even after four decades of effort, Rakic can hardly contain his enthusiasm for his research on the cerebral cortex. "This is the most appropriate study of humankind," he says, "because it is this particular part of the brain that distinguishes us from all other species."

Renowned teacher, researcher named dean of engineering

Award-winning researcher and teacher T. Kyle Vanderlick, PH.D., has been appointed dean of the Faculty of Engineering and the Thomas E. Golden Professor of Engineering at Yale, effective January 1. Vanderlick comes to Yale from Princeton University, where she was chair and professor of chemical engineering.

A leading expert on interfacial forces—interactions that occur near or between surfaces—Vanderlick conducts research that aims to measure, control and understand the properties of interfaces and thin films, especially those with relevance to materials science and biology. Her work has led to new and fundamental insights across a range of areas spanning from metallic adhesion in micro/nano-scale devices to the action of antimicrobial peptides on cell membranes.

In 2002 Vanderlick was awarded both the Princeton Engineering Council Teaching Award and the Princeton President's Award for Distinguished Teaching. Vanderlick has B.S. and M.S. degrees from Rensselaer Polytechnic Institute and a PH.D. in chemical engineering from the University of Minnesota.

Vanderlick succeeds Paul A. Fleury, PH.D., the Frederick W. Beinecke Professor of Engineering and Applied Physics, who has served as dean of engineering since 2000.



T. Kyle Vanderlick

Medicine@Yale

Peter Farley, *Managing Editor*

Contributors: John Curtis, John Dillon, Janet Rettig Emanuel, Michael Fitzsosa, Hannah Hoag, Pat McCaffrey, Kara Nyberg, Karen Peart, Jacqueline Weaver, Sarah C.P. Williams

Photographs: John Curtis, Terry Dagradi, Robert Lisak, Michael Marsland, Princeton University Office of Communications, Harold Shapiro

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.
Telephone: (203) 785-5824
Fax: (203) 785-4327
E-mail: medicine@yale.edu
Website: medicineat.yale.org

Copyright ©2008 by Yale School of Medicine.
All rights reserved.

If you have a change of address or do not wish to receive future issues of *Medicine@Yale*, please write to us at the above address or via e-mail at medicine@yale.edu.

Postal permit held by Yale University,
155 Whitney Avenue, New Haven, CT 06520

Yale School of Medicine
Robert J. Alpern, M.D., *Dean*
Ensign Professor of Medicine

Jancy L. Houck
Associate Vice President for Development
and Director of Medical Development
(203) 436-8560

Mary Hu
Director of Institutional Planning and Communications

Michael Fitzsosa, *Director of Communications*

This issue follows Volume 3, Issue 6 (November/December, 2007).
The January/February, 2008 issue was not published.

Student-run auction benefits seven New Haven-area charities



Potential bidders at the student auction.

The annual student-run Hunger and Homelessness Auction, held last November, raised \$30,000 for seven area charities. According to Barbara Hirschman, a second-year M.D./PH.D. student and one of the auction's two co-chairs, local organizations were asked to submit grant applications, and members of the auction's board, which includes students in medicine, public health, nursing and the Physician Associate Program, paid visits to various agencies to select this year's seven beneficiaries.

The proceeds from the auction will benefit the Emergency Shelter Management Service, the Community Health Care Van, Loaves and Fishes, Domestic Violence Services, the Community Soup Kitchen, the Downtown Evening Soup Kitchen and Caring Cuisine.

For the second year, professional auctioneer Wade Brubacher, father of second-year medical student Jake Brubacher, cut a striking figure in a white cowboy hat as he led the proceedings (see related story, p. 4).

Advances

Health and science news from Yale



Raising the Rae-1 flag

Raising a flag is a good way to send a message. In fact, that's all it takes for a stressed-out, potentially cancerous cell to get the attention of the ever-watchful immune system. Until now, models of immune surveillance have assumed that only foreign danger signals or well-established inflammation could trigger a protective response.

But a new Yale study published in the February issue of *Nature Immunology* reports that cell-surface expression of Rae-1, a protein associated with milder forms of cell dysregulation, is enough to kick the immune system into action.

When the Rae-1 flag was raised in the skin cells of transgenic mice, local T cells and Langerhans cells became activated, changed their shape, communicated and moved out of the area to launch an immune response. It may be the earliest identified immune response to a potentially cancerous cell, says Michael Girardi, M.D., associate professor of dermatology, whose team worked with researchers from King's College London School of Medicine and the University of Minnesota.

"Now that we have a starting point for the immune surveillance of cancer," says Girardi, "we can begin to look at how it all unfolds."

Early treatment could quiet epilepsy

Epilepsy can be controlled by medication, but not cured. Scientists have wondered whether early drug intervention could suppress the development of certain forms of genetic epilepsy, and a new School of Medicine study backs this idea.

Using a rat model of genetic epilepsy, a team led by Hal Blumenfeld, M.D., Ph.D., associate professor of neurology, neurobiology and neurosurgery, showed that early treatment with ethosuximide—an anti-epileptic drug sold by Pfizer under the name Zarontin—reduced the severity of epilepsy in adulthood. Surprisingly, as reported in the December 2007 issue of *Epilepsia*, the effect persisted after therapy was discontinued.

The researchers began treating the rats at 21 days of age, before they had had any seizures, and continued the treatment until they were 5 months old. The early treatment suppressed the seizures and blocked changes in the expression of several ion channels involved in susceptibility to seizures.

The findings support the idea that seizures have to occur at a critical stage of development for the full epileptic profile to develop, but that this ruthless cycle can be stopped by early intervention.

Gene-hunters search the world for treatments

Genetic disease research is a global enterprise in the post-genomic era

Yale researchers are going to the ends of the earth to find the genetic causes of human disease. The inspiration for their globetrotting comes from the work of Richard Lifton, M.D., Ph.D., chair and Sterling Professor of Genetics, who has pioneered the discovery of human disease genes by studying "outliers," people and families with extreme forms of common diseases.

Lifton's technique depends on finding rare families who show severe forms of inherited conditions like high blood pressure, heart attack or stroke. The far-flung families, who might live in Turkey or Tehran, Brazil or the South Pacific, present a worst-case scenario of genetic mutations that, in milder forms, contribute to the far more common types of the same killers. Each time a gene is uncovered in one of these families, it sheds light on the pathways that underlie related but more widespread diseases, and presents potential new targets for therapies. Using this approach, Lifton and colleagues have identified 10 genes that cause very high blood pressure and 10 that cause low blood pressure.

In the past, Lifton says, human genetics occupied itself with truly rare diseases, like hemophilia or inborn errors of metabolism, but that has changed. "With the tools of the human genome project," he says, "we can now begin to figure out the inherited susceptibilities to virtually every common disease that afflicts mankind."

In a recent example, cardiologist Arya Mani, M.D., assistant professor of medicine, identified a family in Iran with early severe coronary artery disease. The affected members had heart attacks before age 50, and, with Lifton's help, Mani showed that their disease traced back to a single genetic mutation. What's more, this single defect caused diabetes, high blood pressure, and high levels of "bad" LDL cholesterol and fats in the blood. This constellation of risk factors for heart disease is termed metabolic syndrome and occurs together in many Americans. The pathway Mani uncovered, which affects all of these risk factors, presents opportunities for developing new medicines to treat metabolic syndrome and prevent heart disease.

Another Lifton trainee, Murat Gunel, M.D., associate professor of neurosurgery and neurobiology and chief of neurovascular surgery, has forged a link between Yale and his native Turkey to study families with a predisposition to stroke.

Other researchers around Yale have taken Lifton's lead and looked at rare cases to learn about more general causes of disease. In 2005, Matthew W. State, M.D., Ph.D., Harris Associate Professor of Child Psychiatry, identified the first gene whose mutation causes Tourette's syndrome, a common development disorder in children. His discovery and concurrent



By studying individuals with extreme forms of common diseases, Richard Lifton has discovered genes that underlie the forms that affect most of us.

findings from Jeffrey R. Gruen, M.D., associate professor of pediatrics, of a gene involved in the learning disability dyslexia were both cited in a list of the top 10 scientific breakthroughs of 2005 by the leading journal *Science*.

An alternative approach to unlocking the genetic secrets of common diseases is also flourishing at Yale. In contrast to rare mutations with dramatic effects, there are numerous common variations in many genes that have relatively small effects on disease on their own, but collectively can add up to a big risk for conditions like heart disease, autism or Alzheimer's disease.

Finding these small effects requires collecting a large number of patients and an equally large number of matched control subjects without the disease. Then, researchers must scan half a million spots on the DNA of each person to find the differences in their genetic codes. After that, sophisticated mathematical models determine if there is an association between particular genetic differences and disease.

Two of the earliest successes of this whole-genome association approach took place at Yale. In 2005, a group led by Josephine J. Hoh, Ph.D., associate professor of epidemiology and of ophthalmology and visual sciences, identified common variants in an immune protein associated with age-related macular degeneration (AMD), the leading cause of blindness among the elderly. In 2006, Hoh joined with collaborators in Hong Kong, comparing Chinese and Caucasian populations with AMD to zero in on a gene involved in the most serious, "wet" form of the disease. Also in 2006, Judy H. Cho, M.D., associate professor of medicine and genetics, uncovered the involvement of another immune signaling molecule, the interleukin-23 receptor, in Crohn's disease, an autoimmune inflammation of the intestinal tract.

A third and extremely active avenue of human genetic research at Yale does not even involve humans, at least not directly. The time-honored staples of basic genetic research—that

Genetics, page 8

MEDICINE » tomorrow

Yale School of Medicine is known worldwide for its cutting-edge research on the genetic bases of human disease. You can help to realize the promise of new treatments, the development of personalized medicine and breakthroughs that will lead to the prevention of disease by supporting our researchers and clinicians. The gift opportunities listed below can fund important work in genetics or in any other area of donor interest.

Professorship **\$3 million**
To assist a distinguished faculty member's research and scholarly activities

Yale Scholar **\$2.5 million**
To support a newly recruited young investigator for four years; gifts are eligible for 100 percent in matching funds from Yale University

Research Fund **\$100,000 or more**
To support research conducted by teams of faculty and graduate students

Technology Fund **\$100,000 or more**
To expand and upgrade technical resources and fund specialized staff

For more information about gift opportunities, visit yaletomorrow.yale.edu/medicine or contact Jancy Houck, Associate Vice President for Development and Director of Medical Development at (203) 436-8560.

Out & about



July 19, 2007: Representatives of the ABB Foundation visited Yale Cancer Center to learn how the foundation's gift to establish a **NEW LUNG CANCER TISSUE BANK** will help to initiate new research into the prevention and treatment of lung cancer. The ABB Group, a technology-based provider of power and automation products, systems, solutions and services headquartered in Zurich, Switzerland, employs over 100,000 people in approximately 100 countries; the ABB Foundation donated \$20,000 to launch the new tissue bank. Profes-

or of Surgery **Frank C. Detterbeck, M.D.**, recently treated ABB U.S. Employee Pat Sclafani of Marlborough, Conn., for a rare cancer of the thymus gland. (From left) **Julie Guarino**, president of the ABB Foundation; **Robert J. Homer, M.D., PH.D.**, associate professor of pathology and medicine; **Lori Lampman**, manager of human resources at ABB Ltd. in Norwalk, Conn.; Detterbeck; **David L. Rimm, M.D., PH.D.**, professor of pathology; **Shevaun Macari**; and **Danielle DeStefano**.



November 9: Students, faculty and members of the community converged on the medical school's Harkness Ballroom for the annual student-run **HUNGER AND HOMELESSNESS AUCTION**, which raised \$30,000 for New Haven-area social service agencies (see related story, p. 2). **1.** (From left) Auctioneer **Wade Brubacher**, father of second-year medical student Jake Brubacher, shares a light moment with **Jessica Beer** and **Thea Cogan-Drew**. **2.** (From left) **Corey Frucht**, **Matty Vestal** and **Heather Speller**. **3.** (From left) **Maya Hasan**, **Anna Engberg**, **Dominique Caruso**, **Sarah Bailey**, **Kathleen Lacci** and **Patricia Peter**.



January 17: In conjunction with the **WORLD PREMIERE OF ANNA DEAVERE SMITH'S LET ME DOWN EASY** at New Haven's Long Wharf Theatre, faculty and friends of the Department of Internal Medicine gathered at Sage Restaurant for an update on the medical school's collaboration with Makerere University and Mulago Hospital in Kampala, Uganda. **1.** Smith (center) with **Ashgar Rastegar, M.D.**, professor of medicine, and **Richard L. Edelson, M.D.**, professor of dermatology and director of Yale Cancer Center. **2.** (From left) **Margaret J. Bia, M.D.**, professor of medicine, **Michele Barry, M.D.**, professor of medicine and public health, and **Rita Berkson**, executive director of the Goldhirsh Foundation. **3.** **David Roer, M.D.**, and **Majid Sadigh, M.D.**, associate professor of medicine. **4.** Emmy and Tony Award-winning actress **Blythe Danner**. **5.** **Nicholas and Sandra DeRoma**. **6.** **Nancy and**



Garry Leonard. **7.** **Stephen A. Stein, M.D.**; **Randolph B. "Randy" Reinhold, M.D.**, chair of surgery at the Hospital of St. Raphael in New Haven; Berkson; and **Mark R. Cullen, M.D.**, professor of medicine and of epidemiology and public health. **8.** **Christopher Woerner** and **Bruce L. McClennan, M.D.**, professor of diagnostic radiology. **9.** **Angie Perroto**, **Patricia King**, Sadigh and **Lynn Gambardella**.



Advances

Health and science news from Yale



Running depression out of our lives

Feeling down? Go for a run and put your genes to work. According to a new Yale study, the well-known antidepressant effects of exercise may be due to genes in the brain that are switched on by physical activity.

In the December 2007 issue of *Nature Medicine*, former graduate student Joshua Hunsberger, Ph.D., and a team led by Ronald S. Duman, Ph.D., Elizabeth Mears and House Jameson Professor of Psychiatry and Professor of Pharmacology, reports that exercise reduced depression-like behavior in mice and also boosted the activity of a gene called *vGF* in the hippocampus, a brain region that has been strongly implicated in depression in humans.

Mice given free access to a running wheel had higher levels of *vGF* expression in the hippocampus than sedentary mice. These results were bolstered by experiments showing that infusing a synthetic form of *vGF* directly into the hippocampus had potent antidepressant effects; conversely, mice in which the *vGF* gene had been knocked down showed more depression-like behavior than those with the gene.

The authors say that the development of new therapies that target *vGF* could have “superior efficacy to existing chemical antidepressants.”

Arthritis therapy stops diabetes in its tracks

In type 1 diabetes, an autoimmune disease, the T cells of the immune system attack the cells of the pancreas that produce insulin, making it impossible for the body to control blood sugar levels. B cells are also involved in the process but their exact role is unclear.

Drugs that deplete B cells have been effective in controlling other autoimmune diseases, such as rheumatoid arthritis, and some forms of lymphoma. Li Wen, M.D., Ph.D., senior research scientist in the Department of Medicine, wondered if the same approach might be useful in treating type 1 diabetes.

Using mice that were specially bred to be predisposed to the disease, Wen and her colleagues found that rituximab, an antibody that binds to B cells, could delay the onset of diabetes in mice that had not yet developed it. As reported in the December issue of *The Journal of Clinical Investigation*, in additional experiments, some mice with diabetes no longer needed insulin after they had received the antibody treatment.

Alumnus is winner of Yale's highest honor

Yale Medal recognizes physician's seven decades of service to alma mater

Samuel D. Kushlan, M.D., received many honors throughout a distinguished career spanning seven decades. But last November brought a particularly proud moment for Kushlan—a “double blue” who graduated from Yale College in 1932 and from the School of Medicine in 1935—when he received the Yale Medal in recognition for his innumerable contributions to his alma mater. The medal, the highest award bestowed by the Association of Yale Alumni (AYA), is given annually to five alumni in honor of outstanding service to the university.

Although Kushlan officially retired from medicine in 1982, a typical morning still finds him at the School of Medicine or Yale-New Haven Hospital attending “morning report” on patients, reading journal articles in the medical library or going to internal medicine grand rounds. At 95, Kushlan still drives almost every day to the hospital where he has worked for 70 years and continues to be a role model for younger colleagues.

Born in New Britain, Conn., in 1912, Kushlan was so inspired by his local doctor that he knew he wanted to be a physician by the age of 10. After graduating from the School of Medicine, he completed his residency at what was then New Haven Hospital, earning a salary of \$25 a month. His main diagnostic tools were taking a medical history and doing a physical exam—X-rays were the only imag-



Samuel and Ethel Kushlan celebrated at the Yale Medal awards ceremony.

ing technique available; and in those pre-penicillin days, the principal medications were aspirin, digitalis, phenobarbital, quinine and morphine. “Medicine was very primitive 70 years ago,” he recalls. Today more than 4,000 medications are listed in the *Physicians' Desk Reference*.

Except for a brief stint at Harvard in 1938, Kushlan spent his entire career at Yale. He established the first endoscopy clinic in Connecticut in 1942 and was the sole member of Yale's gastroenterology section from 1938 until 1955.

From 1967 until his retirement, Kushlan served as the associate physician-in-chief at Yale-New Haven Hospital and as a clinical professor of medicine. When he retired, one of the hospital's medical services was named for him, although he said he feels out of place among the other legendary physicians—Elisha Atkins, M.D.; John P. Peters, M.D.; Gerald Klatskin, M.D.; Allan Goodyer, M.D.; and Robert Donaldson, M.D.—with whom he shares this honor.

Although he says he does more learning than teaching these days, Kushlan still has wisdom to impart from the days when the practice of medicine relied more on observation than on diagnostic tests.

He advises colleagues to use such simple diagnostic methods as having a patient with back pain lie down to determine its source: if the pain goes away, it's muscular; if it doesn't, it's internal.

“I sort of toss in a pearl from time to time to pay my way,” he says.

In addition to his activities at the hospital and the lectures and concerts he regularly attends with Ethel, his wife of 73 years, Kushlan also remains an active member of the executive committee of the Association of Yale Alumni and Medicine. He has established Merit Awards for the Medical House Staff and Digestive Disease Fellows and has volunteered his time and resources to create a Capital Visiting Professorship in Gastroenterology.

“I enjoy the opportunity to be busy,” he says.

Implant lets patients put the best foot forward

All of us seem to know someone who has had a hip replacement or knee replacement (if not two). But the ankle's position in the hierarchy of artificial joints corresponds roughly to its location at the bottom of the body. Now a School of Medicine team—armed with prostheses that better mimic the ankle's structure—aims to raise the stature of this crucial joint.

The development of a prosthetic hip in the early 1960s set the modern standard for joint replacement, followed by advances in other manmade joints. “We know a ton about the knee. We know a ton about the hip,” says John S. Reach Jr., M.D., assistant professor of orthopaedics and the director of the newly reconstituted Yale Foot and Ankle Service. “The foot, in medicine, hasn't been looked at much at all. It just hasn't gotten enough respect. A hip is easy to put in; it's a ball and socket. An ankle is pretty complex. It's small. It's fussy.”

Prosthetic ankles have “lagged behind, but not for lack of trying,” Reach says, but they have come a long way from 19th-century efforts to fashion a ball and stem from elephant tusks. The first modern artificial ankle, developed in the 1970s, was a basic hinge, but doctors learned quickly

that the apparently simple joint is much more complex. The latest generation of prosthetic ankles more closely follows the joint's anatomy, and “look more like what God gave you,” says Reach.



John Reach

The new implant—made of titanium, chromium and plastic—replaces the top of the ankle bone and the base of the shin bone. Because it's modular, each part can be tailored to the patient. In November, Reach performed Connecticut's first total ankle replacement with the new device, called the Inbone, on a 38-year-old man whose life was upended in a bizarre auto accident one Sunday in 1994.

The patient, Damian Diaz, who lives in the Fair Haven neighborhood of New Haven lost an eye, a shoulder, and his lower left leg in the crash, when a wheel came off an axle and burst through the floorboard. He had 30 surgeries, and though he felt lucky to be alive, the pain in his right ankle limited his walking to no more than a few steps. “My bone was disappearing,” Diaz said. “I could not live with the hurt every day.”

Diaz was a good candidate for total ankle replacement. Trauma patients often develop severe ankle arthritis, and though it's less common than hip or knee arthritis, Reach expects the incidence of post-traumatic arthritis to rise—partly because medicine and safety advances enable younger people to survive trauma like that Diaz endured. Car airbags protect the upper body, but “people are left with horribly mangled feet,” he says. “When you have pain in the joints, it's bad. It's bone against bone.”

The first lines of treatment are painkillers and braces. Another established option is fusing the ankle bones, but that can leave patients with a permanent limp and lead to further arthritis and, perhaps, amputation.

However, a recent review of the literature found that 1 percent of patients who had a total ankle replacement needed an amputation, compared to 5 percent of the fusion patients.

Reach suspects that 85 percent of the new prosthetic ankles will last at least eight years, and Diaz says that he's happy so far. “I'm waiting to get used to it, but I'm walking,” he says. “It doesn't hurt any more.”

munobiology research program in the country and is also well known for its strength in dermatology. (Department founder Aaron Lerner, M.D., PH.D., discovered the hormone melatonin, and his work laid the foundation for skin cancer treatments as well as the modern science of dermatology.) The medical school has built a major program in medical oncology in the last three years, recruiting close to a dozen new faculty members with expertise in all the major cancers.

“Those three groups can bring it all together,” says Alpern, adding that support for cancer research and care is a top priority in the medical school’s development plan. “What we have in place is excellent, but we need to grow it.”

Sznol says the gift will enable the Yale program to expand and grow. The SPORÉ grant provides gener-

ous funding for basic laboratory and translational research, as well as limited funding for human studies. The next step—and the essential phase in the process to discover new treatments—is the development of more investigator-initiated clinical trials, which the Milstein Meyer Center will enable by providing funds for research nursing, data management, administrative and regulatory assistance, and other support.

“Clinical research is expensive, and it takes time,” says Sznol, former head of the Biologics Evaluation Section of the NIH Investigational Drugs Branch. “This gift from the Meyers will move us forward in a very significant way. It will improve our ability to design new treatments based on the very strong fundamental science that is already in place here, and ultimately test them in humans. You can’t de-

velop cures in humans without doing clinical research, and treating humans is a lot different than treating mice.”

Roz Meyer says both she and her husband “are the kind of people who roll up our sleeves and jump in.” In 1991 they co-founded New Haven’s Leadership, Education and Athletics in Partnership (LEAP), an academic and social enrichment program designed to help children in New Haven’s high-poverty neighborhoods. The program soon grew to serve thousands of young people in five cities across Connecticut.

Five years later, Meyer and LEAP co-founder Anne Tyler Calabresi, joined by Jean Handley, launched the city’s International Festival of Arts and Ideas, which brings performers and artists from around the world to New Haven annually during two weeks in June.

Like those efforts, the Meyers consider their support for cancer research “a way to make something happen that otherwise would not have been possible.”

“We’d like it to cause people to take responsibility, if they have the capacity, to support the things they care about,” says Roz Meyer. It also brings the couple back full circle to their commitment to New Haven, says Jerry Meyer, who sees medical research at the core of the city’s identity in the post-war, post-industrial era.

“New Haven’s economy used to be armaments, with the Winchester, U.S. Repeating Arms and Marlin firearms factories located here,” says Meyer, who closed his clinical practice in the late 1990s and now works as an artist. “Now our industry is arts and ideas, and Roz and I feel very lucky to be a part of it.”

Dyslexia from page 1

strong alliance in place with Anna Gillingham, a pioneer educator and protégée of Samuel T. Orton, M.D., the father of dyslexia research.

“From that experience, and throughout my life, I have maintained an interest in the teaching of reading and the challenges involved,” Ratner says. “I have discovered that an entire network of helpful ongoing research and teaching has developed around the world and I have long been aware of the important work Sally Shaywitz and her husband, Bennett, were doing at Yale.”

Ratner, an active volunteer in the Cleveland area, is mother to three children and two stepchildren, and a grandmother of 14. According to her daughter, Karen Pritzker, of Branford, Conn., she plays the role of “education and reading maven” to family members and friends, giving counsel about spotting and accommodating learning disabilities, and peppering her advice with the facts about learning and learning styles that she has gleaned over years of classroom teaching, course work and her own reading and research.

Says Sally Shaywitz, “Audrey was interested in reading long before it was fashionable because she really understood children, and she had an insight about the importance of teaching reading and how to get it right.”

Shaywitz has championed the idea that the reading and spelling

difficulties at the heart of dyslexia often occur in tandem with ingenious, imaginative, “out-of-the-box” thinking that dyslexic individuals can draw on to excel in educational and economic systems dominated by the printed word. In *Overcoming Dyslexia*, Shaywitz chronicled the lives of several creative and highly successful Americans with dyslexia, including bestselling novelist John Irving, Pulitzer Prize-winning playwright Wendy Wasserstein and financial-services magnate Charles Schwab.

At the newly formed Yale Center for Dyslexia and Creativity (YCDC), Shaywitz and her colleagues are devising experiments and using brain-imaging techniques to explore these ideas scientifically, and she calls the Ratner Professorship an “anchoring gift” in support of these efforts. “This gift ensures that there will be an ongoing presence at Yale of scholars who are interested in these issues and who have made advancing the cause of dyslexic children and adults their focus,” Shaywitz says. “It links Yale with scholarship in dyslexia in a permanent way, and sends the message that a premier institution like Yale values people who are dyslexic and those who work in the field.”

In an age in which much of a child’s future is determined by high-stakes standardized written tests, Shaywitz says that she and her husband are gratified that their work has provided neurobiological evidence

of the need for extra time for dyslexic individuals taking these tests. The Shaywitzes’ research has shown that a region on the left side of the back of the brain known as the word-form area operates less efficiently in dyslexic subjects than in normal readers. Neural circuits in this area allow normal readers to move from accuracy—reading a word correctly—to fluency, where these readers can simply look at a word and instantly know it. As many as one in five children, however, are dyslexic; they can learn to read accurately, Shaywitz says, but not fluently.

“If you’re a good reader and you can use that word-form area well, you can look at a word and you’re on the express highway to reading. But if you’re a dyslexic, that route is blocked and you have to get off and take a ‘country road’—it’s circuitous, and it’s bumpy,” says Shaywitz. “You can get where you’re going, but it takes a lot longer. Just as a diabetic requires insulin, a dyslexic requires extra time.”

World-renowned heart surgeon Delos M. “Toby” Cosgrove, M.D., a dyslexic, is a case in point. Rejected by 12 out of the 13 medical schools to which he applied because of poor test scores, Cosgrove rose in the ranks of medicine to become CEO of The Cleveland Clinic, one of the world’s premier centers for health care. An acquaintance of both Shaywitz and Ratner, Cosgrove applauds the new Ratner Professorship as “honoring two outstanding women.” Cosgrove



Children visiting Sally Shaywitz’s office at the Child Study Center find a menagerie of stuffed animals and kites.

adds that Shaywitz’s pioneering research has done much to destigmatize dyslexia, spreading the word that people like him are “not dumb, just different.”

For Ratner, seeing Shaywitz named to the professorship established in her name is like completing a circle. “Helping a young person to achieve reading skills has been one of the most rewarding and fulfilling activities in my life,” Ratner says. “Sally Shaywitz has taken all that was known before her time and utilized all the technology of today with her expertise, love and devotion to the task. She is the Queen of Hearts.”

Expert on women’s health issues is honored for leadership

Carolyn M. Mazure, PH.D., associate dean for faculty affairs, professor of psychiatry and of psychology and director of Women’s Health Research at Yale (WHRY), has received the 2007 Marion Spencer Fay Award, which honors a distinguished woman physician or scientist whose national leadership has had a major impact on research and the application of science to health care.

The award recognizes Mazure’s accomplishments as the head of WHRY, an innovative program that spear-

heads new investigations in women’s health, and for her own research



Carolyn Mazure

contributions in the field of depression.

“Professor Mazure is an outstanding national leader in women’s health research, and has pioneered the integration of science, educational outreach and policy development in this field,” says Dean Robert J. Alpern, M.D.

The National Board for Women in Medicine established the award in 1963 in honor of Marion Spencer Fay, the dean and president of Woman’s Medical College of Pennsylvania, now Drexel University College of Medicine (DUCM) from 1946 to 1963.

Today the Institute for Women’s Health and Leadership at DUCM, which addresses health issues of women and promotes women in medical education, oversees the award selection. Lynn Yeakel, the Betty A. Cohen Chair in Women’s Health and

director of the institute, presented the award to Mazure in Philadelphia on December 6.

Past winners of the Marion Spencer Fay Award include Mary-Claire King, PH.D., professor of genome sciences and of medicine at the University of Washington School of Medicine, who is best known for identifying important genes involved in breast cancer, and Catherine D. DeAngelis, M.D., the first woman to be appointed editor of *JAMA: Journal of the American Medical Association*.

Family sharing a risky mutation now shares newfound hope

To head off thyroid cancer, a Yale surgeon operates on six family members

Last June, Beverly Block Lewis, part of a family of cattle farmers from Monroe, Conn., learned that she had medullary thyroid cancer. Her Yale surgeon, Julie Ann Sosa, M.D., who specializes in treating the disease, decided to do genetic tests to determine whether Lewis was carrying genetic mutations that contributed to her illness.

Sosa found that Lewis' 10th chromosome harbored a mutation in a gene known as *MEN2A* that causes a rare and severe form of thyroid cancer. Since this discovery, 13 members of Lewis' extended family were found to carry the mutation and 10 have had their thyroids removed. Six surgeries took place at Yale-New Haven Hospital (YNHH) under the supervision of Sosa, assistant professor of surgery.

Sosa says that the *MEN2A* mutation that the Block family carries is extremely rare and that most families in this country with the condition have been known to researchers for years. Sosa herself follows five such families. "Many endocrinologists go their whole lives without seeing any cases of this mutation," she says.

Lewis already had hypothyroidism, a deficiency of thyroid hormone, which she inherited from her mother's side of the family and was the reason for the routine endocrinology appointments that revealed her

cancer. The family assumed Lewis' thyroid cancer must also have been inherited from the maternal side.

But further testing showed that Lewis inherited the *MEN2A* mutation from her father, Burton Block, who was also found to have asymptomatic thyroid cancer. Two of Beverly's siblings, her son and two nephews were also diagnosed with the mutation. All but her 4-year-old nephew Jake were found to have developed cancer.

"Every diagnosis was a new blow," says Alyce Block, Beverly's mother. "Every time was as hard as the first." Beverly's recently married son Aaron Lewis, 28, says that one of the biggest challenges was thinking about future generations: "Kids that aren't even born yet are going to be affected."

Over the next several months, YNHH became like a second home for family members, who were constantly in and out of the hospital with each successive surgery.

But every operation went well and the family pulled through. After his surgery, 83-year-old Burton also survived a near-fatal car accident that landed him back at YNHH, just doors away from where his son Dan was recovering from his own thyroid surgery.

Though the horizontal scars across their throats are now fading, they serve as reminders to members of the Block family that genetic testing may have helped many of them to avoid a deadly disease.

Last August, more than a year after the family's medical saga began,



(From left) Daniel Block, Jake Block, Aaron Lewis, Alyce Block and Beverly Lewis have faced aggressive thyroid cancer as a family. A mutation inherited from Alyce Block's late husband, Burton Block, causes the rare cancer.

Burton Block died from pancreatic cancer, which was unrelated to the thyroid cancer.

But his strength, Beverly and Alyce Block say, was what helped the family through the year. Standing at Burton's

bedside a month before his death, Beverly told family members, "He's really taught us a tremendous amount about strength and patience."

"And the importance of a close-knit family," added Alyce.

Grants and contracts awarded to Yale School of Medicine

May/June 2007

Federal

Hervé Agaisse, NIH, *High-Throughput Assays for Imaging Human Intracellular Pathogen Infections*, 3 years, \$1,115,907 • **Norma Andrews**, NIH, *Molecular Determinants of Intracellular Survival and Replication in Leishmania*, 4 years, \$3,903,249 • **Jonathan Bogan**, NIH, *Insulin-Stimulated Ubiquitin-Like Modification*, 5 years, \$1,529,795 • **Titus Boggon**, NIH, *Structural Basis of Jak3-Mediated Interleukin-2 Family Signal Transduction*, 5 years, \$2,060,895 • **Alfred Bothwell**, NIH, *Generation of Synthetic Human Islet Microorgans*, 4 years, \$1,355,905 • **Valeria Busygina**, NIH, *Role of BLM Protein Complex in the Maintenance of Genome Integrity*, 1 year, \$49,646 • **Lawrence Cohen**, NIH, *Optical Studies of Neuron Activity and Organization*, 1 year, \$412,500 • **Michael Crair**, NIH, *Yale Core Grant for Vision Research*, 5 years, \$2,423,665 • **John Forrest**, NIH, *Short-Term Research Training: Students in Health Professional Schools*, 5 years, \$1,078,790 • **Nigel Grindley**, NIH, *Structure and Function of DNA Polymerase I of E. coli*, 4 years, \$2,393,726 • **Stuart Hicks**, NIH, *S. typhimurium Leucine-Rich Repeat Effector Proteins*, 3 years, \$153,822 • **Fahmeed Hyder**, NIH, *Core Center for Quantitative Neuroscience with Magnetic Resonance*, 5 years, \$3,730,341 • **Shrikant Mane**, NIH, *GeneChip Automation and MegAllele System for Microarray Analysis at Yale University*, 1 year, \$1,054,868 • **Daniel Mathalon**, NIH, *Functional Brain Abnormalities in the Schizophrenia Prodrome*, 5 years, \$2,559,966 • **Laura Ment**, NIH, *Gene Targets for Intraventricular Hemorrhage*, 5 years, \$8,024,951 • **Drew Murphy**, NIH, *The Effect of MRE11/RAD50 on Fidelity of Synthesis by DNA Poly-*

merase Beta, 1.5 years, \$66,739 • **Chirag Parikh**, NIH, *Novel Biomarkers in Cardiac Surgery to Detect Acute Kidney Injury*, 5 years, \$3,884,530 • **James Poling**, NIH, *Pharmacotherapy and Contingency Management for Opioid and Cocaine Dependence*, 5 years, \$2,136,192 • **Robert Roth**, NIH, *Chronic PCP Primate PFC Dopamine Deficit and Schizophrenia*, 5 years, \$2,615,109 • **David Schatz**, NIH, *Immunoglobulin and T Cell Receptor Gene Assembly*, 5 years, \$1,653,917 • **Gerald Shadel**, NIH, *Mitochondrial Dysfunction and Oxidative Stress in Ataxia-Telangiectasia*, 5 years, \$1,808,971 • **Sally Shaywitz**, NIH, *The Connecticut Longitudinal Study in the Fourth Decade*, 3.5 years, \$3,274,067 • **Mark Shlomchik**, NIH, *LSR II Flow Cytometer Analyzer*, 1 year, \$339,163 • **Hugh Taylor**, NIH, *Alteration of HOX Gene Expression by Endocrine Disrupting Chemicals*, 5 years, \$1,757,111; NIH, *Center for Endometrial Biology and Endometriosis*, 5 years, \$6,492,789 • **Flora Vaccarino**, NIH, *Inhibitory Interneurons in Tourette Syndrome*, 4 years, \$1,042,521 • **Lawrence Young**, NIH, *Visual Sonics Vevo 770 Imaging System*, 1 year, \$274,450 • **David Zenisek**, NIH, *Development of a Model System for Presynaptic Study*, 2 years, \$454,375 • **Tongzhang Zheng**, NIH, *Research Training for Environmental Health Study in China*, 5 years, \$611,250 • **Yufeng Zhou**, NIH, *Structural Basis of the Binding of Blockers to Potassium Channels*, 5 years, \$1,488,450

Non-Federal

David Cone, Nat'l Association of EMS Physicians, *Disaster Triage Research Using Virtual Reality*, 1 year, \$6,500 • **Daryn David**, American

Psychoanalytic Association, *Investigating the Internal Working Model*, 1 year, \$13,287 • **Nancy Dunbar**, Cystic Fibrosis Foundation, *Characterization of Cystic Fibrosis Bone Disease*, 1 year, \$36,500 • **Caroline Easton**, Children's Community Programs of CT Inc., *New Haven Educational Reentry and Delinquency Program*, 1 year, \$90,849 • **Cynthia Epperson**, March of Dimes, *Effectiveness of Cognitive Processing Therapy in Reducing Post-Traumatic Symptoms and Enhancing Birth Outcomes in Pregnant Women with a Previous Pregnancy Loss or Complication*, 3 years, \$220,101 • **Jason Fletcher**, American Educational Research Association, *Examining the Effects of Full Inclusion on the Classmates of Children with Special Needs*, 1 year, \$19,800 • **Gerald Friedland**, Doris Duke Charitable Foundation, *Combating MDR and XDR TB and HIV in Rural South Africa*, 2 years, \$200,000 • **Rosana Gonzalez-Colaso**, Physician Assistant Education Association, *Physician Assistant Utilization Among Children with Special Health Care Needs: Type of Provider and Satisfaction with Care*, 1 year, \$8,000 • **Keith Hawkins**, Hartford Hospital, *Schizophrenia Biomarkers: Memory, Genes and Functional Magnetic Resonance Imaging*, 1 year, \$10,795 • **Amy Justice**, Brigham and Women's Hospital, *Genetic and Inflammatory Factors in Anemia in the Elderly*, 1 year, \$53,218 • **Jonathan Knisely**, Radiation Therapy Oncology Group, *Hypoxia, Stem Cell Markers, and DNA Repair Genes in Glioblastoma Multiforme—Correlation with Prognosis*, 1.5 years, \$50,000; HistoRx, Inc., *Glioblastoma Tissue Microarray Clinical Data Abstraction Project*, 0.5 years, \$41,106 • **Qiang Leng**, Iowa State University, *Pain Receptor Mediated Anti-Inflammatory Activity of Echinacea and Other*

Species, 1 year, \$78,388 • **Sheng-Fu Lo**, Howard Hughes Medical Institute, *The Role of TGF- β , IL-17, and Th17 Cells in Cerebral Aneurysm Formation and Rupture*, 2 years, \$36,000 • **Prakash Nadkarni**, Massachusetts General Hospital, *Cancer Genetics Network*, 5 years, \$659,494 • **Peter Rabinowitz**, Mary Imogene Bassett Hospital, *Occupational Risk Factors for Infection in Northeastern Poultry Workers*, 1 year, \$20,000 • **Lynne Regan**, University of Washington, *Combining Computation and Selection in Protein-Ligand Design*, 0.5 years, \$52,794; Human Frontier Science Program Organization, *The Folding of Helical Repeat Proteins*, 3 years, \$462,000 • **Marc Rosen**, University of California—Los Angeles, *Multi-Site Collaborative Study for Adherence: Virologic and Clinical Outcomes*, \$96,300 • **Eugene Shapiro**, Northern Illinois University, *Long-Term Outcome of Childhood Onset Epilepsy*, 1 year, \$341,575 • **Frederick Sigworth**, Harvard University, *Atomic Resolution in Biological Electron Microscopy*, 1 year, \$273,999 • **Benjamin Turk**, University of Medicine and Dentistry of New Jersey, *Regulation of Metal Ion Homeostasis by Channel Kinases*, 1 year, \$75,994 • **Mary Warner**, Physician Assistant Education Association, *Career Patterns in Physician Assistants: A Retrospective Longitudinal Study*, 1 year, \$10,806 • **Sherman Weissman**, March of Dimes, *Precise Definition of Genomic Alterations Associated with Velo-Cardio-Facial Syndrome (VCFS)*, 3 years, \$325,719 • **John Wysolmerski**, University of Pennsylvania, *Intercellular Signaling in Embryonic and Postnatal Mammary Gland Development*, 10 months, \$13,699

Awards support research on health disparities, depression

Two Yale scientists named Donaghue Investigators by Connecticut foundation

Two research projects by Yale School of Medicine investigators—one on health care disparities, and the other on depression—have been given a boost with five-year, \$600,000 awards from the West Hartford, Conn.-based Patrick and Catherine Weldon Donaghue Medical Research Foundation for Health-Related Research.

The Investigator Awards to Jennifer Prah Ruger, PH.D., assistant professor in the Division of Health Policy and Administration at Yale School of Public Health, and Alexander Neumeister, M.D., director of the Molecular Imaging Program in the Clinical Neuroscience Division of the Depart-

ment of Psychiatry, are intended to support particularly promising and highly talented medical researchers holding academic appointments at Connecticut institutions.



Jennifer Ruger

Ruger is studying how to reduce disparities in health care, specifically among women, adolescents, minorities and other groups. Her goal is to translate her findings into programs that make more efficient use of scarce resources while improving clinical and public-health practice.

Ruger has found that global health inequalities are substantial and growing, and that these disparities are influenced by economic, social and

health-sector variables as well as by geography. She recently co-authored a study showing that those individuals in most need of medical care in Korea, but who can least afford it, spend a far greater percentage of their income on health services than do wealthier citizens.

“The Donaghue Investigator Award,” Ruger says, “will be invaluable in furthering my research on the ethics and economics of health and health care disparities in the United States and across the globe.”

Neumeister is studying the neurobiology of depression and post-traumatic stress disorder. He is particularly interested in the relationship between trauma and stress and the risk of developing depression. Neumeister will conduct brain imaging studies using positron emission

tomography (PET) in collaboration with researchers from the Yale PET



Alexander Neumeister

Center to identify novel targets for drug development. This is of particular relevance since previous research has shown that currently available treatments for people with depression and a lifetime history of severe trauma have only modest benefits.

“This funding will allow us to study a very severely ill patient population which has not yet received sufficient attention and is very difficult to treat,” Neumeister says. “This award will yield important novel results that are expected to benefit people with depression and trauma.”

Advocates for universal preschool share education prize

Three scientists associated with the School of Medicine’s Edward Zigler Center in Child Development and Social Policy (EZC) have won the 2008 Grawemeyer Award in Education from the University of Louisville. The EZC, operated under the aegis of the medical school’s Child Study Center (CSC), is devoted to improving the well-being of children and families by bringing objective child development research into the policy and public arenas.

The award, which carries a \$200,000 cash prize, is shared by Edward Zigler, PH.D., Sterling Professor Emeritus of psychology at Yale; Walter S. Gilliam, PH.D., assistant professor in the CSC and EZC director; and Stephanie Jones, PH.D., a recent doctoral student of Zigler’s who is now assistant professor of psychology at Fordham University.

In a 2006 book entitled *A Vision for Universal Preschool Education*, Zigler, Gilliam and Jones drew on four decades of research to present a compelling case for dramatically increasing access to preschool education in the United States.

Forty states now fund pre-kindergarten programs, Zigler, Gilliam and Jones found, but these programs enroll fewer than 10 percent of all preschoolers.

The Yale team argues that universal preschool would improve the school-readiness of the nation’s young children, fill a gap for working families, lower the high school dropout rate, reduce crime and boost the economy.

The book “stands alone in its field for its accessibility, clarity, timeliness and ability to combine a solid



Edward Zigler



Walter Gilliam



Stephanie Jones

research background with practical recommendations,” said their award nomination.

Zigler is best known for his work on intervention programs for economically disadvantaged children, especially the Head Start program, founded in the mid-1960s.

Gilliam conducts research on the effects of preschool programs on school readiness, while Jones studies the social and emotional aspects of early childhood and adolescence.

The Grawemeyer Foundation, established by industrialist, entrepreneur and University of Louisville alumnus H. Charles Grawemeyer, awards a total of \$1 million each year for outstanding achievements in education,

psychology, music composition, ideas improving world order, and religion.

This is the second year that research at the CSC has been honored by the foundation. The 2007 Grawemeyer Award in Education was awarded to James P. Comer, M.D., the Maurice Falk Professor of Child Psychiatry at the CSC, who founded the School Development Program, which has formulated a strategy for improving education that has been applied in over 1,000 schools worldwide.

Excellence from page 1

Comprised of over 800 School of Medicine physicians in more than 100 specialties and subspecialties, and affiliated with Yale-New Haven Hospital, YMG is one of the largest academic group medical practices in the United States. The continued development of YMG has been one of Alpern’s top priorities since he arrived at Yale in 2004; he named Leffell deputy dean for clinical affairs in 2005.

“David has provided outstanding leadership for YMG. This generous gift from David and Cindy represents another step forward in achieving our vision for Yale to be a clinical center of excellence where patients

can expect to be treated by the best physicians in a respectful and patient-centered manner,” Alpern explains. “Winners of this award will represent everything that our clinical practice is about.”

According to Leffell, also professor of dermatology and surgery and an expert on skin cancer, the School of Medicine’s undisputed strengths in research have often overshadowed the importance of its clinical mission. “It’s not that people at Yale disrespect the practice of medicine, it’s just that historically most people here have been researchers and haven’t fully expressed their commitment to clinical medicine,” Leffell says. “This

gift stems from my belief that Yale can and should be a leader in clinical medicine.”

Leffell believes that Yale’s research tradition needn’t be at odds with the patient care provided by YMG physicians, but rather that the two spheres are complementary. “A core element of my vision for the Yale Medical Group is promoting clinical research and launching new clinical trials, and that’s what can distinguish us from other similar large academic group practices,” he says. “But this can’t be at the expense of top-of-the-line patient service. We should be able to do it all.”

As section chief of YMG’s Dermatological Surgery practice, Leffell has

motivated his colleagues to achieve these goals.

According to surveys by Press Ganey, a leading patient-satisfaction assessment firm, the dermatologic surgery practice—one of the largest in the country, with over 11,000 patient visits per year—ranks first at the medical school and is in the 99th percentile nationwide. In addition, the practice conducts clinical research and trials of new treatment options in cutaneous oncology and related areas.

Of his hopes for the new award, Leffell says, “If fostering clinical excellence enhances Yale’s reputation as a clinical destination of choice, it will be well worth it.”

Genetics from page 3

is, simple model organisms including mice, fruit flies, fish and worms—are increasingly being drafted to study human disease mechanisms. “A lot of biology is conserved from these simple organisms all the way up to humans,” explains Professor of Genetics Tian Xu, PH.D. “So, when we identify mutations in these simple

systems, they are proving to be directly applicable to humans.”

By finding cancer-causing mutations in fruit flies, Xu’s research formed the basis for an experimental drug now in human testing. Recently, Xu developed a novel method for rapidly producing large numbers of mice with single-gene mutations, and he is

working with neuropsychiatrist State to identify mutants with interesting behavioral symptoms. The researchers will then examine those genes in State’s collection of 1,000 families with various neurological conditions. “This will dramatically speed up the process of discovering disease genes in humans,” Xu says.

Even Xu’s mice are international travelers. Much of the breeding work for his project is being done in China, but the mice will soon be shipped to Yale’s new West Campus in West Haven, Conn., where they will be tested for disease-related traits in one of the first projects to make a new home in that new facility.