Medicine@Yale

Advancing Biomedical Science, Education and Health Care

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Neuroscientists target disorders of the brain and spinal cord

Neurodegenerative diseases, such as Alzheimer's, Huntington's and Parkinson's, and injuries to the brain and spinal cord from trauma or stroke are among the most feared of the disorders that afflict humankind.

The economic impact of these diseases is massive, and their toll in human suffering is incalculable. According to the National Institute on Aging, the direct and indirect costs of caring for patients with Alzheimer's disease alone are at least $100 billion per year. With a rapidly aging population, the challenges that neurodegenerative diseases pose for our society will only increase.

Decades of research in molecular and cellular biology and neurobiology have revealed a myriad of potential drug targets to slow or prevent these disorders.

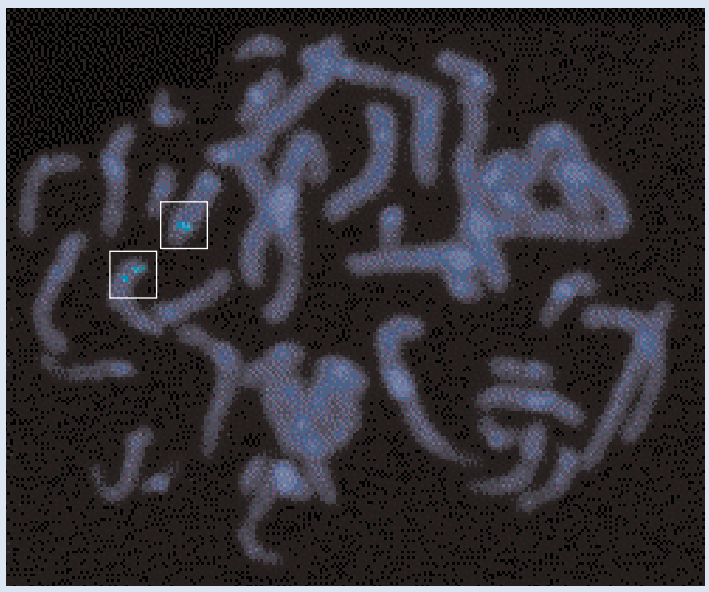
In an effort to aggressively translate these findings into effective therapies, the School of Medicine has formed a new interdepartmental program in Cellular Neuroscience, Neurodegeneration and Repair (CNNR) that will accelerate the pace of Yale's research on neurodegenerative diseases and nerve injury.

The co-directors of the new program, Pietro De Camilli, M.D., Eugene Higgins Professor of Cell Biology, and Stephen M. Strittmatter, M.D., PH.D., Vincent Coates Professor of Neurology and of neurobiology, both members of Yale's Kavli Institute for Neuroscience, will recruit as many as seven new scientists in a variety of disciplines to join them at CNNR and create a core to interconnect the more than 100 neuroscien-

Neuroscience, *page 5*

Pietro De Camilli

Stephen Strittmatter



Gilles de la Tourette (below) recognized that the tic disorder he identified is heritable. (Right) The break in a fluorescent probe (lower box), not seen in a normal chromosome (upper box), shows the precise location of an abnormality that led researchers to a gene associated with Tourette's syndrome.

A team led by Jeffrey Gruen discovered a new gene related to dyslexia.

Making a major impact in *Science*

Tourette's discovery hailed as breakthrough

When French neurologist Gilles de la Tourette first cataloged the persistent muscle tics and involuntary vocal outbursts characteristic of the syndrome that now bears his name, he recognized that the condition ran in families. Now, 120 years later, Yale researchers led by Matthew W. State, M.D., PH.D., Harris Assistant Professor of Child Psychiatry, have identified the first genetic mutation associated with Tourette's syndrome (TS).

Along with a Yale study of dyslexia (story at right), the work was cited in a list of the top 10 scientific breakthroughs of 2005 in the December 23 issue of the journal *Science*.

The gene, which contributes to neuronal development and communication between neurons, accounts for only a small percentage of cases of Tourette's syndrome, but its discovery after years of searching offers the best chance yet to penetrate this socially debilitating condition.

Tourette's, *page 3*

Dyslexia gene also cited among journal's top 10

Long before a child enters school, brain cells are on the move, lining up into carefully wired circuits in preparation for the demanding task of learning to read. Mistakes in this circuit architecture are thought to underlie dyslexia, a reading disability that affects as many as 15 percent of children and runs strongly in families.

In a finding that received worldwide recognition, Yale

Dyslexia, *page 6*

Banner year for Yale as six on faculty join Institute of Medicine

Six Yale researchers, five with appointments at the School of Medicine and one from the School of Nursing, were among the 64 scientists elected in late October to the Institute of Medicine (IOM).

The IOM was formed in 1970 by the National Academy of Sciences to honor professional achievement in the health sciences and to serve as a national resource for independent analysis and policy recommendations on issues related to medicine, biomedical sciences and health.

"This is unprecedented," says Dean and Ensign Professor of Medicine Robert J. Alpern, M.D., noting that, since its founding, no more than three Yale scientists have been elected to the IOM in a single year.

The 2005 elections bring the number of Yale faculty members in the IOM to 37, including three at the School of Nursing, two at the School of Management, two in the Law School and one at Yale-New Haven Hospital, which gives Yale one of the highest concentrations of IOM members of any institution in the nation, Alpern says.

Institute, *page 8*

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Edward Chu is combining modern Western techniques with traditional Chinese medicinal herbs, one example of his efforts to translate basic scientific knowledge into new treatments at the Yale Cancer Center.

Found in translation

Yale's oncology chief is intent on moving cancer discoveries to the bedside

Lifelines
Edward Chu

Edward Chu, M.D., is a man on a mission. Since his appointment as chief of medical oncology and director of clinical research at the Yale Cancer Center (YCC) in 2004, Chu has completed a whirlwind recruiting drive that brought 11 new expert clinical investigators to Yale in just 16 months. This administrative coup—most people in Chu's position would be pleased to fill one or two such positions in a year—is a first stroke in Chu's plan to create a robust translational research program at the cancer center, bringing the knowledge gained from basic scientific research to patient care as quickly as possible.

Acclaimed for his research on tumor resistance to chemotherapy agents and on new compounds for colorectal cancer, Chu came to Yale in 1996 via the National Cancer Institute (NCI), where he was a tenured senior clinical investigator.

Chu has followed in his parents' footsteps—but in reverse. Before they accepted positions at Brown University, both began their professional careers as cancer pharmacologists at Yale. Chu, who grew up near Providence, R.I., graduated from Brown with undergraduate and medical degrees but landed back at Yale, where he continues a family tradition of developing novel treatments for cancer.

Chu's Section of Medical Oncology is one of more than a half-dozen academic units in the School of Medicine that conduct research and provide cancer care under the umbrella of the YCC, which was established in 1974, shortly after President Nixon declared the "war on cancer." Modern chemotherapy was developed and first administered to patients at Yale in 1942, and the YCC was one of the first facilities in the nation to receive the NCI's Comprehensive Cancer Center designation.

By capitalizing on Yale's long-standing tradition in cancer pharmacology, and its well-established strengths in immunobiology and diagnostic imaging, Chu plans to make Yale a center of translational research.

"Everyone uses the term 'translation' these days, but it's extremely difficult to carry off effectively," Chu says. "Our goal is to have really close crosstalk between basic scientists and clinical investigators, and to take findings from the clinic to gain better insight into how various treatments work."

A research area that holds particular personal fascination for Chu is the blending of traditional Chinese medicine with modern cancer therapies.

Along with Henry Bronson Professor of Pharmacology Yung-Chi "Tommy" Cheng, PH.D., Chu and his team are conducting rigorous clinical studies to see whether these 2000-year-old remedies can enhance chemotherapy's effectiveness against cancer cells and/or protect healthy normal cells against the side effects experienced during cancer treatment.

Now that the new group of clinical investigators is settling in at Yale, Chu says, it's time to bring all the pieces together. "We've got tremendous basic science; we've got great core resources. We now have a critical mass of key experts in developing clinical trials," he says. "It won't take very long for Yale to be viewed not just as one of the premier preclinical basic research programs, but one of the preeminent clinical and translational programs in this country."

New collaboration with museum aims to improve science literacy

Amid concern about the effectiveness of science education, epidemiologists at the School of Medicine, educators at Yale's Peabody Museum of Natural History and researchers at the Connecticut Agricultural Experiment Station (CAES) are collaborating on a project to increase science literacy and encourage careers in science.

The initiative, led by Leonard E. Munstermann, PH.D., senior research scientist in epidemiology, has received a five-year, $1.3 million Science Education Partnership Award (SEPA) from the National Institutes of Health (NIH) to stimulate students' interest in science. In the program, to be housed at the Peabody Museum and coordinated by project manager Laura L. Fawcett, M.S.P.H., and science education specialist Terri Stern, researchers and educators will design curricula for grades 5 through 10 that create a deeper understanding of biological science.

"The curricula will feature Lyme disease and West Nile encephalitis because of their public health significance, and because they point to broader biological relationships," says Munstermann, also curator of entomology at the Peabody. Students will explore tick and mosquito life cycles using preserved ticks and the skins and skulls of mammal and bird hosts for Lyme disease and West Nile virus. In springtime, students will capture and examine mosquito larvae from vernal pools.

The project is expected to reach 11,400 students by 2010. "By giving students the chance to participate in hands-on, inquiry-based research projects, we hope to demystify science and make it more accessible," says Barbara M. Alving, M.D., acting director of the National Center for Research Resources (NCRR), a component of the NIH that will administer the grant.

Graduate council bestows top honor on residency dean

Residents at Yale-New Haven Hospital (YNHH) have a gifted mentor in Rosemarie L. Fisher, M.D., professor of medicine and associate dean for graduate medical education, according to the Accreditation Council for Graduate Medical Education (ACGME), which named Fisher one of only two physicians nationwide to receive the 2006 Courage to Lead Award.

Rosemarie Fisher

The award, granted for the first time this year, honors "exemplary leadership; dedication to promoting the professional, ethical, and personal development of residents; and commitment to safe and appropriate care of patients," according to the ACGME.

In addition to serving as associate dean at the School of Medicine, Fisher is director of graduate education at YNHH. In 49 letters to the ACGME in support of Fisher's nomination for the award, colleagues cited Fisher's dedication to residents' training and her unwavering commitment to an open-door policy in addressing their concerns.

"Rosemarie has brought great competence and warmth to her responsibilities as director of graduate medical education," says Peter N. Herbert, M.D., clinical professor of medicine and vice president for medical affairs and chief of staff at YNHH.

Fisher has spent 31 years on the Yale faculty, including 12 as program director for the Department of Internal Medicine's residency program, six as director of graduate medical education, and three as associate dean and director of graduate medical education.

Medicine@Yale

Peter Farley, *Managing Editor*

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Advances

Health and science news from Yale

Take sleep apnea seriously, says study

It can be trying to share a bed with a person affected by obstructive sleep apnea, a common condition in which breathing stops repeatedly during sleep, since loud snoring is a telltale symptom. But a study from the Yale Center for Sleep Medicine (YCSM) provides new evidence that sleep apnea is more than an annoyance.

Since 1997, YCSM researchers had diagnosed sleep apnea in 697 patients using polysomnography, a technique that measures heart rate, breathing and other physiological variables during sleep. A follow-up study begun in 2002 revealed that 9 percent of these individuals suffered strokes or died, compared to only 1.6 percent of a control group.

As reported in *The New England Journal of Medicine* on November 10, after eliminating smoking, alcohol use and hypertension as factors, the scientists found that sleep apnea doubled the risk of stroke or death.

"Sleep apnea is a common and serious problem, but it is also highly treatable," says H. Klar Yaggi, M.D., assistant professor of medicine and lead author. "If you or someone you know has symptoms of sleep apnea, it is important to discuss this with a doctor."

Mad cow's small impact explained?

A recent study by neuropathologist Laura Manuelidis, M.D., professor of surgery, and colleagues in Japan may offer the beginnings of a solution to an epidemiological puzzle.

In 1996, during an epidemic of bovine spongiform encephalopathy (BSE), or mad cow disease, in British cattle, some epidemiologists predicted that up to 100,000 people could contract variant Creutzfeldt-Jakob disease (vCJD), a rapidly progressing, invariably fatal neurodegenerative condition, from BSE-infected beef.

But that nightmarish scenario hasn't yet come to pass: almost 10 years later only 151 cases of vCJD have been verified.

Manuelidis and her team reported in the October 21 issue of *Science* that when neuronal cell cultures were infected with either a weak or sporadic form of CJD or with agents that cause sheep scrapie, a disease similar to CJD, the cultures resisted infection by a more virulent strain of CJD agent.

The team suggests that exposure to less virulent strains of CJD may protect people against the newly evolved bovine agent.

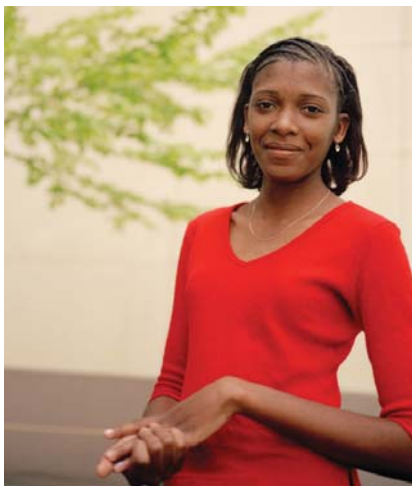
Medical school welcomes first Gilliam Fellows

Howard Hughes initiative aims to diversify graduate biomedical education

At age 10, Meisha Bynoe dreamed of saving lives in her Caribbean homeland, St. Vincent and the Grenadines. As a child, Imran Babar was fascinated with the science underlying life on his family's Minnesota farm. Last fall, both brought their curiosity and passion to Yale to pursue doctorates in the Combined Program in the Biological and Biomedical Sciences (BBS) with the support of Gilliam Fellowships awarded by the Howard Hughes Medical Institute (HHMI).

The fellowships, named for the late James H. Gilliam Jr., an HHMI trustee who was devoted to fostering diversity in science and education, were awarded for the first time this year to a handful of outstanding minority or disadvantaged students in the life sciences. Although African-Americans, Hispanics and Native Americans make up 23 percent of the U.S. population, the National Science Foundation reports that these groups account for less than 5 percent of the nation's scientists and engineers holding doctorates.

HHMI is the nation's largest source of private funding for biomedical research and science education. Following a motto of "people, not projects," the institute is best known for its HHMI investigator program, which grants top scientists generous and flexible contracts, renewable at five- or seven-year intervals, to lead HHMI-supported laboratories at their home institutions. But the institute has also awarded more than $1 billion in grants since 1988 to strengthen science education and to encourage students to pursue careers in the life sciences.


Meisha Bynoe

According to Peter J. Bruns, PH.D., vice president for grants and special programs at HHMI, the institute's program directors throughout the country, including Robert Wyman, PH.D., professor of molecular, cellular and developmental biology at Yale, had been asked to nominate talented students for the Exceptional Research Opportunities Program (EXROP), a summer program in its second year that pairs undergraduate science students with HHMI investigators. From a pool of 84 EXROP students, six with extraordinary promise were chosen to be Gilliam Fellows.

While still an undergraduate at Carleton College in Minnesota, Babar was making substantial research contributions on the role of stem cells in tumor formation to the Massachusetts Institute of Technology (MIT) laboratory of HHMI investigator Tyler Jacks, PH.D., who served as Babar's EXROP mentor during the summer of 2003.


Imran Babar

Babar joined BBS through the Department of Cellular, Molecular and Developmental Biology.

Bynoe, who is a student in the microbiology track of the BBS program, says she finds New Haven to be "cozy" after four years at MIT, in Cambridge, Mass., where she double-majored in biology and music and achieved a perfect grade point average.

Bynoe's EXROP experience with HHMI investigator Richard M. Locksley, M.D., at the University of California at San Francisco in the summer of 2004 was her first look at a immunology lab, and she found the work to be so enjoyable that her childhood dream of becoming a physician has given way to a wish to spend her life in science.

Two Gilliam Fellows now attending other universities did EXROP stints with Yale HHMI investigators. Naira Rezende, now at the Weill Medical College of Cornell University, spent last summer in the laboratory of David G. Schatz, PH.D., professor of immunobiology at the medical school. Alexander Red Eagle, now enrolled at Stanford University, worked with Eugene Higgins Professor of Genetics and Pediatrics Arthur L. Horwich, M.D.

Tourette's *continued from page 1*

Geneticists have been hunting unsuccessfully for genes involved in TS for decades. The disorder, which begins in adolescence, is relatively common, affecting as many as 1 percent of children. But symptoms of TS often overlap with other common diagnoses, including obsessive-compulsive disorder and attention-deficit hyperactivity disorder (ADHD), and there are almost certainly multiple genes that may all lead to increased risk for TS. Add to that the tendency of adults with TS to marry others with similar conditions, and the task of tracking suspect genes through extended families, a staple of genetic analysis, becomes extremely difficult.

To simplify the problem, State adopted a strategy pioneered by his Yale colleague, Chair and Sterling Professor of Genetics and Howard Hughes Medical Institute investigator Richard P. Lifton, M.D., PH.D. "Rather than trying to group together families that may not have the same genetic contribution to TS," State says, "we looked for that one unusual patient who would lead us to a gene."

As reported in the October 14 issue of *Science*, the approach paid off when State's group found a child with both TS and ADHD who had a telltale break on chromosome 13. Alerted by that defect, researchers suspected that there might be a problem with a nearby gene known as *SLITRK1*, because animal studies had already shown that *SLITRK1* plays an important role in brain development. When the team analyzed 174 people with TS, they found three with mutations in *SLITRK1*. No mutations were found in several hundred unaffected people, providing strong evidence that *SLITRK1* was contributing to the disease.


Matthew State


Nenad Sestan

A close collaboration between State and Nenad Sestan, M.D., PH.D., assistant professor of neurobiology, allowed the researchers to quickly determine the biological consequences of one of these mutations. Using sophisticated *in utero* gene delivery techniques, Sestan introduced either normal *SLITRK1* or a gene with one of the mutations found in the subjects with TS into developing mouse neurons. The intact gene caused the neurons to branch out, a necessary step for the proper wiring of neural circuits early in life. But the mutated gene did not support normal branching.

The other mutation, found in two people with TS in the study, was nearly overlooked by the researchers because it occurred in a regulatory part of *SLITRK1* that does not affect protein structure. But further investigation showed that this mutation was not present in several thousand unaffected individuals, and the team's additional experiments suggest that the mutation may cause a lower level of the SLITRK1 protein to be present in some nerve cells in those with TS.

The newfound mutations are rare—only 2 percent of those with TS in the study had them—and how the mutations combine with genetic or environmental factors to increase risk for the disease is unknown. But *SLITRK1* gives researchers a long-awaited starting point for further genetic investigations, says State, who likens the findings to a string that TS researchers can pull to begin unraveling the mysteries of the disorder.

"This is just the first piece of the puzzle," State says. "We hope the clues this gene will give us will have widespread ramifications for understanding the basic biology of this disorder."

For Shoreline heart specialist, prevention is attainable goal

To speak with cardiologist L. Veronica Lee, M.D., assistant professor of medicine, is to stop worrying for a moment about the diet/exercise/motivation conundrum of modern life, especially if you're a middle-aged person who drives everywhere, eats on the go and tends to relax in front of the television. A 10-minute conversation with Lee leaves the reassuring impression that maybe things aren't so complicated after all.

In 15 years as a physician, Lee has seen fad diets come and go, but good health, she believes, depends on balance. And while the low-carbohydrate trend of the past few years may have helped many people to lose weight, it seems to Lee that most of them gain it back over time.

"The reality is we need to have a well-balanced diet. You can go for short-term gains, but if you're throwing your system out of whack, the results are probably going to be short-lived as well," says Lee, who sees patients four days a week in the Yale Medical Group (YMG) practice at the Yale-New Haven Shoreline Medical Center in Guilford and on Fridays in New Haven. "The bottom line is you need a lifestyle you can live with so that you can achieve your target and maintain it. That's how people achieve the most success."

Trained at Columbia University College of Physicians and Surgeons, Brigham and Women's Hospital, the Harvard School of Public Health and Washington University School of Medicine in St. Louis, Lee came to Yale in September from St. Petersburg and West Palm Beach, Fla., where she was in private cardiology practice for three years and developed prevention strategies.

Lee's research focus—and the driving force behind her work with patients—is prevention. Ideally, Lee wants to help patients head off cardiovascular disease entirely, but she also works to prevent it from recurring in patients who have suffered a heart attack. And she has a special interest in preventing heart disease in women.

"Cardiovascular disease is the number one killer in women; stroke and heart attack are very significant players in mortality in women, and the numbers have been climbing," Lee, a fellow of the American College of Cardiology, says. "Men are getting earlier, better and more aggressive treatment. They're cutting back on smoking, they're exercising more than women. Women are lagging behind in exercise, and we're seeing an increase in smoking. Women's rate of heart disease is on the rise."

According to the American Heart Association, more women than men have died of cardiovascular disease—a category that includes coronary heart disease, congestive heart failure, high blood pressure, stroke and diabetes—every year since 1984.

L. Veronica Lee champions prevention and women's cardiovascular health in her practice at the Yale-New Haven Shoreline Medical Center in Guilford, Conn.

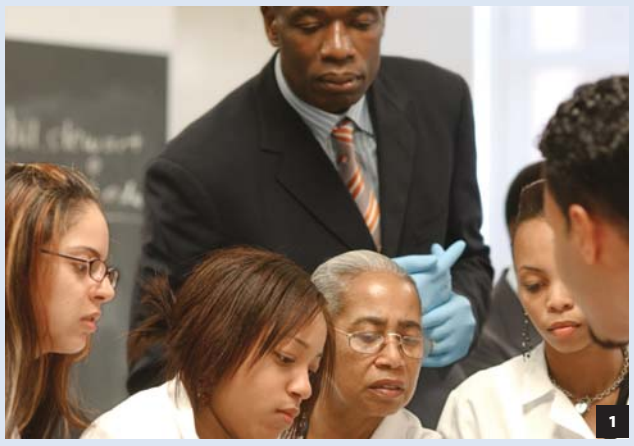
In her practice, Lee helps patients set nutritional goals and works out customized diet and exercise plans to lower the risk of illness. "For everyone, there are different ways of getting themselves off the couch and eating the right things," she says. "I try to assess the approach that's going to work for a particular person."

Lee is part of a new influx of Yale physicians to the Shoreline center, an 80,000-square-foot facility near Interstate 95 that opened in July 2004. YMG, the medical school's 700-member faculty practice, staffs the center's emergency department and its anesthesiology, diagnostic imaging, pathology, laboratory medicine and radiation oncology services. Now specialists in cardiovascular medicine, pediatric cardiology and surgical specialties—including urology, cardiothoracic, hand and cosmetic and reconstructive surgery—are spending one or more days a week in Guilford as a convenience to patients who live east of New Haven.

For Lee, whose exam room window looks out on a grove of oak trees, the Shoreline center provides a perfect setting to convey her message of prevention. "Environment is a key point," she says. "If it's a beautiful location and it's soothing, then it creates a warmer and more nurturing environment that goes along with the whole notion of prevention."

Lee's hopeful outlook would also be soothing to any patient casting aside entrenched old habits on the sometimes difficult road to a healthy lifestyle. "There's no such thing as failure," she says. "If you slip, you just get back up and keep trying."

Out & about



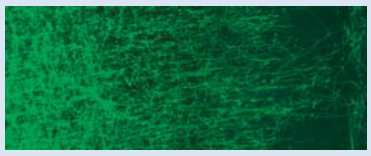
September 21: During the **VISIT OF DIKEMBE MUTOMBO,** the All-Star NBA center and philanthropist met with medical students and joined **Shirley Neighbors**' students from Hill Regional Career High School in New Haven for an anatomy lesson at the School of Medicine. **1.** Mutombo stands behind (from left) **Mariliam Padilla, Monica Daniels,** Neighbors and **Shaylice Bragg** during a lecture in the anatomy lab by medical student **Jason Knight** (back to camera). **2.** Medical students (from left) **Anup Patel, Tracy Wright, Luis Kolb, Ninani Kombo, Chike Brandon, Tejaswini More, Aaron Remenschneider, Emlyn Jones, Sarah Frasure** and **Sara Whetstone** with Mutombo.

October 1: At the **HARVEY CUSHING FAMILY GATHERING,** Cushing's descendants and family members celebrated the eminent neurosurgeon's life and planned for a permanent home at the School of Medicine for his famed collection of brain specimens, photographs, drawings and memorabilia.

1. **Michael Cushing** 2. **Jennie Burnap**
3. **William Cushing** 4. **Harvey Cushing**
5. **Tyler Mortimer** 6. **Bree Mortimer**
7. **Siri Mortimer** 8. **Tony Mortimer**
9. **Morgan Brown** 10. **Betsey Brown** 11. **Sara Wilford** 12. **Christopher di Bonaventura**
13. **Albert Paley** 14. **William Paley** 15. **Alison Paley** 16. **Samuel Paley** 17. **Kate Chiucchini**
18. **Laura Rabbitt** 19. **Kate Roosevelt Whitney** 20. **Amanda Burden** 21. **Peter di Bonaventura**
22. **Franklin Thomas** 23. **Sara di Bonaventura** 24. **Lulie Haddad** 25. **Grace Haddad**
26. **Elizabeth di Bonaventura** 27. **Henry di Bonaventura** 28. **Sarah Rabbitt.**

Advances

Health and science news from Yale



Restoring flexibility to heal broken brains

In early life, the brain is continually sculpted by stimuli from the outside world. But soon, most neural circuits become hard-wired.

Fixed circuits are reliable but costly: the injured brain can rarely repair itself. In 2000, Stephen M. Strittmatter, M.D., Vincent Coates Professor of Neurology, identified Nogo (green in the brain section above), a protein that suppresses self-repair in injured neurons. A report in the September 30 issue of *Science* indicates that Nogo may also lock down cortical wiring during normal development.

The visual cortex is normally divided equally between inputs from each eye. But if one eye is kept shut during a "critical period" before neural circuits are fixed, the active eye appropriates more cortex. However, Strittmatter, Nigel W. Daw, PH.D., professor of ophthalmology and visual science, and colleagues showed that in mice bred to lack the Nogo receptor, an active eye can usurp cortical real estate well past the critical period into adulthood.

Noting that "limited plasticity is central to a range of neurological disorders," Strittmatter is testing Nogo blockers to see if reviving the brain's inborn flexibility can help it to heal after injury.

Cool therapy helps after troubled births

If the placenta or umbilical cord are torn or squeezed before or during childbirth, or if the uterus ruptures, many infants suffer from a severe form of oxygen deprivation known as hypoxic-ischemic encephalopathy, or HIE, that can cause disabilities, such as cerebral palsy, or death.

A new study by a nationwide network of researchers, including Richard A. Ehrenkranz, M.D., professor of pediatrics and of obstetrics, gynecology and reproductive sciences, shows that a simple therapy that lowers newborns' brain temperature can reduce disability and death after HIE.

As reported in the October 13 issue of *The New England Journal of Medicine*, the researchers placed babies with HIE on water-cooled blankets that lowered their body temperature to 92.3 degrees within 6 hours after birth. Only 44 percent of the infants who received the cooling treatment developed disabilities or died, compared to 62 percent of a control group.

The cooling therapy "slows down the injury process caused by birth asphyxia," says Ehrenkranz. "Less injury means a better outcome and fewer cases of cerebral palsy and other complications."

Yale, VA supporting troops on the home front

Experts on PTSD help vets cope with combat trauma from Iraq, Afghan wars

More than 1.2 million Americans have gone to war in Iraq and Afghanistan since September 2001, over a quarter of whom have served more than one tour of duty. This state of affairs has created a heightened sense of urgency among Yale researchers and clinicians who study and treat post-traumatic stress disorder (PTSD) in collaboration with the Veterans Administration (VA).

Yale investigators at the Clinical Neuroscience Division of the VA National Center for PTSD (CND-NCPTSD), located at the VA Connecticut Healthcare System campus in West Haven, Conn., have established a new partnership with psychiatrists at Fort Drum in upstate New York to study how troops react to combat experiences.

Meanwhile, clinicians at the VA's West Haven campus have expanded their staff to care for an expected influx of veterans needing treatment for anxiety and PTSD.

John H. Krystal, M.D., Robert L. McNeil Jr. Professor of Clinical Pharmacology, deputy chair of the department of psychiatry, and director of the CND-NCPTSD, notes that about 196,000 veterans have a diagnosis of PTSD, which costs the VA $274 million per year—13 percent of its total medical costs. With our troops now engaged in two wars, he says, these numbers will only increase.

"Recent survey data suggest that 10 to 20 percent of soldiers participating in combat in Iraq meet criteria for PTSD," says Krystal.

John Krystal

Steven Southwick

Veterans traumatized by war—or people distressed by any other event in which they fear death or great harm to themselves or others—can be diagnosed with PTSD if they meet three criteria: unwillingly revisiting traumatic events in flashbacks or nightmares, hypervigilance and retreating from life and relationships.

Next summer, Krystal and Professor of Psychiatry and Public Health Robert A. Rosenheck, M.D., will begin a $6.9 million nationwide study funded by the VA that will test the effectiveness of the medication risperidone for veterans with chronic PTSD. The drug is a potential alternative to antidepressants, such as Prozac, that are usually prescribed.

The study is the latest in a long-term effort by Yale investigators, who have pioneered PTSD research and clinical care.

In the early 1970s, Yale psychiatrist Arthur S. Blank Jr., M.D., was one of the first clinicians in the nation to develop peer-support programs for veterans suffering from the stress-related symptoms now known as PTSD.

In 1989, when the NCPTSD was established at five campuses across the country, the Clinical Neuroscience Division was based at VA's West Haven campus in order to forge collaborations with the strong basic and clinical neuroscience programs at Yale.

The CND-NCPTSD has gone on to become one of the most important centers advancing our understanding of the neurobiology and treatment of PTSD.

"Very early on, West Haven became a center where they really understood PTSD," says Steven M. Southwick, M.D., professor of psychiatry, a researcher at the West Haven campus of VA Connecticut.

Southwick says that studying the neurobiology of stress responses—finding a physical manifestation of a psychological problem—has helped clinicians to understand PTSD better and to explore more effective treatments. "Before, it was all interpreted psychologically," he says.

To prepare for the needs of returning troops, the VA Connecticut Healthcare System has recently received additional funding to expand clinical services to returning combat veterans, according to Dolores Vojvoda, M.D., assistant professor of psychiatry at the medical school and head of the PTSD and Anxiety Disorder Service in West Haven.

Vojvoda reports that, by December, therapists in her PTSD clinic had treated about 75 Iraq and Afghanistan veterans, and she expects the numbers to grow quickly.

"We are at a critical moment in the lives of the soldiers who have made sacrifices on behalf of every American citizen," says Krystal. "We as a country have to decide whether we are going to return the favor by supporting our soldiers and respecting the sacrifices they have made by making sure they get the treatment they need and by making sure we can improve the treatments we are offering them."

Neuroscience *continued from page 1*

tists who now work across the Yale campus.

"I am very excited about this new neuroscience initiative addressing the basic mechanisms of brain function together with a number of devastating neurological diseases," says Dean and Ensign Professor of Medicine Robert J. Alpern, M.D. "The success of the program is ensured by the extraordinary quality of its two leaders, both of whom have performed groundbreaking research in this arena."

De Camilli says the new program will foster research on molecular and cellular aspects of nervous system function in both health and disease. De Camilli's pioneering work on synaptic vesicles, the cellular packets that deliver neurotransmitters into the junction between nerve cells, is bringing new understanding of normal brain function while also giving insights into pathological mechanisms.

In addition to grants from federal agencies, De Camilli's research receives support from The Human Frontier Science Program Organization as well as the G. Harold and Leila Y. Mathers Charitable Foundation.

"The creation of a program focused both on the cell biology of the nervous system and on its diseases recognizes that innovative research on pathogenetic mechanisms can best thrive in an environment where basic science research is very strong," says De Camilli, who is also a Howard Hughes Medical Institute investigator. "I am delighted to start this new initiative with Dr. Steve Strittmatter, who has already been very successful in bridging fundamental neuroscience with clinically important problems."

Five years ago, Strittmatter identified Nogo, a protein that blocks the regeneration of axons. His laboratory's research on this important regulator (see *Advances,* top left) has suggested potential therapies for brain and spinal cord injuries, stroke and neurodegenerative disorders such as Alzheimer's disease, amyotrophic lateral sclerosis (Lou Gehrig's disease) and multiple sclerosis.

"Establishing a hub for cellular and molecular studies in neuroscience with interdisciplinary and interdepartmental connection holds great promise for many major research advances by Yale neuroscience," Strittmatter says. "This program will illuminate our understanding of how nerve cells function and communicate in the brain, especially as they relate to the development of novel therapies, such as neural repair, for neurodegenerative diseases." Strittmatter's work is supported by The Amyotrophic Lateral Sclerosis Association, the Dr. Ralph and Marian Falk Medical Research Trust and the Christopher Reeve Paralysis Foundation.

Pasko Rakic, M.D., PH.D., the chair and Dorys McConnell Duberg Professor of Neurobiology and director of the Kavli Institute at Yale, said the decision to focus on neurodegeneration, neural repair and the neuronal basis of cognitive function and dysfunction was an outcome of many meetings and deliberations of the School of Medicine's Basic Science Research Strategic Planning Committee.

"Research on neurodegeneration and brain repair is one of the most difficult and most noble goals of neuroscience," Rakic says. "Modern research methods will allow new advances. We are all excited about the prospect of entering this important and fast growing area of biomedical research."

Unlikely allies, common goals in fight against obesity

The sharply rising rate of obesity in America over the past two decades has engendered a fierce public debate, pitting those who hold the food industry responsible for making and promoting unhealthy foods against those who believe that obesity results from a failure of personal responsibility and self-control.

Enter Leslie Rudd, who made his fortune in the food and beverage industry but who also struggled with his weight, and with the resulting stigma, for much of his life. It is Rudd's hope that Yale's new Rudd Center for Food Policy and Obesity, established with his $7.5 million, five-year gift, will represent a fresh start in the fight against obesity and against the discrimination faced by overweight and obese individuals.

The new center's director, Kelly D. Brownell, PH.D., professor and chair of psychology at Yale and professor of epidemiology at the School of Medicine, is a well-known critic of the food industry, but he and Rudd share a strong belief that curbing the obesity crisis will require seismic shifts in our society's approach to food and eating.

"The only hope of preventing obesity lies in understanding and changing the fundamental economic, political and social factors that promote consumption of calorie-dense, nutrient-poor foods along with physical inactivity," says Brownell, who was elected to the Institute of Medicine in October (see related story, page 1). "We believe that real change requires nothing less than real change."

Leslie Rudd speaks at the dedication of the Rudd Center for Food Policy and Obesity as center Director Kelly Brownell (left) and Yale President Richard Levin (center) look on.

Rudd, CEO and principal owner of Kansas-based wine and liquor distributor Standard Beverage Corp., luxury foods purveyor Dean and DeLuca and Rudd Winery, a high-end wine producer in Napa Valley, Calif., sees no contradiction between a life at the heart of the food industry and his founding in 1998 of the Rudd Foundation, which is committed to ending obesity and discrimination against overweight individuals. "I don't think that they're mutually exclusive," he says. "I think that the obesity issue is separate from the enjoyment of food and wine."

Accordingly, a key component of the Rudd Center's mission is to serve as a "safe space," away from the provocative arenas of politics and the media, where leaders of food and agriculture companies can meet with scientists, public health officials and educators for candid exchanges on issues of nutrition and obesity.

The center also plans to monitor and evaluate the food industry's efforts to provide healthier foods and promote healthier eating. Brownell says the center will support corporate campaigns based on solid science but will criticize those found to be short-term, ineffective or misleading.

Using findings by social scientists on effective techniques of persuasion, Rudd Center researchers also plan to create compelling new public health messages that encourage exercise and good nutrition.

The societal stigma surrounding weight has been a major concern of the Rudd Foundation, and the new center will conduct and sponsor research on how weight bias affects emotional well-being in overweight individuals.

"I was once a lot more overweight than I am now," Rudd explains, "and it gave me a first-hand insight into what people who are overweight feel and the discrimination they face."

Rudd believes that the psychological pressure of weight stigma can be so severe as to be disabling, and he sees his achievements in business as a means to help others overcome the physical and psychological burdens of obesity.

"Many overweight people are so held back by this one stigma that they're not very successful," Rudd says. "I became relatively successful. I thought that establishing the center was something that needed to be done, and now there are a lot of people joining us."

Dyslexia *continued from page 1*

researchers have discovered a gene that may cause many cases of dyslexia by interfering with early brain development. The gene, *DCDC2*, is required for neurons to migrate normally and is disrupted in up to 20 percent of people with dyslexia.

"Our results validate and confirm the fact that dyslexia is genetic," says senior researcher Jeffrey R. Gruen, M.D., associate professor of pediatrics and an investigator at the Yale Child Health Research Center. "Based on brain imaging data, we know that dyslexics seem to have a disrupted brain reading circuit, and we think that variants of *DCDC2* could be responsible for disrupting circuit formation during development."

Besides illuminating the cause of dyslexia, the identification of *DCDC2* could lead to genetic tests to identify at-risk children early on, when educational interventions are most effective, Gruen says.

The work, presented at the October meeting of the American Society for Human Genetics, was published in the November 22 issue of the *Proceedings of the National Academy of Sciences*.

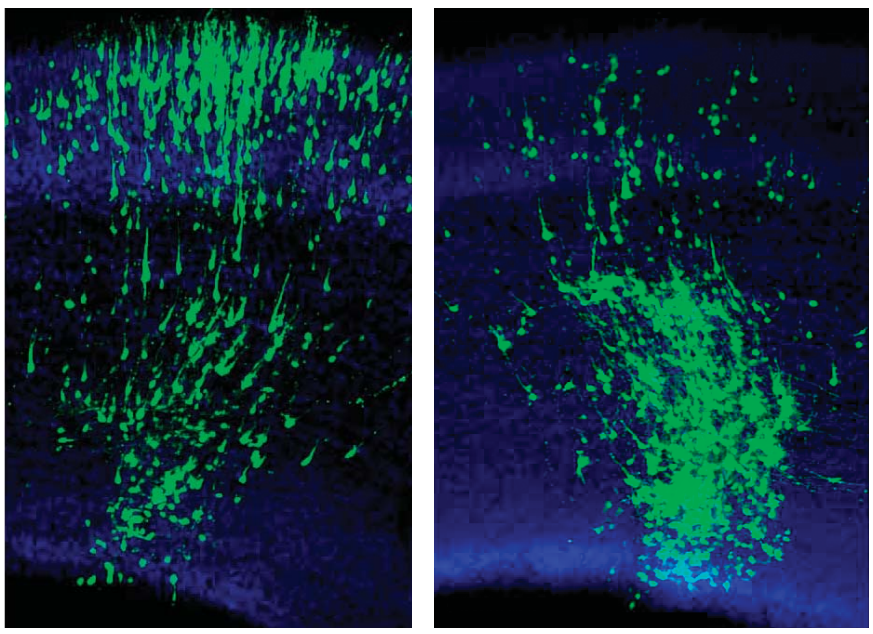
Dyslexia is defined as an impairment in reading ability in people with normal intelligence and adequate educational opportunities. For the last 15 years, researchers have been on the trail of a gene for dyslexia they had traced to human chromosome 6. In 2002, Gruen and colleagues narrowed the search to a stretch of 1.5 million DNA base pairs containing 19 candidate genes, all of which were known to be active in the brain.

To get a closer look at those 19 genes in normal readers and dyslexics, Gruen and his team analyzed 536 parents and children from 153 families, correlating DNA sequences with the children's scores on a battery of reading and comprehension tests.

They quickly saw that in children with low reading scores, sequence variations clustered most often in the area of *DCDC2*. The researchers hit pay dirt when they noticed that in some dyslexic subjects, one copy of the *DCDC2* gene was missing nearly 2,500 "letters" of DNA code. This deletion is uncommon in the general U.S. population, but it was seen in nearly 20 percent of the study participants with dyslexia.

The discovery could lead to genetic tests that would identify children with reading problems early, when interventions are most effective.

The *DCDC2* deletion does not affect the structure or function of the gene's protein product, but Gruen and his colleagues believe it reduces the overall amount of messenger RNA, and hence protein, in nerve cells. They then demonstrated that neurons did not migrate properly in the developing brains of fetal rats in which *DCDC2* expression was experimentally suppressed (see photos above).



(Left) Nerve cells have migrated in an orderly fashion toward the outermost layer of the cortex (top of photo) in the brain of a normal 14-day-old embryonic rat. But neurons in a littermate in which the *DCDC2* gene has been suppressed (right) show abnormal migration.

While the team hasn't yet confirmed that DCDC2 protein levels are lower in dyslexic people, they did establish that in normal adult humans the gene is most active in brain regions involved in reading.

The newly found gene has no relation to IQ, Gruen is quick to point out. And thanks to the flexibility of the brain's circuitry early in life, he says that, with early intervention, dyslexic children may be able to compensate for their disability by training neural circuits other than those affected by the gene when they learn to read.

"If children with dyslexia can get the right education program early on, they will be successful," Gruen says. "We're hoping that someday we can use genetic information to match kids to their ideal intervention as early as possible."

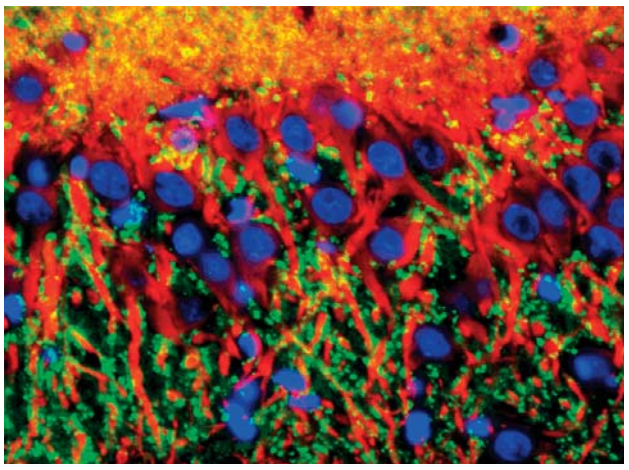
Grants and contracts awarded to Yale School of Medicine, *July/August 2005*

Federal

Serap Aksoy, NIH, *Trypanosome Gene Expression in Tsetse*, 2 years, $163,500 • **Robert Alpern**, NIH, *Regulation of Renal Bicarbonate and Chloride Absorption*, 5 years, $2,043,750 **Roland Baron**, NIH, *Role of the c-SRS Proto-Oncogene in Osteoblasts*, 5 years, $1,798,500 **Sumita Bhaduri-McIntosh**, NIH, *Early Cellular Immune Responses to EBV*, 4 years, $535,680 **Angelique Bordey**, NIH, *GABA Signaling in the Postnatal Subventricular Zone*, 4 years, $1,483,007 • **Robert Camp**, NIH, *Qualitative Analysis of Tissue Biomarkers and Pathways*, 2 years, $281,220 • **Michael Caplan**, NIH, *Ion Pump Partners: Regulators of Sorting and Function*, 4 years, $1,702,179 • **Sonia Caprio**, NIH, *Pathophysiology of Type 2 Diabetes in Youth*, 5 years, $2,043,750 • **R. Todd Constable**, NIH, *Epileptogenic Tissue Localization Using EEG-fMRI*, 4 years, $1,500,511 • **Joseph Craft**, NIH, *Immune Responses in Lupus*, 5 years, $1,635,000 • **Ralph DiLeone**, NIH, *Role of the Orexin Neuropeptide in Responses to Morphine*, 5 years, $1,455,000 • **Daniel DiMaio**, NIH, *Cell Transformation by Bovine Papillomavirus*, 5 years, $2,630,896 • **Ronald Duman**, NIH, *Antidepressants and Signal Transduction and Gene Expression*, 5 years, $1,818,750 • **Jack Elias**, NIH, *Protease/Cathepsin-Mediated Apoptosis in COPD*, 4 years, $1,635,000 • **Jorge Galan**, NIH, *Molecular Genetic Analysis of* Salmonella *Cell Invasion*, 1 year, $2,343,717 • **Joel Gelernter**, NIH, *Genetics of Opioid Dependence*, 5 years, $5,779,192 • **Sankar Ghosh**, NIH, *Subversion of Innate Immune Responses by* Brucella, 2 years, $433,750 • **Thomas Gill**, NIH, *Epidemiology of Disability and Recovery in Older Persons*, 5 years, $3,152,866 • **Daniel Goldstein**, NIH, *Strategies to Enhance Immunity in Aging*, 3 years, $648,000 • **Carlos Grilo**, NIH, *Patient-Oriented Research with a Focus on Eating and Weight Disorders,* 5 years, $597,160 • **Steven Hebert**, NIH, *Structure and Function of ROMK Channel in Kidney*, 4 years, $1,370,692 • **Zeev Kain**, NIH, *Parent/Health Care Provider Behaviors & Child's Anxiety*, 5 years, $2,659,446 **Harlan Krumholz**, NIH, *Telemonitoring to Improve Heart Failure Outcomes*, 4 years, $6,664,663 • **Nian Liu**, NIH, *Content-Based Indexing and Retrieval of Brain Odor Maps*, 3 years, $470,339 • **Angeliki Louvi**, NIH, *Development of Choroid Plexus and the Blood-CSF Barrier*, 2 years, $395,933 • **Shrikant Mane**, NIH, *Yale Microarray Center for Research on the Nervous System*, 5 years, $6,509,106 • **Linda Mayes**, NIH, *Cortical Maturation and ERPs in Cocaine-Exposed Children*, 5 years, $631,800 **Diane McMahon-Pratt**, NIH, *Intervenable Host* Leishmania (Viannia) *Interactions*, 5 years, $5,166,089 • **Thomas Morgan**, NIH, *Genetic Risk Factors for Myocardial Infarction*, 5 years, $846,072 • **A. David Paltiel**, NIH, *Evaluating the Link Between HIV Prevention and Treatment*, 3 years, $1,487,112 • **Jordan Pober**, NIH, *Human CTL-Mediated Injury of Graft Endothelial Cells*, 5 years, $2,177,410 • **Marc Potenza**, NIH, *fMRI of Craving in Addictions: Gender Differences*, 5 years, $1,604,920 • **Kenneth Pugh**, NIH, *Neurobiological Foundations in Reading (Dis)Ability*, 5 years, $2,970,826 • **Timothy Quan**, NIH, *The Role of Epstein-Barr Virus in Systemic Lupus Erythematosus*, 5 years, $613,967 **Gary Rudnick**, NIH, *Structure and Function of NSS Transporters*, 4 years, $1,238,981 • **Charles Sanislow**, NIH, *Cognitive Control in Borderline & Trauma Psychopathology*, 5 years, $887,895 **William Sessa**, NIH, *Regulation of Vascular Remodeling & Angiogenesis by Nogo*, 5 years, $2,043,750 • **Nenad Sestan**, NIH, *Molecular Control of Cortical Neural Stem Cells*, 5 years, $1,717,912; NIH, *Neurobiology of Speech and Language Development*, 4 years, $1,512,376 **Albert Shaw**, NIH, *Top3 Homologues in Lymphocyte Genome Stability and Aging*, 5 years, $1,417,925 • **Dieter Söll**, NSF, *Expanding the Genetic Code with Phosphoserine and Pyrrolysine*, 1 year, $171,569 • **Stephen Strittmatter**, NIH, *Axonal Growth Cone Signal Transduction*, 4 years, $1,512,376 • **Zhaoxia Sun**, NIH, *SCO, a Zebrafish Model, Links Cilia and Kidney Cysts*, 5 years, $1,921,125 • **Patrick Sung**, NIH, *DNA Repair Genes & Proteins of the RAD52 Group*, 5 years, $1,941,565 • **Edwin Thrower**, NIH, *Pancreatic Zymogen Activation in a Reconstituted System*, 2 years, $260,800 • **Helen Treloar**, NIH, *Development of the Primary Olfactory Pathway*, 5 years, $1,430,625 • **Marietta Vazquez**, NIH, *Epidemiology of Human Metapneumovirus Infection*, 5 years, $676,986 **Marney White**, NIH, *Craving, Binge Eating, and Obesity*, 5 years, $671,571 • **John Wysolmerski**, NIH, *Function of the Calcium-Sensing Receptor in the Breast*, 5 years, $1,675,875

Non-Federal

Patrick Allen, National Alliance for Research on Schizophrenia and Depression, *Analysis of Protein Phosphatase-Mediated Glutamate Receptor Regulation*, 2 years, $60,000 • **George Anderson**, University of Pittsburgh, *Neurobiology, Impulsivity and Alcoholism*, 4 years, $45,404 • **Titus Boggon**, American Society of Hematology, *Structure/Function Studies of Janus Kinase Family Members*, 1 year, $50,000 • **Alfred Bothwell**, Robert Leet and Clara Guthrie Patterson Trust, *Bioengineering Functional Islets for Treatment of Type 1 Diabetes*, 1 year, $59,999 **H. Kim Bottomly**, Mount Sinai School of Medicine, *Immuno-biology of Peanut Allergy and Its Treatment: A Prototype*, 5 years, $239,654 **Demetrios Braddock**, American Cancer Society, Inc., *Molecular Determinants of Nucleic Acid Recognition by KH Domains*, 2 years, $720,000 • **Christopher Breuer**, American Surgical Association, *Investigating the Growth Potential of Tissue-Engineered Venous Conduits in a Juvenile Lamb Model*, 2 years, $75,000 **Darlene Brunzell**, National Alliance for Research on Schizophrenia and Depression, β2 *Nicotinic Acetylcholine Receptors Affect Schizophrenia Phenotypes via Modulation of CREB*, 2 years, $59,968 • **João Cabral**, American Heart Association (Heritage Affiliate), *Biophysical Studies of a Bacterial Cyclic Nucleotide-Regulated Channel*, 3 years, $198,000 • **Cecilia Canessa**, American Heart Association (Heritage Affiliate), *Functional Analysis of SGK1* in Vivo, 3 years, $198,000 • **Daniel Chase**, National Parkinson Foundation, Inc., *Identification of the Molecular Mechanisms of Dopamine Signaling*, 1 year, $40,000 • **Yung-Chi Cheng**, Kagoshima University, *Novel Nucleoside Reverse Transcriptase Inhibitors Active Against Multi-Drug Resistance HIC-1*, 1 year, $35,736 **Hongbo Chi**, Arthritis National Research Foundation, *SIPI-Mediated Regulation of Autoimmune Disease*, 1 year, $50,000 • **Chuhan Chung**, American Liver Foundation, *Hepatocellular Carcinoma and Hepatic Stellate Cells Express Antiangiogenic Pigment Epithelium-Derived Factor; Epigenetic Regulation of PEDF Occurs Through DDR2 Activation on HSC*, 3 years, $225,000 • **David Cone**, National Academies of Emergency Dispatch, *Can EMD Conserve Scarce EMS Resources?*, 1 year, $3,500 **Vladimir Coric**, National Alliance for Research on Schizophrenia and Depression, *Endocannabinoid Receptor Modulation and Obsessive-Compulsive Disorder: A Double Blind, Placebo-Controlled Pilot Study of Dronabinol Addition in Serotonin-Reuptake Inhibitor-Resistant OCD*, 2 years, $59,760 • **Kristina Crothers**, American Lung Association, *Chronic Obstructive Pulmonary Disease in HIV-Positive Compared to HIV-Negative Patients*, 1 year, $40,000 • **Madison Cuffy**, The Thoracic Surgery Foundation for Research and Education, *The Role of Indoleamine 2,3-Diosygenase (IDO) on Modulation of Immune Responses in Inflammatory Arterial Diseases*, 2 years, $50,000 • **Jan Czyzyk**, American Cancer Society, Inc., *Alternative Effectors of Ras GTPase in T Cell Activation*, 4 years, $720,000 • **Pietro De Camilli**, G. Harold and Leila Y. Mathers Charitable Foundation, *Molecular Mechanisms of Synaptic Vesicle Biogenesis*, 3 years, $1,650,179 **Marie Egan**, Cystic Fibrosis Foundation, *Cystic Fibrosis Center*, 1 year, $55,310 • **Barbara Ehrlich**, American Society of Nephrology, *Regulation and Function of Polycystin-2*, 1 year, $50,000 • **Richard Flavell**, Bill and Melinda Gates Foundation, *A Mouse Model to Evaluate Live Attenuated Vaccine Candidates*, 5 years, $16,968,506; Alzheimer's Association, *An Inducible Mouse to Elucidate the Role of Immunity/Inflammation in AD*, 3 years, $234,498 • **Gerald Friedland**, Virginia Commonwealth University, *Opioids and HIV Medications: Interactions in Drug Users*, 1 year, $37,632 • **Mark Gerstein**, Rutgers University, *Structural Genomics of Eukaryotic Domain Families*, 5 years, $230,041 • **Daniel Goldstein**, American Society of Transplantation, *Role of the Innate Immune Ligand Heat Shock Protein 70 in Transplantation*, 2 years, $80,000 **Jonathan Grauer**, Medtronic, Inc., *New Zealand White Rabbit Pseudarthrosis Study Evaluating* INFUSE *and* CRM *Products*, 1 year, $210,138 • **Handan Gunduz-Bruce**, National Alliance for Research on Schizophrenia and Depression, *GABA-Glutamate Interactions and Psychosis*, 2 years, $30,000 • **Ann Haberman**, The S.L.E. Foundation, Inc., *How Germinal Centers Select High-Affinity B Cells: Determination of Cellular Interactions and Migratory Behavior via Intravital Microscopy*, 3 years, $150,000 • **Ala Haddadin**, Union Mutual Foundation, *High-Dose Statin Therapy in the Preoperative Period*, 2 years, $25,000 • **Bryan Hains**, Pfizer, Inc., *Pifzer Scholars in Pain Medicine*, 2 years, $123,000 • **Martha Harding**, AGA Foundation for Digestive Health and Nutrition, *Hepatitis C Virus Infection of Human Liver-Chimeric Mice*, 3 years, $195,000 • **Lise Heginbotham**, American Heart Association (Heritage Affiliate), *Regulation of Ca^{2+} Transport Proteins*, 3 years, $198,000 • **Josephine Hoh**, The Ellison Medical Foundation, *Trans-Racial Gene Mapping for Age-Related Macular Degeneration*, 4 years, $200,000 • **Akiko Iwasaki**, Burroughs Wellcome Fund, *Stromal Cell Contributions in Innate and Adaptive Immune Response to Mucosal Viral Infection*, 5 years, $400,000 • **Jeffrey Kahn**, American Heart Association (Heritage Affiliate), *The Role of a Novel Human Coronavirus in Kawasaki Disease*, 3 years, $198,000 • **Insoo Kang**, American Foundation for AIDS Research, *The Effect of Aging on IL-7 Mediated CD8+ T Cell Survival*, 2 years, $60,000 • **Anil Karihaloo**, National Kidney Foundation, *VEGF Signaling in Renal Tubular Epithelia*, 1 year, $100,000 **Stuart Katz**, American Heart Association, *Erythropoietin in Acute Myocardial Infarction*, 1 year, $66,000 • **Barbara Kazmierczak**, L2 Diagnostics, LLC, *Virulence Typing of* Pseudomonas *Clinical Isolates*, 1 year, $158,204 **Judith Kidd**, University of Florida, *Taste Psychophysics*, 1 year, $76,779 • **Fadi Lakkis**, American Society of Nephrology, *Model Organism to Study Innate Allorecognition*, 1 year, $50,000 • **Angelika Lampert**, Epilepsy Foundation of America, *Control of Excitability in Rodent Spike-Wave Seizures by Voltage-Gated Sodium Channels*, 1 year, $40,000 • **Brian Leaderer**, Brigham and Women's Hospital, *Gene by Environment Interactions in Asthma and Allergy*, 1 year, $185,331 • **Patty Lee**, American Lung Association, *Mechanisms of VEGF and HO-1*, 1 year, $60,000 • **Xin Li**, Arthritis Foundation, *Role of* Borrellia burgdoferi *NapA in Lyme Arthritis*, 2 years, $150,000 **Yi-Hwa Liu**, American Heart Association (Heritage Affiliate), *Development of Quantitative High Resolution and High Sensitivity for Targeted Molecular Imaging*, 3 years, $198,000 • **Elias Lolis**, The Campbell Foundation, *CXCR4 Allosteric Agonists*, 1 year, $11,603 • **Gero Miesenböck**, The Dana Foundation, *Illuminating the Function of Hypothalamic Feeding Circuits*, 3 years, $300,000 • **Angus Nairn**, Rockefeller University, *Molecular Actions of Neuroleptic Drugs*, 1 year, $288,288 • **Michael Nitabach**, Whitehall Foundation, Inc., *Clock-Membrane Coupling in Circadian Pacemaker Neurons*, 1 year, $75,000 • **Aldo Peixoto**, Satellite Research, *Hemodynamic and Hormonal Response to Dialysate Sodium Individualization in Hemodialysis Patients*, 1 year, $50,000 **Patricia Preisig**, University of Texas Southwestern Medical Center at Dallas, *The Formulation of a Rational Therapy of Nephrolithiasis*, 3 years, $123,703 • **Timothy Quan**, Arthritis Foundation, *The Role of Epstein-Barr Virus in Systemic Lupus Erythematosus*, 2 years, $150,000; Abbott Laboratories, Inc., *The Role of Epstein-Barr Virus in Systemic Lupus Erythematosus*, 1 year, $72,000 • **Gary Rudnick**, National Alliance for Autism Research, *Mutation Associated with Asperger's Syndrome—Effect on Amine Transporter System*, 2 years, $120,275 **Raymond Russell**, Dr. Robert C. Atkins Foundation, *Effects of a High-Protein Ketogenic Diet on Myocardial Metabolism*, 1 year, $91,615 **Kristi Sacco**, National Alliance for Research on Schizophrenia and Depression, *Effects of Atomoxetine on Cognitive Function in Schizophrenia*, 2 years, $60,000 • **Mary Schwab-Stone**, Fundación Quiera, *Quiera-Yale Children of the Street*, 1 year, $10,211 • **Gerald Shadel**, A-T Childrens' Project, *Aberrant Regulation of Mitochondrial DNA in Ataxia-Telangiectasia*, 2 years, $42,263 • **Arthur Simen**, National Alliance for Research on Schizophrenia and Depression, *Quantitative Trait Mapping in a Large Mormon Pedigree with Severe Depression and Anxiety*, 2 years, $60,000 **Albert Sinusas**, GE Healthcare Ltd., *Evaluation of Ventricular Remodeling in Animals Using SPECT Imaging After Myocardial Infarction*, 7 months, amount confidential **William Sledge**, Eli Lilly and Company, *YNHH Recidivist Program Prevention Evaluation with Six Sigma Methodology*, 1 year, $129,553 • **Stefan Somlo**, The Joseph LeRoy and Ann C. Warner Fund, Inc., *ARPKD Research*, 1 year, $25,000 • **Julie Sosa**, Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Neurocognitive Changes in Primary Hyper-parathyroidism*, 3 years, $179,374 • **Julie Staley-Gottschalk**, National Alliance for Research on Schizophrenia and Depression, *Antidepressant-Mediated Adaptations in Nicotinic Acetylcholine Receptor Expression*, 2 years, $60,000 • **Mary Tomayko**, Dermatology Foundation, *Phenotypic and Functional Analysis of Memory B cells*, 3 years, $165,000 • **Flora Vaccarino**, National Alliance for Autism Research, *Molecular Mechanisms of Cerebral Cortical Overgrowth*, 2 years, $119,276 • **Lisa Walke**, American Geriatrics Society, *Barriers to and Facilitators of Effective Symptom Management in Older Adults with Chronic Obstructive Pulmonary Disease*, 2 years, $130,000 • **Li Wen**, American Diabetes Association, Inc., *The Role of Toll in Autoimmune Diabetes*, 3 years, $300,000 • **Kevin White**, University of California–Riverside, *Molecular Bases of Ecdysteroid Action in the Mosquito*, 5 years, $157,982 • **Catherine Yeckel**, American Diabetes Association, Inc., *Mild Cold Exposure: A Non-Pharmacological Approach to Improve Insulin Sensitivity In Obese Youth*, 3 years, $414,000 **Mark Yeckel**, National Parkinson Foundation, Inc., *Dopaminergic and Cholinergic Control of Inhibitory Connectivity Between Direct and Indirect Output Pathways of the Neostriatum Background*, 1 year, $40,000 • **Jiasheng Zhang**, American Society of Nuclear Cardiology, *Imaging of Matrix Metalloproteinase Activity in Thoracic Aortic Aneurysm: A Pilot Study*, 1 year, $25,000



With support from the G. Harold and Leila Y. Mathers Charitable Foundation, Professor of Cell Biology Pietro De Camilli studies synaptic vesicles. In this micrograph of rat hippocampus, an enzyme involved in the synthesis of PIP_2, a lipid that is crucial to vesicle formation, is labeled in green.

CORRECTION: The listing in Volume 1, Issue 3 for Brian Leaderer's 5-year NIH grant, *Indoor and Outdoor NO_2 and Asthma Severity in Children*, was incorrect. The correct grant amount is $6,544,369, for 5 years.

Cell biologist Mellman elected to European academy

Ira Mellman, PH.D., chair and Sterling Professor of Cell Biology, is one of three American scientists elected as foreign members of the European Molecular Biology Organization (EMBO) at the organization's annual meeting in Warsaw in October.

Ira Mellman

Membership in EMBO is a life-long honor and scientists are elected on the basis of proven excellence in research. Among the organization's members are some of Europe's leading researchers, including 38 Nobel Prize winners.

EMBO was established in 1964 to create a central molecular biology laboratory and to build a network that would enhance interactions among European laboratories. Currently there are more than 1,200 EMBO members in Europe, and only 60 investigators outside of Europe have been named as associate members.

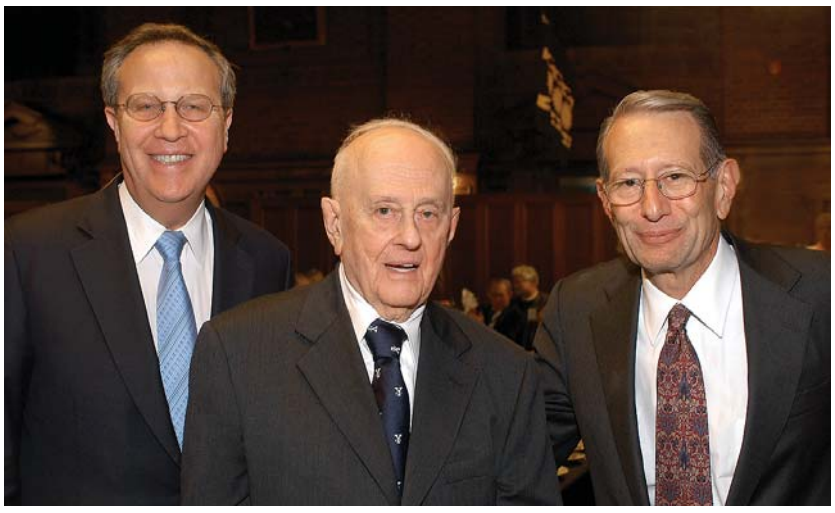
Mellman uses a combination of biochemical, genetic and imaging methods to understand complex functions of cell biology, especially in the immune system. Another area of his research involves the molecular mechanisms that sort, target and transport cell membrane components to appropriate locations in different types of cells.

After receiving his undergraduate degree at Oberlin College, Mellman earned his doctorate in genetics from Yale in 1978. He began his academic career as a postdoctoral fellow and an assistant professor at Rockefeller University and then joined the Yale faculty in 1981.

From 1997 to 2001 Mellman served as founding director of Yale's Combined Program in Biological and Biomedical Sciences, which united all the disparate department-based graduate programs at the School of Medicine and the main Yale campus.

Mellman, who holds a joint appointment in the Department of Immunobiology, is editor-in-chief of *The Journal of Cell Biology* and is on the editorial boards of *Cell* and *The Journal of Experimental Medicine*. He is an affiliate member of the Ludwig Institute for Cancer Research and was named scientific director of the Yale Cancer Center in 2003.

He holds a senior fellowship at Lincoln College, University of Oxford, where he served as Newton-Abraham Professor. Mellman is also a fellow of the American Academy of Arts and Sciences; a member of numerous advisory boards in the public and private sectors in the U.S., Europe and Australia; the recipient of an NIH MERIT award and the Yale Science and Engineering Society Medal. Mellman has delivered endowed lectures throughout the world, including the NIH Director's Lecture.



Nicholas Spinelli celebrates his Yale Medal with Yale President Richard Levin (left) and Association of Yale Alumni Chair Edward Dennis (right).

Alumnus receives Yale Medal for his decades of service

At the end of World War II, Nicholas P.R. Spinelli, M.D., took leave from his Army unit in Germany and hitched a ride on a cargo plane to Rome. From there he traveled to Faeto, a village in southern Italy overlooking the Adriatic Sea that his parents had left 30 years earlier, and where the villagers celebrated the arrival of their native son. "I was there for three nights," says Spinelli, a 1941 alumnus of Yale College and 1944 alumnus of the School of Medicine. "I had to make rounds and visit every sick person in the village."

His triumphant return to his family's ancestral community was the result of his parents' belief in education and Spinelli's own belief in the value of his education at Yale. Had they stayed in Italy, Spinelli said, his parents would never have been able to educate their yet unborn children, Nicholas and his sister, Viola. "Education was a passion with both my parents," he says. "That was why they were working so hard."

Throughout his career, Spinelli has shown his loyalty to Yale by raising money for the medical school, joining with his classmates to establish a scholarship fund, serving as the medical school's director of alumni affairs and sponsoring the first White Coat ceremony, in which newly admitted medical students receive white physician's coats from leaders of the School of Medicine, in 1992.

In November the Association of Yale Alumni awarded Spinelli the Yale Medal, which, since 1952, has honored outstanding service to the university. In this recognition, Spinelli joins such other medical school graduates and faculty members as pediatrician Grover F. Powers, M.D.; Russell B. Scobie, M.D.; William L. Kissick, M.D., M.P.H., DR.PH.; Muriel DuBrow Wolf, M.D.; and former Dean Milton C. Winternitz, M.D.

Spinelli's path to Yale began in Stratford, Conn., where his parents had settled. His father ran several businesses, including a gas station and a restaurant on the Boston Post Road, then the main thoroughfare between New York and Boston.

In 1937 Spinelli entered Yale College, planning to become a writer. At the end of his freshman year, however, he took a job in a biology laboratory, where a professor encouraged him to study medicine, and in the fall of 1941 he entered the School of Medicine.

A few months later, while preparing for an anatomy exam, he heard President Roosevelt announce on the radio that the nation was at war. Spinelli and his 43 classmates were inducted into the Army, and their medical education was accelerated to meet wartime needs. Upon his discharge Spinelli returned to Stratford to practice internal medicine. A heart attack forced his retirement in 1958, but he began a second career as director of medical education at Bridgeport Hospital. In the 1980s his second career gave way to a third, as director of alumni affairs at the medical school. His main concern there was on what he called "incubating alumni," strengthening relations with students and bringing them into the fold by including them in alumni events. At that time he helped create the Committee on the Well-being of Students, which makes a report each year on issues of concern to students.

Perhaps his greatest gift to the medical school was at his 40th reunion in 1984, when he asked his classmates to contribute to a scholarship fund over the next decade. By then, he said, the fund would be large enough to offer its first scholarship. In 1994, with 100 percent participation from the class, the fund helped to support a first-year student; it can now assist up to three students through their first year. "I have gotten letters from students who have been given the scholarship, saying how important it was and how they couldn't have gone to medical school without it," Spinelli says.

For his service to Yale, Spinelli received the Distinguished Service Award from the Association of Yale Alumni in Medicine in 1987 and the Peter Parker Medal in 1994. In recognition of his contributions to the medical school, two rooms were dedicated in Spinelli's honor in 2000, one at the PVA/EPVA Neuroscience and Regeneration Research Center at the VA Connecticut Healthcare System in West Haven and the other at the medical school's Office of Alumni Affairs.

But no honor, he says, surpasses one he received when he was 16 years old: "The greatest gift I got was the letter saying I was accepted to Yale."

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The six elected in October, who were honored at a December reception in the Medical Historical Library, are Kelly D. Brownell, PH.D., chair and professor of psychology, professor of epidemiology and director of the Rudd Center for Food Policy and Obesity (see related story, page 6); Pietro De Camilli, M.D., Eugene Higgins Professor of Cell Biology, Howard Hughes Medical Institute investigator and co-director of the newly formed program in Cellular Neuroscience and Neurodegeneration Research (see related story, page 1); Margaret Grey, R.N., DR.PH., dean of the School of Nursing; Joseph Schlessinger, PH.D., chair and William H. Prusoff Professor of Pharmacology; Gerald I. Shulman, M.D., PH.D., Howard Hughes Medical Institute investigator and professor of medicine and of cellular and molecular physiology; and Joan A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry and Howard Hughes Medical Institute investigator.

New Institute of Medicine members (clockwise from lower left) De Camilli, Shulman, Steitz, Brownell, Grey and Schlessinger with Deputy Dean Carolyn Slayman and Dean Robert Alpern.

Brownell is best known for his efforts to curb obesity. De Camilli, a cell biologist, studies synaptic vesicles, which deliver neurotransmitters into the junctions between nerve cells. Schlessinger studies growth factor receptors and the intracellular signaling pathways they activate. Shulman is an expert on insulin resistance in type 2 diabetes mellitus and the benefits of exercise in diabetes management. Steitz discovered snRNPs, small particles inside cells that are necessary to convert genetic information into active proteins. Grey studies children's adaptation to chronic illnesses, particularly type 1 diabetes.