Medicine@Yale

Advancing Biomedical Science, Education and Health Care

Volume 3, Issue 2 March/April 2007

New PET center will aid drug development

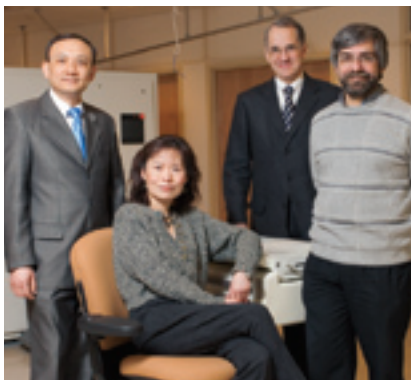
State-of-the-art scans unveil biological processes in the living human body

Although molecular medicine has made striking advances in recent years, for many diseases physicians are still stumbling in the dark, able to glean clues to a therapy's effectiveness only by studying changes in symptoms. In many cases, patients may continue to deteriorate while their doctors seek the best treatment. Researchers at Yale's new Positron Emission Tomography (PET) Center hope to bring light into this darkness and speed the development of new medications by developing novel imaging tools that reveal otherwise hidden molecular abnormalities.

The development of the center was made possible, in part, by Pfizer, the pharmaceutical company, which contributed $5 million to help establish it and provides $2 million annually to support PET imaging studies of mutual research interest to Pfizer and Yale.

The center's faculty also hopes to build additional alliances with other companies, but the majority of the research conducted at the center is anticipated to be supported by federal research grants.

PET, *page 6*



The PET center's senior faculty are Director James Frost (second from right), Henry Huang (left) and Co-Directors Yu-Shin Ding (seated) and Richard Carson.

A passionate venture

Alum's $2.5 million gift to Yale Scholars program spurs study of Alzheimer's

Henry F. McCance, M.B.A., has a special knack for spotting talent and helping young people to realize their aspirations. Over the course of a 40-year career at Greylock Partners, a venture capital firm in Waltham, Mass., McCance and his partners have shepherded almost 300 software companies from idea to reality, a track record that earned him the National Venture Capital Association's Lifetime Achievement Award in 2004.

When a family member was diagnosed with early Alzheimer's disease seven years ago, McCance decided to apply the skills he had honed during his four decades at Greylock into a plan of attack on the disease, which has stubbornly resisted effective diagnosis. In 2005, McCance co-founded the Cure Alzheimer's Fund (CAF), which explicitly adopted a venture capital approach to fund research "with the highest probability of slowing, stopping or reversing Alzheimer's disease by 2016."

So when McCance first heard about the School of Medicine's Yale Scholars initiative, which provides support to outstanding young faculty members as they embark on research careers, the concept had a familiar

Henry McCance applauds the "can-do spirit" of the Yale Scholars initiative.

and appealing ring. McCance got on board enthusiastically with a $2.5 million gift endowing the Henry F. McCance Yale Scholar, an honor that will be bestowed every four years on a new faculty member in the medical school's program in Cellular Neuroscience, Neurodegeneration and Repair. Yale University will match McCance's gift to create a $5 million total endowment, and McCance has contributed an additional $250,000 in current-use funds to ensure that the first McCance Yale Scholar recruit will receive support immediately.

"Startups are often founded by and take their vision from a young, talented person who really 'doesn't know any better' than to take on the incumbent legacy of a corporate giant," says McCance, a 1964 alumnus of Yale College. "They haven't been told it can't be done, so they go do it. The idea of supporting the best up-and-coming research talent under the Yale Scholars program embodies that sort of entrepreneurial can-do spirit."

Robert J. Alpern, M.D., dean and Ensign Professor of Medicine, says, "I am delighted that Henry has chosen to support our efforts to find a treatment for Alzheimer's, and I am especially excited that he will do this through the Yale Scholars program, which focuses support on young investigators."

Yale ties are strong in McCance's family. His father, Thomas McCance, a member of Yale's Class of 1925, was a partner at Brown Brothers Harriman and Co. in New York City, and his brother, Thomas McCance Jr., graduated from the university in 1955. Henry says that his father's example inspired him to study economics at Yale. "I grew up with it at the kitchen table, and then continued at Yale."

McCance went on to earn a master's degree at Harvard Business School and then worked for two years for the Department of Defense during

McCance, *page 8*

A 'country doctor' gives back to Yale by aiding students

When the late John E. Borowy, M.D., enrolled in the School of Medicine in 1946 after serving in World War II, he had few financial resources to fall back on. According to Borowy's nephew, Louis "Skip" DeBeradinis, his uncle's working-class parents were elderly and infirm, and Borowy relied on the GI Bill and income from odd jobs to make his way through medical school.

John Borowy

Borowy, a revered "country doctor" in his hometown of Stamford, Conn., for 45 years, recalled his days as a member of the School of Medicine's Class of 1950 with affection and gratitude, says DeBeradinis. Borowy, who died in February 2006, had no children. He left virtually his entire estate to the medical school to endow a $2.4 million scholarship fund, a legacy that will benefit deserving medical students for years to come.

"I am so grateful to John Borowy and his nephew, Louis DeBeradinis," says Robert J. Alpern, M.D., dean of the School of Medicine. "Dr. Borowy's appreciation for his Yale education and the commitment of his estate to scholarships for our students was an

Borowy, *page 6*

Inside this issue

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A weekly radio show is just one of the many ways in which Kenneth Miller reaches out to cancer patients and their families. Miller also writes books on cancer for a lay audience, and he leads a regular forum where Yale Cancer Center staff can provide support for one another.

A commitment to compassion

Oncologist grapples with the personal impact of cancer on families and caregivers

Throughout his 18 years as an oncologist, Kenneth D. Miller, M.D., has always tried to go above and beyond what many consider to be adequate care for patients and their families. But it wasn't until his wife was diagnosed with acute leukemia in 1999 that he gained a personal understanding of what it is like to live with cancer. That experience prompted him to reflect on how patients are cared for not just during treatment but afterward, and it has culminated in his work as the first director of supportive oncology services at Yale Cancer Center (YCC).

Miller, assistant professor of medicine, traces his interest in oncology to his childhood in Hartford, when he accompanied his father to the medical appointments of a number of friends who had cancer. After graduating from Tufts University School of Medicine, Miller returned to Connecticut for his residency at Yale-New Haven Hospital and then completed two fellowships, one in hematology at the National Institutes of Health and another in medical oncology at the Johns Hopkins Oncology Center.

He practiced medical oncology in the community, and then went on to work for Connecticut Hospice as associate medical director for two years. Miller took a position at YCC in 2005.

With support from the Kenneth B. Schwartz Center, Miller has instituted a regular forum in which YCC doctors, nurses and social workers discuss the difficult emotional and social issues that can arise when caring for patients who are severely ill. Although the sessions focus on the caregivers' feelings, their ultimate aim is to provide more compassionate care to patients.

Miller's parents lost many friends to cancer as they aged, but today patients are surviving longer, sometimes with acute disease, creating a new demand for strategies to address psychosocial as well as medical issues. In October 2006, as part of Yale's effort to offer patients a broader range of care, Miller helped open the Connecticut Challenge Adult Survivorship Clinic, where he serves as medical director.

Lifelines
Kenneth Miller

The clinic, named for an annual bicycle ride in Fairfield, Conn., that benefits survivorship programs at YCC, helps patients who have finished treatment to reflect on the experience and begin to rebuild their lives.

Another of the clinic's programs assists cancer survivors who are still undergoing treatment and are experiencing complications.

"There is a spectrum of things that happen to people who have been through the cancer experience," Miller says, "and we're trying to address some of these issues in a meaningful way." Miller is also in the process of building a palliative care team at Yale to ensure that people receive the same level of medical attention at the end of life as they do while they are undergoing treatment. "We're all going to reach the end of life," he says. "Everyone we treat should be offered the best that we can give in terms of holistic and compassionate care."

Along with Edward Chu, M.D., professor of medicine and YCC deputy director (see related story below), Miller co-hosts the weekly *Healthline* show on WTIC-AM radio in Hartford. He frequently gives lectures to spread his message about how caregivers can contribute to patients' quality of life, and he is distilling his insights into a book, tentatively entitled *Walking in Our Patients' Shoes: The Role of Empathy in Medicine*. Another book, *Choices in Breast Cancer,* is now in press.

Miller says that caring for his patients, developing programs to help improve the quality of life for cancer survivors, and working on end-of-life issues are all pieces of the same puzzle: how to provide compassionate care to cancer patients at every stage of their illness. "It all fits together as a package."

Medical oncologist is appointed deputy director of Cancer Center

Edward Chu

Yale Cancer Center (YCC) is expanding, and so is the role of Edward Chu, M.D. Chu has been appointed deputy director of YCC, where he will also continue to direct the center's clinical research initiatives and serve as chief of medical oncology.

Chu, professor of medicine and pharmacology, graduated from Brown University with undergraduate, master's and medical degrees. He came to Yale in 1996 from the National Cancer Institute, where he was a tenured senior clinical investigator. He is internationally known for his research on tumor resistance to chemotherapy and on new compounds for colorectal cancer.

Over the last two years, Chu has recruited 11 clinical investigators from around the country as part of his plan to transform Yale into a center of translational research.

"Ed's experience and dedication will be a tremendous asset as Yale Cancer Center continues to grow and enters a new phase of expansion with the opening of our new clinical facility in 2009," said YCC Director Richard L. Edelson, M.D.

Chu moves into his new position in the footsteps of José Costa, M.D., who helped lead the center for 10 years, developing research programs and guiding YCC through two comprehensive grant submissions to the National Cancer Institute. Costa, professor of pathology and medicine, remains an active member of the Cancer Center and vice chair of the Department of Pathology.

Cell-signaling expert will lead vascular biology

William C. Sessa, PH.D., an expert on blood vessel function in health and disease, has been named director of the medical school's Program in Vascular Biology and Transplantation (VBT). Sessa, vice chair and professor of pharmacology, has served as deputy director of VBT since 2005.

Founded in 2000, VBT was the School of Medicine's first interdepartmental research program explicitly focused on translating laboratory discoveries into practical treatments for disease. The 35 members of the program, drawn from numerous basic science and clinical departments, study the role of vascular biology in heart disease and peripheral vascular diseases, cancer and stroke. Faculty also search for ways to improve outcomes in organ-transplant patients.

William Sessa

Sessa studies the signals sent by various proteins and by the gas nitric oxide in endothelial cells that form a thin lining inside blood vessels. When these signals are disrupted, vascular disease can result.

As director, he succeeds Jordan S. Pober, M.D., PH.D., the VBT program's founder and professor of pathology, immunobiology and dermatology. Pober will now head the medical school's program in Human Translational Immunology.

"VBT is lucky to have Bill Sessa, an outstanding vascular biologist who is deeply committed to the application of basic research to real clinical problems," says Pober. "I expect him to lead the program in new directions and toward ever greater achievements."

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Peter Farley, *Managing Editor*

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Photographs and Illustrations: American Association for the Advancement of Science, Hal Blumenfeld, John Curtis, Terry Dagradi, Louis DeBeradinis, ©Images.com/CORBIS, Yong Woo Jung, Robert Lisak, Mark Ostow, Margaret Sasaki, William Simpson, Hannah Fairfield Wallander
Design: Peter W. Johnson, Maura Gianakos/Yale RIS

Medicine@Yale is published six times each year by the Office of Institutional Planning and Communications, Yale School of Medicine, 300 George St., Suite 773, New Haven, CT 06511.
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Advances

Health and science news from Yale

Breathing easier about lung injury?

Patients with heart or lung problems, including premature babies, are given supplemental oxygen. But this intervention is sometimes too much of a good thing, because prolonged high concentrations of oxygen can cause hyperoxic acute lung injury, or HALI, in which the lungs' capillaries become leaky.

The protein angiopoietin-2 (Ang2) destabilizes blood vessels, so Jack A. Elias, M.D., the Waldemar Von Zedtwitz Professor and chair of internal medicine, led a study to see whether Ang2 might contribute to HALI.

In the November 5, 2006 issue of *Nature Medicine*, Elias's team reported high Ang2 levels and greater cell death in fluids and lung tissue taken from mice, adult humans and premature infants after exposure to high oxygen levels. But mice treated with RNA that suppressed Ang2 expression had far less damage, and mice bred to lack Ang2 lived significantly longer than their counterparts, raising the possibility that drugs designed to curb Ang2 could protect patients against HALI.

Vineet Bhandari, M.B.B.S., M.D., D.M., assistant professor of pediatrics and first author, says that the study was true bench-to-bedside research. "All the work was initially done on mice ... and then we showed its clinical relevance in human patients with acute lung injury."

Changes in Medicare help prevent cancers

When Medicare coverage expanded to include screening for colon cancer, early diagnosis and treatment also increased, according to a report by School of Medicine researchers in the December 20, 2006, issue of *JAMA: The Journal of the American Medical Association*.

Medicare reimbursement rules first changed in 1998 to cover screening colonoscopies for patients at risk for colon cancer. In 2001 coverage was expanded to include all Medicare recipients.

A team led by Cary P. Gross, M.D., associate professor of medicine, found that colonoscopies have increased by 600 percent since the first Medicare change. The percentage of patients diagnosed at an early stage increased from 22.5 percent to 25.5 percent since 1998; after 2001, that percentage rose to 26.3.

"These data strongly support initiatives to increase access to and use of screening colonoscopy, yet more work needs to be done, as many eligible patients still are not receiving appropriate screening for colorectal cancer," Gross says.

Immunology comes of age at medical school

Top-ranked, influential research group now a full-fledged department

Ever since Edward Jenner first prevented smallpox infection by injecting an English boy with cowpox virus in the 1790s, scientists have worked to conquer infectious diseases by understanding and strengthening the immune response. Yet as recently as three decades ago, the most basic principles of modern immunology eluded researchers, who were scattered across university departments, working largely in isolation.

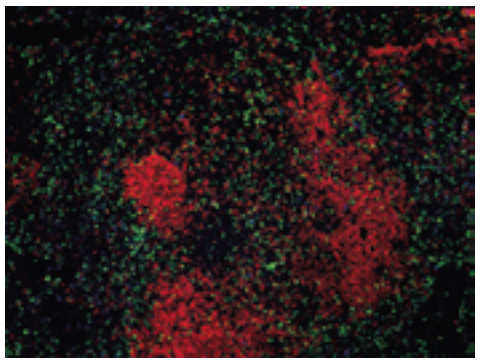
At the School of Medicine all that began to change in 1988. The administration decided to continue the work of the late Richard Gershon, M.D., who had established an immunology division within the pathology department, by recruiting Richard A. Flavell, PH.D., to create the Section of Immunobiology, one of the first freestanding groups in the country devoted to teaching and research in immunology.

Almost 20 years later, Flavell, now Sterling Professor of Immunobiology, continues to lead the School of Medicine's immunologists, but in January his Section of Immunobiology became a full-fledged academic department. What started out in 1988 as a handful of scientists has grown to include 13 world-renowned researchers, including four investigators of the highly competitive Howard Hughes Medical Institute and two members of two of the world's most prestigious scientific societies: the National Academy of Sciences (NAS) and the United Kingdom's Royal Society. "We strategized about it and planned very carefully what we wanted to build, and that's what we built," says Flavell.

Yale's newly christened Department of Immunobiology was named the best in its field in the United States in a *Chronicle of Higher Education* survey published in January. In 2006, department members had over $18 million in combined federal and non-federal research funding; between 1999 and 2006 the faculty collectively published more than 70 scientific articles in the top science journals *Science, Nature* and *Cell*.

A prime example of the department's far-reaching influence is the discovery of the so-called *toll*-like receptors of the innate immune system in the 1990s. At that time, most immunology researchers were focused on the adaptive immune system, which quickly creates custom-made B and T cells that target specific bacterial or viral invaders. But the late Charles A. Janeway Jr., M.D., wondered how the adaptive immune system is able to act so precisely every time the body is invaded by an infectious microbe.

In a scientific tour de force published in 1997 in the journal *Nature*, Janeway and Ruslan M. Medzhitov, PH.D., professor of immunobiology, showed that *toll*-like receptors, a component of the innate system, provide the adaptive system with the necessary advance intelligence to do its job.



In this image, made by postdoctoral associate Yong Woo Jung, PH.D., in the laboratory of Susan Kaech, PH.D., assistant professor of immunobiology, CD8 T cells (green) are responding to viral infection in the spleen. B cells are seen in red.

"It was like saying there are only four planets in the solar system and then one day somebody comes along and says, no, there are eight," says David G. Schatz, PH.D., professor of immunobiology.

According to the National Library of Medicine, nearly 6,000 scientific articles on *toll*-like receptors have been published in the wake of Janeway and Medzhitov's seminal article, but this is just one of many important contributions that have emanated from the department.

Flavell has focused on genetics by examining how different genes contribute to the decision-making process that gives rise to two important immune cells known as Th1 and Th2 cells, which regulate the type of immune response generated by the body. Flavell's lab has identified molecules involved in activating and differentiating T cells that could be useful for treating HIV and cancer.

T cells are also an area of interest for Kim Bottomly, PH.D., Yale's deputy provost for science, technology and faculty development and professor of immunobiology, dermatology and molecular, cellular and developmental biology. Bottomly's lab has shown that the immune response to allergens, such as those that provoke asthma, stems from their similarities to microbes that jump-start the immune system.

Understanding the immune response is also crucial to untangling how it goes awry in autoimmune diseases. Peter Cresswell, PH.D., professor of immunobiology, dermatology and cell biology, studies how proteins get broken down and then "displayed" by antigen-presenting cells that allow T cells to recognize them.

Schatz is focusing on two proteins he discovered that are involved in antibody production and without which there would be no adaptive immune response.

Sankar Ghosh, PH.D., professor of immunobiology, molecular biophysics and biochemistry and molecular, cellular and developmental biology, has concentrated on a protein called NF-κB that allows *toll*-like receptors to send signals. NF-κB is involved in every kind of inflammatory process, from the redness that results when a splinter penetrates the skin to cancer.

The explosive growth of knowledge from the Department of Immunobiology's basic research over the last two decades has led to an increasing awareness that the clinical relevance of immunobiology goes far beyond protection against disease. Immune mechanisms may lie at the root of numerous chronic diseases, including cancer, coronary artery disease and Alzheimer's disease. The department remains in the scientific vanguard with the recently launched Human and Translational Immunology program, which will work on applying lessons learned in the lab to human beings.

Immunobiology chair named to Institute of Medicine

Richard A. Flavell, PH.D., chair of the new Department of Immunobiology at Yale and an internationally recognized scientist, was named to the Institute of Medicine (IOM) in October.

The IOM was established in 1970 by the National Academy of Sciences and is recognized as a national resource for independent, scientifically informed analyses and recommendations on issues related to human health. Those elected to the institute have made significant contributions to the advancement of medical science, health care and public health, and election is considered one of the highest honors in the health sciences.

Flavell, the Sterling Professor of Immunobiology, studies the molecular basis of T-cell differentiation in the immune system. His research team has used genomic approaches to identify the genes that are selectively expressed in T-cell lineages, and has used gene targeting, transgenic mice, and retroviral technology to elucidate the function of these genes and their target sequences.

Richard Flavell

A Howard Hughes Medical Institute investigator, Flavell also studies the mechanisms of programmed cell death using mice lacking death-effector molecules, and he investigates the molecular and cellular bases of autoimmune disease.

"Richard's research is outstanding, clearly placing him among the best immunologists in the world," says Dean Robert J. Alpern, M.D., Ensign Professor of Medicine. "This is combined with a talent for leadership that has allowed him to cultivate an immunology program that is unsurpassed anywhere. His wisdom and experience should prove valuable to the Institute of Medicine."

Out & about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October 12: WTNH meteorologist **"Dr. Mel" Goldstein** celebrated his 10th year as a cancer survivor with friends and colleagues at **THE WONDER OF IT ALL**, a reception and concert held at the New Haven Lawn Club. The event helped double the Dr. Mel Goldstein Multiple Myeloma Research Fund at Yale Cancer Center (YCC), pushing the fund above $200,000. Goldstein established the fund in 1999, three years after being diagnosed with multiple myeloma. **1.** (From left) **Richard L. Edelson**, M.D., professor of dermatology and director of YCC, with Goldstein. **2.** An avid jazz fan and pianist, Goldstein performed "The Circle," a song he composed for the occasion, accompanied by the John Pizzarelli and John Oddo Quartet featuring the Legends of Jazz. **3.** (From right) **Ron Shaw**, president and chief executive officer of the Pilot Pen Corporation of America, and WTNH anchor **Jocelyn Maminta** presented Goldstein with a signed photograph, *Sunrise on the Sound*, donated by photographer Harold Shapiro. **4.** Congresswoman **Rosa L. DeLauro** (D-Conn.) was in attendance.


1

December 12: **1.** The Yale Cancer Center (YCC) hosted **Christian McEvoy**, cofounder of **COAST TO COAST: A RUN FOR SURVIVORSHIP**, when he arrived in New Haven on a five-month, 3,500-mile run across the country to raise awareness and funds for cancer survivors. **2.** McEvoy (center in white shirt) joined **Richard L. Edelson**, M.D., director of YCC (on McEvoy's left) and **Kenneth D. Miller**, M.D., director of the Connecticut Challenge Adult Survivorship Clinic (on McEvoy's right), along with YCC staff and cancer survivors before the group took a ceremonial 1.5 mile run through the city.

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November 18: The Commons at Yale's Woolsey Hall was the setting for the third annual **DISCOVERY TO CURE GALA**, which raised over $345,000 to support research on early detection of and new treatments for ovarian, cervical and uterine cancers. **Peter E. Schwartz**, M.D., the John Slade Ely Professor of Obstetrics, Gynecology and Reproductive Sciences, was honored with the announcement of an endowment established in his name by friends, colleagues, patients and family. **1.** (From left) **Kenneth Schwartz** and **Michelle Fantaci**; **Andrew Schwartz** and **Kelly Arnett**, PH.D., Peter Schwartz and **Arlene Schwartz**; **Anne and Bruce Schwartz. 2. José Costa**, M.D., professor of pathology and medicine and vice chair of the Department of Pathology, (left) with Connecticut Attorney General **Richard Blumenthal**. **3.** (From left) Honorary Discovery to Cure Chair **Rosanne Malouf**, **Donna Malouf**, and **Thomas J. Rutherford**, PH.D., M.D., associate professor of obstetrics, gynecology and reproductive sciences. **4.** (From left) **Richard L. Edelson**, M.D., professor of dermatology and director of Yale Cancer Center; **Ruth Edelson**; Discovery to Cure Chair **Debra Levin** and **Marshall Levin**.


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Jan 25: At the New Haven Lawn Club, **Robert J. Alpern**, M.D., dean and Ensign Professor of Medicine, hosted a **LUNCHEON FOR RETIRED AND EMERITUS FACULTY** who reside in the New Haven area. **1. Arthur Ebbert Jr.**, M.D., professor emeritus of medicine and former deputy dean of the medical school (left), with **Wayne O. Southwick**, M.D., former chair and professor emeritus of orthopaedics and rehabilitation. **2.** (From left) **Arthur B. DuBois**, M.D., professor emeritus of epidemiology, **Brenda Ritchie**, **G. Eric Schonewald**, development officer for the medical school, and **J. Murdoch Ritchie**, PH.D., professor emeritus of pharmacology. **3.** (From left) **Jack R. Cooper**, PH.D., professor emeritus of pharmacology, **David Seligson**, M.D., SC.D., professor emeritus of laboratory medicine, **Charles M. Radding**, M.D., professor emeritus of genetics, **Robert E. Handschumacher**, PH.D., professor emeritus of pharmacology and **Peter Lengyel**, PH.D., professor emeritus and senior research scientist in molecular biophysics and biochemistry. **4. Robert H. Gifford**, M.D., professor emeritus of medicine and former deputy dean for education.

Advances

Health and science news from Yale

Inclined by genes toward nicotine

Nearly 5 million people die prematurely each year from diseases related to smoking. Yet the World Health Organization estimates that more than a billion people smoke, a testament to tobacco's addictive nature.

Growing evidence indicates that some of the tendency for nicotine dependence is inherited. Using DNA from smokers in African-American and European-American families, Joel Gelernter, M.D., professor of psychiatry, genetics and neurobiology, and colleagues recently linked several genetic regions to nicotine dependence.

Many of these regions had already been targeted by other researchers, but in a new finding reported in the January issue of *Biological Psychiatry*, the Gelernter team has shown that a region of chromosome 5 that contains several genes is strongly associated to nicotine dependence in the African-Americans in the study.

"These data add to the growing evidence for specific locations for genes that influence risk for nicotine dependence," says Gelernter, who now hopes to zero in on the specific gene or genes that influence nicotine dependence.

Missing molecule puts neurons off track

During fetal development, different types of neurons must journey to their proper place in the brain's cerebral cortex. A wrong turn along the way may have devastating results, including periventricular heterotopia (PVH), a congenital brain malformation that can cause epilepsy, mental retardation and deficits in learning and memory.

PVH is associated with mutations in a gene known as *Filamin-A*, but little has been known about how these mutations cause neurons to go astray. Research led by Pasko Rakic, M.D., PH.D., professor and chair of neurobiology and director of Yale's Kavli Institute for Neuroscience, has now implicated MEKK4, an intracellular signaling molecule that contributes to proper neuronal migration.

In the December 7, 2006, issue of *Neuron*, Rakic's team showed that MEKK4 regulates levels of Filamin-A protein in the developing brains of mice and that mice engineered to lack MEKK4 had impaired neuronal movement and an increased incidence of PVH.

The findings shed new light on PVH and on cortical development, "a dynamic and complex process that, in humans, occurs during gestation over many months and is regulated by numerous molecules," says Rakic.

Yale research makes *Science*'s 'top 10' list

Faculty, alumnus research cited by premier journal as "breakthroughs" of 2006

The research of two School of Medicine researchers and a Yale alumnus—work on the genetics of a devastating eye disorder, the capacity of stem cells to make identical copies of themselves and the decoding of the Neanderthal genome—has been recognized by the journal *Science* as among the top 10 scientific breakthroughs of 2006.

The journal cited two genomic studies of age-related macular degeneration (AMD) led by Josephine J. Hoh, PH.D., associate professor of epidemiology and of ophthalmology and visual science, along with several other AMD studies, as representing significant progress against the disease, the most common cause of blindness in people over the age of 50. AMD attacks the central area of the retina known as the macula, resulting in progressive loss of vision.

In 2005, Hoh and colleagues compared the DNA of patients with AMD to those who didn't have the disease in order to home in on genetic differences between the two groups. The team eventually linked a variant of a gene on chromosome 1 known as *CFH* with the milder "dry" form of AMD. Last year a group led by Hoh went on to identify a single change in a gene on chromosome 10 that leads to a significantly increased risk of developing the more aggressive "wet" form of the disease.

"Discovery of the association of *CFH* and AMD changed the direction of macular degeneration research," Hoh says, adding that one of the most rewarding aspects of her work has been the collaboration it has sparked with other scientists.

Haifan Lin, PH.D., professor of cell biology and director of the Yale Stem Cell Center, was one of four scientists whose laboratories were listed as contributing to breakthroughs in the understanding of small RNA molecules known as Piwi-interacting RNAs, or piRNAs. Lin's lab first discovered *piwi/argonaute* genes, which are essential for the self-renewal of stem cells, in 1998. But it was not understood what roles these genes play in stem cell division until last year, when Lin's group showed that Piwi/Argonaute proteins bind to piRNAs.

"Despite their tiny size, Piwi-interacting RNAs probably have important functions," notes Lin, who describes them as "tiny, but mighty." Now that Lin has discovered that piRNAs help cells to differentiate into many different cell types, he is trying to find out how they control gene activity inside the cell. This work may have important implications for the understanding of infertility and cancer; because of their tiny size, the molecules could also be more easily used as therapeutic molecules.

Yale alumnus Jonathan Rothberg,

PH.D., also appeared on the top 10 list. Rothberg, who received his doctorate from the university in 1991, is founder and chairman of the board of 454 Life Sciences, a Branford, Conn., company that created technology for the rapid sequencing of genomes. (The sequencer Rothberg's company developed played a role in the discovery of piRNAs; two of the labs in *Science*'s top 10 list used the technology, and stem cell expert Lin is currently using it in his work.)

Rothberg and his collaborators in Germany and Croatia took the No. 2 slot on *Science*'s list for successfully analyzing 1 million base pairs in DNA taken from a 38,000-year-old Neanderthal fossil.

Neanderthals are the extinct hominid group most closely related to contemporary humans and believed to have diverged from modern humans about half a million years ago. The DNA analysis has revealed that the difference between the modern human and the Neanderthal genome is just one base pair in 2,000.

According to Rothberg, the 454 Life Sciences team is poised to sequence the entire Neanderthal genome within two years.

"For the first time," he says, "Neanderthal gives us a handle on understanding human intellect, one of the great mysteries left in science."

High school partnership celebrates 10 years

It's a common sight on any medical school campus: students being asked to identify and explain the function of a muscle on a cadaver they're working with in the anatomy lab. But on a recent afternoon, the students in question weren't enrolled at the School of Medicine, but high school students participating in the Anatomy Teaching Program, one of several ways in which the medical school collaborates with Hill Regional Career High School, a New Haven magnet school just a stone's throw from campus.

Career High attracts students from the New Haven area who hope to work in health care, business or computer technology. Though the medical school's partnership with the high school began informally in 1993 with the anatomy program, this year marks the 10th anniversary of a more formal partnership that has enabled Career High's students to benefit from a wide range of the expertise and resources available at Yale.

The collaboration now has many facets. For a medical careers class, for example, faculty from the Department of Epidemiology and Public Health visit Career High during the first semester to speak about career options; during the second semester, the high school students complete an internship in clinics and laboratories at Yale. To help Career High students understand cell structure, the Department of Epidemiology and Public Health donated a research-quality electron microscope to their school. The medical school assisted Career High in equipping its science labs, and students in the high school's Advanced Biology class come to the School of Medicine twice a month with their teacher, Shirley Neighbors, to get help with course material from medical students.

Medical student Terri Huynh (right) teaches Career High students in the medical school's anatomy lab.

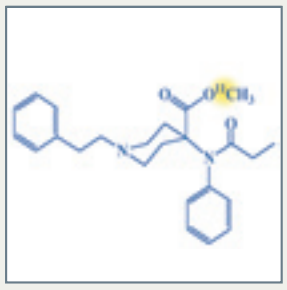
In Career High's anatomy course, also taught by Neighbors, two classes meet twice each month in the medical school's anatomy lab. First- and second-year medical students overseen by William B. Stewart, PH.D., associate professor and chief of the section of anatomy and experimental surgery, volunteer as instructors. In small groups, the students explore such topics as cardiovascular health, energy metabolism and infectious diseases. "One of the ideas is that these kids will become community ambassadors for health," says Stewart.

Thanks to the SCHOLAR initiative (Science Collaborative for Hands-On Learning and Research), a three-week summer residential science program for students entering grades 10 through 12, Career High students have had a chance to become more fully immersed in all Yale has to offer. SCHOLAR students, who normally participate in the program for three years, study science at the college level and conduct research under the supervision of Yale faculty.

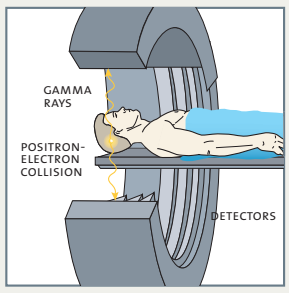
Neighbors believes that, in addition to her students, medical students and society as a whole will see benefits from the Yale-Career High partnership. As she watched second-year medical student Rebecca Bruccoleri explain in a recent class how food is converted to energy, she observed, "If they can find time to do this as a med student, you can imagine what kind of doctors they'll be."

PET *from page 1*

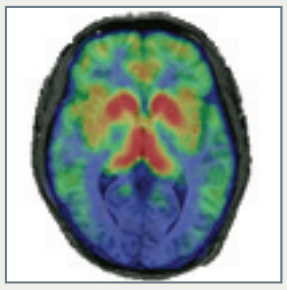
A window into the body



In positron-emission tomography, or PET, a tiny amount of a radioactive atom (here, carbon-11, with a 20-minute half-life) is chemically attached to drug molecules or other biologically active substances. The radiolabeled compound is injected, and quickly accumulates at particular cell-surface receptors or other sites in the body's organs.



The tracer rapidly decays and emits positrons, which collide with electrons, causing both particles to be annihilated. Pairs of gamma rays arise from these collisions, traveling out of the body in opposite directions. A ring of detectors in the PET imaging equipment records the arrival of the positrons in each pair.



Computers calculate the gamma rays' origin, and hence where inside the body the radiolabeled substance bound to its molecular target. These data can be converted into color-coded maps. This image shows the binding levels of carbon-11 carfentanil to opioid receptors in the brain, with areas of highest concentration in red.

At a January 18 ceremony marking the official opening of the new 22,000-square-foot facility, George Mills, M.D., director of the Division of Medical Imaging and Radiopharmaceutical Drug Products at the Food and Drug Administration's Center for Drug Evaluation and Research, said that PET is "the essential foundation" of the agency's efforts to streamline the development of new medicines.

Also in attendance were Pfizer CEO Jeffrey B. Kindler, J.D., Yale President Richard C. Levin and senior leaders from Pfizer and Yale who played key roles in conceiving the center, including Diane K. Jorkasky, M.D., Pfizer's vice president of worldwide research operations, Dean Robert J. Alpern, M.D., James A. Brink, M.D., professor and chair of diagnostic radiology, and psychiatry Chair Benjamin S. Bunney, M.D.

In PET, minute amounts of radioactive material known as tracers are chemically attached to drug molecules or other biologically active substances, such as glucose. When these chemically tagged compounds are injected into a patient's body they bind to specific organ sites, which can be detected and converted into images by the PET scanner (see "A Window into the Body," above). Researchers and clinicians use this information to study changes in organ function as a result of disease or in response to treatment and to determine how much of a drug compound has successfully reached its desired target. PET enables researchers to study the safety and efficacy of different drug doses and to identify biological markers of disease that can aid in diagnosis.

The heart of the new center is a cyclotron encased in a lead radiation shield filled with water; the shield weighs over 100,000 pounds. Within a concrete vault the cyclotron accelerates atomic particles to produce short-lived radioactive isotopes. In an adjacent room, radiochemists collect the isotopes and attach them to appropriate molecules, and the labeled compounds are immediately injected into patients. Then patients lie within the PET scanner, a machine much like a CT scanner that is able to image the accumulation of labeled compounds in specific regions in the body. Yale's new center boasts one of only 18 PET scanners in the world that can image the human brain at a resolution of 2.5 millimeters.

"The work we do here will build the knowledge we need to develop diagnostic imaging agents coupled to personalized therapy," says J. James Frost, M.D., PH.D., M.B.A., professor of diagnostic radiology and psychiatry, chief of nuclear medicine at Yale-New Haven Hospital and director of the new center, located at 801 Howard Avenue in New Haven. Joining Frost as co-directors are lead physicist Richard E. Carson, PH.D., professor of diagnostic radiology and biomedical engineering and lead radiochemist Yu-Shin Ding, PH.D., professor of diagnostic radiology. Completing the senior faculty team is Henry Huang, PH.D., a radiochemist and associate professor of diagnostic radiology.

Pfizer has already used the School of Medicine's new PET facilities to study a small group of patients to determine how much of a new drug for depression would be required to reach its target in the brain in adequate amounts, and how much would generate unacceptable side effects, according to Jorkasky.

Researchers are usually required to give dosages that escalate over a period of several months to large numbers of patients in order to establish the safest and most effective dose of a drug. "If we are able to avoid the need to do large-scale clinical studies like that, we'll be saving tons of money and time, and, most important, we won't expose patients needlessly to a drug that may not have any benefit," says Jorkasky. Frost says that the center will serve as a core facility for the entire medical school in that some biomarkers discovered in the course of research projects with Pfizer or other companies will be available for faculty research projects.

Along with cardiology and oncology, the center's major areas of focus are Alzheimer's disease, schizophrenia, depression, obesity, post-traumatic stress disorder and other conditions that are difficult to diagnose and treat. Frost hopes that the center's research will help to identify biomarkers for subtypes of these diseases, which can help determine the best treatment for specific individuals. "Ultimately this will benefit our patients," Frost says. "That's the key."

The FDA's Mills was enthusiastic in his praise for the new center, which he said is equipped with "one of the most intensely high-resolution scanners that's out there." In particular, Mills lauded the alliance between Yale and Pfizer and the strong links between preclinical and clinical research, animal and human studies, and PET imaging and drug development.

"I've seen the critical pathway, and it's here," Mills told attendees. "You've got it."

Borowy *from page 1*

unusually thoughtful way for him to say thanks. Over many years it will help many students acquire a Yale medical education."

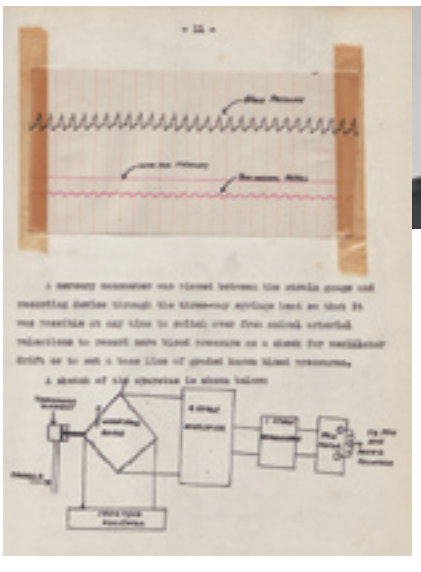
Born in Stamford in 1921, Borowy entered the University of Connecticut in 1938. War was on the horizon, and he joined the Army Air Corps Reserve while in college, graduating in 1942 with a B.S. degree and a second lieutenant's commission.

Almost immediately, Borowy was deployed to the European Theater, followed by a stint in the North African Campaign. He rose to the rank of captain, and eventually was placed in charge of communications on Ascension Island in the South Atlantic Ocean, then a major way station for coded military messages sent between Europe, Africa and the United States. The island was also a refueling stop for planes returning from Europe and Africa, and DeBeradinis says that Borowy's encounters with wounded soldiers on the island were instrumental in his decision to attend medical school.

When settling Borowy's estate, DeBeradinis was surprised as he thumbed through his uncle's medical school thesis, which described a novel method of measuring blood pressure; the pen-and-ink wiring diagrams and meticulously plotted graphs on the yellowing pages (see photo) reveal a technically inclined side of Borowy that his nephew had never known. "He was never really a handy guy when it came to doing anything around the house," DeBeradinis, president of National Meter Industries in Bedford, N.H., recalls with a chuckle. "I used to go over to change light bulbs for him."

But Borowy was "a brilliant, brilliant man," DeBeradinis hastens to add. An avid amateur historian with a special interest in military history who "could recite dates, times and places of all these events that changed history," Borowy had a library of more than 800 books, which DeBeradinis has donated to the Ferguson Library in Stamford.

When Borowy opened his practice in 1954 specializing in pulmonary medicine, Stamford had a far more rural character than it does today, and DeBeradinis says that his uncle's practice retained an old-fashioned flavor—his ledgers show payments in the form of apple pies. "He was very caring, very considerate and concerned for his patients, and gave a lot more than just medical care," says DeBeradinis. "He would make house calls when patients were too sick to come to his office, and he did that right up until he retired from practice in 1999."



(Left) A page from John Borowy's 1950 medical school thesis. (Above) Borowy in 1943.

After retiring, Borowy continued to visit former patients and volunteered at Stamford Hospital and at the VA Connecticut West Haven Healthcare System, where he had been a resident for two years in the mid-1950s.

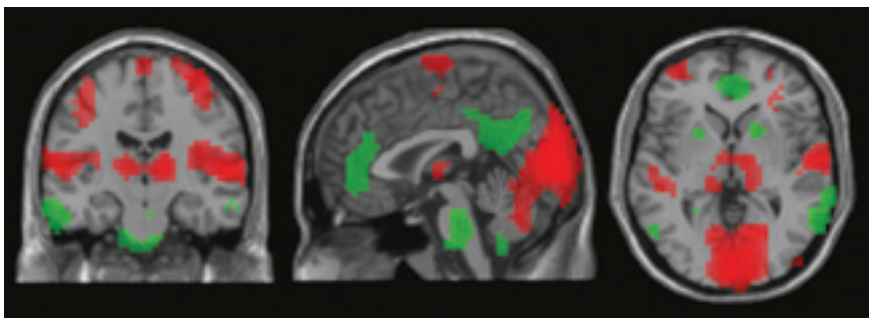
"Everyone knew him as a simple and unpretentious but caring, experienced, qualified physician who was respected by his patients" says Frank R. Coughlin Jr., M.D., a member of the medical school's Class of 1952 who frequently worked with Borowy in his chest surgery practice in Stamford. "The generosity of this gift was a surprise, and a very pleasant one."

DeBeradinis says that his uncle's belief in the importance of good doctoring only grew when his own health began to fail several years ago and he found himself on the other end of the stethoscope.

Of Borowy's bequest, DeBeradinis says that it was his uncle's belief that students with the potential to become skilled and caring doctors should never be held back by financial need. "This was his way of giving back to the community."

Grants and contracts awarded to Yale School of Medicine

July/August 2006



With support from the National Institutes of Health, Hal Blumenfeld, M.D., PH.D., associate professor of neurology, neurobiology and neurosurgery, is performing neuroimaging studies of epilepsy. This image shows brain areas involved in absence seizures in a 12-year-old girl.

Federal

Hervé Agaisse, NIH, *High-Throughput Screen for Compounds Affecting Intracellular Pathogen Infection*, 1 year, $82,500 • **Robert Beech**, NIH, *A Genetic Model for the Role of Neurogenesis in Antidepressant Response*, 2 years, $379,125 **Andrea Benin**, NIH, *Outpatient EHRs: Using Electronic Data to Improve Health and Health Care*, 3 years, $486,000 • **Zubin Bhagwagar**, National Alliance for Research on Schizophrenia and Depression, *A Proton MRS Study of GABA and 5-HT Interactions*, 2 years, $60,000 **Daniel Biemesderfer**, NIH, *Megalin Function in the Normal and Diseased Kidney*, 5 years, $1,694,325 • **Hal Blumenfeld**, NIH, *Functional Neuroimaging in Childhood Absence Epilepsy*, 3.5 years, $1,889,682 • **Arthur Broadus**, NIH, *PTHrP Function in the Periosteum and Entheses*, 2 years, $330,000 • **Robert Bruce**, NIH, *Substance Abuse, HIV and HVC Treatments to Improve Health Outcomes in Drug Users*, 5 years, $870,852 • **Sonia Caprio**, NIH, *Pathophysiology of Metabolic Defects of Juvenile Obesity*, 5 years, $916,605 • **Judy Cho**, NIH, *IBD Consortium Genetics Research Center*, 1 year, $319,573; NIH, *IBD Genetics Consortium Data Coordinating Center*, 1 year, $922,200 • **Robert Constable**, NIH, *Towards an Improved Understanding of BOLD Signal Changes*, 5 years, $1,847,260 • **Nihal Delanerolle**, NIH, *Proteomic Profiles in Human Temporal Lobe Epilepsy*, 2 years, $408,375 • **Caroline Easton**, NIH, *A Therapy Approach for SADV*, 3 years, $873,000 **Erol Fikrig**, NIH, *Immunotherapeutics for Treatment of Flavivirus Infection*, 5 years, $6,982,520 • **Durland Fish**, U.S. Department of Agriculture, *Northeast Regional Tick Control Project*, 1 year, $208,544 • **Terri Fried**, NIH, *Treatment Goals at the End of Life*, 3 years, $1,272,050 • **Frank Giordano**, NIH, *Zinc Finger Proteins to Modify Heart Function*, 5 years, $2,066,250 • **Charles Greer**, NIH, *Neuron Glial Interactions*, 5 years, $1,575,361 • **Ruth Halaban**, NIH, *Yale SPORE in Skin Cancer*, 5 years, $11,500,000 • **Graeme Hammond**, NIH, *MHC Suppression as a Model for Transplant Tolerance*, 2 years, $453,750 • **Kevan Herold**, NIH, *Phase II Trial of HoKT3γ*, 4 years, $2,157,201 • **Margaret Hostetter**, NIH, *Developmental Adaptation: Child Health Research Center*, 4 years, $2,106,443 • **Jeannette Ickovics**, NIH, *Integrating Prenatal Care to Reduce HIV/STDs Among Teens: A Translational Study*, 5 years, $4,511,882 **Mustafa Khokha**, NIH, *Role of Gremlin in Embryonic Development*, 1 year, $121,770 • **Diane Krause**, NIH, *Epithelial Engraftment of Bone Marrow Derived Stem Cells*, 3 years, $743,500 **Daeyeol Lee**, NIH, *Dynamics and Neural Mechanisms of Decision Making*, 1 year, $56,110 **Douglas Leslie**, NIH, *Patterns of Service Use and Costs Associated with Autism*, 3 years, $586,800 • **Ming Li**, NIH, *TGF-beta 1 Regulation of Peripheral T Cell Tolerance*, 5 years, $691,200 **Annette Molinaro**, NIH, *Statistical Methods for Predicting Survival Outcomes from Genomic Data*, 3 years, $478,269 • **Dhasakumar Navaratnam**, NIH, *Studies on Hair Cell BK Channels*, 5 years, $1,859,625 • **Laura Niklason**, NIH, *Novel Cellular Life Span Extension for Tissue Engineering*, 1 year, $187,977 • **Michael Nitabach**, NIH, *Transgenic Tethered Spider Toxins*, 4.5 years, $1,815,282 • **Peter Novick**, NIH, *Genetics of Secretion in Yeast*, 5 years, $2,182,490 • **J. Peter Olausson**, Nat'l Alliance for Research on Schizophrenia and Depression, *Reinforcement of Neuroprotection for Stress Hormone-Induced Hippocampal Damage by FGF Signaling Pathways*, 2 years, $60,000 • **Godfrey Pearlson**, NIH, *Reward, Impulsivity and Cocaine Addiction: fMRI Studies*, 4 years, $1,618,069 • **Marina Picciotto**, NIH, *Antidepressant Effect of Nicotinic Receptor Blockade*, 10 months, $1,580,604 **Douglas Rothman**, NIH, *Acquisition of a 7T Human MR System for the Development of Ultra High Resolution Whole Brain MRSI and MRI*, 1 year, $2,000,000 • **David Rothstein**, NIH, *Peripheral Mechanisms of Immunologic Tolerance*, 5 years, $7,039,959 • **Gerard Sanacora**, NIH, *Studies of Amino Acid Neurotransmitter Contributions to Depression*, 5 years, $634,230 **Alan Sartorelli**, NIH, *Hypoxia-Activated O6-Benzylguanine Prodrugs*, 3 years, $880,401 **Alan Sartorelli**, NIH, *Development of Anticancer 1.2-Bis(sulfonyl)hydrazines*, 4 years, $1,214,240 • **Samuel Sathyanesan**, NIH, *Choroid Plexus and Antidepressants: Genomics and Proteomics*, 2 years, $337,582 • **Nenad Sestan**, Nat'l Alliance for Research on Schizophrenia and Depression, *Characterization of a Novel Candidate Gene in Schizophrenia*, 2 years, $60,000 • **Eugene Shapiro**, NIH, *Effectiveness of Vaccines in Clinical Practice*, 5 years, $760,280 **Mark Shlomchik**, NIH, *Role of B Cells and DCs in Lupus Pathogenesis*, 5 years, $2,339,919 **Warren Shlomchik**, NIH, *Dendritic Cell Subsets and Paths of Maturation in GVHD*, 5 years, $2,066,250 • **Julie Staley-Gottschalk**, NIH, *Cognition, Tobacco Smoke and Nicotinic Receptor Occupancy*, 1.5 years, $336,257 **Thomas Steitz**, NIH, *Structure of DNA and RNA Polymerases and their Functional Complexes*, 4 years, $1,564,921 • **Lisa Suter**, NIH, *The Cost-Effectiveness of MRI in Early Rheumatoid Arthritis*, 5 years, $663,525 • **Eugene Swenson**, NIH, *Liver Injury and Repopulation by Bone Marrow Stem Cells*, 5 years, $671,290 • **Hemant Tagare**, NIH, *Segmentation of Ultrasound Images*, 4 years, $1,556,175 • **Cenk Tek**, Nat'l Alliance for Research on Schizophrenia and Depression, *Mental Transformations in Schizophrenia in Relation to Negative Symptoms and Deficit Syndrome*, 2 years, $59,992 • **Benjamin Turk**, U.S. Department of the Army, *Identification of Substrates and Inhibitors of the Anthrax Lethal Factor*, 1 year, $259,928 • **Sandra Wolin**, NIH, *Antibodies to Ro Ribonucleoproteins as Biomarkers in Sjogren's Syndrome*, 2 years, $431,122

Non-Federal

Jonathan Bogan, W. M. Keck Foundation, *Regulation of Glucose Transporter Trafficking*, 5 years, $1,000,000 • **Titus Boggon**, American Society of Hematology, *Structure/Function Studies of Janus Jinase Family Members*, 2 years, $150,000 • **Elizabeth Bradley**, John D. Thompson Hospice Institute for Education, Training and Research, Inc., *Improving Care for Patients with Irreversible Conditions and Their Families*, 1 year, $100,000 • **Pia Britto**, Russell Sage Foundation, *Man Ana: An Investigation of Ethnic Identity Formation of Muslim Arab Children in the United States*, 2 years, $103,510 **Herta Chao**, American Association for Cancer Research, *The Detection of Pharmacodynamic Changes in Circulating Tumor Cells in Response to Chemotherapy Using Novel Robotic Epifluorescent Microscopy Platform*, 2 years, $100,000 **Katarzyna Chawarska**, Autism Speaks, *Face and Gaze Processing in the Second Year of Life: Comparison between ASD, DD and Typical Infants*, 2 years, $119,979; Autism Speaks, *Why and When Do Children with Autism Develop Difficulties Recognizing Faces?*, 2 years, $100,000 **Haijun Chen**, American Heart Association, *The Molecular and Structural Basis of Beta-Subunits MinK and MiRP1*, 4 years, $260,000 **Lei Chen**, Ambulatory Pediatric Association, *Training of Pre-Hospital Personnel in the Use of Laryngeal Mask Airways in Simulated Pediatric Arrest Scenarios*, 1 year, $8,000 • **Hongbo Chi**, Arthritis Foundation, *Regulation of Immune Response and Systemic Autoimmunity by SIP Signaling*, 2 years, $150,000 • **Susan Compton**, ACLAM Foundation, *Murine Norovirus Pathogenesis and Transmissibility*, 1 year, $24,998 **R. Todd Constable**, The John B. Pierce Laboratory Inc., *Cognitive and Affective Influences on Central Taste Processing*, 5 years, $100,707 **Vladimir Coric**, Obsessive Compulsive Foundation, Inc., *A Double-Blind, Placebo Controlled Trial of N-Acetylcysteine in SRI-Resistant OCD*, 1 year, $36,600 • **Priscilla Dannies**, Elsa U. Pardee Foundation, *Enhancing the Ability of Human Growth Hormone to Reduce Tumor Burden in a Mouse Model of Human Ovarian Cancer*, 1 year, $131,631 • **Alan Dardik**, American Vascular Association, *Flow Responses to Carotid Angioplasty*, 1 year, $75,000 • **Enrique De La Cruz**, American Heart Association, *Actin Filament Cooperativity and Actin Binding Protein Function*, 3 years, $198,000 • **Ronald Duman**, Sepracor Inc., *Influence of Eszopiclone on Neurogenesis and Cell Proliferation in Adult Limbic Brain Structures*, 1 year, $80,025 **Richard Flavell**, American Diabetes Association, Inc., *Prevention of Type 1 Diabetes by TGF-Beta-Induced Regulatory T Cells*, 3 years, $300,000 • **Gerald Friedland**, University of Natal, *Collaborative AIDS Program of Research in South Africa (CAPRISA)*, 1 year, $19,282 **David Geller**, American Heart Assoc. (Heritage Affiliate), *Renal and Extrarenal Effects of Aldosterone*, 3 years, $198,000; Amgen Nephrology Institute, *Molecular Mechanisms of Hypertension in the Metabolic Syndrome*, 1 year, $58,868 **Satish Ghatpande**, Charles H. Hood Foundation, *Novel Mechanisms of Embryo Protection: The Role of Adenosine Action in the Developing Heart*, 2 years, $150,000 • **Daniel Goldstein**, Society of Geriatric Cardiology, *Role of Aging in Vascular Injury*, 1 year, $10,000 • **Fred Gorelick**, Brentwood Biomedical Research Inst., *Alcohol and the Exocrine Pancrease ER Stress Responses*, 1 year, $32,600 • **Jonathan Grauer**, Medtronic, Inc., *Modeling the Deleterious Effect of Infection on Posterolateral Lumbar Fusion in a Rabbit Model and Evaluating the Potential Effect of BMP2 to Overcome this Effect*, 1 year, $155,362 **Kalpana Gupta**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Cranberry for UTI Prevention in Nursing Home Residents*, 2 years, $238,710 • **Bryan Hains**, International Association for the Study of Pain, *Sodium Channel Blockers and Pain after Spinal Cord Injury*, 1 year, $5,000 • **James Hill III**, Albert Einstein Healthcare Network, *The Impact of Healthy Work Organization on Return to Work Outcomes in an Aging Workforce*, 3 years, $190,374 • **Selby Jacobs**, State of Connecticut Department of Mental Health and Addiction Services, *PCP: Person-Centered Care for Psychosis*, 1 year, $432,166 • **Sven-Eric Jordt**, State of Connecticut Department of Public Health, *Sensory Irritant Receptors in the Pathogenesis of Smoking-Induced Lung Disease*, 2 years, $299,723 • **Anil Karihaloo**, American Heart Assoc. (Heritage Affiliate), *Role of VEGF in Renal Ischemic Repair*, 3 years, $198,000 **Haifan Lin**, Stem Cell Research Foundation, *Translation Regulation of Stem Cell Self-Renewal*, 2 years, $80,575 • **Kangmo Lu**, American Diabetes Association, Inc., *New Risk Factors for Diabetic Retinopathy*, 1 year, $100,000 **James Macy**, ACLAM Foundation, *Strategies for MPV Screening*, 1 year, $25,000 • **Arya Mani**, American Heart Assoc. (Heritage Affiliate), *Mapping a Gene for Premature Coronary Artery Disease*, 3 years, $198,000 • **Ira Mellman**, Sandler Program for Asthma Research, *Dendritic Cell Biology and Asthma*, 3 years, $750,000 **Guillermo Mor**, The Johns Hopkins University, *Multiplex Protein Test for Early Detection of Ovarian Cancer*, 1 year, $50,000 • **Laura Niklason**, Texas A&M University, Ex Vivo *Delineation of Mechanisms of Cerebral Vasospasm*, 3 years, $89,182 • **Marcella Nunez Smith**, Robert Wood Johnson Foundation, *Minority Faculty in Academic Medicine: How to Successfully Support Diversity*, 1 year, $49,868 • **A. David Paltiel**, Massachusetts General Hospital, *The Cost-Effectiveness of Preventing HIV Complications*, 1 year, $22,287 • **Chirag Parikh**, American Heart Assoc. (Heritage Affiliate), *A Pilot Study Investigating Novel Biomarkers in Cardiac Surgery to Detect Acute Kidney Injury*, 1 year, $74,931; The Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Novel Biomarkers to Detect Delayed Graft Function*, 3 years, $197,144; Satellite Healthcare, Inc., *The Diagnostic and Prognostic Value of Biomarkers for Acute Kidney Injury in Critically Ill Patients*, 3 years, $150,000 • **Albert Perrino**, Alcoholic Beverage Medical Research Foundation, *Heightened Pain Processing in Individuals at Risk for Alcoholism*, 6 months, $40,000 **Edward Perry**, Alcoholic Beverage Medical Research Foundation, *Interactive Psychopharmacologic Effects of Alcohol and Nicotine in Humans*, 2 years, $90,000 • **George Porter**, Charles H. Hood Foundation, *Calcium Channels Regulate the Formation of the Cardiac Outflow Tract from the Anterior Heart Field*, 2 years, $150,000 • **Nandhini Ramamoorthi**, Arthritis Foundation, *Tick Salivary Protein, Salp 15 and Control of Lyme Arthritis*, 2 years, $150,000 • **Jill Reiter**, Breast Cancer Alliance, Inc., *Quantitative Analysis of EGFR Variants in Breast Cancer*, 2 years, $125,000 • **Scott Rivkees**, Chemical Diversity Labs, Inc., *Identification of Novel ACTH Antagonists*, 1 year, $183,356 **Haleh Saadat**, Foundation for Anesthesia Education Research, *Implementation and Testing of a Wellness Program Conducted with Anesthesiology Residents at Yale*, 2 years, $100,000 • **Robert Sherwin**, American Diabetes Association, Inc., *CNS Responses to Hypoglycemia in Diabetes*, 4 years, $180,000 • **Warren Shlomchik**, The Leukemia & Lymphoma Society, *Memory T Cells for Immune Reconstitution Post-Allogenic Stem Cell Transplantion*, 5 years, $550,000 • **Peter Smith**, ACLAM Foundation, *Mouse Parvovirus: Effects of Immune Status and Pregnancy on Duration and Potential Reactivation of Viral Shedding*, 1 year, $25,000 **Julie Sosa**, American Geriatrics Society, *A Multi-Institutional Randomized Controlled Trial Measuring the Effects of Surgery on Depression, Memory and Concentration Among Elderly Patients with Asymptomatic Primary Hyperparathyroidism*, 2 years, $150,000 • **Matthew State**, Tourette Syndrome Association, Inc., *Investigation of SLIT and Trk-Like Family 1 (SLTRK1): A New Candidate Gene for Tourette Syndrome*, 1 year, $75,000 • **Meredith Stowe**, The Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Reducing Isocyanate Exposure in the CT Autobody Industry*, 3 years, $91,180 • **Lynn Sullivan**, Robert Wood Johnson Foundation, *Reducing HIV Sexual Risk Behaviors in Patients Receiving Treatment for Opioid Dependence*, 3 years, $46,183 • **Lisa Suter**, Arthritis Foundation, *Defining Best Practices for MRI in Rheumatoid Arthritis*, 2 years, $150,000 • **Ning Tian**, Research To Prevent Blindness, Inc., *Research to Prevent Blindness Dolly Green Scholar*, 1 year, $70,000 • **Susumu Tomita**, Esther and Joseph Klingenstein Fund, Inc., *Regulation of Excitatory Synaptic Strength in the Brain*, 3 years, $150,000 • **Elizabeth Triche**, State of Connecticut Department of Public Health, *Genetics and Smoking in Pregnancy*, 2 years, $349,893 • **Marianne Ulcickas Yood**, Henry Ford Health System, *Oral Antidiabetic and Insulin Use Among Patients with Diabetes*, 2 years, $35,000 • **Jack Van Hoff**, St. Baldrick's Foundation, *St. Baldrick's Foundation Award*, 1 year, $25,000 • **Joanne Weidhaas**, State of Connecticut Department of Public Health, *Analysis of miRNA Mutations in Lung Cancer*, 2 years, $265,050 • **Stuart Weinzimer**, Juvenile Diabetes Research Foundation International, *Advanced Studies of Closed Loop Glucose Control on Type 1 Diabetes*, 2 years, $618,082 **Erin Wolff**, University of California—San Francisco, *Regulation of HOXA 10 by Putative Co-Factor Spastin*, 1 year, $119,450 • **Xuchen Zhang**, American Heart Assoc. (Heritage Affiliate), *Role of HO-1 and STAT3 in Oxidant-Induced Lung Injury*, 3 years, $198,000

Scientist is honored by foundation for research on lupus

Immunobiologist unveils molecular mechanisms of autoimmune disease

The S.L.E. Lupus Foundation, the nation's leading organization providing patient services, education and funding for lupus research, has named Mark J. Shlomchik, M.D., PH.D., professor of laboratory medicine and immunobiology, its scientific honoree for the year 2006.

Shlomchik studies the role of B cells, immune system cells produced in bone marrow, in systemic lupus erythematosus (SLE) and other autoimmune diseases.

Normally B cells help to protect the body from infectious agents, but in SLE unknown environmental or genetic factors cause these cells to go awry and to produce antibodies to DNA, RNA and other proteins found in every cell in the body. For this reason lupus affects many of the body's own organs, especially the heart, joints, skin, lungs, blood vessels, liver, kidneys and nervous system. These "autoreactive" B cells also cause the immune system's T cells to target these organs, leading to further damage.

SLE is a chronic condition with a vicious cycle: as the body's damaged tissue becomes inflamed, more autoreactive B cells are produced. For reasons that are not fully understood, the symptoms of lupus—joint pain, fever, skin disorders and fatigue, among others—wax and wane, occurring in intermittent bursts known as "flares." The most common treatments used during flares are corticosteroids or other drugs that suppress the immune system. But these drugs have serious side effects, including increased susceptibility to infection, obesity, diabetes, osteoporosis, hypertension and cataracts, so there is an urgent need to understand the cellular and molecular mechanisms that cause flares and to develop new drugs to prevent them.

Margaret G. Dowd, executive director of the S.L.E. Lupus Foundation, celebrates with Mark Shlomchik at the foundation's annual gala.

As part of this effort, Shlomchik, has focused his recent research on the so-called *toll*-like receptors (TLRs) of the innate immune system (see related story, page 3).

It had long been suggested that B cells might become autoreactive by somehow recognizing DNA or RNA in the cells that form the body's organs. During the past five years, it was shown that TLR9 and TLR7, both of which are expressed on B cells, are specific, respectively, for DNA and RNA.

Following up on this work, Shlomchik and his colleagues reported in 2006 in the journal *Immunity* that lupus-prone mice lacking TLR9 and TLR7 did not generate antibodies against DNA and RNA, and that lupus-like symptoms in mice lacking TLR7 were far less severe.

These findings suggest that developing drugs that target TLRs could be valuable new treatments for lupus and other autoimmune diseases.

After receiving his M.D. and PH.D. degrees from the University of Pennsylvania, Shlomchik joined the Yale faculty as an assistant professor in 1993 and rose through the ranks to become professor in 2004.

He serves on the scientific advisory board of the S.L.E. Lupus Foundation's Lupus Research Institute and is co-chair of its Novel Research and Peer Review task forces. He is also Associate Director of the Yale-New Haven Hospital Blood Bank.

The foundation paid tribute to Shlomchik at its annual gala, held last December at the Marriott Marquis hotel in New York City, saying that he had brought "invaluable insight, encouragement, and direction to the Lupus Research Institute, helping to take it to new levels of scientific excellence."

The event's master of ceremonies was NBC Sports and HBO sportscaster Bob Costas, and entertainment was provided by soprano Barbara Cook, a star of the musical theater for over 50 years.

The foundation also honored James D. Robinson III, M.B.A., chairman of the board of Bristol-Myers Squibb, for his company's development of abatacept (Orencia), a non-steroidal anti-inflammatory agent. Abatacept has won Food and Drug Administration approval for the treatment of rheumatoid arthritis and is now being tested in a multicenter Phase II trial for treating and preventing lupus flares.

Awards & honors

Miguel Coca-Prados, PH.D., professor of ophthalmology and visual sciences, recently completed a professorship at Pfizer's Groton laboratories as the 2006 Yale-Pfizer Global Discovery Visiting Professor. Now in its third year, the Visiting Professor Program is a 12-week sabbatical in which an outstanding Yale faculty member consults and conducts research on Pfizer's campus in southeastern Connecticut. Coca-Prados studies the way in which gene mutations that cause glaucoma alter the normal function of the cells in the eye in which they are expressed.

Joshua A. Copel, M.D., professor of obstetrics, gynecology and reproductive sciences and pediatrics, was awarded the Dru Carlson Award for Research in Ultrasound and Genetics in February at the 27th annual meeting of the Society for Maternal-Fetal Medicine (SMFM). The award was established in memory of Dru Carlson, M.D., an SMFM member known for her expertise in ultrasound and genetics research who died in 2003. Copel, also vice chair and director of Obstetric-Gynecological Ultrasound at Yale, is an authority on high-risk pregnancies, prenatal diagnosis, fetal surgery, amniocentesis and first trimester screening and chorionic villus sampling.

Sankar Ghosh, PH.D., professor of immunobiology, molecular biophysics and biochemistry, and molecular, cellular and developmental biology, has received the Ranbaxy Research Award in basic research for the year 2005. The award is given by the Ranbaxy Science Foundation, a non-profit organization established by Ranbaxy Laboratories, India's largest pharmaceutical company. The award was presented in March at the foundation's 13th annual symposium in New Delhi. Ghosh studies the role of the regulatory protein NF-κB in immune responses and disease, and explores the therapeutic potential of inhibiting the protein.

Alan E. Kazdin, PH.D., the John M. Musser Professor of Psychology, Child Psychiatry and at the Institute for Social and Policy Studies at Yale, has been named president of the American Psychological Association, the largest association of psychologists in the world. Kazdin, who also directs the Yale Parenting Center and Child Conduct Clinic, began his leadership of the 150,000-member organization on January 1 as president-elect and will continue in 2008 as president. Kazdin is interested in advancing psychological science and service on a world stage in the areas of diversity, children and families and social policy.

Anthony Koleske, PH.D., associate professor of molecular biophysics and biochemistry and neurobiology, has been awarded the $500,000 Established Investigator Award from the American Heart Association. The award supports midterm investigators with unusual promise, a record of accomplishments and a demonstrated commitment to cardiovascular or cerebrovascular science. The award will help fund Koleske's research into how cells sense differences in their arterial environment and respond by redirecting their migration. Understanding these cues may lead to treatments to block the formation of atherosclerotic plaque.

Glenn C. Micalizio, PH.D., assistant professor of chemistry, has been named an Eli Lilly Grantee for Organic Chemistry. The award includes a two-year unrestricted grant of $100,000, which Micalizio will use to continue his research on synthesis of complex biologically active organic molecules. He will also participate in the 13th biennial Lilly Grantee Symposium in March 2008 in Indianapolis. Micalizio's research focuses on simplifying the process of molecular synthesis by developing new ways to form carbon–carbon bonds between molecules.

McCance *from page 1*

the Vietnam War. Venture capital was a new idea then, but McCance moved into the field soon after. "In 1966 it was a nascent industry, and I wanted to get away from the 28,000-person office building that the Pentagon represented into something very entrepreneurial."

When Greylock began aggressively investing in software companies in the 1970s, that industry was out of favor with investors, but it soon became McCance's specialty. "Most people thought that hardware investments were more interesting and exciting," McCance says. "We took a contrarian view. Now software touches every part of our lives in business and in the home."

McCance says he now devotes about 40 percent of his time to his new foundation, sounding a clarion call about the urgent need to cure Alzheimer's disease. He sees philanthropic channels like the Yale Scholars initiative and the CAF as necessary in an age of across-the-board cuts in National Institutes of Health research funding, and as a remedy for disproportionately low funding for Alzheimer's disease in particular.

"Even though the disease was discovered 100 years ago, there is remarkably little understanding of the disease or effective therapeutics," he says. "Statistics say that two out of five people will have Alzheimer's by age 85 if there isn't a cure. If you compare the research dollars spent on this disease to HIV/AIDS, cancer or heart disease, it's out of synch. We're not spending enough in this country to cure this disease."