Medicine@Yale

Advancing Biomedical Science, Education and Health Care

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Leading scientist is appointed new chair of Cell Biology

Membrane traffic expert will head a department that has shaped the field

James E. Rothman, PH.D., one of the world's foremost experts on membrane trafficking, the means by which proteins and other materials are transported within and between cells, has been named the Fergus F. Wallace Professor of Biomedical Sciences and chair of the School of Medicine's Department of Cell Biology. Rothman will come to Yale from Columbia University's College of Physicians and Surgeons, where he is now a professor in the Department of Physiology and Biophysics, the Clyde and Helen Wu Professor of Chemical Biology and director of the Columbia Genome Center.

In addition to directing Cell Biology, Rothman is the first recruit to Yale's recently opened West Campus in West Haven, Conn., where he will launch a Center for High-Throughput Cell Biology. At the new center, multidisciplinary teams of scientists will develop tools and techniques to rapidly decipher the cellular functions of the 25,000 known protein-coding genes in the human genome, providing fresh insights into disease and new molecular targets for therapy. Under Rothman's leadership the Department of Cell Biology will be significantly expanded, and will be co-located at the West Campus along with its present location at the main campus of the School of Medicine.

James Rothman

For his decades of seminal research on the transport of molecules

Chair, *page 6*

An indelible smile, and a caring heart

The Class of 2008 mourns the death of a compassionate classmate

On the morning of Saturday, April 19, Mila Rainof, a member of the School of Medicine's Class of 2008, was struck by a car as she crossed a busy street at the northern edge of the medical campus. Rainof, who was scheduled to begin a residency in emergency medicine in Oakland, Calif., in June, died the next day of severe head injuries. At a medical school "town meeting" called by Dean Robert J. Alpern, M.D., on the Monday after Rainof died, Alpern said, "The medical school family has lost a member—way too young in age."

The Class of 2008 is a close-knit group, said class co-president Kristina Zdanys. The loss of any of its members would have been deeply felt, but Rainof was special. "Whenever she walked into a class or [the student cafeteria], she was always smiling or had something nice to say," Zdanys said. One month later, as a procession of the 96 members of her class walked to Yale's Old Campus for Commencement ceremonies, each graduate paused at the corner of York Street and South Frontage Road, where one by one, they placed a carnation in remembrance of Rainof, a beloved classmate who would not be with them on that joyous day. Because she had fulfilled all of the School of Medicine's requirements for graduation, Rainof was awarded the M.D. degree posthumously as a member of the Class of 2008.

JOHN CURTIS

A makeshift memorial to Mila Rainof with flowers, photos and tributes appeared at the intersection of York Street and North Frontage Road, where Rainof was involved in a fatal accident in April. Classmates have established a memorial scholarship fund in Rainof's name, and the Section of Emergency Medicine will give an award each year to the School of Medicine graduate going into emergency medicine who best exemplifies Rainof's compassionate approach to patient care.

In the wake of her death, Rainof's friends and classmates found many ways to honor her. Her close friends stood by Rainof's parents and sister when they came to New Haven and organized a memorial service in the medical school's Rose Garden, where friends remembered Rainof and called upon those gathered to perpetuate her memory by treating others with the same warmth, compassion and kindness that she showed to all. "Like everyone else," said her boyfriend and classmate James Troy, "I was instantly won over by her amazing smile. All of us who spent time with her had no choice but to love her." Friend and classmate Ellen House, who shared clinical rotations with Rainof, said that patients asked for "the smiley one." She mourned for Rainof and for

Rainof, *page 6*

New aid policy will lower tuition debt, widen career choices

The School of Medicine has overhauled its financial aid policy with a major boost in aid to middle-income families by reducing the required parental contribution for families making less than $100,000 per year, medical school Dean Robert J. Alpern, M.D., announced in April.

This change is made possible by the addition to the school's budget of approximately $1.1 million in new need-based scholarship funds from endowment income.

According to Richard Belitsky, M.D., deputy dean for education, the rising pressure of student debt has been accelerating a trend in career choices away from primary care and other lower-paying specialties. In addition to making medical school significantly more affordable for middle-income families, the new policy will also lower financial barriers for students who wish to enter less lucrative fields of medicine. "Our goal is to reduce the debt burden on students and replace it with scholarship aid, so they can make career choices based on what they want to do, rather than what pays the most," said Belitsky.

Richard Belitsky

Aid, *page 6*

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TERRY DAGRADI

Linda Mayes (left), an expert on the effects of stress on the developing brain, with postdoctoral associate Michael Crowley and Crowley's daughter, Lia. Lia is wearing a net containing dozens of electrodes, which detect the differences in electrical potentials across the surface of the brain. By studying changes in these potentials in response to various stimuli, Mayes can monitor the brain function of children who have undergone stress early in development.

Finding blooms amid the ashes

Researcher seeks keys to children's resilience in the face of trauma

"You don't grow up as a Southerner without wondering how people come to be who they are. It's just a part of the culture." So says Linda C. Mayes, M.D., who ought to know, having grown up in the small town of Winchester, Tenn., at the foot of the Cumberland Plateau.

Mayes has built on this cultural touchstone in her scientific contributions to our knowledge of human development. Now the Arnold Gesell Professor of Child Development in the Child Study Center (CSC), she has conducted seminal studies of how stress-induced disturbances in early brain development affect children's later ability to recognize and regulate their emotions.

As a young woman, Mayes moved from Winchester to the mountains of Sewanee, Tenn., to attend college at the University of the South. There, she immersed herself in the history and literature of the post-Civil War South and came away impressed by the extraordinary burst of literary creativity that took place in the wake of the region's wartime trauma and humiliation.

"I've always been interested in the idea that when a culture is undergoing tremendous transition, oftentimes you see a great flowering of the arts." In the field of child development, Mayes explains, researchers "often talk about the capacity to preserve imaginative play. If a child preserves creativity despite horrific trauma, it's often a sign of adaptability and some spark of health."

During medical school training and a pediatrics residency at Vanderbilt University School of Medicine, Mayes specialized in neonatology, with a special interest in the work of the intensive-care nursery. At first, she was captivated by the rapid changes seen in sick infants as they struggle toward wellness, but soon found herself drawn to longer-term questions. "What I ultimately found most intriguing about neonatology was what happened to the infants after they left the nursery," she says, "how their life stories evolved and their long-term outcome after we had done the best we could with medicine."

Arriving at Yale as a Robert Wood Johnson General Pediatrics Fellow in 1992, Mayes began collaborating with the late William Kessen, PH.D., who believed that research ties with pediatricians would strengthen developmental psychology, which he saw as in danger of becoming isolated from children's real-world, day-to-day lives. Other research partnerships with developmental pediatrician Richard H. Granger, M.D., and legendary child psychiatrist and CSC director Donald J. Cohen, M.D., both also now deceased, profoundly shaped her views as well.

Lifelines
Linda Mayes

Trained as a child and adult psychoanalyst, Mayes maintains a clinical practice at the Child Study Center, using play-centered therapy techniques with children as young as 3 years who suffer from trauma or loss of a loved one. In 2007, she was appointed special advisor to Dean Robert J. Alpern, M.D., a position in which she oversees scientific integrity in research conducted at the School of Medicine.

In her own behavioral neuroscience research, Mayes uses dense-array electroencephalography (EEG) to measure subtle changes in brain function that result from early childhood stress, whether caused by prenatal exposure to cocaine or broader, more all-encompassing stressors such as poverty and violence. In long-term studies at Yale, Mayes has found that early cocaine exposure disrupts the regional specialization of the cortex necessary for efficient learning and effective emotional control. These changes themselves lead to an increased vulnerability to drug addiction, a vicious intergenerational cycle that Mayes hopes her work can help to bring to an end. In partnership with the Anna Freud Centre in London, where she is a member of the directorial team, Mayes and her colleagues have recently developed a parallel EEG lab and they are developing clinical interventions for at-risk families and adolescents.

"The families involved in our longitudinal research let us stay in their lives for such a long time, because that's the only way to really find anything out," says Mayes. "We are studying adolescents who are now 15 and 16 years who we have known since they were newborns. It's a real honor."

Online: Yale Netcast
"Teen brains wired to take risks"

Expert on internal workings of bacteria is new HHMI investigator

Christine Jacobs-Wagner, PH.D., the Maxine Singer Associate Professor of Molecular, Cellular and Developmental Biology at Yale, has been named an investigator of the Howard Hughes Medical Institute (HHMI), a non-profit medical research organization that is one of the nation's largest philanthropies.

Jacobs-Wagner is one of the world's leading authorities on the internal organization of bacteria. Working with the bacterium *Caulobacter crescentus*, a common inhabitant of freshwater lakes and streams, Jacobs-Wagner and colleagues discovered that the organism contains intermediate filaments, a cytoskeletal structure previously thought to be present only in animal cells.

Christine Jacobs-Wagner

According to the online Human Intermediate Filament Database, 79 diseases, including amyotrophic lateral sclerosis (Lou Gehrig's disease), Parkinson's disease and some forms of cataracts, have been associated with defects in intermediate filaments. Jacobs-Wagner says that *C. crescentus* offers an excellent model system for understanding these structures.

HHMI's 298 investigators, selected through rigorous national competitions, include 12 Nobel Prize winners and 122 members of the National Academy of Sciences.

Jacobs-Wagner, who received her doctorate at the University of Liège, Belgium, becomes one of 17 scientists at Yale who now hold the prestigious appointment.

Local doctor begins new leadership role in clinical practice

Following an exhaustive national search, Ronald J. Vender, M.D., clinical professor of medicine and a nationally recognized gastroenterologist, has been named chief medical officer (CMO) of Yale Medical Group (YMG), the clinical practice staffed by faculty of the School of Medicine. In this newly created position, Vender, reporting to YMG CEO David J. Leffell, M.D., will assume operational responsibilities and will work to continue to advance the medical school's health care mission. Vender was also appointed as the medical school's associate dean for clinical affairs.

Ronald Vender

Vender will work with medical school and hospital leadership on strategic planning; achieving high satisfaction from patients and referring physicians; ensuring patient safety and high-quality, cost-effective patient care; and establishing measures to ensure excellence in clinical care.

Vender, who graduated from the School of Medicine in 1977 and completed his internship, residency and a fellowship at Yale-New Haven Hospital (YNHH), has held leadership roles at several New Haven-area hospitals, including YNHH, Milford Hospital and the Hospital of St. Raphael, where he has served as section chief of gastroenterology since 1993. In 1997 he founded, with two colleagues, the Gastroenterology Center of Connecticut, a private practice with offices in Hamden, Milford and Guilford.

Vender has twice received the Vincent DeLuca Award for Outstanding Teacher of Gastroenterology. In May, he received the Distinguished Clinician Award from the American Gastroenterological Association.

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Peter Farley, *Managing Editor*

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Advances

Health and science news from Yale

A replacement for hormone replacement?

Estradiol, a naturally occurring female sex hormone, supports skeletal health by balancing the ongoing processes of bone resorption and bone formation. When used as a component in estrogen replacement therapy for post-menopausal women, however, estradiol has been linked to increased risk of some kinds of cancers.

Working with rat-derived osteoblasts, cells that can build bone, School of Medicine scientists have isolated a substance that mimics estradiol but is functionally and chemically different, making it a possible new candidate for hormone replacement.

Studies in the laboratories of Thomas L. McCarthy, PH.D., and Michael Centrella, PH.D., of the Department of Surgery, identified the estrogen-like substance, which triggered several of the biochemical responses induced by estrogen receptor activation. They published their findings in the May 13 edition of the *Proceedings of the National Academy of Sciences USA*.

The scientists hope the osteoblast-derived molecule, which they labeled Ob-SERM, may be developed into a safer alternative to traditional estrogen replacement.

Clearing out Alzheimer's plaques

Alzheimer's disease (AD) patients tend to have elevated levels of TGF-ß, or transforming growth factor beta, an immune system molecule that plays a key role in activating immune response to injury.

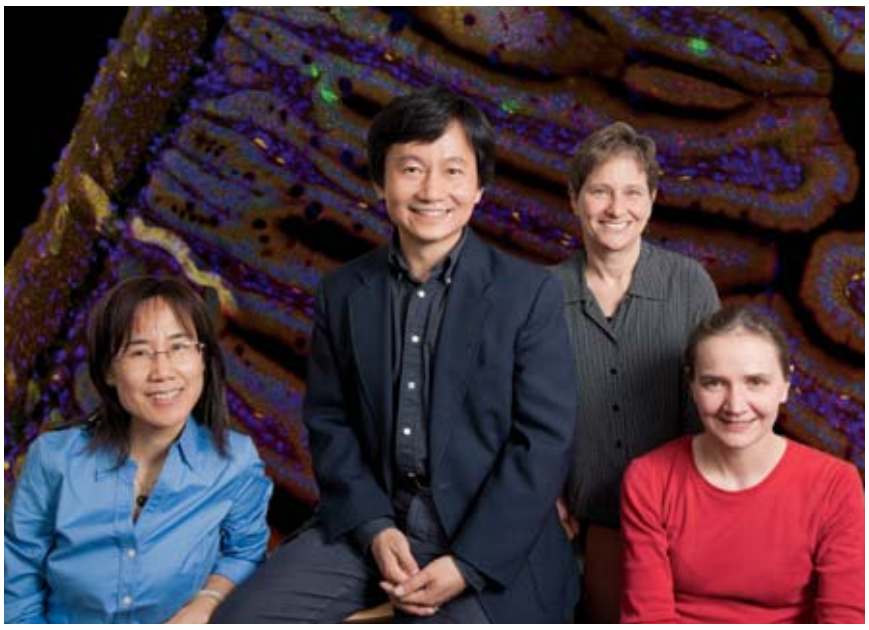
A multi-center group of researchers has found that blocking TGF-ß pathways in mice genetically engineered to display symptoms of AD clears the amyloid plaques in the brain that are a hallmark of the disease. Mice with tamped-down TGF-ß also show minor improvements navigating certain mazes.

In the June issue of *Nature Medicine*, a team led by Terrence C. Town, PH.D., of Cedars-Sinai Medical Center in Los Angeles, and Richard A. Flavell, PH.D., chair and Sterling Professor of Immunobiology and Howard Hughes Medical Institute investigator, reports that interrupting TGF-ß pathways in the mice allowed immune cells to engulf and digest about 90 percent of the plaques in their brains. "It was like a vacuum cleaner had removed the plaques," says Flavell.

Town, the study's lead author, says that if these results are supported by studies in humans, "we may be able to develop a drug that could be introduced into the bloodstream to cause peripheral immune cells to target the amyloid plaques."

A 'Shangri-La' for stem cell research at Yale

A focus on the basics of stem cell biology is Yale's unique approach



HAROLD SHAPIRO, MICROGRAPH COURTESY OF HAIFAN LIN.

(From left) Caifong Qiu, Director Haifan Lin, Associate Director Diane Krause and Natalia Ivanova are advancing research and building new scientific collaborations at the Yale Stem Cell Center. The micrograph in the background shows embryonic stem cells in the intestine of a mouse.

This summer marks the second anniversary of the opening of the Yale Stem Cell Center (YSCC). By any measure, say YSCC Director Haifan Lin, PH.D., professor of cell biology, and Associate Director Diane S. Krause, M.D., PH.D., professor of laboratory medicine and pathology, the center has been a smashing success.

Before the center opened its doors, there was only one laboratory at Yale involved in human embryonic stem cell (hESC) research. Today, there are 12, an enormous leap forward for the medical school and the state of Connecticut, according to Lin, who calls stem cells "the next frontier of biomedical research."

This increase in capacity is critical because hESCs have many advantages over the so-called adult stem cells that can be gathered from tissues such as bone marrow or skin cells: hESCs are easier to collect, they can be grown in large numbers and they in principle can differentiate into any of the cell types that make up the diverse tissues—heart, bone, brain, muscle, and more—of the human body. Although very recent advances in reprogramming adult cells to act more like embryonic stem cells may ultimately help bypass ethical issues, for now, hESCs remain the gold standard against which reprogrammed cells are measured, and the best hope for future medical advances.

The YSCC's state-of-the-art facilities have enabled more researchers to enter the field by helping them scale both the regulatory and technical hurdles involved in stem cell research, Lin says. The center, which occupies the second floor of the new research building at 10 Amistad St., consists of four "cores": stem cell culture, directed by Caihong Qiu, PH.D.; imaging; cell sorting and analysis; and genomics.

Because the space used for hESC research is not supported by federal funds, researchers there are not restricted by government regulations that limit support for hESC research to an approved list of already established stem cell lines. "So far, we have been using the approved cell lines, but we are capable of deriving our own lines, or using non-approved cells lines here," Lin says of the YSCC. "This building is like a Shangri-La for stem cell research."

Part of what made the center possible is a 2005 state law that established Connecticut as a safe haven for hESC research and established the Connecticut Stem Cell Research Program in the state's Department of Public Health, which will provide $100 million to fund hESC research over 10 years. In the first year of that initiative, Yale received $7.7 million, of which $2.5 million went to Lin to establish the stem cell culture core facility. Krause received $1 million to expand her work on leukemia to include studies on hESCs. Michael Snyder, PH.D., professor of molecular, cellular and developmental biology and of molecular biophysics and biochemistry, received $3.8 million to investigate how hESCs differentiate into brain cells. Three other researchers also received smaller seed grants to support new projects.

In the second round of grants, announced in March, Yale received $5.6 million out of the total $10 million put up by the state. The YSCC itself received $1.8 million, and the rest was awarded to 11 faculty members based on original research proposals.

Among the researchers supported by the latest state funding are D. Eugene Redmond Jr., M.D., who received $1.12 million to support his work using hESCs to replace the neurons that die off in Parkinson's disease. Dianqing Wu, PH.D., professor of pharmacology, Laura E. Niklason, M.D., PH.D., associate professor of anesthesiology and biomedical engineering, and Flora M. Vaccarino, M.D., associate professor of neurobiology, each received nearly $500,000 to study heart, blood vessel and neuronal stem cells, respectively. In addition, seven other labs received smaller seed grants to work on both basic and clinical applications of stem cells.

The benefits of the YSCC go beyond Yale. The mission of the center, says Lin, is to provide a centralized source of technical expertise to the community, including colleagues at other institutions. Researchers at the University of Connecticut and Wesleyan University, who have also shared in the state's stem cell funds, have access to the Yale core facilities for their work.

Besides its new labs, the stem cell center boasts 38 affiliated faculty members from departments across Yale, and six months ago Lin and Krause welcomed their first new faculty recruit, Natalia Ivanova, PH.D., assistant professor of genetics and the Robert T. McCluskey, M.D. Yale Scholar. Ivanova is a leader in the use of gene expression profiling to trace the pathways by which undifferentiated embryonic stem cells progress to mature cell types. Much of her

Stem Cells, *page 8*

MEDICINE tomorrow

Scientists at the Yale Stem Cell Center believe that understanding the most basic mechanisms of stem cell biology will lead to more successful clinical applications. The potential impact of stem cell research on human health is enormous. You can help accelerate the pace of this research by supporting Yale's scientists and clinicians. The gift opportunities listed below can fund work in stem cell research or any other area of donor interest.

RESEARCH FUND
$100,000 or more
To support focused research conducted by teams of faculty and graduate students

TECHNOLOGY FUND
$100,000 or more
To expand and upgrade technical resources and fund specialized staff

YALE SCHOLAR
$2.5 million
To support a newly recruited young investigator, like stem cell researcher Natalia Ivanova; gifts are eligible for 100 percent in matching funds from Yale University

PROFESSORSHIP
$3 million
To assist a distinguished faculty member's research and scholarly activities

For information about these or other gift opportunities, visit www.yaletomorrow.yale.edu/medicine or contact Jancy Houck, associate vice president for development and director of medical development, at (203) 436-8560.

Out & about


1


2

ELAINE UBIÑA (4)


3


4

April 26: The 9th annual **LA CASSA MAGICA**, a black-tie gala to benefit Yale Cancer Center (YCC), was held at The Belle Haven Club in Greenwich, Conn. The event raised over $420,000 to support clinical trials of new cancer treatments at YCC. **1. Chris and Gina Lemmon**, vice chairs (along with Blythe Danner, not pictured) for this year's event. **2. Debbie and Louis Chênevert**. **3.** From left: **Duke Brodsky**, **Susan Owens and Howard Brodsky**. **4.** From left: **Beck Gilbert**; **Paula Zahn**; **Richard L. Edelson**, M.D., YCC director and professor of dermatology; **Kathryn Anderson Adams**, chair; and **George Crapple**. Gilbert, Zahn, Anderson Adams and Crapple are all members of the YCC board.

BARBARA WATTS

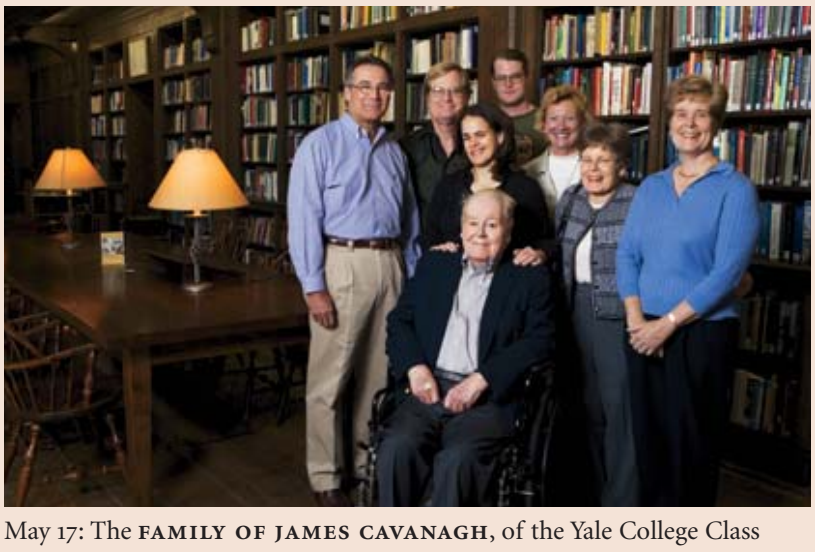
April 27: In the **ANNUAL FACULTY/STUDENT SOFTBALL GAME**, the student team, inspired by graduating captain **Misaki Kiguchi** '08 and co-captain **Saif Rathore** '09, redeemed themselves after losing two of the previous three games to the heroic team led by Dean **Robert J. Alpern**, M.D., known far and wide as "Bob's Bulldogs." (Alpern donates chances to join the game to bidders at the medical students' annual Hunger and Homelessness Auction in support of local charities.) Solid fielding, strong hitting, and clever base running characterized the play of the students—a startling change from previous years—while Alpern's usually flawless team made a number of surprising errors in the field, contributing to a final, rather lopsided score that nobody seems to remember. Front row, from left: **Elizabeth H. Bradley**, PH.D., M.B.A., professor of public health; **Patrick Maloney** '10; **Peter M. Glazer**, M.D., PH.D., the Robert E. Hunter Professor of Therapeutic Radiology; Alpern; **Adam Kaye** '09; **Richard A. Silverman**, director of admissions; Rathore; **Matthew McRae** '09; and **Susan A. Sansone**, registrar, M.D./PH.D. Program. Back row, from left: **Robert Heimer**, PH.D., professor of epidemiology and pharmacology; **Joseph E. Craft**, M.D., professor of medicine and immunobiology; **David L. Rimm**, M.D., PH.D., professor of pathology; M.D./PH.D. student **Adriana Blakaj** '13; **Scott Kennedy** '08; Kiguchi; **Gregory Nelson** '08; **Mark Schlangel** '10; **Christopher Spock** '09; **Daniel Solomon** '10; **Matthew Hornick** '10; **Gabriel Widi** '08; and **Reid Sansone.**

ROBERT MACK

May 6: The Art Place Quilters at Yale, sponsored by the School of Medicine's office of Facilities Operations have made over 30 **LAP QUILTS FOR VETERANS** receiving dialysis or chemotherapy at the VA Connecticut Healthcare System (VACHS) in West Haven, Conn. From left: **Sharon H. Croteau**, chief of voluntary services at VACHS; **Barbara Tracy**; **Lorraine F. Roseman**, operations manager and customer advocate at the medical school; **Jean LaCamera**; **Sue Turbert**; and **Kim Roberts**. (Not pictured: Lauretta Grau, Helen Collibee, Janice Baker and Barbara Judisch.)

TERRY DAGRADI

May 15: Members of the **CONNECTICUT BRAIN TUMOR ALLIANCE** (CTBTA), a foundation created by **Susan Lemkuil** to support brain tumor research and treatment at Yale, presented a check for $15,000 to the Department of Neurosurgery. Back row, from left: **John DeStefano Jr.**, mayor of the city of New Haven; **Dennis D. Spencer**, M.D., the Harvey and Kate Cushing Professor of Neurosurgery; **Joseph M. Piepmeier**, M.D., the Nixdorff-German Professor of Neurosurgery; **David Lemkuil**; and **Andy Pace**. Front row, from left: **Tracy Gamer-Fanning**, CTBTA president; **Kim Hodnett**; **Stacey Mairano**; Susan Lemkuil; **Jennifer Pace**; **Joachim M. Baehring**, M.D., associate professor of neurology and neurosurgery; and **Ron Mairano**.



JULIE BROWN HARWOOD

May 17: The **FAMILY OF JAMES CAVANAGH**, of the Yale College Class of 1942, gathered in the School of Medicine's Medical Historical Library before a luncheon at the venerable Mory's to celebrate Cavanagh's gift of $500,000 to support medical education at Yale. Cavanagh (seated) was joined by (from left) stepson **Gary A. Santora**; son **James F. Cavanagh**; granddaughter **Gayle E. Maslow** (with hands on Cavanagh's shoulders); grandson **Thomas M. Cavanagh**; daughter-in-law **Sara Z. Cavanagh**; daughter **Catharine C. Maslow**; and daughter **Sheila P. Marshall**. (Not pictured: Charles H. Cavanagh, Sarah Cavanagh and Connor P. Cavanagh.)

Advances

Health and science news from Yale

Feminine pharaoh: a genetic anomaly?

Akhenaten, a pharaoh of Egypt's 18th dynasty, is portrayed (see photo) with a thin neck, elongated head, large buttocks, breasts and a prominent belly. These depictions have long intrigued Egyptologists, who have suggested that he was portrayed in this way for religious reasons, or that artists exaggerated his physical characteristics.

ROGER WOOD/CORBIS

But Irwin M. Braverman, M.D., professor of dermatology, believes that ancient artists accurately captured the signs of two genetic conditions: aromatase excess syndrome, in which excess estrogen production can lead to feminization of the male body and early puberty in females, and craniosynostosis, a developmental defect that alters normal skull growth.

The pharaoh's daughters are depicted with breasts, large hips and buttocks at age three and seven in some carvings, and a number of his relatives are shown with identical abnormalities, suggesting genetic causes, says Braverman, who presented his findings at the 14th annual Historical Clinicopathological Conference in May.

No mummy of Akhenaten exists, but Braverman says it may be possible to confirm his retrospective diagnosis with genetic tests on the mummies of Akhenaten's kin.

Natural selection tames alcohol use

It is well known that some East Asians have a low tolerance for alcoholic drinks because they carry variants of genes that help regulate alcohol metabolism.

New research by Kenneth K. Kidd, PH.D., professor of genetics, and first author and postdoctoral associate Hui Li, PH.D., suggests that some environmental change in East Asia during the past few thousand years promoted the spread of one such variant protecting certain ethnic groups from vulnerability to alcoholism.

The new study, published in April in the online journal *PLoS ONE*, reports that a variant of a gene known as ADH1B became widespread specifically among the speakers of the Hmong and Altaic language families because of some relatively recent difference in these groups' environments. Any number of factors—the variant may have conferred resistance to a novel parasite or toxin, for example—could have triggered the genetic change, the researchers say.

That these populations are less prone to alcoholism as a result is happenstance, Kidd says, but "something important in recent human history has affected the genetic composition of many East Asian populations."

Opening up the lines of communication

Gift supports training in medical Spanish for Yale physicians

HAROLD SHAPIRO

In creating a course in medical Spanish at the School of Medicine, Fred and Linda Kantor found a perfect fusion of their longstanding interests in medicine and in New Haven's Hispanic community.

To be successful, the doctor-patient relationship requires clear communication above all else. When a doctor doesn't speak the native tongue of a patient, translators are often called in to help, but because one's health is an intimate and private matter, introducing a third party into a medical discussion is not an ideal solution.

For Linda Kantor, of Orange, Conn., these issues are more than theoretical. Kantor is a founder and vice president of the Board of Directors of Casa Otoñal ("Autumn House"), a campus-like complex of buildings dedicated to housing the elderly of New Haven's Hispanic community. "We've found that when some of our elderly are at the hospital, many times they have to bring along a child or a grandchild as an interpreter," she explains. "But it's not ethically or medically a good idea to have an 8 year old in an Ob/Gyn clinic translating for a grandmother." According to Kantor's husband, Yale immunologist Fred S. Kantor, M.D., the Paul S. Beeson Professor of Medicine, even having the services of a professional translator has its limits. "As a physician, it's wonderful to have a capable translator, but it's not the same as having even rudimentary Spanish" when treating a Spanish-speaking patient, he says.

Michael Vlock, a Branford, Conn.-based executive and philanthropist who has known the Kantors since he was 10 years old—they were close friends of his parents—recently joined his wife, Karen Pritzker, in making a $250,000 gift to the School of Medicine to honor the couple's lifetime of service to Yale and to New Haven. Vlock and Pritzker asked the couple to help choose how the money would be spent. "With this wonderful gift and its income, we didn't want to sponsor an annual lecture or a prize," says Fred Kantor. "Our task was to integrate our interests—medicine, the Hispanic community and the elderly."

The result was a course in "medical Spanish" taught in Yale-New Haven Hospital's Fitkin Amphitheatre last fall. The course drew 60 students and was taught in four sections, twice a week, by Tricia Walter, M.A., a lecturer in Yale's Department of Latin American Studies. Fred Kantor, who took the course himself, says it has been a real boon to his practice of medicine. "I had no knowledge of Spanish at all, and even after one semester I found I could communicate better with the patients," he says. "Their faces brighten when they realize that somebody is trying to communicate with them in their language."

Vlock is pleased that his donation provided the foundation for an initiative that is so much in keeping with the Kantors' varied commitments to the community. "Their ties to both the School of Medicine and to the Hispanic community are very deep," Vlock says. "Their convictions as to the significance and potential lifesaving capacity of teaching medical Spanish were pretty persuasive, and Karen and I are thrilled to be able to empower them, given all that they've done for my family and for the community."

Although elementary Spanish does not negate the need for a trained interpreter, Linda Kantor says that even a rudimentary knowledge of Spanish will make a difference to doctors and patients. "For physicians to at least have a modicum of Spanish, to be able to introduce themselves, to say 'I hope you feel better,' and to be able to ask some pertinent questions in Spanish," she says, "will help to put both the patient and the physician more at ease, and lead to better medical practice."

The kindest cut: single-port surgery at Yale

About 8 percent of the population has an appendectomy at some point in their lives, usually prompted by an attack of acute appendicitis. Until about 2000, appendectomies were performed using traditional "open" surgery techniques, in which surgeons gained access to the abdomen through a single, fairly large incision. For the past decade or so, appendectomies have more commonly been performed laparoscopically, with surgical instruments and a fiber-optic video camera inserted through three small incisions in the abdomen.

In the latest advance for this relatively common procedure, Kurt E. Roberts, M.D., assistant professor of surgery, has pioneered a new laparoscopic technique that requires only a single 11-millimeter incision, or "port." In July 2007, Roberts performed the world's first true single-incision, or single-port, laparoscopic appendectomy at Yale-New Haven Hospital, when he removed the appendix of a 22-year-old woman using only one small incision in the navel. He has since performed 12 more single-port appendectomies, and he has also broadened the technique to complete 4 single-port umbilical hernia repairs and, recently, 10 gall bladder removals.

Kurt Roberts

"This is exciting news because a single-port appendectomy performed with only one small incision is even less invasive than the widely performed three-port laparoscopic appendectomy, which uses three incisions," explains Roberts. "One incision equates to even less pain and shorter recovery time for the patient than the usual three." Similarly, Roberts is now able to remove the gall bladder through only one incision in the navel, an operation traditionally performed with four incisions.

In recent years, the trend in abdominal surgery has been to reduce the number of incisions whenever possible. Roberts' procedure, nicknamed the "puppeteer technique," involves entering the abdomen, grasping the appendix, dissecting and removing it, all through one tiny incision. Because the surgical port is hidden in the navel, Roberts says, an already small incision becomes nearly invisible once the wound has healed, resulting in "tremendous medical and cosmetic benefits for the patients."

Roberts is keenly interested in applying his single-port methods in natural orifice transluminal endoscopic surgery, or NOTES, a growing trend in which operations are performed through bodily orifices such as the mouth, or, in women, the vagina. Using NOTES, surgeons can avoid visible scarring, significantly reduce post-operative pain and gain unprecedented access to internal organs. Roberts believes that surgery is at the beginning of a revolution in which many procedures, including hernia repair and gastric banding for the treatment of obesity, may soon be performed using these new techniques of single-port surgery and NOTES.

Rainof *from page 1*

"all the future memories of Mila that I will never have."

Karen J. Jubanyik, M.D., assistant professor of surgery, recalled a difficult shift she worked in the Emergency Department at Yale-New Haven Hospital the day after Rainof died.

"It was a typical Monday. The ambulance bay looked like Noah's ark; they were coming in two by two. I had intubated two patients by 8 a.m. A woman with a breech baby came in active labor, looking like she was going to deliver on our doorstep. And more than a few patients were looking for specific narcotic medications by name . . . I just thought, 'What would Mila do?' She would dig in hard and contribute in every way possible. She would go to the patient's bedside, hold their hand and genuinely listen to them, without judgment. Her life will go on if we all take what we learned from Mila and incorporate it into our daily life, in the world of medicine and at home. And if we teach this by example to those around us, Mila's impact on this world can grow exponentially." Friend and classmate Maggie Samuels-Kalow said, "Mila was the person that you wanted at your side when the patient was getting sicker and you didn't know what to do."

A group collected photos and remembrances for a book to be given to Rainof's family, while other students also organized efforts to work with the city of New Haven to improve safety at intersections near the medical school. A cherry tree has been planted in her honor on Harkness Lawn.

The Mila Rainof, M.D. Memorial Fund and a new award for graduates entering emergency medicine have been established at the School of Medicine to honor and perpetuate her compassionate spirit and humanistic approach to medicine. For details on the fund or award, please contact Jancy Houck, director of medical development, at (203) 436-8560.

Chair *from page 1*

between intracellular compartments and across cell membranes, Rothman has received numerous honors, including Columbia's Louisa Gross Horwitz Prize and the Lasker Award for Basic Medical Research, two prizes that are sometimes colloquially referred to as "pre-Nobels" because so many recipients of the Horwitz and Lasker awards have gone on to become Nobel laureates. Much of this work was done using a "cell-free" approach, in which Rothman isolated intracellular components crucial to molecular transport in a laboratory dish. This strategy allowed him to perform elegant, focused experiments that sidestepped the complexity of working with complete cells.

"Jim Rothman is one of the most brilliant researchers of our time," said Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. "When Jim started his career, a number of successful biochemists were recognizing the importance of studying molecular processes in cell-free systems, but no one imagined that you could study vesicle trafficking in a cell-free system. Jim had the courage to try and the skills to succeed, and this bold approach revolutionized the field. Jim continues to bring this combination of brilliance and intensity to his research, and now also to the continued development of an exceptional cell biology department."

Carolyn W. Slayman, PH.D., Sterling Professor of Genetics and deputy dean of academic and scientific affairs, added, "Jim Rothman has helped to shape the field of cell biology over the past two decades, and it will be exciting to have him join the scientific community at Yale."

Rothman has many personal and scientific connections to Yale. He graduated *summa cum laude* from Yale College in 1971 with a degree in physics, and conducted research as an undergraduate in Yale's Department of Molecular Biophysics and Biochemistry with Eugene Higgins Professor Donald M. Engelman, PH.D. (then an assistant professor) and Harold J. Morowitz, PH.D., now Clarence J. Robinson Professor of Biology and Natural Philosophy at George Mason University in Fairfax, Va.

Both of Rothman's children are Yale College graduates, and his spouse, Joy Hirsch, PH.D., is a former professor at Yale School of Medicine who now directs the Program for Imaging and Cognitive Sciences at Columbia University.

"My life's work on membrane trafficking in cells was inspired by the discoveries of George Palade, who founded Yale's cell biology department in 1973, and indeed founded the field of cell biology as we know it today," Rothman said. "It is a privilege to lead the department he began as we redefine molecular cell biology and catalyze its impact on medicine, and a unique pleasure to return to Yale."

George E. Palade, M.D., a Nobel Prize-winning cell biologist, led Yale's department for its first decade and established its current directions. Beginning in the 1950s, electron microscope images made by Palade and other scientists revealed that tiny spherical sacs known as vesicles encapsulate and shuttle proteins, hormones, neurotransmitters and other substances between intracellular organelles and to the cell surface. In these micrographs, vesicles were seen to fuse with membranes, spilling their contents into intracellular organelles, or, in the case of the membrane at the cell surface, into the extracellular space, where the released vesicular cargo could interact with neighboring cells or enter the bloodstream to affect distant ones. This latter process, known as exocytosis, is basic to life and occurs in organisms as diverse as yeast and humans; in our own case, exocytosis underlies physiological functions ranging from the secretion of insulin to the regulation of the brain neurotransmitters responsible for movement, perception, memory and mood. Rothman discovered the molecular mechanisms and machinery responsible for these and related processes.

After graduating from Yale, and basic science training as a medical student at Harvard Medical School (HMS), Rothman soon resolved to learn more about the mechanisms of vesicular transport. He shifted his focus to basic science, earning a PH.D. in biological chemistry from HMS in 1976. He then spent two years as a postdoctoral associate in the laboratory of Harvey F. Lodish, PH.D., a preeminent biochemist at the Massachusetts Institute of Technology.

In 1978, Rothman moved to the Department of Biochemistry at Stanford School of Medicine as an assistant professor. At this time, he and Randy W. Schekman, PH.D., of the University of California, Berkeley, conducted parallel research programs, using biochemical and genetic techniques to identify and characterize the proteins that are necessary for vesicle transport, and for the docking and fusion of vesicles with membranes. For this early work, Rothman and Schekman have shared many awards.

Rothman continued his research at Princeton University from 1988 until 1991, when he became the founding chair of the Department of Cellular Biochemistry and Biophysics at Memorial Sloan-Kettering Cancer Center in New York as well as vice chair of the Sloan-Kettering Institute.

In 1993, Rothman discovered a complex of vesicle membrane proteins that he implicated in membrane fusion, and based on this discovery he formulated the "SNARE hypothesis," which has become highly influential in the study of membrane trafficking.

This hypothesis posits that distinctive, complementary protein complexes known as SNAREs, expressed on both vesicles and target membranes, first ensure that different classes of vesicles bind to appropriate membranes and then unleash biochemical changes leading to fusion of vesicles with those membranes and the delivery of the vesicles' cargo to its proper destination.

Rothman has given invited lectures on his work throughout the world, and has served on the editorial boards of *Science* and *Cell*.

He is a member of the National Academy of Sciences and the Institute of Medicine, a fellow of the American Academy of Arts and Science, and a foreign associate of the European Molecular Biology Association.

Rothman succeeds Ira Mellman, PH.D., a distinguished cell biologist and immunologist who was chair and Sterling Professor of Cell Biology at the School of Medicine until 2007, when he joined the biotechnology company Genentech as vice president for oncology research.

Since Mellman's departure last year, former chair James D. Jamieson, M.D., PH.D., professor of cell biology and director of the medical school's M.D./PH.D. Program, has served as interim chair of the Department of Cell Biology.

Aid *from page 1*

In an e-mail to the medical school community, Alpern wrote, "It is critical to the health of medicine and to society in general that medical education is available to students from all segments of society. Medical schools also have an obligation to prepare students for careers in all the specialties, so that patients with every kind of medical need can be served."

Beginning with the 2008 academic year, no contribution toward tuition will be expected from parents earning less than $100,000 whose assets are typical of their income level. Contributions from parents earning more than $100,000 will be calibrated according to a sliding scale based on a realistic assessment of income and assets. The change will apply to both current and newly enrolled students.

The school is also raising its "base loan" amount (which students are expected to cover by taking out a loan before receiving scholarships and grants) from $17,000 to $18,000, but this amount will remain among the lowest of all peer private institutions.

The total cost of medical school at Yale in 2008–2009 will be $62,010 for an incoming student, including tuition, room, board, books, transportation and other expenses. The average medical education debt of School of Medicine students who graduated with outstanding loans in 2007 was $115,000, compared to a national average of $157,000 for graduates of private medical schools. The average debt figure is estimated at $125,000 for this year's graduating class at Yale. In 2007–2008, medical students at Yale received $7.3 million in grants and $9.2 million in student loans. Overall, 87.6 percent of Yale medical students receive some form of financial aid.

The new policy reflects a growing trend among universities with large endowments to make more financial aid available. Yale College announced in January that it would reduce the cost of undergraduate education by up to 50 percent for families with need. Families earning up to $60,000 a year will make no contribution and families earning up to $120,000 will pay no more than 10 percent of their income toward Yale College costs.

Belitsky said, "If you're without any resources, there's scholarship money available to pay for medical school, and if you're wealthy, there's family money to pay for it. What we've found is that it's the middle-income families who have been taking it on the chin." Alpern added, "The school's previous financial-aid formula assumed that families earning as little as $45,000 a year could contribute to their children's medical school costs, when in fact, they often cannot. We're correcting that now."

Grants and contracts awarded to Yale School of Medicine

September/October 2007

Federal

Nadia Abdala, NIH, *Alcohol and HIV Risk Reduction in St. Petersburg, Russian Federation*, 4 years, $2,757,715 • **Norrina Allen**, Agency for Health Care Research and Quality (AHRQ), *Geographic Patterns in Recurrent Stroke Rates by Gender and Race*, 18 months, $37,519 • **Frederick Altice**, Health Resources and Services Administration, *Special Projects of National Significance*, 4 years, $1,600,000 • **George Anderson**, NIH, *Neuroendocrine, Pharmacology, and Genetics Core Resource*, 5 years, $1,620,365 • **Karen Anderson**, NIH, *Universal Technology for Profiling the Dynamics of Normal and Oncogenic Signaling*, 2 years, $363,569 • **Amy Arnsten**, NIH, *Ionic and Second Messenger Basis of Stress-Induced Prefrontal Dysfunction*, 5 years, $1,654,000 • **Andrew Bellemer**, NIH, *Mechanisms for Inhibition of Neurotransmitter Release by the G Protein Galphao*, 3 years, $93,967 • **Jeffrey Bender**, NIH, *Molecular Models of Estrogen-Induced Vascular Protection*, 6 months, $371,250 • **Zubin Bhagwagar**, NIH, *A Study of GABA and 5-HT Interactions to Test a Molecular Model of Vulnerability to Depression*, 5 years, $904,796 • **Hilary Blumberg**, NIH, *Stress, Neurodevelopment and the Emergence of Addictive Behaviors in Adolescence*, 5 years, $992,250 • **Michael Bracken**, NIH, *National Children's Study*, 5 years, $15,053,669 **Elizabeth Bradley**, Agency for Health Care Research and Quality (AHRQ), *Hospital Strategies to Improve Outcome Performance*, 4 years, $1,085,403 • **Ronald Braithwaite**, NIH, *A Computer Simulation of the Sub-Saharan HIV Pandemic That Can Estimate Benefit and Value from Alcohol Interventions*, 5 years, $2,144,325 **Matthew Burg**, NIH, *Reducing Vulnerability to ICD Shock Treated Ventricular Arrhythmias*, 5 years, $2,929,047 • **Michael Cappello**, NIH, *Research Training in Pediatric Infectious Diseases*, 5 years, $610,290 • **Harvey Chin**, NIH, *Defining Effects of Myosin VII Structure and Kinetics on Hereditary Deafness*, 2 years, $81,944 **Judy Cho**, NIH, *IBD Genetics Consortium Data Coordinating Center*, 5 years, $5,703,845; NIH, *Yale University IBD Genetics Research Center*, 5 years, $1,858,550 • **Paul Cleary**, Agency for Health Care Research and Quality (AHRQ), *Consumer Assessment of Healthcare Providers and Systems*, 5 years, $7,354,181 • **Lawrence Cohen**, NIH, *Scan of Protein Space for Optical Voltage Probes*, 5 years, $5,049,153 • **David Cone**, Centers for Disease Control and Prevention (CDC), *E-Semble Virtual Reality Software for Mass Casualty Triage System*, 1 year, $15,000 **Joan Cook**, NIH, *Dissemination of Empirically Supported Psychotherapies*, 2 years, $341,086 **Michael Crair**, NIH, *Development and Plasticity at Thalamocortical Synapses*, 5 years, $1,339,539 **Kristina Crothers**, NIH, *Longitudinal Studies of HIV-Associated Lung Infections and Complications*, 5 years, $3,964,897 • **Dianne Duffey**, NIH, *Mechanisms of ATF2 in Survival of Head and Neck Cancer*, 1 year, $135,000 • **Jasmine Escalera**, NIH, *Activation of TRPA1 Irritant Receptors by Acrolein Fungal Toxicants*, 3 years, $122,916 **Andrew Flannery**, NIH, *Molecular Interactions Involved in Calcium-Regulated Phagocytosis*, 3 years, $153,822 • **Terri Fried**, NIH, *Expanding Treatment Options for Older Persons*, 5 years, $914,037 • **Jorge Galán**, NIH, *The Type III Secretion Effector Protein Interactome*, 2 years, $454,395 • **Alison Galvani**, NIH, *Optional Influenza Vaccine and Population Adherence*, 3 years, $625,925 • **Joel Gelernter**, NIH, *Alcohol Dependence Genetics in a Large Chinese Pedigree*, 2 years, $345,280 • **Peter Glazer**, NIH, *Targeted Correction of the Human Beta-Globin Gene*, 4 years, $1,648,410 • **Fred Gorelick**, NIH, *Exocrine Pancreatic Zymogen Activation*, 5 years, $1,224,014 • **Shannon Gourley**, NIH, *Role of Amygdalostriatal CREB Activity in Persistent Depressive-Like Behavior*, 2 years, $50,697 **Traci Green**, NIH, *Substance Use, HIV Infection and Mortality in a Cohort of Aging Veterans*, 2 years, $66,310 • **Carlos Grilo**, NIH, *Treatment of Binge Eating in Obese Patients in Primary Care*, 5 years, $1,695,520 • **David Hiller**, NIH, *Mechanism of Peptidyl Transfer by the Ribosome Deduced by Kinetic Isotope Effects*, 2 years, $96,472 • **Mark Horowitz**, NIH, *Control of Osteogenesis and Adipogenesis by EBF*, 4 years, $1,283,082 • **Karl Insogna**, NIH, *Microcomputed Tomography Device (Scanco Micro CT35)*, 1 year, $233,348 • **Paul Ivancic**, Nat'l Center for Injury Prevention and Control (NCIPC), *Prevention of Neck Injuries in Older Adults during Rear Motor Vehicle Collisions*, 3 years, $808,284 • **Leslie Jacobsen**, NIH, *Prenatal Cocaine Exposure: Studies of Brain Function*, 20 months, $455,153 **Insoo Kang**, NIH, *Investigating Membrane-Associated T Cell Receptor Signaling in Human CD8+ T Cell Subsets*, 2 years, $270,600; NIH, *Aging and IL-7-Mediated CD8+ T Cell Survival*, 5 years, $1,695,350 • **Kenneth Kidd**, Dept. of Justice (U.S.), *Population Genetics of SNPs for Forensic Purposes*, 18 months, $911,125; Nat'l Science Foundation (NSF), *ALFRED: A Resource for Research and Teaching Human Evolution*, 2 years, $248,516; Nat'l Science Foundation (NSF), *ALFRED: A Resource for Research and Teaching Human Evolution*, 3 years, $370,691 • **Harlan Krumholz**, NIH, *Young Women with Acute Myocardial Infarction*, 4 years, $9,848,211 • **John Krystal**, NIH, *Cortical GABA Function in Alcoholism*, 5 years, $3,318,900 • **Gary Kupfer**, NIH, *Functional Characterization of the Fanconi Anemia Core and D2 Complexes*, 3 years, $1,008,219 • **Daeyeol Lee**, NIH, *Stress, Prefrontal Cortex, and Decision Making*, 5 years, $1,240,500 • **John Leventhal**, NIH, *Integrating Well-Woman and Well-Baby Care to Improve Parenting and Family Wellness*, 2 years, $454,605 • **Paul Lizardi**, NIH, *Probes for Detection of DNA Accessibility in Chromatin*, 3 years, $1,129,191 • **Charles Lockwood**, NIH, *Progestin Effects on Uterine Hemostatsis and Angiogenesis*, 5 years, $2,163,672 • **Carolyn Mazure**, NIH, *Interdisciplinary Research Education*, 5 years, $857,917 • **Sherry McKee**, NIH, *Modeling Stress-Precipitated Smoking Lapse for Medication Development*, 5 years, $1,240,500 • **Diane McMahon-Pratt**, NIH, *Integrated Functional Genomics: On the Road to Leishmaniasis Control*, 1 year, $4,000; NIH, *Multidisciplinary Parasitology Training Program*, 5 years, $1,176,943 • **Ewan McNay**, NIH, *Insulin in the Hippocampus: Memory Enhancement and Impact of Type 2 Diabetes*, 5 years, $1,529,950 **Yorgo Modis**, Dept. of the Army, *The Structural Basis of Pathogen Recognition by Receptors of the Innate Immune System*, 1 year, $178,655 • **Alexander Neumeister**, NIH, *Norepinephrine Transporter Imaging in Alcohol Dependence and Obesity*, 5 years, $1,240,500 • **Laura Niklason**, NIH, *Enabling Strategies for Growing Collagenous Tissues*, 4 years, $2,061,843 • **Stephanie O'Malley**, NIH, *Naltrexone for Heavy Drinking in Young Adults*, 5 years, $3,062,762 • **Godfrey Pearlson**, NIH, *Bipolar and Schizophrenia Consortium for Parsing Intermediate Phenotypes*, 4 years, $3,195,446 • **Joao Pedra**, Centers for Disease Control and Prevention (CDC), *Critical Role of the ASC/Caspase-1 Pathway in Tick-Borne Rickettsiosis*, 3 years, $450,000 • **Marc Potenza**, NIH, *fMRI of Stress and Self-Control in Smoking and Obesity*, 5 years, $1,002,822 **Enrique Pouget**, NIH, *Male-Female Sex Ratio and Risk for HIV/STI Among African-American Women*, 1 year, $40,972 • **Ann Rasmusson**, NIH, *GABAergic Neurotransmission in PTSD*, 18 months, $356,980 • **Jill Reiter**, Dept. of Defense (U.S.), *Soluble EGFR Isoforms in Cell Growth Control*, 1 year, $119,763 • **Bruce Rounsaville**, NIH, *Clinician Scientist Training in Substance Abuse Research*, 5 years, $4,840,939 • **Mehran Sadeghi**, NIH, *Molecular Imaging of Vascular Remodeling*, 5 years, $1,622,500 • **David Schatz**, NIH, *Interdisciplinary Immunology Training Program*, 5 years, $2,816,856 • **Richard Schottenfeld**, NIH, *Drug Counseling and Abstinent-Contingent Take-Home Buprenorphine in Malaysia*, 5 years, $1,614,643 • **Jody Sindelar**, NIH, *Stressors and Their Impact on Health-Related Addictions: Smoking, Drinking, Body Mass Index*, 5 years, $1,211,112 • **Rajita Sinha**, NIH, *Human Subjects Core: Protocols, Statistics, and Collaborative Method Development*, 5 years, $2,962,253; NIH, *ORWH: SCOR on Sex and Gender Factors Affecting Women's Health*, 5 years, $5,255,014; NIH, *Interdisciplinary Research on Stress, Self-Control and Addiction*, 5 years, $5,742,328 • **Robert Soufer**, NIH, *Neurobehavioral Correlates of Mental Stress Ischemia*, 5 years, $2,397,801 • **Julie Staley-Gottschalk**, NIH, *Neuroreceptor Imaging of Tobacco Smokers*, 5 years, $504,467 • **Jane Taylor**, NIH, *Stress-Induced Compulsive Behaviors: CRF Regulation*, 5 years, $1,057,800 • **Derek Toomre**, NIH, *Novel TIRF Microscopy for Analyzing Trafficking and Signaling at the Cell Cortex*, 5 years, $2,481,250 • **Xiao-Jing Wang**, NIH, *Recurrent Neural Circuit Basis of Time Integration and Decision Making*, 5 years, $1,860,938 • **Joanne Weidhaas**, NIH, *Defining the Genetic Basis of the Radioresponse Using a* C. elegans *Tissue Model*, 5 years, $555,660 • **Stuart Weinzimer**, NIH, *Yale Study of Closed-Loop Automated Glucose Control for Hypoglycemia Prevention*, 5 years, $1,197,606 • **John Wysolmerski**, NIH, *The Effect of PTHrP during Lactation*, 4 years, $1,308,611 • **Huiping Zhang**, NIH, *Association and Function of Opioid Receptor Gene Variants to Substance Dependence*, 2 years, $176,324 **Zhengdong Zhang**, NIH, *Gene Regulation in Metastasis and New Methods to Analyze Its Microarray Profiles*, 2 years, $178,496 • **Hongyu Zhao**, Nat'l Science Foundation (NSF), *Collaborative Research: A General Framework for High-Throughput Biological Learning: Theory Development and Applications*, 3 years, $359,997

COURTESY OF E-SEMBLE

With funding from the Centers for Disease Control and Prevention and the Laerdal Foundation for Acute Care, David Cone, associate professor of surgery and director of emergency medical services, is exploring the use of TabletopVR VirtualVictim, virtual reality software designed by Dutch firm E-Semble, to compare triage systems in emergencies involving mass casualties.

Non-Federal

Vikki Abrahams, Lupus Foundation of America, *Mechanisms of Antiphospholipid Antibody-Induced Pregnancy Complications in Patients with APS*, 1 year, $60,000 • **Anna Cali**, Thrasher Research Fund, *Intrahepatic Fat Accumulation, Total and HMW Adiponectin, and the Metabolic Syndrome in Obese Youth*, 1 year, $26,750 • **Jodi Carlson**, Animal Welfare Institute, *Development of a Booklet on the Pair Housing of Macaques*, 6 months, $3,000 • **Sreeganga Chandra**, American Parkinson's Disease Association, Inc., *Delineating the Physiological Function of Synucleins*, 1 year, $50,000 • **Lauren Cohn**, Juvenile Diabetes Research Foundation Int'l, *Inhaled Insulin and Lung Immunity*, 1 year, $110,000 **Miriam Delphin**, Advocates for Human Potential, Inc., *Shared Decision Making*, 6 months, $10,000 • **Michael DiGiovanna**, The Breast Cancer Research Foundation, *Activated HER2 as a Predictor of Therapeutic Response and as a Target in Novel Combination Therapies*, 1 year, $100,000 • **Yu-Shin Ding**, Pfizer Inc, *Feasibility Study into NET Occupancy Determination with PET Radioligand [C-11]MRB([C-11]MeNER)*, 9 months, $212,195 • **Ronald Duman**, Sepracor Inc., *Influence of Eszopiclone on Chronic Unpredictable Stress (CUS): Blockade of the Anti-Neurogenic and Anhedonic Effects of CUS*, 1 year, $148,575 • **Richard Edelson**, Union Mutual Foundation, *Investigations in Transimmunization*, 1 year, $25,000 • **Terri Fried**, Robert Wood Johnson Foundation, *Evolving Toward Effective and Efficient Health Care Decision Making Based on Health Outcomes Priorities Among Adults with Multiple Health Concerns*, 2 years, $224,986 • **John Geibel**, AstraZeneca AB, *Zinc is a Potent Inhibitor of Acid Secretion*, 1 year, $250,000 • **Mark Gerstein**, Wellcome Trust, *Integrated Human Genome Annotation: Generation of a Reference Gene Set*, 9 months, $177,403 **Jeffrey Gruen**, JS Genetics, *Molecular Diagnosis of Dyslexia*, 6 months, $36,409 • **Lyndsay Harris**, The Breast Cancer Research Foundation, *Biomarker Incubator to Define and Validate Predictors of Response to Paclitaxel and Trastuzumab*, 1 year, $223,911 • **Kevan Herold**, Juvenile Diabetes Research Foundation Int'l, *Preclinical Studies of Anti-CD3 mAb and IL-1Ra*, 1 year, $110,280; University of Michigan Health System, *Brehm Coalition Award*, 2 years, $500,000 • **Pei Hui**, Third Wave Technologies, Inc., *A Study to Evaluate the Analytical and Clinical Performance of the Invader HPV Reagents*, 1 year, $47,190 • **Shuta Ishibe**, American Society of Nephrology, *Role of the Met Receptor in Kidney Development and Repair*, 2 years, $200,000 • **Robert King**, Tourette Syndrome Association, Inc., *A Genetic Linkage Study of GTS*, 1 year, $140,356 • **Steven Kleinstein**, Mount Sinai School of Medicine, *Modeling Viral Immunity and Antagonism*, 3 years, $794,542 • **Jeffery Kocsis**, Nat'l Multiple Sclerosis Society, *Therapeutic Potential of Cellular Transplantation into a Focal Model of EAE*, 3 years, $463,694 • **Themis Kyriakides**, Georgia Institute of Technology, *Regenerative Acellular Biomaterials Derived from Embryonic Stem Cells*, 2 years, $21,009 • **Paul Lombroso**, The Institute for the Study of Aging, Inc., *Screening for Inhibitors of STEP*, 1 year, $100,000 • **Mark Mamula**, L2 Diagnostics, LLC, *EGFR Peptides as Vaccines in Anti-Tumor Immunity*, 18 months, $96,144 • **Rory McCrimmon**, Juvenile Diabetes Research Foundation Int'l, *Restoring Hypoglycemia Counterregulation in T1DM*, 3 years, $495,000 • **Thomas McMahon**, Columbia University-Teachers College, *Maternal Drug Use, Psychopathology and Child Adaptation*, 5 years, $889,255 • **Gil Mor**, The Johns Hopkins University, *Multiplex Serum Biomarker for Ovarian Cancer*, 2 years, $267,985 **Angus Nairn**, Brown University, *Structural and Functional Analysis of Signaling Proteins in Dendritic Spines*, 1 year, $23,703 • **Alexander Neumeister**, Nat'l Alliance for Research on Schizophrenia and Depression, *Contribution of Early Life Trauma on Serotonin 1b Receptor Expression in Depression*, 2 years, $99,040 **Karin Provost**, American Thoracic Society, *Airway Epithelial Regulation of Allergic Airway Response*, 1 year, $50,000 • **David Reiss**, Oregon Social Learning Center, *Early Growth and Development Study*, 5 years, $292,366 • **Scott Rivkees**, JS Genetics, *Newborn Screening for Sex Chromosomes Disorders*, 1 year, $109,379 **Gerard Sanacora**, Nat'l Alliance for Research on Schizophrenia and Depression, *The Effect of Stress and Antidepressants on Amino Acid Neurotransmission and Glial Cell Function*, 2 years, $98,952 • **Alan Sartorelli**, Nat'l Foundation for Cancer Research, *Development of a Rapid Simple Quantitative Assay for AGT, the Resistance Protein for Cloretazine and Other 06-Guanine Targeting Drugs, for the Selection of Patients with a High Probability of Response*, 1 year, $75,000 • **Heather Scobie**, Cancer Research Fund of the Damon Runyon-Walter Winchell Foundation, *Defining the Functional Interface Between* Campylobacter jejuni *and its Mammalian Host Cells*, 3 years, $140,000 **Stephen Strittmatter**, F. M. Kirby Foundation, Inc., *Stroke Research Project*, 1 year, $100,000 **Susumu Tomita**, Alfred P. Sloan Foundation, *Research Fellowship*, 2 years, $90,000 • **Fred Volkmar**, The Nancy Lurie Marks Foundation, *Undergraduate Education in Autism*, 2 years, $35,051 • **Anne Williamson**, ITN Energy Systems, Inc., *Wireless Multimodal Brain Monitoring*, 1 year, $29,223

Pioneering brain scientist is winner of inaugural Kavli Prize

Shares $1 million award for 30 years of research on the developing brain

In May, Pasko Rakic, M.D., PH.D., the Dorys McConnell Duberg Professor of Neurobiology and professor of neurology at the School of Medicine, was named one of the inaugural recipients of the Kavli Prize in Neuroscience for his key role in changing our understanding of the cerebral cortex, the seat of human cognitive function.

The $1 million Kavli Prizes, which will be presented biannually for achievements in neuroscience, nanoscience and astrophysics, are a partnership of the Norwegian Academy of Science and Letters, the Oxnard, Calif.-based Kavli Foundation, and the Norwegian Ministry of Education and Research.

Rakic, a neurosurgeon-turned-neuroscientist, was honored along with Sten Grillner, PH.D., professor of neuroscience at Sweden's Karolinska Institute, and Thomas M. Jessell, PH.D., professor of biochemistry and molecular biophysics and Howard Hughes Medical Institute investigator at Columbia University for "discoveries on the developmental and functional properties of neuronal circuits."

"Together Rakic, Jessell and Grillner have managed to decipher the mechanisms that govern the formation and functioning of the complex networks of the neural system to a level of understanding never previously achieved," said Jon Storm-Mathisen, professor of anatomy at the University of Oslo and chair of the Kavli Neuroscience Prize Committee. "The insight spans from the level of signaling molecules to cell and network wiring and action, to behavior. The new knowledge carries promise for future treatments of brain disorders by repairing damaged circuits."

For the past three decades, Rakic has carried out pioneering studies of how neurons in the developing cerebral cortex are generated and how they assemble themselves into the highly ordered, distinctively layered and densely interconnected circuits that direct higher order sensory and motor functions.

"Pasko Rakic has contributed much to our understanding of brain function, defining the mechanisms by which cortical neurons move to the proper location within the cerebral cortex," says Dean Robert Alpern, M.D., Ensign Professor of Medicine. "He is an outstanding scientist who has not only made significant contributions himself, but has developed an exceptional department of neurobiology here at Yale."

Early in his career, Rakic discovered that previously enigmatic support cells known as radial glia serve as guides for the migration of cortical neurons in the developing brain, and he showed how this process is critical for the organization of the multilayered structure of the cerebral cortex.

His "radial unit hypothesis" set the stage for our current view of the steps involved in the evolution of ever more complex and sophisticated brains among the vertebrates. Rakic's four-dimensional model of developmental events over time, from the initial divisions of neuronal stem cells through their migration and stratified settlement in cortical columns, is reproduced in virtually every basic neuroscience textbook.

Rakic also introduced the influential idea that different regions of the cerebral cortex acquire many of their specialized anatomical and functional properties through genetic programs intrinsic to the cortex itself.

Pasko Rakic

The Kavli Prize is named for, and funded by, Fred Kavli, an entrepreneur and philanthropist who was inspired to seek a career in science and engineering while marveling at the northern lights in the skies above the tiny Norwegian village where he grew up. He later moved to the U.S., where he founded the Kavlico Corporation, which became one of the world's largest suppliers of sensors for aeronautic, automotive and industrial application.

In addition to funding the new prizes, Kavli has established 15 research institutes devoted to neuroscience, nanoscience and astrophysics at leading academic institutions around the world. Since 2005, Rakic has been director of the Kavli Institute for Neuroscience at Yale.

At a ceremony in New York announcing the prizes, Kavli said, "The Kavli Prizes were created to recognize achievements in three exceptionally exciting fields which we believe promise remarkable future discoveries and benefits for humanity in the 21st century and beyond."

Yale researcher is lauded for neuropsychiatric discoveries

In April, Amy F.T. Arnsten, PH.D., professor of neurobiology and psychology, was one of 11 scientists to receive a Distinguished Investigator Award from the National Alliance for Research on Schizophrenia and Depression (NARSAD) for her research on the genetic basis of schizophrenia. According to NARSAD, the award was established "to support highly significant research by established scientists . . . who are on the cusp of a breakthrough, or who are poised to test an innovative new idea that has the potential to make a significant advance in a given area of research."

Arnsten's research group has made important contributions to understanding the prefrontal cortex, the most evolved part of the brain. The prefrontal cortex is key for abstract thought and goal-directed behavior, and is weakened in mental illnesses such as attention deficit hyperactivity disorder (ADHD), post-traumatic stress disorder (PTSD), bipolar disorder and schizophrenia. Research in the Arnsten lab has revealed many of the chemical influences at work in the prefrontal cortex, which has led to new treatments for ADHD (guanfacine) and PTSD (prazosin).

Recently, Arnsten has expanded on the insights gained in her research to explore whether a loss of function in the gene *Disrupted-in-Schizophrenia 1*, or *DISC1*, in the prefrontal cortex leads to a collapse of neural networks and loss of dendritic spines—protrusions on nerve cells that play a key role in the transmission of signals from cell to cell—and ultimately to the cognitive dysfunction that is characteristic of schizophrenia. This research is conducted in collaboration with Yale experts, including Arthur A. Simen, M.D., PH.D., assistant professor of psychiatry; Nenad Sestan, M.D., PH.D., assistant professor of neurobiology; Alvaro Duque, PH.D., and Min Wang, PH.D., both associate research scientists in neurobiology; and Constantinos Paspalas, PH.D., of the University of Crete.

The highly competitive Distinguished Investigator Award, which is given to investigators of brain and psychiatric disorders who have established themselves as leaders in their fields, includes a one-year grant of $100,000.

"Dr. Arnsten exemplifies the kind of individual we try to single out for the Distinguished Investigator Award—an outstanding scientist, representing the very best in the field, with an important body of work behind her and currently pursuing innovative and promising research," says Geoff Birkett, president and CEO of NARSAD. Jack Barchas, M.D., chair and Barklie McKee Henry Professor of Psychiatry at Weill Medical College of Cornell University and a 1961 graduate of Yale School of Medicine, chaired the committee that selected the winning proposals. "The work of Dr. Arnsten is extremely impressive," Barchas says, "and, like that of our other 10 Distinguished Investigator awardees, has very real potential to produce insights that will lead to new approaches to treatment for serious mental illness."

Amy Arnsten

In addition to Arnsten's award, two medical school scientists in the Department of Psychiatry were also honored by NARSAD with Young Investigator Awards, created to help the most promising scientists who are now entering research . . . to generate pilot data necessary for larger grants." The awards carry grants of $60,000 each distributed over two years.

Savita G. Bhakta, D.P.M., a postdoctoral associate who does research at the VA Connecticut Healthcare System in West Haven, Conn., plans to gain a better understanding of the neurochemistry of schizophrenia by studying how cannabinoids (chemical compounds found in marijuana) induce schizophrenia-like behavioral and cognitive effects in healthy people and exacerbate symptoms in patients with schizophrenia. Fei Wang, PH.D., associate research scientist, will use multimodal magnetic resonance imaging technology to study adolescents with bipolar disorder to identify abnormalities in brain circuitry serving the emotional processing that are implicated in the illness.

The Long Island, N.Y.-based NARSAD is the world's largest donor-supported organization supporting research on brain and behavior disorders. Since 1987, NARSAD has awarded more than $230 million to nearly 2,700 scientists.

Online: Yale Netcast
"This is your brain on stress"

Stem Cells *from page 3*

groundbreaking work had been done with mouse stem cells, but funds from Connecticut's initiative are allowing her to expand her studies to hESCs. Ivanova's work exemplifies the philosophy of the center and its founders—to keep a focus on basic questions of stem cell biology, with the idea that this will lead to clinical applications.

As Lin explains, "We actually know very little about stem cells, and that makes me feel that some people are jumping ahead too fast. If we don't know how they work, how can we harness their potential?" This vision dovetails well with the medical school's strength in basic research, and makes the YSCC a unique player in the stem cell field. "Few other places have been focusing on really understanding the inner workings of stem cells," he says. "We think we can and believe that by doing that we will generate more impact and speed the development of cures."

In that effort, state support has been a critical factor, but it is only the beginning. "We will be eternally grateful for the support from the state, but we have to think of their contribution as seed money," Lin says. "Stem cell research in still in its infancy. Our center is a new baby that has been born, but now we need to feed it and let it grow up. One thing we know is that this baby is full of potential."

Online: Yale Netcast
"The 'lead-by-science' approach to stem cell research"