

Medicine@Yale

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Smilow Cancer Hospital, a 'great achievement,' welcomes patients



Joel Smilow addresses attendees of the hospital's opening day celebration.

New \$467 million facility built with gift from alumnus offers patient-centered care

Gray skies overhead could not dampen the celebratory mood on the grounds of Yale-New Haven Hospital (YNHH) on the afternoon of October 21, where a dedication ceremony marked the grand opening of Smilow Cancer Hospital at Yale New Haven—a moment

of triumph for Yale University, the School of Medicine, and YNHH.

"It is a day of hope," said Yale President Richard C. Levin. "It is a day of inspiration, a day that we've all waited for for many years, and it will allow this hospital and this medical school to take their places among the leaders in the world in the care and treatment of cancer." The ceremony, held in an outdoor plaza at the foot of the new 14-story building, was attended by

hundreds of faculty, staff, and donors, and featured a performance by the Trinity Boys Choir and a lineup of speakers including Connecticut Governor M. Jodi Rell; Levin; medical school Dean Robert J. Alpern, M.D.; Marna P. Borgstrom, M.P.H., CEO and president of YNHH; Bonnie Kaplan Tymniak, a lymphoma survivor; and the hospital's namesake and major donor, Joel E. Smilow.

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The tiniest scale yields the biggest prize

Nobel Prize is awarded for atomic-level studies of cell structure basic to life

A telephone ringing before daybreak is unlikely to appear on anyone's list of favorite sounds, but for Thomas A. Steitz, PH.D., it may now rank with the sweetest music.

In the early morning hours of October 7, Steitz, Sterling Professor of Molecular Biochemistry and Biophysics, learned in a call from Sweden that he would share the 2009 Nobel Prize in Chemistry for his seminal research on the structure of the ribosome, a cell organelle that is vital to protein synthesis and to the action of many antibiotics.

Later that day, at a press conference packed with media representatives and well-wishers in the President's Room of Yale's Woolsey Hall, a reporter asked Steitz where he was when he heard the news.

"I was in bed," a cheerful Steitz deadpanned, to laughter from the crowd. "It was 5:30 a.m., maybe a little bit before that. The telephone rang and Joan [Joan A. Steitz, PH.D., Thomas Steitz's wife, also Sterling Professor of Molecular Biochemistry and Biophysics] answered it and said, 'It's for you.' So I went



A beaming Thomas Steitz gave a press conference on the afternoon of the announcement of his Nobel Prize in Chemistry.

over and it turned out to be from Stockholm. Very exciting."

Some of Steitz's apparent calm may have been due to the fact that his name has been frequently included on informal short lists of potential Nobelists ever since 2000, when he and a team including longtime Yale collaborator Peter B. Moore, PH.D., Sterling Professor of Chemistry, published a pair of papers in the journal *Science* on the structure and function

of the ribosome as determined by X-ray crystallography.

The ribosome is an asymmetrical structure consisting of a large and small subunit. In the two *Science* articles, hailed as "landmark publications" in an accompanying commentary, Steitz and colleagues described and depicted the structure of the large, protein-synthesizing portion of the ribosome in

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Brothers follow parents' example to help fight cancer

It would be an understatement to say that philanthropy runs in the family of Richard S. Sackler, M.D., and his brother, Jonathan Sackler. The names of their parents, Richard and Beverly Sackler, adorn cultural and scientific centers around the world, from the Sackler Galleries at the Royal Academy of Arts in London, to the famed Sackler Wing of New York's Metropolitan Museum, to the just-launched Raymond and Beverly Sackler Institute for Biological, Physical, and Engineering Sciences at Yale (see related story, page 4).

So it's only fitting that both Richard Sackler and his wife, Beth, and Jonathan Sackler and his wife, Mary Corson, each head charitable

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Jonathan and Richard Sackler

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JULIE BROWN

"It's been a really wonderful experience for us. This has been kind of my baby," says Lynn Tanoue, professor of medicine and violinist, of the Yale Medical Symphony Orchestra. Begun with a simple e-mail, the orchestra now has weekly rehearsals, and has played three concerts to packed houses in the medical school's Harkness Auditorium.

If you rent timpani . . .

A busy, award-winning clinician finds her way back to the music she loves

Lynn T. Tanoue, M.D., studied the violin through childhood, high school, and college. She played as a student at the School of Medicine in the late 1970s, alongside undergraduates in the Yale Symphony Orchestra and in a New Haven community orchestra.

But Tanoue's free time was soon scarce. "I know a lot of people who studied an instrument all the way through college," says Tanoue, professor of medicine. "But then you go to medical school, and your instrument winds up in the closet."

After a chance encounter with an old friend, Tanoue has now returned to her musical roots. At a wedding in 2007 Tanoue spoke to Lisa M. Wong, M.D., a pediatrician, violinist, and president of the Longwood Symphony Orchestra, a group of musically minded physicians and medical students in the Boston area. Speaking with Wong inspired Tanoue to approach Thomas P. Duffy, M.D., director of Yale's Program for Humanities in Medicine, about building an orchestra at the School of Medicine.

Duffy, professor of medicine, secured funding, and Tanoue sent a school-wide e-mail advertising an open sight-reading in Harkness Auditorium. "I got back hundreds of responses—'Great idea. Sign me up. Here's what I play,'" recalls a beaming Tanoue.

They came—and the Yale Medical Symphony Orchestra was born. Tanoue hired Adrian Slywotzky, a doctoral student at Yale School of Music, to conduct. She scheduled weekly rehearsals, selected medical artwork for promotional posters, and rented timpani. "We've given three concerts at Harkness," Tanoue says, and each time the auditorium has been packed. "There clearly is a musical soul to the medical center that was waiting to be discovered."

Tanoue's musical homecoming is reminiscent of her return to the School of Medicine in 1991. After she received her medical degree, Tanoue remained at Yale for a residency in internal medicine and a fellowship in pulmonary and critical care. But after completing her fellowship in 1989, she found herself looking for a new home, and she worked for two years in private practice in the New Haven community. "It was probably the best thing I ever did, to leave for a little while," she says. "I learned an enormous amount very quickly."

Tanoue's departure from Yale coincided with the appointment of asthma researcher Jack A. Elias, M.D. (now chair of the Department of Internal Medicine) as section chief of pulmonary and critical care medicine. Tanoue returned to Yale in 1991 to work with Elias on complementing Yale's world-class research by hiring

first-rate pulmonary clinicians and building clinical programs. Under their leadership, the number of Yale clinicians in pulmonary medicine has increased from three to 16, and the Winchester Chest Clinic at Yale-New Haven Hospital (YNHH) now offers state-of-the-art specialty care in every aspect of chest medicine.

The daughter of an accomplished surgeon and a graduate of the same Honolulu high school that produced AOL founder Steve Case and President Barack Obama, Tanoue, now interim section chief, directs the Winchester Chest Clinic and co-directs, with lung cancer expert Frank C. Detterbeck, M.D., professor of surgery, the Thoracic Oncology Program (TOP) at Yale Cancer Center. The TOP, which has burgeoned as a successful multidisciplinary program, is participating in translational research efforts at the medical school, most notably with David L. Rimm, M.D., PH.D., professor of pathology, to better predict lung cancer outcomes using molecular technologies.

And yet Tanoue, winner of the 2009 David J. Leffell Prize for Clinical Excellence, somehow still has time for music. Known as modest when discussing her career achievements, she describes the orchestra's creation with a sort of surprised delight. But to colleagues who watched her build the clinical arm of pulmonary medicine at Yale, and to others who know her determination, the story is not, in the end, such a surprise.

School of Medicine remembers a student of 'joy and warmth'



Natasha Collins

In September, friends, family, classmates, and teachers gathered in Yale's Battell Chapel to remember and honor Natasha Collins, a member of the medical school's Class of 2012 who died

of leukemia on August 12 at the age of 26. With words, music, and singing, those present recalled a young woman of sensitivity, honesty, compassion, joy, and warmth.

"It was one of my favorite moments of each day—walking in, sitting next to her, and seeing her smile," said classmate Whitney Sheen, as she recalled attending lectures with Collins, who played violin in the Yale Medical Symphony Orchestra.

About five years ago, Collins was diagnosed with acute myelogenous leukemia and had been in remission after chemotherapy and a cord blood transplant. When the cancer returned in February, her classmates launched an international search for a bone marrow donor, but the effort was complicated because Collins was biracial, and an exact match was elusive.

At an August meeting held to inform the medical school community of the circumstances of Collins's passing, Associate Professor of Medicine Mark D. Siegel, M.D., who oversaw Collins's care in her final days, said, "The leukemia got to the point where her only chance for survival was to go with a transplant with a slight mismatch." After the transplant Collins developed a severe form of a liver syndrome, which led to multiple organ failure.

"What a great doctor she would have been," said Nancy R. Angoff, M.P.H., M.D., associate dean for student affairs. "What better doctors we can each be because of her. She will shine on in us and make us better people and better doctors."

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Expert on severe mental illness is new director of mental health center

Michael J. Sernyak, M.D., professor of psychiatry, has been appointed director of the Connecticut Mental Health Center (CMHC), a partnership between Yale and the state of Connecticut's Department of Mental Health and Addiction Services (DMHAS) that was established in 1966.

Sernyak, who specializes in the treatment issues of the severely mentally ill, was nominated to the directorship by Yale University following a national search, and was appointed by Thomas A. Kirk Jr., PH.D., who retired as DMHAS commissioner in June.

Sernyak succeeds Selby C. Jacobs, M.D., who is retiring at the end of the academic year.

The CMHC, an urban community mental health center that provides outpatient psychiatric services for over 7,000 New Haven-area residents each year, is housed with the Abraham Ribicoff Research Facilities, laboratories that have furthered our understanding and treatment of mental illnesses including schizophrenia, depression, and drug and alcohol addiction.

Sernyak, a nationally recognized health services researcher, has studied how antipsychotic medications may contribute to the development of diabetes in psychiatric patients, and has examined issues involving the delivery of medical care to patients with schizophrenia.



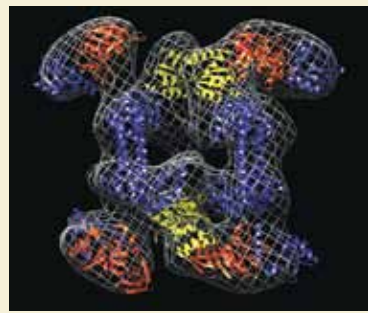
Michael Sernyak

After graduating from Amherst College with a B.A. in physics and astronomy in 1983, Sernyak obtained his M.D. at Jefferson Medical College. He completed an internship at Greenwich Hospital, and a residency in psychiatry at Yale in 1987. He then served as unit chief of the Psychosis Studies Unit at CMHC for five years.

In 1996, Sernyak joined the staff at the VA Connecticut Healthcare System (VACHS) in West Haven, Conn., and in 2001 he was appointed chief of the Psychiatry Service at VACHS.

Advances

Health and science news from Yale



FRANZISKA BLEICHERT

Images help scientists think outside the box

Cell structures known as box C/D guide ribonucleoproteins (RNPs) help to maintain the integrity of ribosomes, which synthesize proteins in all forms of life on Earth (see related story, page 1).

A team in the lab of Susan J. Baserga, M.D., Ph.D., used electron microscopy to discern the structure of the box C/D RNP in *Methanocaldococcus jannaschii*, a hardy microbe found in Antarctic ice and in boiling vents on the ocean floor.

Conventional models have proposed that box C/D RNPs are composed of one RNA molecule and pairs of core proteins. But as reported in the September 11 edition of *Science*, first author Franziska Bleichert, M.D., and the Yale group found that the *M. jannaschii* box C/D RNP was instead made up of two RNAs and four copies of each of the three core proteins (see image above).

"It looks like a Wheat Thin with feet," says Baserga, professor of molecular biophysics and biochemistry. "When you can discern structure, you can often figure out function."

Giving a gut punch to Parkinson's disease

Obesity is a well-known risk factor in diabetes, heart disease, and cancer. Now, scientists are finding links between obesity and neurodegenerative diseases such as Parkinson's disease (PD) as well.

PD is caused when dopamine-producing nerve cells die off in a part of the brain that governs movement. In the November 11 issue of *The Journal of Neuroscience*, a team led by Tamas L. Horvath, D.V.M., Ph.D., chair and professor in the section of comparative medicine, and also professor of obstetrics, gynecology, and reproductive sciences and of neurobiology, conclude that ghrelin, a hormone produced by the stomach, can protect these neurons from death, and that obesity-related declines in ghrelin may raise the risk of PD.

Dopamine cells in mice lacking ghrelin that were exposed to a cell-killing toxin died off in substantially greater numbers than in normal mice; administration of ghrelin reversed this effect.

"Because this hormone originates from the stomach, it is circulating normally in the body," Horvath says, "so it could easily be used to boost resistance to Parkinson's or it could be used to slow the development of the disease."

Yale mourns loss of a bright young light

An idealistic and dedicated woman, graduate student Annie Le planned to devote her life to medical research

On October 12, a memorial service that mixed prayer, remembrances, and music was held at Yale's Battell Chapel for doctoral student Annie Marie Le, 24, whose body was found on September 13 in the School of Medicine's Amistad Street Research Building, where she had been conducting experiments. Le's death was ruled a homicide, and a laboratory technician has been charged with her murder.

In remarks to the assembled mourners, Yale President Richard C. Levin said, "Yale remains a close community. When tragedy strikes we all feel it intensely. The fabric of the whole here is very tightly knit; when one thread is pulled the afghan unravels. We are, by nature, not isolated from each other, but interconnected." Levin called Le "a model student for the Yale of the 21st century... And it is in our hearts that Annie's spirit will live."

During the service, solo piano and violin performances punctuated prayers and remarks by Levin; Yale's University Chaplain and Roman Catholic Chaplain; Jon Butler, Ph.D., dean of Yale's Graduate School of Arts and Sciences; and several of Le's personal acquaintances.

Le, of Placerville, Calif., came to Yale in 2007 as a graduate student in the Combined Program in the Biological and Biomedical Sciences after earning her undergraduate degree in cell and developmental biology at the University of Rochester.

At Yale, she worked in the laboratory of her advisor, Anton M. Bennett, Ph.D., associate professor of pharmacology, whose research focuses on a family of

enzymes that regulate cell signaling, with emphasis on the role these enzymes may play in human disease.

Le, who had dreamed of a career at the National Institutes of Health after her graduate training, was exploring how metabolic stresses influence an enzyme believed to be involved in controlling mitochondrial function in muscle cells, possibly leading to metabolic disease.

"Annie came to Yale with high expectations and was truly excited about the bright prospects of a career in research," Bennett said. "She showed that she was more than ready to do what was expected of her." Bennett characterized Le as "a dreamer with clear visions and plans, who knew that she had

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(Below) In September, students, faculty, and staff gathered on Yale's Cross Campus for a candlelight vigil in memory of pharmacology graduate student Annie Le (left), whose murder in a medical school research building shook the Yale community and the nation.



MICHAEL MARSLAND

Advocate for women's health research is honored

In an October 29 ceremony held at the Hartford Marriott Downtown, Carolyn M. Mazure, Ph.D., director of Women's Health Research at Yale (WHRY), was inducted into the Connecticut Women's Hall of Fame.

Mazure, professor of psychiatry and psychology and associate dean for faculty affairs, was honored for her work in founding WHRY, for her wide-ranging influence on biomedical research and health care, and for her own research on gender-specific aspects of depression which has shown, for example, that stress is a more potent pathway to depression for women than for men.

Mazure founded WHRY in 1998 with the support of The Patrick and Catherine Weldon Donaghue Medical Research Foundation based on the premise that understanding gender differences is vitally important to the health of both women and men.

The WHRY program, which is dedicated to exploring the wide range of conditions that are more prevalent in women, or for which the causes, treatment, or prevention have gender-specific differences, has grown to become a national model for initiating and fostering interdisciplinary research on women's health and gender differences, and for disseminating findings with real-world benefits to the community.

The program is now constructed around research "cores" devoted to a

range of areas in women's health. In a recent line of research under the umbrella of the Women and Trauma core, WHRY scientists are conducting one of the first studies of how women veterans returning from combat zones in Iraq and Afghanistan readjust to civilian life.

The WHRY's Pilot Project Program provides Yale scientists with "seed" funding that allows them to generate the data they need to obtain external grants from the National Institutes of Health. All told, over \$4 million in such grants have allowed Yale researchers to obtain more than \$40 million in external funding to extend their research.

Also honored at the October event were Connecticut's three women hospital presidents and CEOs, including

Marna P. Borgstrom, M.B.A., CEO of Yale-New Haven Hospital.

The Connecticut Women's Hall of Fame, founded in 1993, showcases the outstanding contributions of Connecticut women to their communities, their state, and the nation.

Prior inductees affiliated with the School of Medicine include Joan A. Steitz, Ph.D., Sterling Professor of Molecular Biophysics and Biochemistry, and the late Patricia Goldman-Rakic, Ph.D.

Steitz, discoverer of small nuclear ribonucleoproteins, intracellular complexes that play a key role in the splicing of pre-messenger RNA, the earliest product of DNA transcription, was inducted into the Connecticut Women's Hall of Fame in 2008.

Goldman-Rakic, who died in 2003, was a pre-eminent investigator of the workings of the prefrontal cortex, seat of all higher-level cognitive functions in the brain. She was inducted to the Connecticut Women's Hall of Fame posthumously in 2008.

Carolyn Mazure is one of three inductees into the Connecticut Women's Hall of Fame in 2009.



COURTESY OF WHRY

Out & about

August 25: The 99 members of the Class of 2013 set Harkness Auditorium alight with nervous excitement at this year's **WHITE COAT CEREMONY**, in which new students receive physician's jackets, formally marking their entrance into the medical profession. **1. Justin M. Steinberg**, M.B.A., '13 with his wife, **Kimberly E. Steinberg**, and daughter, **Marjorie**. **2. Brooks Van Udelsman** '13 with his parents, **Robert Udelsman**, M.D., M.B.A., M.S.B., chair and William H. Carmalt Professor of Surgery and chief of surgery at Yale-New Haven Hospital (YNHH), and **Nikki J. Holbrook**, PH.D., adjunct professor of medicine. **3.** A white coat is readied for its new owner by **Thomas J. Lynch Jr.**, M.D., director of Yale Cancer Center and physician-in-chief at YNHH's Smilow Cancer Hospital, who delivered this year's keynote speech. **4. Laura Huang** '13 wears her new white coat alongside her mother, **Lin-Lan Tang**, M.D. (left) and sister, **Stephanie Huang**.



October 8: Leaders of Yale and University College London (UCL) and their associated hospitals were joined by former British Prime Minister **Tony Blair** (right) to sign an agreement creating the **YALE-UCL COLLABORATIVE ON BIOMEDICINE**, a new partnership in biomedical research and clinical care. (From left) **David Fish**, M.D., professor of epilepsy and clinical neurophysiology at UCL and managing director, UCL Partners; **Malcolm Grant**, CBE, L.L.D., president and provost of UCL; Yale President **Richard C. Levin**; and Yale-New Haven Hospital CEO **Marna P. Borgstrom**, M.P.H. Blair, founder of the Tony Blair Faith Foundation, is teaching a "Faith and Globalization" seminar at Yale for the second year.

September 21: **LATVIAN PRESIDENT Valdis Zatlers**, M.D. (left), an orthopaedic surgeon who trained as a fellow at Yale in 1990–91, met with Dean and Ensign Professor of Medicine **Robert J. Alpern**, M.D., at the School of Medicine during a wide-ranging six-day trip to the United States. Zatlers spoke to Yale students in political science and international relations and to residents in orthopaedics. Zatlers received his fellowship training under the auspices of the Keggi Orthopaedic Foundation (KOF), an organization founded and led by **Kistaps J. Keggi**, M.D., clinical professor of orthopaedics and rehabilitation. Founded in 1988, KOF has brought more than 250 health and education professionals from the former Soviet republics and Vietnam to the United States for education.



October 16: An **INAUGURAL SYMPOSIUM AT THE RAYMOND AND BEVERLY SACKLER INSTITUTE FOR BIOLOGICAL, PHYSICAL, AND ENGINEERING SCIENCES** was held at Yale's West Campus. The day-long event, which featured talks by internationally renowned scientists from diverse fields, celebrated both the gift by the Sacklers that helped establish the institute and the arrival of the first class of graduate students in the Integrated Graduate Program in Physical and Engineering Biology. (From left) **Martin Chalfie**, PH.D., chair and William R. Kenan Jr. Professor of Biological Sciences at Columbia University, who shared the 2008 Nobel Prize in Chemistry for the discovery and development of green fluorescent protein; **Peter Salovey**, PH.D., Yale University provost, Chris Argyris Professor of Psychology, and professor of epidemiology and public health; **Beverly Sackler**; **Raymond R. Sackler**, M.D.; and **Lynne J. Regan**, PH.D., professor of molecular biophysics and biochemistry and of chemistry, and director of the new Sackler Institute, which is dedicated to promoting research that bridges the gaps between traditional scientific fields.

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to work hard to achieve those dreams," and noted that she never complained. "Instead, she asked, 'How can I help?' And she always did." Le's research is slated to be published in a paper that she co-authored, Bennett said. "We dedicate this paper in her memory."

Le was born in San Jose, Calif., and spent most of her childhood in Placerville. She graduated from Union Mine High School in 2003, at the top of her class of 362. As a college student at Rochester, she met her fiancé, Jonathan Widawsky, now a graduate student in physics at Columbia University.

A eulogy composed by Le's family read, in part, "Annie was loved by everyone who knew her and special to all those who came in contact with her. She was a kind-hearted human being who was devoted to her family and friends, always sacrificing her time to help others. Her laughter was infectious and her goodness was ingenious. ... She was a considerate daughter, a thoughtful sister, a generous niece, a spirited cousin, a loving granddaughter, and a gracious friend. We will always remember her beautiful smile, her fun-loving spirit, and the joy that

she brought to us all. Annie Marie Le will be profoundly missed."

Le is survived by Widawsky; her father and his wife, Mr. and Mrs. Hoang Le; her mother, Vivian Van Le; her brother, Chris Tri Le; her half-siblings, Martin Le and Emmie Le; her guardian parents, Mr. and Mrs. Robert Linh Nguyen and their three children, Dan, Ryan, and Sean Khiem; her grandmother, Thang Thi Vu, as well as several aunts, uncles, and cousins.

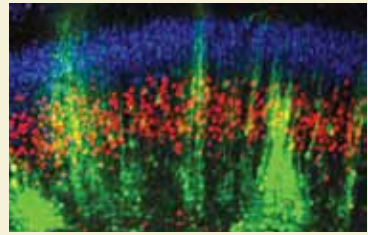
Memorial donations may be directed to the Annie Le Fellowship, Yale Office of Development, P.O. Box

2038, New Haven, Conn., 06521-2038. Donations may also be made in Annie's memory to the "I Have a Dream" Foundation, 330 Seventh Avenue, 20th Floor, New York, N.Y., 10001, and online at <https://secure.virtualatlantic.com/ihad/ssl/donation.aspx>.

During Le's funeral in El Dorado Hills, Calif., in late September, her mother read a poem in Vietnamese, translated into English by Le's brother Chris, that included these lines: "I sang lullabies by your side this week, like I did when you were a baby, wishing you a peaceful sleep."

Advances

Health and science news from Yale



COURTESY OF PASKO RAKIC

Neurons shouldn't always stick together

The cerebral cortex is organized into contiguous cellular columns—the sort of ordering a dozen pencils takes on if tightly wrapped with a rubber band. These columns form during embryonic development, when neurons shimmy up spoke-like radial glial cells until they reach their proper location in the cortex.

However, some neurons in each column shift away from the glial spoke to form interconnections with neurons in neighboring columns, ensuring a proper neuronal “blend” to perform specific functions. Scientists believe that disturbances in this process may cause psychiatric disorders.

In the September 24 issue of *Nature*, a group led by Pasko Rakic, M.D., Ph.D., the Dorys McConnell Duberg Professor of Neurobiology, reports that in mice lacking genes for the receptor EphA, neurons formed tight, even single-file columns, while overexpression of EphA caused too much lateral drift (green in image). In normal mice, appropriate numbers of neurons drifted to neighboring columns to perform their assigned duties.

“This so-far unrecognized mechanism . . . seems to be essential for the proper intermixing of neuronal types in the cortical columns,” the authors write.

Can an old antibody learn a new trick?

Antibody-based drugs, which harness and enhance the power of the immune system, have been useful in treating many diseases. However, most are expensive, have unacceptable side effects, or cannot be orally administered.

In papers published on the Web on October 19 and November 4 by the *Journal of the American Chemical Society*, David A. Spiegel, Ph.D., M.D., assistant professor of chemistry, and colleagues describe a new strategy employing small molecules that direct antibodies to kill prostate cancer cells or cells infected with the HIV virus.

The molecules built by the Spiegel team are “bifunctional”—they have been designed to lock onto diseased cells and also onto anti-DNP, an otherwise passive antibody that is naturally present in many people and can be easily and safely induced in others.

“Instead of trying to kill the pathogens directly, these molecules manipulate our immune system to do something it wouldn't ordinarily do,” says Spiegel. “This is an entirely new approach to treating these two diseases.”

Clinical research: the next generation

Translational medicine initiative sees educational success stories as it hits the three-year mark

In 2006, former National Institutes of Health (NIH) Director Elias Zerhouni, M.D., launched the Clinical and Translational Science Awards (CTSA) program, part of his ambitious “Roadmap” initiative aimed at speeding the translation of biomedical laboratory discoveries to the bedsides of patients in need.

Much of the impetus for the CTSA program came from a widespread appreciation that the challenges of clinical and translational research had become so daunting that an entire generation of physicians and scientists were shying away from careers in these fields. In addition to standard medical and scientific training, today's clinical and translational researchers often need special expertise in biostatistics, genetics, and computation, as well as knowledge of the strict regulations governing biomedical research with human subjects. To be truly successful, investigators must work comfortably in an emerging scientific culture based on interdisciplinary teams of physicians, scientists, and nurses. To reverse the alarming decline in the numbers of clinical and translational researchers, the CTSA program included a “Scholars” component, which provides support for education for the young scientists who will make up the next generation of investigators.

In a happy coincidence, a strategic plan commissioned by Dean Robert J. Alpern, M.D., completed in 2004, had targeted clinical and translational research as a priority for the School of Medicine, which led to the creation of the Yale Center for Clinical Investigation (YCCI). With educational, clinical, and community-based components, the YCCI's structure mapped perfectly onto the goals Zerhouni hoped to accomplish with the CTSA, and the School of Medicine was named a recipient in the program's first crop of grants—a \$57.3 million award that remains the largest grant ever received by Yale in its 300-year history.

“When YCCI was established, I viewed the commitment to train the next generation as perhaps our most important goal, and we're now beginning to reap the fruit of our efforts to educate young clinician-researchers,” says C.N.H. Long Professor of Medicine Robert S. Sherwin, M.D., YCCI director and an internationally recognized diabetes researcher. Over the past three years, Sherwin says, over 30 junior faculty holding M.D.s or Ph.D.s have received support through the CTSA as YCCI Scholars, and the program has given them the wherewithal to seek out and obtain about \$42 million in research grants of their own. These YCCI Scholars have published more than 113 papers (with an additional 31 in press), given conference presentations, and collaborated with colleagues both nationally and internationally.

“The CTSA has provided crucial support to a broad group of people,” says Judy H. Cho, M.D., associate professor of medicine and YCCI's co-director for education. “We have M.D.s without much research experience, and Ph.D.s with a lot of research experience who do not have adequate experience or exposure to clinical research issues to gather data for grant funding.”

Sacklers from page 1

foundations of their own—the Richard and Beth Sackler Foundation and the Bouncer Foundation.

In keeping with their family's longstanding generosity to Yale, the brothers' respective foundations have now joined forces to donate a \$3 million endowment establishing the Richard Sackler and Jonathan Sackler Professorship, expressly intended to be held by those appointed as director of Yale Cancer Center (YCC).

“The Sackler family has a rich tradition of philanthropy, having provided significant support at Yale,” says Dean Robert J. Alpern, M.D. “They are actively involved in medical school programs, with Richard serving on Yale Cancer Center's Advisory Board and the Dean's Council. I am

most appreciative of this most recent gift, which will honor and support all future Yale Cancer Center directors.”

Richard Sackler, co-chairman of Stamford, Conn.-based Purdue Pharma and adjunct professor of genetics at Rockefeller University, says, “My father raised Jon and me to believe that philanthropy is an important part of how we should fill our days.” He explains that the new gift was inspired by his years of association with Richard L. Edelson, M.D., the Aaron B. and Marguerite Lerner Professor of Dermatology, who served as YCC director for five years until this past spring and, among other achievements, oversaw approval of the newly opened Smilow Cancer Hospital (see related story, page 1). “What he accomplished

is terrific,” says Sackler, who credits Edelson with laying a solid foundation for the hiring of the current YCC director, Thomas J. Lynch Jr., M.D., whom Sackler calls a “world leader with a clear vision.”

For Jonathan Sackler's part, his “deep interest in science and technology and in education,” led the Stamford-based Bouncer Foundation (named, he says, for a beloved family dog) to help establish the professorship. “This is the first significant gift that my brother and I have made together,” says Richard Sackler, who says it took little prompting on his part to convince Jonathan to endow the professorship. “When I described the gift to him, he very quickly said, ‘This is something we can do—so let's do it.’”



ROBERT A. LISAK

As Co-Director for Education in the Yale Center for Clinical Investigation, physician-scientist Judy Cho, M.D., an expert on the treatment and genetic bases of inflammatory bowel disease, serves as a mentor to junior faculty members who aspire to careers in clinical and translational research.

In addition, the YCCI Scholars are eligible to receive a new Master of Health Science Research degree through a special YCCI program offering courses in epidemiology, biostatistics, informatics, practical and ethical issues in clinical and translational research, and topics in human investigation and grant writing.

“The important thing isn't the degree, it's the training,” says Eugene D. Shapiro, M.D., professor of pediatrics and of epidemiology and public health, who, along with Cho, is co-director for education at YCCI. “The new master's program fills a need by providing training for young investigators in areas that are critical for successfully conducting clinical and translational research.”

Barbara Alving, M.D., director of the NIH's National Center for Research Resources, the agency that oversees the CTSA program, says that educational opportunities that encourage physicians and scientists to venture beyond their comfort zones are invaluable. “The training that investigators receive through the CTSA Scholars program enhances their ability to work in interdisciplinary teams,” says Alving, “providing increased opportunities for collaboration and broader research perspectives.” According to Shapiro, these benefits are crucial to advancing medicine. “We're trying to give these folks additional skills that will lead to success for them, and lead to success for humanity as a whole by providing new discoveries and better ways to deliver medical care,” he says. “Our educational programs give people more tools, but I think they also inspire people.”

 Yale Netcast
“Tailoring Research to Promote Better Health”

Grants and contracts awarded to Yale School of Medicine

January–April 2009

Federal

Nadia Ameen, NIH, *Functional Relevance of CFTR Trafficking in Vivo to Intestinal Disease*, 4 years, \$1,406,752 • **Choukri Ben Mamoun**, U.S. Army Medical Research Acquisition Activity, *Two New Plant-Like Pathways Link Hemoglobin Degradation to Lipid Biogenesis in *Falciparum Malaria**, 1 year, \$228,167 • **Zubin Bhagwagar**, NIH, *A PET Study of 5-HT_{1B} Receptor Binding as a Novel Biomarker for Cocaine*, 1 year, \$212,250 • **Linda Bockenstedt**, Nat'l Research Fund for Tick-Borne Diseases, Inc., *Real-Time Imaging of Vector-Borne *Borrelia burgdorferi* Infection in Mice*, 1 year, \$60,000 • **Marcus Bosenberg**, NIH, *The Role of Beta-Catenin Signaling in Malignant Melanoma*, 1 year, \$469,373 • **Martina Brueckner**, NIH, *Cilia in Cardiac Morphogenesis*, 5 years, \$2,052,375 • **David Calderwood**, NIH, *Integrin–Filamin Interactions in Migration and Signaling*, 4 years, \$1,356,968 • **Lloyd Cantley**, NIH, *HGF Signaling in Kidney Repair*, 4 years, \$1,514,326 • **Kelly Cosgrove**, NIH, *GABAergic Mechanisms of Comorbid Alcohol and Nicotine Dependence*, 5 years, \$2,504,378 • **Peter Cresswell**, NIH, *Molecular Aspects of Human CDld Functions*, 5 years, \$1,628,186 • **Alan Dardik**, NIH, *Molecular Regulation of Vein Graft Adaptation*, 5 years, \$2,399,015 • **Nihal deLanerolle**, NIH, *Efficacy of Erythropoietin (EPO) and EPO Analogues in the Treatment of Epilepsy*, 2 years, \$398,235 • **Deepak D'Souza**, NIH, *Imaging Nicotinic Acetylcholine Receptors in Schizophrenia*, 3 years, \$873,711 • **Richard Flavell**, NIH, *The Role of Bcl-Rambo in Thymic Involution*, 5 years, \$2,068,750 • **Joel Gelenter**, NIH, *Genetics of Alcohol Dependence in American Populations*, 5 years, \$3,018,367 • **David Glahn**, NIH, *Genetics of Brain Structure and Function*, 2.5 years, \$989,343; NIH, *Influence of Psychosis on Brain–Behavior Endophenotypes for Bipolar Disorder*, 4 years, \$2,092,560; NIH, *Genetics of Brain Structure and Function—Genome Wide Association*, 5 years, \$3,595,574 • **Danielle Guez**, NIH, *FACS: A Novel Method to Study Neurons Altered during Cocaine Sensitization*, 3 years, \$117,508 • **Shangqin Guo**, NIH, *MicroRNA Regulation of Stem Cell Self-Renewal*, 5 years, \$756,409 • **Sairy Hernandez**, NIH, *T B Cell Helpers in Immunity and Autoimmunity: Development, Maintenance and Migration*, 3 years, \$100,428 • **Mark Hochstrasser**, NIH, *Degradation of Short-Lived Regulatory Proteins in Yeast*, 5 years, \$1,807,996 • **Elizabeth Jonas**, NIH, *Mitochondrial Ion Channels in Hypoxic Neurons*, 5 years, \$2,148,484 • **Mark Kidd**, NIH, *Mechanisms of Abnormal Enterochromaffin Cell Secretion of Serotonin in Crohn's Disease*, 4 years, \$1,331,861 • **Ami Klin**, NIH, *Perception of Social and Physical Contingencies in Infants with ASD*, 5 years, \$2,068,750 • **Patty Lee**, NIH, *Innate Immune Mechanisms in Emphysema*, 4 years, \$2,068,750 • **Elias Lolis**, NIH, *Regulation of CXCR4 by Cognate and Non-Cognate Ligands*, 5 years, \$2,049,100 • **Chao Ma**, NIH, *Antigen-Specific Immune Mechanisms of Neuronal Hyperexcitability and Chronic Pain*, 2 years, \$398,235 • **Arya Mani**, NIH, *The Genetics and Pathophysiology of Impaired Wnt Signaling in Metabolic Syndrome*, 4 years, \$1,655,000 • **Graeme Mason**, NIH, *Role of Acetate in Heavy Drinking*, 2 years, \$455,125; NIH, *GABA Effects of Nicotine in Men and Women*, 5 years, \$1,856,250 • **Christian Matranga**, NIH, *Investigating the Role of RNA Helicases in RNAi and Innate Immunity*, 3 years, \$148,134 • **Ruslan Medzhitov**, NIH, *Toll Pathway and Control of Adaptive Immune Responses*, 5 years, \$2,105,573 • **Thomas Murray**, NIH, *The Regulation of Pseudomonas aeruginosa Surface Colonization*, 3 years, \$395,685 • **Alexander Neumeister**, NIH, *Serotonin 1B Receptor Imaging in PTSD with and without Comorbid Depression*, 2 years, \$354,772 • **Mona Nolde**, NIH, *The Role of Mammalian PIWI Proteins and piRNAs in Hematopoiesis and Leukemia*, 3 years, \$153,822 • **Chirag Parikh**, NIH, *Identifying Acute Tubular Necrosis in Cirrhosis Patients with Renal Dysfunction*, 2 years, \$455,125 • **Christopher Pittenger**, NIH, *Targeting Glutamate in OCD: A Placebo-Controlled, Double-Blind Augmentation Trial of Glutamate-Modulating Agent Riluzole in Treatment-Resistant OCD*, 3 years, \$636,750 • **Marc Potenza**, NIH, *International Society for Research on Impulsivity Scientific Meeting*, 1 year, \$39,627 • **Jennifer Prah Ruger**, NIH, *Economic Evaluation of Drug Abuse Treatment and HIV Prevention Services for Pregnant Women*, 4 years, \$2,702,314 • **Vincent Quagliarello**, NIH, *A Ran-*

domized Controlled Trial to Reduce Pneumonia in Nursing Home Residents, 5 years, \$6,603,979 • **Mladen-Roko Rasin**, NIH, *Molecular Control of Corticospinal System Formation by Intermediate Targets*, 2 years, \$180,496 • **Matthew Roberts**, NIH, *Structural Insights of Postsynaptic Scaffolds and Signaling Complexes*, 2 years, \$82,148 • **John Rose**, NIH, *Novel Vaccines for Broad Protection against Avian Influenza*, 4 years, \$1,655,000 • **William Sessa**, NIH, *Endothelial NOS by Protein–Protein Interactions*, 5 years, \$2,431,955 • **Erik Shapiro**, NIH, *Magnetic Resonance Imaging of Neurogenesis*, 2 years, \$398,235 • **Robert Sherwin**, NIH, *Enhancing Clinical Investigation by Improved Clinical Research Management*, 5 years, \$136,160 • **Warren Shlomchik**, NIH, *Leukemia Stem Cells Essential Targets for GVL and Mediators of GVL-Resistance*, 5 years, \$1,438,520 • **Rajita Sinha**, NIH, *Chronic Alcohol and Brain Stress Circuit Response*, 5 years, \$2,606,037; Brookhaven Nat'l Laboratory, *The Prefrontal Cortex in Salience and Control in Cocaine Addiction: pHfMRI Study*, 4 years, \$136,188 • **Dieter Söll**, NIH, *Studies on Transfer RNA*, 4 years, \$6,091,595 • **David Stern**, NIH, *Signaling by Neuregulins and ErbB4 in Breast Cancer*, 5 years, \$1,758,407 • **Carlos Stocco**, NIH, *Molecular Pathways Controlling Ovarian Gene Expression*, 5 months, \$320,243 • **Vinita Takiar**, NIH, *Exploiting AMPK to Slow Polycystic Kidney Disease*, 1 year, \$45,972 • **Peter Tattersall**, NIH, *Molecular Genetics of Parvoviral DNA Replication*, 5 years, \$2,597,026 • **Flora Vaccarino**, NIH, *Morphogenesis and Function of the Cerebral Cortex*, 5 years, \$2,042,428 • **Joanne Weidhaas**, NIH, *Let-7 MicroRNAs in Lung Cancer: Altering Growth and Radioresistance*, 5 years, \$1,707,161 • **Marney White**, NIH, *Placebo-Controlled RCT of Bupropion for Binge Eating*, 2 years, \$152,400 • **Dianqing Wu**, NIH, *Wnt Signaling*, 5 years, \$1,595,961 • **Ying Xia**, NIH, *A New Strategy for Protection from Cerebral Ischemia*, 5 years, \$2,068,750

Non-Federal

Vikki Abrahams, Alliance for Lupus Research, *Effect of Antiphospholipid Antibodies on Trophoblast Function in Pregnancy*, 16 months, \$73,284 • **Ali Abu-Alfa**, Genzyme Corporation, *Genzyme Educational Conference*, 1 year, \$5,475; Abbott Laboratories Inc., *Medical Education Lecture Series*, 9 months, \$12,000 • **Eitan Akirav**, Juvenile Diabetes Research Foundation Int'l, *Glucose and the Islet Vasculature: Key Players in Beta Cell Proliferation*, 2 years, \$91,772 • **Robert Beech**, California Bipolar Foundation, *Predicting Response using Expression Differences in Clinical Treatment of Bipolar Disorder (PREDICT-BD)*, 1 year, \$49,891 • **Choukri Ben Mamoun**, Burroughs Wellcome Fund, *Function and Regulation of Host and Parasite Nutrient Transporters during Malaria Infection*, 2.5 years, \$250,000 • **Thomas Biederer**, Dana Foundation, *Molecular Mechanisms Underlying the Structural Plasticity of Central Synapses*, 3 years, \$200,000 • **Elizabeth Bradley**, William J. Clinton Foundation, *Ethiopia Hospital Management*, 1 year, \$141,813; South Essex Partnership NHS Foundation Trust, *SEPT Leadership Workshop*, 6 months, \$54,000 • **Judy Cho**, Crohn's & Colitis Foundation of America Inc., *Mapping Rare Variants and Expression Quantitative Trait Loci Contributing to Crohn's Disease Pathogens*, 3 years, \$386,100 • **Lynn Cooley**, Muscular Dystrophy Association, *Genetic Analysis of Muscle Function and Muscle Disease at the Single-Cell Level*, 3 years, \$320,000 • **Joseph Craft**, Lupus Foundation of America, *Mechanisms of Autoantibody Production in Lupus*, 1 year, \$66,000 • **Michael Crowley**, Bial Foundation, *When Rejection Hurts: Probing the Neural Basis of Childhood Social Exclusion with a Dense-array EEG*, 20 months, \$16,461 • **Enrique De La Cruz**, American Heart Association, Nat'l Center, *Mechanics of Cooperative Cofilin–Actin Filament Interactions and Severing*, 5 years, \$500,000 • **Linda Degutis**, State of Connecticut, *Yale Center for Public Health Preparedness Training and Technical Assistance*, 10 months, \$111,000 • **Michael DiGiovanna**, Breast Cancer Alliance, Inc., *Co-Targeting IGF-I Receptor and HER2 in Breast Cancer*, 1 year, \$100,000; Connecticut Breast Health Initiative, Inc., *Combination Targeting of IGF-I Receptor and HER2 in Breast Cancer*, 1 year, \$33,000 • **Ronald Duman**, Repligen Corporation, *Influence of Uridine on Behavior and Trophic Factor*

Expression in the Chronic Unpredictable Stress (CUS) Model of Depression, 1 year, \$59,430 • **Marie Egan**, Cystic Fibrosis Foundation, *Yale–Cystic Fibrosis Therapeutics Development Center*, 1 year, \$64,800 • **Liana Fraenkel**, Arthritis Foundation, *Improving Patient Willingness to Accept Escalation of Therapy in RA*, 2 years, \$194,986 • **Alison Galvani**, Howard Hughes Medical Institute, *Workshop on Mathematical Modeling of Infectious Disease Epidemiology and Control, Durban, South Africa*, 1 year, \$30,000; World Health Organization, *Integrated Tsetse Fly Ecology and Genetics for Improved HAT Control*, 1 year, \$20,000 • **Antonio Giraldez**, Muscular Dystrophy Association, *The Role of MicroRNAs in Muscle Development and Muscular Dystrophy*, 3 years, \$401,300 • **Michael Girardi**, Skin Cancer Foundation, *Investigating the Immunogenomic Landscape of Cutaneous T-Cell Lymphoma*, 1 year, \$10,000 • **Daniel Goldstein**, American Heart Association, Nat'l Center, *The Interplay of Aging, Viral Immunity and Atherosclerosis*, 5 years, \$500,000 • **Jonathan Grauer**, Stryker Spine, *Biochemical Comparison of Uniaxial Screws and Monoaxial Screws*, 1 year, \$26,685 • **Elena Grigorenko**, Florida State University, *Research Supplement to Promote Diversity in Health-Related Research*, 1 year, \$66,129 • **Erol Gulcicek**, Columbia University, *Yale Proteomics Core for Biodefense*, 5 years, \$659,008 • **Michelle Hampson**, Dana Foundation, *Brain and Immuno-Imaging*, 3 years, \$199,482 • **Keith Hawkins**, Hartford Hospital, *Adolescent Maturation of Brain Network Integration for Executive Control Abilities*, 6 months, \$33,893 • **Kristina Herbert**, Damon Runyon Cancer Research Foundation, *Regulation and Mechanism of pri-miRNA processing by Drosha and DGCR8*, 3 years, \$140,000 • **Zhiwei Hu**, Breast Cancer Alliance, Inc., *Targeting the Tumor Blood Vessels for Photodynamic Therapy of Chemoresistant Breast Cancer*, 1 year, \$100,000 • **John Huang**, Allergan Sales, Inc., *2008 Horizon Grants Program*, 1 year, \$50,000 • **Peter Jatlow**, University of Connecticut Health Center, *Maternal Genetics: Cigarette Smoking and Infant Birth Rate*, 10 months, \$9,000 • **Jing Jin**, American Foundation for AIDS Research (amfAR), *Cellular Factors Required for HIV Cell-to-Cell Transmission*, 3 years, \$375,000 • **Richard Kibbey**, American Diabetes Association, Inc., *Characterization of Phosphoenolpyruvate Carboxykinase-2 as a Mitochondrial GTP*, 3 years, \$298,350 • **Harriet Kluger**, American Cancer Society, Inc., *Developing an Assay to Predict Sorafenib Response in Renal Cell Carcinoma*, 4 years, \$900,000 • **Priti Kumar**, Hanyang University, Korea, *Human T Cell Specific RNAi-Based Nanomedicine for AIDS*, 4 years, \$1,114,875 • **Gregory Larkin**, American Foundation for Suicide Prevention, *Suicide Clusters across the Globe: Geospatial Trends from America, Ireland, and New Zealand*, 2 years, \$99,988 • **Csaba Leranth**, Passport Foundation, *Negative Effects of Bisphenol A on the Brain*, 2 years, \$20,000 • **William Lin**, American Skin Association, *Investigating the Immunogenomic Landscape of Cutaneous T-cell Lymphoma*, 1 year, \$7,000 • **Z. Ping Lin**, Wendy Will Case Cancer Fund, Inc., *Role of Ribonucleotide Reductase in Cell Cycle Checkpoints and DNA Damage Repair*, 1 year, \$30,000 • **Thomas Lynch**, American Cancer Society, Inc., *Yale Cancer Center ACS Institutional Research Grant*, 3 years, \$420,000 • **Mark Mamula**, Alliance for Lupus Research, *Antigen Trafficking between APCs as Therapeutic Target for Lupus*, 2 years, \$494,598 • **Linda Mayes**, University of Maryland, *Behavioral*

Measurement of Negative Reinforcement in Adolescent Alcohol Use/Abuse, 1 year, \$12,979 • **Thomas McMahon**, State of Connecticut Judicial Department, *Juvenile Justice Urban Cities Pilot*, 6 months, \$119,526 • **Asht Mishra**, Epilepsy Foundation of America, *Neuroimaging Biomarkers and Prevention of Spike Wave Epileptogenesis*, 1 year, \$45,000 • **Deepak Narayan**, Plastic Surgery Education Foundation, *Spitzoid Nevi Versus Melanoma by Cellular Gp100, Nedd9, and Gab2*, 1 year, \$5,000 • **Elaine O'Keefe**, Association of Schools of Public Health, *An Introduction to Public Health Careers for Middle and High School Students*, 9 months, \$30,000 • **Alexander Panda**, Preeclampsia Foundation, *TLR Expression and Function of Peripheral Blood Immune Cells in Preeclampsia*, 1 year, \$25,000 • **Lynne Regan**, Joan's Legacy, *Development of a Novel Class of Therapeutics for Small Cell and Non-Small Cell Lung Cancer*, 2 years, \$100,000 • **David Rimm**, Ensemble Discovery Corporation, *Proposal for Collaboration on EGFR/ERBB Dimer Detection in Human Breast Cancer and Correlation with Drug Resistance*, 1 year, \$76,262; Susan G. Komen Breast Cancer Foundation, *In Situ Detection of Cancer to Predict Non-Nodal Metastasis in Breast Cancer*, 3 years, \$600,000 • **Scott Rivkees**, United Cerebral Palsy Research and Education Foundation, *Prevention of Cerebral Palsy with Sulfonyleurea Agonists*, 2 years, \$100,000 • **John Rose**, Columbia University, *Development of Novel Vaccines for High Priority Pathogens*, 5 years, \$1,861,875 • **David Silverman**, American Heart Association, Nat'l Center, *Noninvasive Assessment of Regional Changes in Perfusion during Hypovolemia and LBNP*, 1 year, \$22,000 • **Albert Sinusas**, Massachusetts General Hospital, *Absolute Quantification of Myocardial Blood Flow Using Rb-82 PET*, 6 months, \$22,432 • **Lawrence Solomon**, CT Hospice, Inc., *Hospice Palliative Medicine Fellowship*, 5 months, \$100,000 • **Christopher Spock**, Plastic Surgery Education Foundation, *Micro RNA and Classification of Hemangiomas*, 1 year, \$10,000 • **Matthew State**, University of Illinois, *PET Evaluation: Tourette Syndrome*, 1 year, \$165,132 • **Stephen Strittmatter**, Cure Alzheimer's Fund, *Specificity and Mechanism of AB-Oligomer Action through Prion Protein*, 1 year, \$100,000; Dr. Ralph and Marian Falk Med. Res. Trust, *Axonal Regeneration Therapy for Spinal Cord Injury*, 3 years, \$1,119,000 • **Babak Tahvildari**, Robert Leet and Clara Guthrie Patterson Trust, *Functional Organization and Connectivity during Active Cortical Network*, 2 years, \$92,000 • **William Tamborlane**, Donaghy Medical Research Foundation, *Changing Life-Styles for Better Health: A Model Program for Community Health*, 4 years, \$926,586 • **Diana Vesely**, Arthritis Foundation, *Langerhans Cell Induction of T Regulatory Cells and Lyme Arthritis*, 2 years, \$100,000 • **Jun Yu**, American Heart Association, Nat'l Center, *The Role of Nogo-B on Vascular Remodeling and Atherogenesis*, 4 years, \$308,000 • **James Yue**, Stryker Spine, *Retrospective Review of Anterior Cervical Decompression and Fusion vs. Laminoplasty vs. Laminectomy for the Treatment of Cervical Myelopathy and Myeloradiculopathy*, 11 months, \$44,109 • **Hitten Zaveri**, American Epilepsy Society, *Fourth International Workshop on Seizure Prediction*, 1 year, \$10,000 • **Edward Zigler**, Smith Richardson Foundation, Inc., *Edward Zigler Center in Clinical Development and Social Policy*, 2 years, \$300,000 • **Howard Zonana**, University of Massachusetts, *An Observational Descriptive Study of IRB Practices*, 16 months, \$24,000

MEDICINE » tomorrow

Almost a century ago, John W. Sterling, of the Yale College Class of 1864 (right), ably demonstrated the ability of one person to shape an institution. Sterling made a bequest to Yale that funded a building boom in the 1920s and 1930s that literally defined the campus, raising many of the university's signature structures. The Sterling bequest extended to faculty and students as well: to this day, the 36 Sterling Professorships are the highest honor bestowed on Yale's faculty—including Thomas Steitz, recipient of the 2009 Nobel Prize for Chemistry, whose achievements are chronicled in this issue of *Medicine@Yale*.

Creating new endowed professorships is one of the medical school's highest priorities. At no point in history has medical research made advances at the pace seen in the last 10 years, and this progress will pale by comparison to what we are poised to accomplish in the years ahead. Providing steady, secure support for the scientific pursuits of our very best faculty members is one way to sustain our rapid progress in understanding and treating illness.

A \$3 million gift will create an endowed professorship in your name or a loved one's name. Please consider a donation today.



YALE MANUSCRIPTS & ARCHIVES

Haloarcula marismortui, an evolutionarily ancient, single-celled, “extremophile” organism that thrives in the highly salty, oxygen-poor depths of the Dead Sea. Extremophiles have played an important role in the recent history of structural biology (see related story, page 3) because their proteins are unusually stable in the laboratory and relatively easy to crystallize for X-ray analysis.

Since structures as basic to life as the ribosome have been highly conserved over the course of evolution, the insights that Steitz and colleagues gained in their studies of *H. marismortui* have broad ramifications. In a notable example, many widely prescribed antibiotics work by binding to the ribosomes of infectious bacteria and disrupting their function, and knowledge of ribosome structure is now leading to better strategies to combat drug-resistant bacterial strains.

By providing the first detailed 3-D reconstructions of the ribosome (Steitz and colleagues imaged the *H. marismortui* ribosome at a resolution of 2.4

angstroms—for comparison, this sheet of paper is about 1 million angstroms thick), the Steitz lab conclusively showed that the ribosome was not an RNA framework that made it possible for protein enzymes to catalyze the chemical reactions involved in synthesizing other proteins, but the opposite: in the ribosome, proteins provide a stabilizing scaffold for a dense mass of RNA helices that catalyze these reactions themselves (see image at right).

In addition to settling these structural questions, the *Science* papers provided intriguing evidence in support of the “RNA world” hypothesis, which proposes that life forms dependent on RNA as both an information-carrier and enzyme were abundant before the rise of DNA and protein-based organisms.

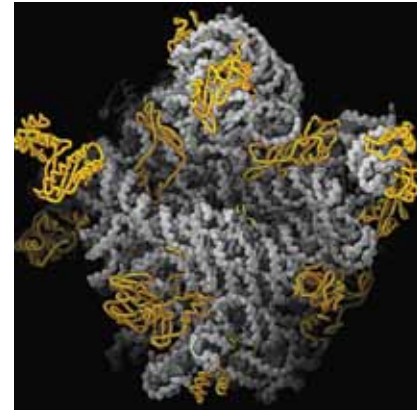
Steitz shares the Nobel Prize equally with Ada E. Yonath, PH.D., of the Weizmann Institute of Science in Israel, who pioneered the crystallization of the *H. marismortui* ribosome, and Venkatraman Ramakrishnan, PH.D., of the MRC Laboratory of Molecular Biology in Cambridge, United Kingdom.

Ramakrishnan, who was a post-doctoral associate in Moore’s Yale lab 30 years ago (“It’s good to see one’s ‘children’ doing well,” said Moore) went on to solve the structure of the small subunit of the ribosome in another extremophile, *Thermus thermophilus*, a bacterial denizen of super-hot deep-sea vents.

Along with Moore and William L. Jorgensen, PH.D., Sterling Professor of Chemistry, Steitz is a co-founder of Rib-X Pharmaceuticals, Inc., a New Haven-based drug discovery company that is applying knowledge of ribosome structure to the creation of new, more effective classes of antibiotics.

At the October press conference, Steitz made a plea for the support of basic science, pointing out designing antibiotics was “the furthest thing from our minds” when his team first decided to crack the secrets of ribosomal structure.

Recalling the daunting technical challenges that faced him and his colleagues, he said, “It seemed a little like climbing Mount Everest. We knew it



COURTESY OF THOMAS STEITZ

In this image from one of the classic *Science* articles published in 2000 by Thomas Steitz and colleagues, the large subunit of the ribosome is seen to be primarily composed of RNA helices (gray), interspersed with stabilizing protein backbones (gold).

was doable in principle but we did not know if we would ever get there.” But when he saw a detailed image of the ribosome for the first time, he added, it was “the most exhilarating moment I have experienced in science.”

 Yale Netcast
“Mapping the Ribosome”

Hospital from page 1

“Yale University, Yale School of Medicine, and Yale-New Haven Hospital together have a long tradition of excellence in cancer care,” Alpern said. “The first chemotherapy was given by Yale physicians in 1942 at what was then called New Haven Hospital, ushering in the age in which we could treat and cure patients. There’s a new age coming with much better treatments, and we now have the Smilow Cancer Hospital, and for that we are incredibly grateful to Joan and Joel Smilow, and to many other donors. We’ll be able to do state-of-the-art research, and we will be educating, in this hospital, the next generation of clinicians and researchers.”

Borgstrom’s remarks opened the afternoon’s proceedings. “Like most great achievements,” she said, “this point represents the intersection of ideas and people. More than six years ago, we knew that we had to increase Yale-New Haven Hospital’s patient care capacity. It took a lot of time, and it took a lot of hard work on the part of many people to make this idea a reality.”

With his wife, Joan, Smilow, a member of the Yale College Class of 1954 and the former CEO, chairman, and president of Playtex, has given generously to his alma mater for decades. In the fall of 2007, Smilow gave a transformational gift that allowed construction of the long-planned cancer hospital to move ahead.

“The one question that people have asked me the most in the last couple of years is, would I have done it if I had known what was going to happen in the country in the following two years?” Smilow said in his remarks at the grand opening. “I long ago learned that paper assets were not nearly as important as real assets that either you would personally enjoy, or that would benefit other people. The answer is yes.”

The Smilows’ philanthropy has endowed six coaching positions in Yale athletics and enabled the renovation of the old Lapham Field House, now called Smilow Field Center. Smilow also stewarded the major gifts component of Yale’s capital campaign in the 1990s and, more

recently, helped to implement a \$120 million gift from his class, the largest in Yale’s history. Smilow received the Yale Medal, the university’s highest honor, in 1993.

Smilow Cancer Hospital has been under construction since 2006. When it is fully complete in April 2010, the new facility will bring all of the inpatient and outpatient cancer services at Yale into one building, and it is expected to become the most comprehensive cancer care facility in New England.

The hospital was designed with an explicit commitment to personalized cancer care. A multi-specialty team of physicians and nurses is mobilized to treat each patient, and the teams are housed together in suites, dedicated to different forms of cancer, that facilitate collaboration among the various disciplines involved in cancer treatment.

These interdisciplinary teams will have easy access to conference rooms where they can view diagnostic-quality images on large screens and interact with local colleagues or, using telemedicine technology, with experts at distant sites.

“The opportunity for expanded patient services and improved multidisciplinary team care in Smilow Cancer Hospital will have profound implications for cancer patients,” said Professor of Medicine Thomas J. Lynch Jr., M.D., director of Yale Cancer Center and physician-in-chief at the new hospital. “Each patient will receive their cancer care from a team of specialized physicians who are experienced in treating their particular type of cancer. The new facility will make these interactions seamless for our patients.”

With 500,000 square feet of space, the hospital, which cost an estimated \$467 million, boasts a rooftop garden with trees and fountains, and a lobby with saltwater aquariums.



PARK PLACE PHOTOGRAPHERS, INC.

George Posener, of Orange, Conn., was present at the Smilow Cancer Hospital’s opening. Posener, who celebrates his 98th birthday this December, recently made a gift to the new hospital, having previously established endowments at the School of Medicine that support stem cell research and training of fellows in the Department of Surgery’s Section of Trauma and Surgical Critical Care and in the Department of Internal Medicine’s Section of Hematology.

Lynch sees the opening of the hospital as just one of several developments advancing cancer treatment and research at Yale. In the short term, the new hospital offers multidisciplinary team care and a much greater availability of clinical trials to patients.

But in the long term, coupled with the opening of the new Cancer Biology Institute at Yale’s West Campus, Lynch says, the Smilow Cancer Hospital will raise YNH into the top echelon of the nation’s cancer research and care facilities.

“Yale’s always done wonderful basic science, and it’s always had wonderfully compassionate doctors. But it’s never put the whole package together for cancer,” Lynch says. The opening of the new hospital and the development of West Campus are “giving Yale the ability to put together a truly comprehensive program in cancer. The medical school and the hospital have come together in an unprecedented way to say that cancer really matters here—cancer is something that we’re going to use the resources of one of the world’s great universities to fight.”

 Yale Netcast
“More Clinical Trials Needed”



ROBERT A. LISAK

(From left) Robert Alpern; Richard Levin; Joel and Joan Smilow; Marna Borgstrom; Joseph R. Crespo, chair of the Yale-New Haven Hospital (YNHH) Board of Trustees; Thomas Lynch; Bishop Theodore L. Brooks Sr. of Beulah Heights First Pentecostal Church, a YNHH trustee; Bonnie Kaplan Tymniak; and New Haven Mayor John DeStefano took part in the Smilow Cancer Hospital ribbon-cutting.

Expert on visual development is first Ziegler Professor

Michael C. Crair, PH.D., who studies the development, structure, and function of the visual system, has been named the inaugural William Ziegler III Associate Professor of Vision Research.

Crair, a faculty member in the Department of Neurobiology, uses a broad range of experimental techniques, including in vitro and in vivo electrophysiology and optical imaging, to explore how genes and the environment guide the development of sensory maps in the brain, especially those that underlie vision. In addition to shedding light on the



Michael Crair

general question of how the brain is wired up during development, research in Crair's lab has advanced understanding of how genetic instructions and sensory experience interact during brain development.

Crair joined the School of Medicine faculty in 2007 as associate professor of neurobiology and of ophthalmology and visual science. He is director of

the Vision Core Facility, overseeing the molecular and cellular biology equipment, microscopes, and other technologies used in vision research at Yale. He also serves as director of graduate studies for the Department of Neurobiology.

Crair received his PH.D. in physics from the University of California, Berkeley, and completed postdoctoral studies in neuroscience at Kyoto University in Japan, and at the University of California, San Francisco.

He has received numerous honors for his work, including a NARSAD—Sidney R. Baer Jr. Foundation Young

Investigator Award. He has been named an Alfred P. Sloan Foundation Research Fellow, a John Merck Fund Scholar, and the March of Dimes Foundation's Basil O'Connor Fellow.

The new professorship was created by the family of the late William Ziegler III, of Darien, Conn., a longtime member of the Yale Eye Center Advisory Board.

Ziegler, who died in 2008, was an avid sailor and environmentalist. He was chair and CEO of American Maize-Products Company and later of Swisher International Inc.

Neurology chair, MS researcher named Gilbert Glaser Professor

David A. Hafler, M.D., chair and chief of neurology at Yale School of Medicine (YSM) and Yale-New Haven Hospital (YNHH), has been named the first



David Hafler

Gilbert H. Glaser, M.D., Professor.

Hafler, a leader in the effort to better understand the molecular basis of multiple sclerosis (MS), joined the faculty of the School of Medicine

this September. An authority on the mechanisms of autoimmunity and inflammatory diseases of the central nervous system, he was previously director of molecular immunology in the neurology department at Harvard Medical School, where he was the Jack, Sadie, and David Breakstone Professor of Neurology (Neuroscience) and a neurologist at Brigham and Women's Hospital.

Hafler has been a major force in defining the causes of multiple sclerosis. He was among the first to apply the technique of T-cell cloning to human disease, identifying the targets of activated immune cells in patients with MS.

More recently, Hafler became an associate member of the Broad Institute at Harvard and MIT, and founded an international collaboration with

scientists from the University of Cambridge and the University of California, San Francisco. The group led an initiative to explore the genetic basis of MS, culminating in the first whole genome scan identifying MS-associated genes, work published in 2008 in *The New England Journal of Medicine*.

The new professorship honors Gilbert H. Glaser, M.D., professor emeritus of neurology and chair of the medical school's Department of Neurology from 1971 to 1986.

Glaser, who was the department's founding chair, is widely acknowledged as one of the founders of the field as a distinct medical specialty. His work in neurology and neuroscience as both an investigator and a teacher advanced both disciplines nationally and internationally. In particular, Glaser's research on epilepsy, which included one of the first identifications of a specific location of epileptic discharges in the brain, has helped to improve both surgical and non-surgical treatments of the disorder. Yale's epilepsy program under Glaser's leadership was one of the nation's first and has evolved into one of the most active and advanced in the world.

Glaser received the W. G. Lennox Award from the American Epilepsy Society in 1963, and served as president of the American Academy of Neurology from 1973 through 1975.

Nixdorff-German Professor is neurosurgeon and geneticist

Murat Günel, M.D., recently named the Nixdorff-German Professor of Neurosurgery, combines a neurosurgical practice with research in the genetics of neurovascular disease. His main clinical interest is the treatment of intracranial aneurysms (ICAs), weaknesses in the brain's blood vessels that can balloon, putting pressure on brain



Murat Günel

tissue, or rupture, causing hemorrhagic stroke. He is chief of the Section of Neurovascular Surgery at Yale-New Haven Hospital (YNHH).

Günel, also professor of neurobiology and of genetics, is co-director of the Yale Program on Neurogenetics. In his research, he has explored the genetic risk factors for neurovascular disease, including ICAs and cerebral cavernous malformations, a less serious vascular irregularity in the brain.

In a paper in *Nature Genetics* in December 2008, Günel and colleagues reported variations in three genetic regions associated with a greater risk of ICA and proposed a likely causative role for two specific genes. The study population has since grown to 15,000 people, and Günel says that more detailed genetic data on aneurysm risk should soon emerge from his research.

Günel received his medical degree from Istanbul School of Medicine, in Turkey, and completed his residency in neurosurgery at YNHH in 1998. That same year, he joined the Yale faculty as an assistant professor of neurosurgery. Since 2001, he has been chief of the Section of Neurovascular Surgery.

Among other organizations, Günel is a member of the American Association of Neurological Surgeons (AANS), the Congress of Neurological Surgeons (CNS), and the Academy of Neurological Surgeons. He is currently serving a term as president of the Joint Cerebrovascular Section of the AANS/CNS.

The Nixdorff-German Professorship was established in 1974 with a bequest from Elizabeth S. Nixdorff in memory of her late husband, Charles Edward Nixdorff, and "in recognition of the many contributions to medicine" of William J. German, M.D. German's neurosurgical career at the School of Medicine spanned four decades. He retired as professor of surgery and chief of the Section of Neurosurgery in 1968.

In a 1981 obituary of German published in the *Journal of Neurosurgery* and written by the late Yale neurosurgeons William F. Collins, M.D., and Lycurgus M. Davey, M.D., German was remembered as "an unpretentious, kind, dignified, expert in his profession, and, perhaps most of all, a friend to everyone who knew him."

Harris Professor probes development of social cognition in autism

Kevin Pelphrey, PH.D., the newly designated Harris Family Associate Professor of Child Psychiatry in the Child Study Center, focuses his research on the brain mechanisms underlying the development of different aspects of social cognition.

Pelphrey's interests include the development of social perception, the perception and regulation of emotion, and the development of theory of mind, a crucial cognitive capacity defined as the ability to make inferences about others' mental states.

Scientists believe that some of these capacities appear to be impaired in children with autism spectrum disorders (ASD) and other neurodevelopmental



Kevin Pelphrey

disorders. By comparing the typical development of social cognition with its development in ASD using magnetic resonance imaging, eye-tracking, and virtual-reality techniques, members of the Pelphrey laboratory are working to uncover the building blocks of complex, multifaceted, social cognitive abilities.

Pelphrey completed his doctorate in psychology at the University of North Carolina, Chapel Hill, in 2001. Subsequently, he held a postdoctoral fellowship in cognitive neuroscience

at Duke University. He remains a core faculty member at Duke University's Brain Imaging and Analysis Center.

Pelphrey is a frequent scientific collaborator with colleagues in Yale's Department of Psychology, and is a member of the Interdepartmental Neuroscience Program and the Cognitive Science Program.

Pelphrey's honors include a Scientist Career Development Award from the National Institutes of Health (NIH), a John Merck Scholars Award in the Biology of Developmental Disabilities in Children, the A. Richard Newton Breakthrough Research Award from the Microsoft Corporation, and the American Psychological Association's

Boyd McCandless Award for a distinguished early career theoretical contribution in Developmental Psychology.

He is a member of the NIH's Child Psychopathology and Developmental Disabilities Study Section, and a reviewing editor of *Frontiers in Neuroscience* and a member of the editorial boards of *Autism Research* and the *Journal of Autism and Developmental Disorders*.

In addition, Pelphrey serves as a reviewer for over twenty other scientific journals. He is a member of the Society for Personality and Social Psychology, the International Society for Autism Research, and the Society for Neuroscience, among other organizations.