Medicine@Yale

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Advancing Biomedical Science, Education, and Health Care

Honoring an RNA pioneer, backing science's next generation

In 2007, Natalia B. Ivanova, PH.D., arrived at the School of Medicine with ambitious plans. A rising star in stem cell biology, she had just left a postdoctoral fellowship at Princeton, and her first order of business was to hire a team for her Yale laboratory.

Most medical investigators are funded not from a central budget, but through grants from the government or other institutions. Young scientists are pressed to win support from these backers, who tend to favor established researchers. But Ivanova, assistant professor of genetics, had a leg up: she was the medical school's first recruit to benefit from the Yale Scholars initiative, which provides young scientists with support that allows them to focus on science during their earliest years as independent researchers rather than scramble for funding.

The brainchild of Dean Robert J. Alpern M.D., the Yale Scholars Award provides $250,000 per year for four years to cover salary and start-up costs for a promising new faculty member at the School of Medicine.

"This was a tremendous advantage, allowing me to get right to work on my ideas," Ivanova says, adding that the promise of support from the Robert T. McCluskey, M.D., Yale Scholar Fund sealed her decision to come to Yale. That fund

HAROLD SHAPIRO

(From left) Joan Steitz has been honored by a new Yale Scholar fund endowed by Donald McCluskey, the eighth such fund in the initiative launched by Dean Robert Alpern in 2005.

was endowed in 2006 by Donald S. McCluskey, M.ENG., an alumnus of Yale College and the Faculty of Engineering, to honor his brother (now deceased), a Yale College alumnus and physician-scientist at Harvard Medical School and Massachusetts General Hospital for five decades.

Now McCluskey has created a second Yale Scholar endowment, named for Joan A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry, Howard Hughes Medical Institute investigator, and pioneer in the study of RNA.

Steitz has said that she "fell in love with RNA" as a college student in the early 1960s, and she maintained that focus through graduate school and postdoctoral training. She joined the School of Medicine faculty in 1970, and within // Scholar *(page 7)*

A firm foothold in the genetics of autism

New study applies advanced genomics in a carefully assembled population to yield some of the first solid data in autism genetics

Matthew W. State, M.D., PH.D., had never seriously considered a career in genetic research until 1995, when he spent a few months in a child psychiatry ward during his residency at the University of California, Los Angeles. There he cared for a few children with Prader-Willi syndrome, a rare genetic disorder caused when all or part of a seven-gene stretch of chromosome 15 is missing. Children with Prader-Willi tend to be intellectually delayed and prone to compulsive behaviors such as skin-picking and uncontrollable eating.

"These kids just had one region lost, but it led to a variety of psychiatric manifestations," State recalls. "It made me start thinking, quite naively, about studying rare mutations as a way of understanding disorders that are much more common in the population." The notion led State, at age 35, to enroll in the graduate program in genetics at Yale, where others were thinking along the same lines. Most famously, faculty member Richard P. Lifton, M.D., PH.D., now chair and Sterling Professor of Genetics, had discovered a trove of new genes involved in hypertension by screening families with rare, extreme blood pressure disorders.

In recent years, State, now the Donald J. Cohen Professor in the Child Study Center, professor of psychiatry and genetics, and co-director of the Yale Program on Neurogenetics at the School of Medicine, has been employing the latest genomic technologies to take the same general approach

EVAN MCGLINN

Matthew State led one of three new genomic studies that provide some of the strongest evidence to date on genetic causes of autism.

to the notoriously diverse autism spectrum disorders. Studies have found dozens of genetic blips in people with autism, which is characterized by repetitive behaviors and problems in communication and social interactions, but researchers have struggled to sort out which of these gene variants are harmful and which benign.

State and several other groups around the country have attacked this problem by focusing on an unusual group of study participants known as the Simons Simplex Collection (SSC). Assembled and maintained with funding from the New York City-based Simons Foundation, // Autism *(page 7)*

Office supporting student research celebrates 25 years

John Forrest

Women who Google the phrase "increase chances of conceiving twins" are advised to try eating yams. Parents of children suffering from a middle ear infection might be advised to "wait and see" before starting antibiotics. These disparate pieces of advice both stem from thesis research by Yale medical students that was overseen by the Office of Student Research, which celebrated its 25th anniversary in February.

"Not all student theses lead to changes in standards of care, but many of them do," says John N. Forrest, M.D., who founded the Office of Student Research 25 years ago and has remained its director ever since.

During that time the office has evolved to become the main funding source for medical student research, introduced // Student research *(page 7)*

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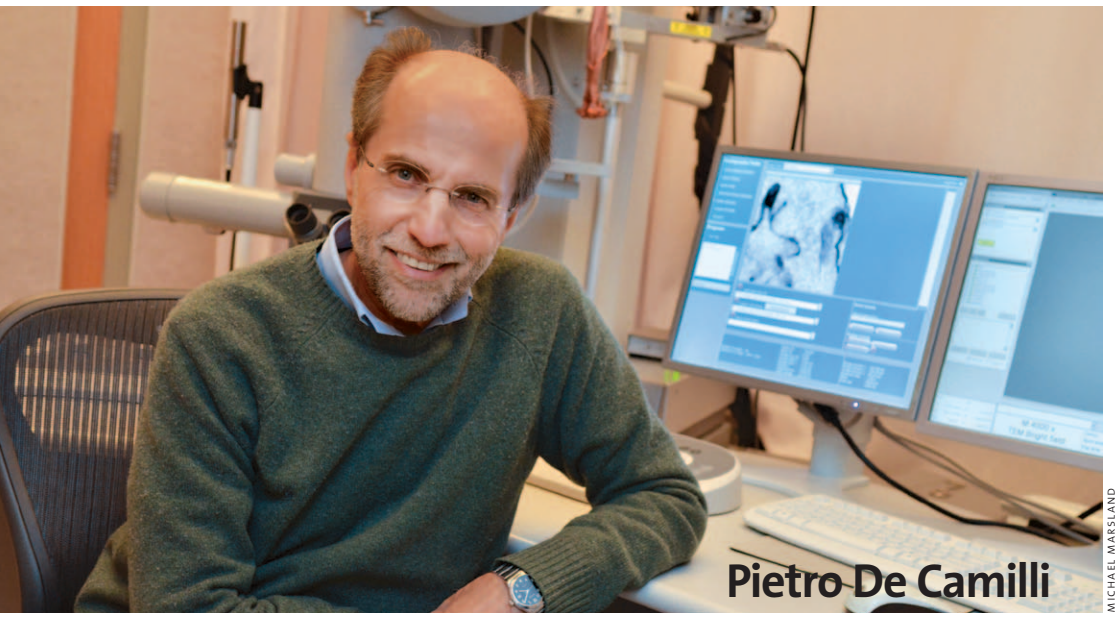

MICHAEL MARSLAND

One of the world's leading researchers in the cell biology of the synapse, Pietro De Camilli has catalogued and characterized a host of proteins involved in synaptic vesicle trafficking. Vesicles, which are crucial to brain function, are spherical sacs shaped from nerve cell membranes that are loaded with neurotransmitters. At synapses, vesicles fuse with the membrane and empty their cargo to send a chemical message. Then the membrane reshapes to form a new vesicle, and the cycle begins anew.

Cycle of life

After three decades in basic science, a biologist circles back to medicine

The poet William Carlos Williams exalted the ordinary: "So much depends," he wrote, "upon/a red wheel/barrow." Seen from the vantage point of Pietro De Camilli, M.D., the seemingly unremarkable fact that cell membranes can bend into different shapes is likewise invested with the greatest importance, for life itself—and every thought, emotion, and memory—depends upon it.

As a child, De Camilli spent each year's four-month school vacation in his mother's ancestral village by Lake Maggiore, in northern Italy. There he developed the "passion for understanding nature" that drew him to biology. Because little rigorous advanced training in general biology was available in Italy at that time, De Camilli enrolled in medical school. He had little interest in a career as a physician, but relished the chance to be "exposed to one organism, from molecules to mind."

His early research was in endocrinology, specifically on how hormones are secreted from cells in a process called exocytosis. This manner of secretion is ubiquitous in biology, but is particularly crucial in the nervous system. In neurons, the membrane is shaped into spherical sacs called vesicles that carry neurotransmitters to synapses. There they fuse with the synaptic membrane and empty their cargo, passing on to other cells the chemical messages that allow the brain to function.

De Camilli soon shifted his focus to neurobiology, and in 1978 he joined the Yale laboratory of Paul Greengard, PH.D., who went on to win the Nobel Prize for his studies of synaptic transmission. As a cell biologist, De Camilli's favored tool was the microscope, and he needed time to adjust to Greengard's biochemistry lab, in which "they studied the nervous system with a Waring blender," isolating proteins from homogeneous solutions of brain tissue using chromatography.

But in a "magic moment" De Camilli realized that antibodies being developed by his colleagues could be used with light and electron microscopy to localize subcellular proteins. Before long he had characterized synapsin, the first synaptic vesicle protein to be understood in any depth, and after launching his own Yale lab, he continued to build an inventory of such proteins.

But De Camilli, now the Eugene Higgins Professor of Cell Biology and professor of neurobiology, gradually became intrigued with the question of how new vesicles form after neurotransmitters are released. In this process, called endocytosis, intracellular proteins bend the now-flat synaptic membrane back into a proper-sized sphere, which pinches off and migrates into the cell. This newly born vesicle is loaded with a neurotransmitter, and the secretory cycle begins anew. "These processes are so fundamental that what you learn can be applied to every cell," says De Camilli, whose wide-ranging work on every step in this progression has earned him election to the National Academy of Sciences and appointment as a Howard Hughes Medical Institute investigator.

De Camilli's career seems itself to be unfolding in a cycle. Mouse strains with defective vesicle trafficking that were created in his lab to explore basic biology turned out to have characteristics seen in various human diseases, rekindling De Camilli's interest in concepts he learned in medical school. In 2006 he joined with Stephen M. Strittmatter, M.D., PH.D., the Vincent Coates Professor of Neurology and professor of neurobiology, to launch the program in Cellular Neuroscience, Neurodegeneration, and Repair, which aims to rapidly translate lab discoveries into new treatments for neurodegenerative diseases and injuries of the brain and spinal cord.

"Basic science helps us understand medicine," he says, "but increasingly," as genomics inspires experiments based directly on human biology and disease, "medicine has become a tool of science."

Specialist in pancreatic cancer lauded for outstanding patient care

Ronald R. Salem, M.D., Lampman Professor of Surgery, professor of diagnostic radiology, and chief of the medical school's Section of Surgical Oncology, is the recipient of the 2011 David J. Leffell Prize for Clinical Excellence.

Salem's accomplishments since his arrival at Yale 22 years ago include establishing the Oncologic and General Surgery group, now one of the busiest clinical practices in the Department of Surgery. A specialist in treating pancreatic cancer Salem is an expert in performing the Whipple procedure, in which the head of the pancreas is removed.

At an April 9 ceremony, Dean and Ensign Professor of Medicine Robert J. Alpern, M.D., characterized Salem as "absolutely dedicated to patient care. … He works with extreme compassion, and his extraordinary caring nature is evident to all of his patients."

Ronald Salem

Colleagues who nominated Salem for the prize praised "his availability, his calm disposition during critical moments, and above all his counsel."

Salem earned his medical degree at the University of Rhodesia and completed a general surgery residency at the Royal Postgraduate Medical School at Hammersmith Hospital in London. He was chief resident and a research fellow at the New England Deaconess Hospital and the Dana Farber Cancer Center in Boston.

The annual prize was established in 2008 by David J. Leffell, M.D., the David Paige Smith Professor of Dermatology, professor of surgery, and deputy dean for clinical affairs, and his wife, Cindy, to mark Leffell's 30th Yale College reunion. The award recognizes a faculty member who exemplifies clinical expertise, skilled teaching, and the highest standards of care and compassion for patients.

Pediatric Surgery announces arrival of new section chief

Michael Caty

In March, the School of Medicine and Yale-New Haven Children's Hospital (YNHCH) announced the appointment of Michael G. Caty, M.D., M.M.M., as chief of the Section of Pediatric Surgery and surgeon-in-chief at YNHCH.

Caty comes to Yale from the Women and Children's Hospital of Buffalo, where he was surgeon-in-chief, director of pediatric surgical services, and professor of surgery and pediatrics at the University at Buffalo School of Medicine and Biomedical Sciences.

"Dr. Caty is a skilled surgeon, researcher, and academician who brings more than two decades of experience to his role as our new pediatric surgeon-in-chief," said Robert Udelsman, M.D., M.B.A., chair and William H. Carmalt Professor of Surgery, and surgeon-in-chief at Yale-New Haven Hospital.

Caty is board certified in pediatric and general surgery. His clinical interests include neonatal surgery, thoracic surgery, intestinal motility disorders, pediatric surgical oncology, pediatric laparoscopy, and minimally invasive thoracic surgery. He earned his B.S. at Boston College and his M.D. at the University of Massachusetts Medical School. He trained in general surgery at the University of Michigan, and also completed a residency in pediatric surgery at Children's Hospital Boston and Harvard Medical School. Caty is a member of the American College of Surgeons and a number of other professional societies.

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Human stem cells play by own rules

ISTOCKPHOTO

Three genes in a constant interplay with one another determine the fate of embryonic stem cells (ESCs). The genes—*Nanog*, *Oct4*, and *Sox2*—have been extensively studied in mice, but little is known about how these genes regulate human stem cells.

ESCs are medically important, because they can differentiate into any of the myriad cell types that make up tissues. Each gene in the *Nanog*/*Oct4*/*Sox2* trio plays a vital part in directing cells to commit to one cell fate versus another. Yale Stem Cell Center scientist Natalia Ivanova, PH.D., assistant professor of genetics, and colleagues mapped out the role of each of these genes in human embryonic stem cells (hESCs) by selectively inactivating them during hESC maintenance and differentiation. In the April 6 issue of *Cell Stem Cell*, Ivanova and her team report that *Nanog*, *Oct4*, and *Sox2* do not have the same functions in hESCs and mouse cells.

There are restrictions on the use of hESCs in research, but "it is difficult to deduce from the mouse how these cells work in humans," says Ivanova. "Human networks organize themselves quite differently."

No turning back the biological clock

Assisted reproductive technologies (ARTs), such as in vitro fertilization, are so established that pregnancy at any age may seem both reasonable and achievable—views that more and more women hold, according to a new report from Yale researchers. The reality is that despite medical advances, women who wait until their early forties to have children face significant risks of infertility or complications during pregnancy. The new study urges concerted public and professional education to address the "alarming" misperceptions of ARTs.

"We're seeing more and more patients upset after failing in having their own biological child after age 43," says Pasquale Patrizio, M.D., M.B.E., professor of obstetrics, gynecology, and reproductive sciences and director of the Yale Fertility Center.

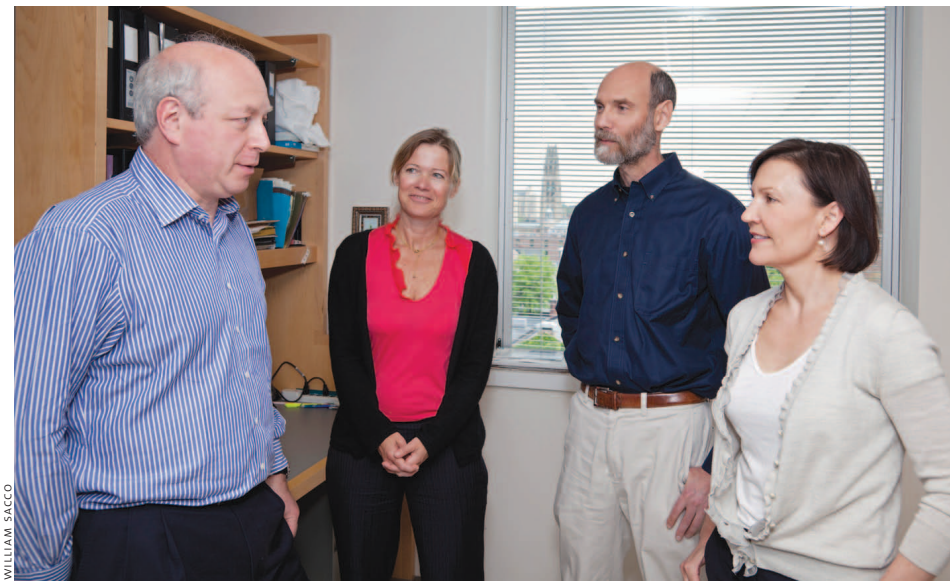
In an advance online edition of *Fertility and Sterility*, Patrizio's team writes that among women aged 43 and older employing ARTs, only about 4 percent eventually give birth, a number 10 times lower than that for women under 35. The researchers urge that women be better informed of these odds, and of the options to cryopreserve their oocytes while at their "fertility peak years" (under 35) or use donated oocytes, methods that have achieved high success rates in older women but are lesser-known than other ARTs.

Cardiovascular science as social network

In bringing cardiovascular researchers together under one roof, Yale center gathers momentum and funding, stimulates scientific collaboration

There is strength in numbers, and in unity, as members of the Yale Cardiovascular Research Center (YCVRC) know. Less than a year after moving into new laboratory space expressly designed to foster collaboration and shared resources, the 16-person team, led by YCVRC Director Michael Simons, M.D., has received a $9.5 million five-year Program Project Grant (PPG) from the National Heart, Lung, and Blood Institute, a component of the National Institutes of Health. The grant will support research on the molecular basis of arteriogenesis—the process by which new arterial blood vessels are formed—with the aim of developing a new framework for drug discovery and other therapeutic advances.

Since his arrival at Yale from Dartmouth Medical School in 2008, Simons, a leading researcher on the role of arteriogenesis in cardiovascular diseases, has created a unique scientific climate at the YCVRC that has attracted top scientists he describes as "stars." In turn, the expansion and diversification of YCVRC faculty has opened up new research directions and new avenues of funding. The new PPG is a concrete recognition of the unusually complementary and interrelated research projects happening at the YCVRC, says Simons, the Robert W. Berliner Professor of Medicine, professor of cell biology, and chief of the Section of Cardiovascular Medicine. It reflects an upward spiral in cardiovascular research at Yale—research that may lead to new arteriogenic therapies for illnesses like atherosclerosis, in which buildup of cholesterol and fatty materials causes an artery wall to thicken, and metabolic syndrome, a combination of medical disorders that can jointly lead to cardiovascular disease and diabetes. "This would not have happened three years ago," he says, "because we would not have had the people."



WILLIAM SACCO

YCVRC Director Michael Simons with (from left) Anne Eichmann, Martin Schwartz, and Karen Hirschi.

Scientific diversity

One of the YCVRC team's greatest strengths is its scientific diversity. For instance, Martin A. Schwartz, PH.D., professor of medicine and cell biology, is an expert in the way "fluid shear stress," the friction of flowing blood against the endothelium (cells that line all blood vessels), regulates their behavior. As part of the new PPG, Schwartz's lab will study how increased flow leads to the growth of new arteries. Recruited to Yale in 2011 from the University of Virginia, Schwartz is one of the newest members of the YCVRC and the PPG team.

Shear stress, Schwartz explains, is "the critical stimulus" in the formation of collateral arteries that grow around blocked arteries, a kind of natural bypass. Following the occurrence of an arterial blockage, as happens in a heart attack, for example, "some people can make these collateral arteries pretty efficiently, and some people don't," he says. The making of these collateral arteries is critical to recovery. For more than 10 years, Schwartz has investigated the mechanisms underlying this phenomenon experimentally, and he has made real progress. "We're now at the point where we can apply our understanding to the problem of flow-dependent artery remodeling" in human patients.

Anne Eichmann, PH.D., M.SC., professor of medicine, was recruited to the Center in 2010 from the Collège de France. Eichmann studies the factors that determine where the cells in blood vessels and lymphatic vessels grow. "We know about the factors that tell endothelial cells how to grow, but we're much less familiar with the cues that tell them *where* to grow," she says.

Among Eichmann's other areas of interest is neurovascular biology—specifically, to understand how the vascular and nervous systems influence each other's growth and function. The vascular and nervous systems appear to be more closely related than previously thought: "In multicellular organisms," Simons explains, "the nervous system evolved first, and the vascular system followed, and it's beginning to look like they used the same set of molecules." This connection holds tremendous potential for biomedical research, says Simons. "It turns out that the vasculature controls the function of the nervous system, and the nervous system controls the function of the vasculature. There's a huge overlap between neurobiology and vascular biology, and we're trying to build a program that takes advantage of the expertise Yale has in those fields."

Eichmann has explored the effects of the interactions between nerves and arteries on blood pressure; and another recent recruit, Jean-Léon Thomas, PH.D., M.SC., associate professor of neurology, has pursued research on the relationship between vasculature and brain function. In 2011, Thomas, Eichmann, and colleagues reported in the journal *Genes & Development* that they had identified stem cells in the brain that replace damaged nervous tissue, and that a protein called vascular endothelial growth factor (VEGF) receptor 3 acts directly in these stem cells to stimulate the creation of new nerve cells in adults—findings that have implications for neurodegenerative diseases such as Alzheimer's and Parkinson's.

Another recent addition to the YCVRC is Karen K. Hirschi, PH.D., professor of cardiology, who joined the faculty in the fall of 2011. Hirschi studies signaling pathways that regulate endothelial cell differentiation, specialization, and growth during early vascular development. Her lab is also using this basic biological information to direct the fate of human pluripotent stem cells (both embryonic and induced), which can become any cell type, specifically toward vascular cells. Hirschi's aim is to understand how to get human stem cells to efficiently become vascular endothelial cells, so they can be used to form new blood vessels in regenerative medicine strategies.

Other recent recruits include Daniela C. Tirziu, PH.D., instructor in medicine, who specializes in cell-to-cell communications in the heart; Daniel Greif, M.D., assistant professor of medicine, who works on pulmonary artery development and function; Hyung Chun, M.D., assistant professor of medicine, whose interests // Center *(page 6)*

A legacy of achievement

For two centuries, Yale School of Medicine has been a center of important advances in science and medicine. The physicians and scientists of the Yale Cardiovascular Research Center were drawn to the School of Medicine because of its superb faculty and outstanding core research facilities.

The generosity of individual donors allows us to sustain Yale's groundbreaking research on the prevention and treatment of heart disease and vascular disease. With independent funds, Yale researchers are able to harness the power of cutting-edge technology and pursue tomorrow's most significant health breakthroughs.

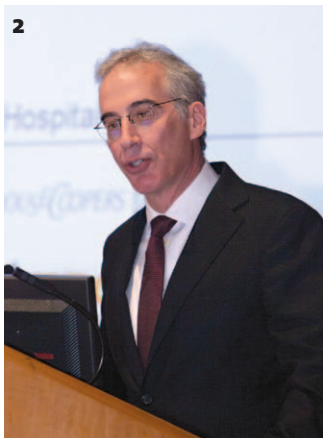
To learn more about cardiovascular research at the School of Medicine and ways you can contribute, please contact May Cahill, director of principal gifts, at 203-436-8528, or at may.cahill@yale.edu.

OUT & ABOUT

January 27, 2012 A reception was held in the medical school's Historical Library honoring the appointment of **Steven M. Southwick**, M.D., as the first **Greenberg Professor** of Psychiatry, Post-Traumatic Stress Disorder, and Resilience (see related story, page 8). The professorship was created in 2010 with a gift from **Glenn H. Greenberg**, of the Yale College Class of 1968. (From left) **Linda Vester Greenberg**; Glenn Greenberg; **Robert J. Alpern**, M.D., dean and Ensign Professor of Medicine; and Southwick, also professor in the Child Study Center.

TERRY DAGRADI

February 28, 2012 At a panel discussion called **"Personalized Medicine: How Far Off?"**, sponsored jointly by Yale's Office of Cooperative Research and the New Haven-based bioscience advocacy group CURE (Connecticut United for Research Excellence), medical school faculty and biotech entrepreneurs discussed the status and trajectory of medicine in the post-genomic age. 1. **Richard P. Lifton**, M.D., PH.D., chair and Sterling Professor of Genetics and professor of medicine. 2. **Paul R. Pescatello**, J.D., PH.D., CEO of CURE, moderated the discussion. 3. **Thomas J. Lynch,** M.D., Richard Sackler and Jonathan Sackler Professor of Medicine, director of Yale Cancer Center, and physician-in-chief of Smilow Cancer Hospital at Yale-New Haven.



WILLIAM SACCO (3)

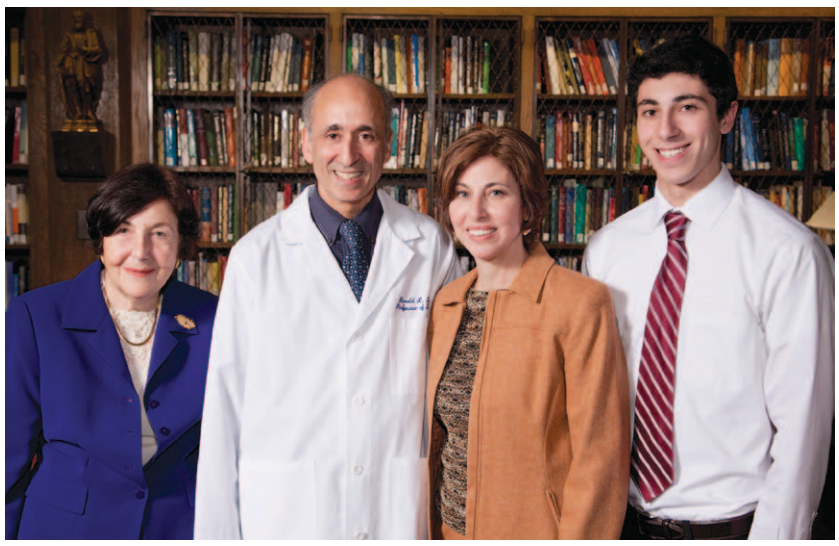
JOHN CURTIS (5)

March 16, 2012 Each spring, fourth-year students at medical schools across the country eagerly anticipate **Match Day**, when students receive word of acceptance in residency training programs. At Yale, medical students gathered with friends, family, and faculty members in Harkness Ballroom to await the news. 1. **Alisse Hauspurg** and a friend share a hug. 2. (From left) **Alicia Little**, **Charisse Orme**, and **Katherine Uyhazi**. 3. **Julius Oatts** (left) and **Lilangi Ediriwickrema**. 4. **Whitney Sheen**. 5. (From left) **Adelina Hung**, **Fayola Edwards**, and **Odayme Quesada**.

February 24, 2012 More than 70 second-year medical students participated in the production of this year's **Second-Year Show**, entitled "The iPocalypse." 1. **Jessi Gold** playing Margaret J. Bia, M.D., professor of medicine and director of the medical school's Clinical Skills Program. 2. **Alex Kula** sang and played the guitar in the show's finale. 3. **Kelsey Loeliger** and the Class of 2014 sang and danced in the show's final musical number. 4. **Samantha Wang**, one of the show's directors, played an evil management consultant hired by Deputy Dean for Education Richard Belitsky, M.D., the Harold W. Jockers Associate Professor of Medical Education and associate professor of psychiatry, who devises a plan to eliminate the venerable Yale System of medical education. 5. Loeliger (left) and **Juliet Fraser** (right) in the musical number "Defying Belitsky."

JOHN CURTIS (5)

April 9, 2012 This year's **David J. Leffell Prize for Clinical Excellence** was awarded to **Ronald R. Salem**, M.D., Lampman Professor of Surgery professor of diagnostic radiology, and chief of the Section of Surgical Oncology (see related story, page 2). Pictured here at a reception in the medical school's Historical Library are (from left) Salem's mother-in-law, **Blanche Feldman**; Salem; Salem's wife, **Sharon Salem**; and son, **Daniel Salem**.



HAROLD SHAPIRO

Just seven minutes curbs alcohol abuse

ISTOCKPHOTO

If someone ends up in a hospital's emergency department (ED) with signs of harmful drinking habits, as few as seven minutes of counseling by a physician can motivate them to cut back their alcohol consumption, says a new study by Yale researchers.

On average, the nearly 900 patients enrolled in the study, published in an advance online edition of *Annals of Emergency Medicine*, consumed around 20 drinks in the week prior to visiting the ED. When the researchers followed up a year later, that number had decreased to 17 drinks per week for patients with no interventions and to 14 for those who received counseling in the hospital. Moreover, the counseled patients reported fewer binge drinking episodes than those who received no counseling. Patients in the intervention group were also less likely to drive after having three or more drinks.

"A short intervention has great potential to increase the health of the public," says Gail D'Onofrio, M.D., M.S., professor and chair of the Department of Emergency Medicine and leader of the new study.

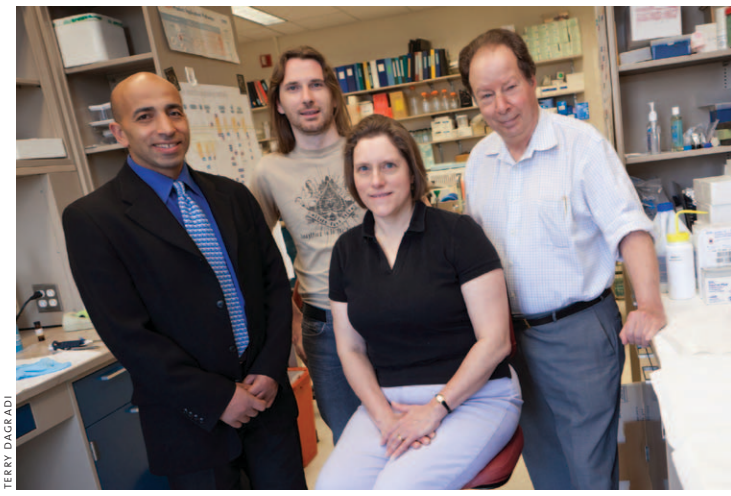
Is cell phone use risky during pregnancy?

Chatting on a cell phone may become the next taboo for pregnant women. A recent study led by Hugh S. Taylor, M.D., professor and chief of the Division of Reproductive Endocrinology and Infertility in the Department of Obstetrics, Gynecology, and Reproductive Sciences, found that when pregnant mice were exposed to cell phone radiation during pregnancy, their offspring were more hyperactive and forgetful than usual.

Taylor and colleagues attached cell phones on active calls—and therefore producing radiation—to the cages of 33 pregnant mice and left them there for the full 17 days of gestation. After the birth of the offspring, the scientists tested the memory, hyperactivity, and anxiety of the newborn mice. Those born to mothers with cell phones on their cages scored higher on measures of hyperactivity and lower on tests of memory and anxiety than mice born to mothers without the cell phone exposure, the researchers reported in the March 15 issue of the journal *Scientific Reports*. The team also found that certain neurons in the prefrontal cortex of the brains of offspring exposed to radiation had decreased activity, which may explain their behaviors. More work is needed, they say, to determine a safe level of cell phone radiation for pregnant women.

Stopping malaria dead in its tracks

Cross-campus collaborators work toward the elusive goal of effective treatment, eliminating drug resistance and side effects in the bargain



TERRY DAGRADI

(From left) The School of Medicine's Choukri Ben Mamoun and Yoann Augagneur have joined with Sidney Altman (right) and Donna Wesolowski (second from right) to design a malaria-fighting compound that could provide the basis for effective, less toxic treatments, against which the malaria parasite would be unlikely to develop drug resistance.

For parasites like those that cause malaria to thrive in the human body, they must produce proteins that drive their growth, reproduction, and nutrition. Existing malaria drugs work by blocking parts of this protein machinery, but the pathogens frequently become resistant to these drugs by evolving ways to block the drugs from binding to or passing through their external membranes.

Now, Yale researchers have discovered a different approach that works against malaria parasites and other pathogens by destroying the genetic material that encodes some of these pathogens' most vital proteins.

Over the past few years, Sidney Altman, PH.D., Sterling Professor of Molecular, Cellular, and Developmental Biology, has developed a technique to destroy specific pieces of a cell's messenger RNA (mRNA) with a compound called a peptide-morpholino oligomer (PMO) conjugate. He and his colleagues have shown that PMO conjugates can kill bacteria, including *E. coli* and staph bacteria, by stopping the production of proteins the pathogens require to survive.

When the PMO binds its targeted mRNA sequence, this structure is recognized by an enzyme in human red blood cells that destroys the mRNA, preventing it from being transcribed into proteins in the pathogen.

"We think that this technique has general importance and has lots of applications," says Altman, who shared the 1989 Nobel Prize in Chemistry for helping to establish that RNA can act as an enzyme as well as a carrier of genetic information.

For the new work, Altman collaborated with malaria expert Choukri Ben Mamoun, PH.D., associate professor of internal medicine and microbial pathogenesis, and Ben Mamoun's postdoctoral fellow Yoann Augagneur, PH.D., to test whether the PMO conjugates are effective against *Plasmodium falciparum*, the parasitic species that causes the most severe cases of malaria. As a proof of concept that PMO conjugates could enter *P. falciparum* cells and cause its mRNA to degrade, the team of scientists developed a PMO that binds the mRNA coding for an enzyme known as gyrase, the same type of sequence that Altman had targeted in other pathogens.

"There are genes that we know are essential to the parasite but we can't knock them out using classical genetics," says Ben Mamoun. "But using this oligomer, we can block the genes and study what happens." As reported in the April 2 issue of the *Proceedings of the National Academy of Sciences*, when the gene for gyrase was blocked, the malaria parasites died. "The next step is to test new targets and optimize the conjugates," says Augagneur. "We can use different conjugates against the same mRNA targets and improve the activity by two- to three-fold, and we can also find new targets." The drugs are an optimal way to target the malaria parasite, he says, because resistance, a problem with many other drugs, is unlikely to develop against the PMOs. "In principle, there wouldn't be resistance because you would need several mutations right next to each other in order to stop the conjugate from working."

And because you can selectively choose where on a stretch of mRNA the PMO binds, scientists can select sequences that don't resemble any human genes, so the PMO won't interfere with normal body processes.

"All existing anti-malarial drugs have side effects and some of them are very severe," says Ben Mamoun. "But, although we haven't done human trials yet, we would predict that these oligomers would be quite safe because of their specificity and selectivity."

While Ben Mamoun and Augagneur pursue new ways to use the PMOs against malaria parasites, members of Altman's lab plan to move on to other types of pathogens.

"There are lots of parasites that affect human cells and we just have to find out which ones are attractive as targets of this drug," says Altman. "It's very easy to redesign our compound to attack anything we want to look at."

Cross-country walk seeks 'altruistic' organ donors

Donating part of his liver and a kidney to two different recipients he had never met was not enough for Harry Kiernan. The Vietnam veteran and firefighter is now taking his efforts to raise awareness about organ donation—including so-called altruistic donations like his, in which recipients are not related or known to the donor—many steps further by walking across the United States.

Kiernan's 3,300-mile journey began March 18 in Glastonbury, Conn., and he reached Yale-New Haven Hospital (YNHH) the next day, where a ceremony for "Walk of 2012" took place under the Donate Life flag near the hospital's entrance. Sukru H. Emre, M.D., professor of surgery and pediatrics and the transplant surgeon who performed Kiernan's liver donation surgery, was on hand to wish Kiernan well and commend him for his generosity.

Emre presented Kiernan with an appreciation plaque from the Yale-New Haven Transplantation Center (YNHTC) on behalf of patients on the transplant waiting list for his dedication and service.

WILLIAM SACCO

Sukru Emre (left) and Harry Kiernan kicked off Kiernan's "Walk of 2012" on the Yale-New Haven Hospital grounds on March 19. Kiernan, a Vietnam veteran, firefighter, and liver and kidney donor, is walking across the U.S. to raise awareness about organ donation.

"Mr. Kiernan is one of our heroes. He saved two patients' lives by donating one of his kidneys and a part of his liver," said Emre, chief of the Section of Transplantation Surgery and YNHTC director (donated parts of the liver grow back in donors and grow to the proper size in recipients). Emre pointed out that, like Kiernan, many altruistic donors are veterans, firefighters, or policemen. "These individuals were on front lines in many life-and-death situations and they know how to sacrifice for others," he said.

In the U.S., only two percent of organ donations from living patients are altruistic donations. With each step he takes from east to west, Kiernan, founder of the National Living Organ Donors Foundation, hopes to increase the number of organ donations, from both deceased and living donors, nationwide.

After leaving New Haven, Kiernan set off for New York City and expects to arrive in Los Angeles during the first week of July.

// Center *(from page 3)* include pulmonary hypertension; Suk-Won Jin, PH.D., and Stefania Nicoli, PH.D., both assistant professors of medicine who use zebrafish as a research model; John Hwa, M.D., PH.D., associate professor of medicine; Kathleen Martin, PH.D., associate professor of medicine; Daniel L. Dries, M.D., M.P.H., associate professor of medicine and medical director of the Yale Center for Advanced Heart Failure; and Yibing Qyang, PH.D., assistant professor of medicine and of pathology. Qyang, like Hirschi, studies stem cells—particularly cardiovascular progenitor cells (CPCs), which are capable of making nearly an entire heart during formation—and is working to better understand the biology of CPCs with the aim of developing and enhancing therapies for disease and injury.

Abundant resources

Since Simons' arrival in 2008, grant funding for cardiovascular research at Yale has nearly tripled, increasing from about $8.5 million to about $24 million in 2012. This amount includes a five-year $6 million grant from the Paris-based Fondation Leducq under the auspices of its Transatlantic Networks of Excellence in Cardiovascular and Neurovascular Research program, awarded in 2010. The School of Medicine, at which the Leducq grant is supporting YCVRC research on the link between arteriogenesis and metabolism, is one of just six research institutions taking part in this international project, which is built around frequent and close communication.

But it's not simply funding that has enticed leading cardiovascular researchers to set up shop at the School of Medicine. Another crucial factor is the "unique environment" of the YCVRC, Simons says, a collegial place where "everybody has a say. People help each other, and we have several fantastic interaction forums." These include a weekly faculty gathering held in a purpose-built lunchroom in the center's suite at 300 George Street (see photo). "If you're there, you could be asked to talk off the cuff about what you do," Simons explains. "All our joint funding has come out of this faculty lunch."

Cardiovascular medicine is a scientific success story, as research has led to effective medications to manage cholesterol as well as angioplasty and stents, which allow doctors to widen narrow or blocked blood vessels. "But there has never been a medication that changes the nature of disease," Simons says. "All the currently available treatments—and they're very good—do not address the underlying biology of disease, and they basically palliate. The question is: how can you understand what's going on?"

Collaboration

YCVRC members collaborate very closely with other groups at the medical school. One notable relationship is that between the YCVRC and the Vascular Biology and Therapeutics (VBT) Program. Formed in 2000, VBT was the medical school's first interdepartmental research program explicitly focused on translating laboratory discoveries into practical treatments for disease. Now led by William C. Sessa, PH.D., the Alfred Gilman Professor of Pharmacology, VBT's diverse and collaborative design served as a model for the YCVRC, and functions as its "sister" program.

VBT members meet with YCVRC scientists in regular joint lab meetings. A leading researcher on blood vessel function and vascular disease, Sessa is one of the new PPG's seven investigators. The others are Tirziu; Simons; Schwartz; Themis Kyriakides, PH.D., associate professor of pathology and of biomedical engineering; Laura E. Niklason, M.D., PH.D., professor of anesthesiology and of biomedical engineering, a pioneer in tissue engineering; and Albert J. Sinusas, M.D., professor of medicine and of diagnostic radiology, a YCVRC member and an expert in advanced cardiovascular and molecular imaging. All seven scientists are members of VBT.


ROBERT LISAK

"We see VBT and the YCVRC as a single program, because people interact so effectively—at seminars and retreats, and at joint lab meetings," Sessa says. "There are common research interests, and everyone is secure enough with their own work to champion collaborative interactions. Michael Simons' recruitment gave us a partner in cardiology to synergize with."

Other budding YCVRC collaborations involve the Departments of Neurology, Ophthalmology, and Psychiatry. Each month, YCVRC scientists convene with colleagues from the Department of Neurology at a neurovascular meeting to explore the implications of vascular research in the brain. For instance, Jaime Grutzendler, M.D., associate professor of neurology and of neurobiology, studies the brain's microvasculature—its smallest blood vessels—and is interested in "vascular dementia," or the ways neurovascular defects contribute to cognitive decline in the elderly. The expertise of YCVRC scientists like Eichmann, Hirschi, and Thomas, who all work in areas related to neuroscience, is something Grutzendler is now able to tap into.

Ophthalmology is closely linked to neurovascular research, says Hirschi, because "the retina is a neural tissue. Several of us in the YCVRC are interested in ophthalmological disorders that occur because of dysregulated blood vessel formation—or [as with diseases like "wet" macular degeneration], when there's an overgrowth of blood vessels in the eye that inhibits vision."

In May, the YCVRC and VBT will convene an international neurovascular symposium in New Haven jointly with University College London (UCL) scientists, many of whom "work on [neurovascular interactions and] eye disease," Hirschi says. "We hope to form collaborations so that we can do studies for eye disease [similar to our studies on the neurovasculature of the brain]."

In the area of psychiatry, too, there is much overlap. Thomas, for instance, studies the effects of VEGF signaling on behavior, and is working jointly with colleagues in the Department of Psychiatry to gauge the links between VEGF and behavioral outcomes like depression and anxiety.

"The symposium enables everyone to share his or her work, get a feel for what everyone else is doing, and identify mutual interests on which we can build joint research programs and training opportunities," Hirschi says.


TERRY DAGRADI

(Above) In the lunchroom at the Yale Cardiovascular Research Center (YCVRC), faculty members, postdoctoral fellows, and graduate students can mingle informally.

(Left) Members of the YCVRC in the center's suite at 300 George Street. The suite's physical design reflects its collaborative culture.

Scientists from Yale and UCL are also collaborating on a project recently funded by a European Community (EC) grant, administered by the European Union. Sinusas, Tarek Fahmy, PH.D., associate professor of biomedical engineering, Simons, and Niklason are working jointly with colleagues at UCL, with U.K.-based Ark Therapeutics, and also with teams of scientists in Germany and Finland, to design and test a new technology designed to improve healing around implanted vascular stents. The technology involves using magnetized biodegradable stents, which will attract stem cells that have been loaded with iron particles; and, additionally, stents in which viral vectors have been embedded, to promote the adhesion of stem cells. The aim of the new technology—which the scientists hope will be tested in human patients within four years—is to alleviate circulatory problems arising from obstructive blood clots and narrowed blood vessels in patients with coronary stents.

The four-year $4.5 million grant is the first EC grant to fund the work of American scientists, Simons says, and could not have been possible without the existence of the Yale UCL Collaborative, which was created in 2010. "This grant is unique in that it brings together several biotech companies and academic institutions that have complementary expertise," Sinusas says.

Thanks to advances in genome sequencing technologies, and in particular to state-of-the-art genetic screening capabilities now offered by the Yale Center for Genome Analysis, YCVRC scientists are increasingly able to rely on genetic analyses of individual patients in conducting basic research—with the hope that this research can then be brought "back to the bedside" as therapy for disease. Cardiovascular genetics efforts at the YCVRC, led by Arya Mani, M.D., associate professor of medicine and of genetics, working together with colleagues from UCL and Yale's Department of Genetics, have already resulted in "significant new insights in our understanding of early atherosclerosis and metabolic syndrome," Simons says.

Scientists have traditionally believed that cardiovascular illnesses are caused by numerous small changes in many genes. But "it appears now that there are a number of genes in which a single mutation will give you a significant phenotype," Simons says—which increases the odds that scientists can identify the gene variants that cause a particular disease, understand that disease's biology, and find new therapies.

// Scholar *(from page 1)* five years she had discovered "initiator regions," sites in messenger RNA (mRNA) strands that mark where the cell's protein-making machinery begins translating mRNA into proteins. In a classic paper published five years later, Steitz showed that RNA-protein complexes in the cell nucleus called snRNPs are critical to "splicing," by which non-coding sequences are excised from pre-mRNA to form mRNA. In the decades since, RNA biology has exploded, and Steitz continues to explore RNA's diverse and powerful roles in the cell.

"Dean Alpern envisioned an environment where new faculty members are free to work on their best ideas," says McCluskey, whose new gift brings the total number of Yale Scholar funds to eight. "I am happy to name this new fund in honor of Joan Steitz, a scientist who exemplifies the power of original thinking." To sustain the funds, gifts like McCluskey's two $2.5 million donations establishing Yale Scholar Funds are matched by a commitment from Yale University—evidence of the program's importance to recruiting and jump-starting research.

"A Yale Scholar Award allows a new scientist to gain traction on a research idea even if it is not a conventional one," Alpern says. "A Yale Scholar has the latitude to take novel approaches, to adopt new techniques or to work at the intersection of disciplines where it is harder to find grants. By year five the researcher should be well positioned to attract his or her own funding."

Today, Ivanova continues her work at the Yale Stem Cell Center (see "Advances," page 3), and her position as a McCluskey Scholar has passed to Andrew Goodman, PH.D., assistant professor of microbial pathogenesis, who studies microbial communities in the human gut.

"I am deeply grateful to Mr. McCluskey for his generous support," Alpern says. "Natalia Ivanova and Andrew Goodman are at the start of a long line of distinguished McCluskey Scholars, and by September we will announce our first Steitz Scholar. This remarkable legacy will shape the School and the discoveries we can make here for generations to come."

// Student research *(from page 1)* a fifth year of medical school for research, expanded Student Research Day—an annual event at which students present their work in posters and oral presentations to peers and faculty—and "created ideal faculty-student pairs," Forrest says. Those student-faculty matches allowed students like Obinwanne Ugwonali, M.D. '99, to find the link between yams and twin births through research in Nigeria, and Khoonyen Tay, M.D. '06, to explore the options for treating a middle ear infection in children.

At its founding, the Office of Student Research had limited funding, and could only support student research during the first summer of medical school. Today, the office funds students during periods of research throughout medical school, typically during the summer between the first and second years, but often extending to a fifth year. Each year more than 200 students receive funding from Forrest's office, mostly via an NIH Training Grant that has been continuously renewed for 25 years. Also providing funding are Yale's Clinical and Translational Science Award from the NIH, the Howard Hughes Medical Institute, the Sarnoff Cardiovascular Research Foundation, the Doris Duke Charitable Foundation and donations to Yale from individuals. A recent re-application for the NIH training grant earned a perfect score, which Forrest says is a testament to the faculty-student pairs and the volume and quality of publications and national presentations arising from Yale medical students' research. The budget for the Office of Student Research now exceeds $2.5 million per year.

Under Forrest's leadership, Student Research Day has been transformed into an eagerly anticipated annual event. "In the 60s and 70s," he says, "there was a modest student research afternoon where the prize-winning thesis was presented." Today, the event (held this year on May 8) includes a poster session with about 90 posters, oral presentations by authors of the highest-rated theses, and the Farr Lecture, which has featured scientific leaders, including Nobel laureates.

Hardean Achneck, M.D. '05, now assistant professor of surgery at Duke University School of Medicine, credits his fifth year at Yale with teaching him to think like a researcher."The general principles that have helped me in my research career basically started with research at Yale," says Achneck, who still considers his faculty advisor, John Elefteriades, M.D., professor and chief of cardiothoracic surgery, a mentor.

"It's often a lifelong friendship that's formed between the mentor and the student with publications, presentations, and all the like that follow," Forrest says. "It is that faculty-student pair that deserves the emphasis and the celebration."

// Autism *(from page 1)* the SSC includes blood samples and extensive medical information from 2,700 families in which one child has been diagnosed with autism. The families are recruited from 13 clinics across the country, each using the same precise measures to confirm autism diagnoses. Researchers collect blood samples from not only the children with autism, but from parents and unaffected siblings. The term "simplex" in the SSC's name refers to the fact that the collection includes only families with a single child with autism and at least one unaffected child, making it easier to draw precise genetic comparisons between affected and unaffected family members.

In a much-publicized study published April 4 in *Nature*, State's team screened about 10 percent of SSC participants. But rather than sequencing the entire genome of each participant, which is for now prohibitively expensive, the researchers focused on the "exome," those portions of the genome that code for proteins. By applying this technique to the SSC's unique population, the research fingered three genes that almost certainly contribute to autism, and about a dozen others that are strong contenders. Two accompanying papers in *Nature* turned up yet more candidates.

As the cost of genome sequencing continues to plummet, State and others will screen more and more SSC children. Based on previous work and the findings published in *Nature*, he estimates that the total number of autism-linked genes will hit 500 or more—a greater cause for optimism than it might seem. "Even though there are many, many regions in the genome involved, I believe they will converge on a small number of pathways," State says. And, he adds, those specific networks will make the best targets for new treatments.

The SSC was launched in 2008 to help solve a puzzle. "We knew that children with autism don't usually get married and don't have children, and yet the rate of autism isn't decreasing," says Gerald D. Fischbach, M.D., scientific director of the Simons Foundation's Autism Research Initiative. "So where is it coming from?"

One leading hypothesis was that some portion of autism cases are caused by spontaneous—so-called *de novo*—genetic variations, rather than those inherited from parents. A 2007 *Science* paper reported that 10 percent of individuals with autism carry *de novo* copy number variations (CNVs), stretches of DNA that are either deleted or duplicated, compared with just 1 percent of controls. Last year, State's team and an independent group screened the SSC samples for *de novo* CNVs and confirmed that these variations crop up more often in children with autism than in controls.

But CNVs are large, sometimes encompassing thousands of base pairs of DNA and dozens of genes, making it difficult to draw conclusions about which individual genes are implicated in a disease. The new studies, in contrast, read families' genomes letter-by-letter, so researchers can zoom in on variants affecting just one letter.

After screening 928 SSC participants, State and colleagues found 125 single-letter *de novo* mutations in the children with autism, compared with 87 such mutations in unaffected siblings. That's a statistically significant difference, but also highlights a basic problem: Since healthy people carry so many mutations that don't seem to do any harm, how do we know which ones in the autism group are important? "Sorting out the stuff that's damaging from the stuff that's not is extremely difficult," State says. "One of the major preoccupations of the paper was finding an unbiased way of doing that."

The researchers reasoned that a gene was more likely to be meaningful if it carried new mutations in more than one unrelated child with autism. They also placed special focus on mutations that are highly damaging to protein production. Once those criteria were plugged into the proper statistical analyses, from over 238 families studied the researchers ended up with just one gene, called SCN2A, that is strongly associated with autism.

Another group of researchers, led by Evan Eichler, PH.D., of the University of Washington, did a similar search in a separate group of 677 SSC participants. When State's group applied their statistical approach to the combined data from both studies, three genes made the cut: SCN2A, KATNAL2 and CHD8.

"Each one of these genes is a whopper," Fischbach says. "Because of the design of these experiments, using both parents and unaffected siblings, this is about as sure as one can be about a genetic cause." These gene candidates have intriguing biological roles in brain cells. SCN2A, for example, makes a protein that helps control the transmission of electrical impulses across nerve cell membranes; a handful of people with epilepsy or intellectual disability have been reported to carry glitches in the gene.

State, Eichler, and Michael Wigler, PH.D., of the Cold Spring Harbor Laboratory are working on sequencing the rest of the participants in the SSC, and based on the mutation rate reported in the *Nature* papers, they estimate they will find at least 25 genes solidly linked to autism in the SSC alone. What's still unclear, however, is how much of the broader population of children with autism may also carry glitches in these genes—or how many of these genes will also figure into other psychiatric disorders, such as schizophrenia, bipolar disorder, and obsessive-compulsive disorder.

There's also the more mysterious issue of environmental and developmental contributions to developmental disorders. And all three *Nature* papers shed light on a factor that's been much talked-about: paternal age. The data show that as the age of the father increases, so does the number of spontaneous mutations carried by his child, which makes sense since sperm tend to acquire more genetic mutations as a man ages. "It's a very strong correlation—there's no question," State says. Still, a father's age probably plays a minor role in overall autism risk. The average age of men when they fathered children with autism was only 1.1 years higher than when they fathered unaffected siblings. And when paternal age was left out of the analysis, children with autism were still found to carry more mutations than unaffected siblings.

But State sees a broader lesson to be learned from this finding. "It shows that as you get more insight at the molecular level, you can begin to understand what mechanisms might be behind some of these environmental influences," he says. "As you move forward in clarifying the genetics, you're also going to clarify the environmental factors, and vice versa."

Expert on the effects of post-traumatic stress named the inaugural Greenberg Professor

Steven M. Southwick, M.D., a widely recognized expert on the psychological and neurobiological effects of extreme psychological trauma, has been named the inaugural Greenberg Professor of Psychiatry, Post-Traumatic Stress Disorder, and Resilience.

Southwick, also professor in the Child Study Center, has published extensively on the phenomenology and neurobiology of post-traumatic stress disorder (PTSD), the longitudinal course of trauma-related psychological symptoms, memory for traumatic events, treatment of PTSD, and on neurobiological and psychological factors associated with resilience to stress. He has worked with a range of stress-sensitive and stress-resilient individuals, including combat veterans with PTSD, civilian children and adults with PTSD, stress-resilient prisoners of war, and active Special Forces soldiers.

A 1974 graduate of Yale College, Southwick earned his M.D. at George Washington University. He completed his internship at the Johns Hopkins Hospital and a residency in psychiatry at Yale School of Medicine. He currently serves as an adjunct professor at Mt. Sinai School of Medicine and medical director of the Clinical Neurosciences Division of the National Center for Posttraumatic Stress Disorder.


Steven Southwick

Southwick has earned numerous awards in recognition of his clinical and research accomplishments and his teaching. These include selection by Yale's Psychiatry Residents' Association as Outstanding Psychiatry Faculty Teacher, an honor he has received three times; the Stephen Fleck Award for a Yale faculty clinician; and the Connecticut Psychiatric Society's Roger Coleman Memorial Award.

The professorship was created with a gift from Glenn H. Greenberg, of the Yale College Class of '68, to enhance understanding and advance treatment of psychological trauma, PTSD, and resilience.

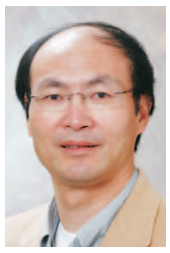
Biostatistician, substance abuse researcher is appointed Susan Dwight Bliss Professor

Heping Zhang, PH.D., a specialist in research on substance use, statistical methods in genetic studies of substance use, and research training in mental health epidemiology, has been appointed as the Susan Dwight Bliss Professor of Biostatistics in the School of Public Health.

Zhang has developed statistical methods and software to analyze data related to a broad range of health outcomes including pregnancy outcome, mental health, and substance use. He has published over 180 research articles.

In 2005, Zhang founded the Yale Collaborative Center for Statistics in Science (C2S2) to foster collaboration on statistical methods and technologies, particularly for understanding the etiology of pregnancy outcomes and to evaluate treatment effectiveness for infertility. In only a few years, his center has emerged as a major national resource for reproductive sciences.

He directs a training program for pre- and postdoctoral students,


Heping Zhang

which is funded by the National Institute of Mental Health, and he is a fellow of the American Statistical Association and of the Institute of Mathematical Statistics. Zhang was named the 2008 Myrto Lefokopoulou Distinguished Lecturer by the Harvard School of Public Health and a Medallion Lecturer by the Institute of Mathematical Statistics.

Zhang has also received a FIRST Award from the National Institute of Child Health and Human Development and an Independent Scientist Award from the National Institute on Drug Abuse.

In 2009, Zhang, who received his doctorate from Stanford University. was a Chang-Jiang Scholar with the Chinese Ministry of Education. In 2011, he received the Royan International Award on Reproductive Health.

Biostatistician who focuses on genetics and molecular biology named Hiscock Professor

Hongyu Zhao, PH.D., a biostatistician whose work is focused on developing mathematical, statistical, computational, and visualization tools needed to address scientific problems in molecular biology and genetics, has been appointed the Ira V. Hiscock Professor of Biostatistics in the School of Public Health.

Zhao, also professor of genetics and of statistics, is a leader in statistical genetics, computational biology, genetic epidemiology, and human genetics, and has developed novel statistical methods and showed how they can be applied to the study of many diseases, including cancer, obesity, hypertension, mental retardation, HIV/AIDS, substance dependence, and immunological disorders.

He has also contributed to genomic and proteomic analysis through the development of powerful statistical methods for pathway reconstructions using different types of genomic data, network analysis,


Hongyu Zhao

protein-protein interaction network inference, DNA copy number analysis, and pathway-based analysis.

Zhao's accomplishments and professional service have been recognized with many distinguished honors, including election as a fellow of the American Statistical Association, the Institute of Mathematical Statistics, and the American Association for the Advancement of Science.

Zhao is editor or associate editor of many statistical and biological journals, and is a past recipient of the Mortimer Spiegelman Award, given by the American Public Health Association to a top statistician in public health under the age of 40.

He received his B.S. from Peking University in Beijing, China, and his doctorate from the University of California-Berkeley.

Environmental health scientist with a focus on cancer risks is designated Bliss Professor

Tongzhang Zheng, D.SC., has been named the Susan Dwight Bliss Professor of Environmental Health Sciences in the School of Public Health. Zheng studies environmental pollution and human health, particularly in cancer epidemiology and etiology related to environmental hormone disruptors, genetic susceptibility, and the interaction of genes and the environment.

Zheng's research emphasizes the role of organochlorine compounds—such as polychlorinated biphenyls (PCBs), dichlorodiphenyltrichloroethane (DDT), and other pesticides—in the etiology of several major cancers in the United States, including breast, non-Hodgkin's lymphoma, Hodgkin's disease, multiple myeloma, and testicular cancer.

Zheng has shown that immunosuppression due to increasing exposure to ultraviolet radiation and hair dye use may be partly responsible for a worldwide increase in non-Hodgkin's lymphoma. In addition, he has


Tongzhang Zheng

examined the relationship between circadian rhythm disruption and the risk of female breast cancer, and found evidence that exposure to a higher level of light at night increases risk of the disease.

Zheng has worked with numerous Chinese government officials and scientists to develop educational and research programs in China that have benefited Yale faculty and students. He helped develop three major cohort studies and a case-control study of liver cancer in China.

He is also the co-scientific director of two summer programs that train epidemiologists and biostatisticians worldwide. In 1992 he was chosen as Teacher of the Year by students at the School of Public Health.

Zheng received his doctorate from Harvard University.