

Scientists honored for research unveiling molecular machines

The month of May brought the good news that two School of Medicine scientists, each of whom have done pathbreaking work on molecular machines involved in human disease, had received high honors for their research.

On May 1 Jorge E. Galán, PH.D., D.V.M., chair and Lucille P. Markey Professor of Microbial Pathogenesis and professor of cell biology, was elected a member of the National Academy of Sciences (NAS), one of the most

prestigious honors in science. On the 29th, Arthur L. Horwich, M.D., was named a winner of the Shaw Prize in Life Science and Medicine, along with his longtime scientific collaborator Franz-Ulrich Hartl, M.D., DR.MED., of the Max Planck Institute of Biochemistry in Germany.

Galán is renowned for his research on the cell biology, biochemistry, immunobiology, and structural biology of the bacterial pathogens *Salmonella* and

Campylobacter, which together cause most of the world's food-borne illness.

Galán's group has thoroughly characterized the *Salmonella* "needle complex," a syringe-like organelle through which the bacterium injects bacterial proteins into host cells during infection, modulating the function of those cells for its own advantage. In 2004, Galán and colleagues used cryoelectron microscopy to visualize the three-dimensional structure of the needle complex. For his wide-ranging research, in 2011 he was awarded the Koch Prize, the leading international scientific award in microbiology.

The NAS, an organization of scientists and engineers dedicated to the furtherance of science and its use for the general welfare, was established in 1863. The Academy acts as an official adviser to the federal government in any matter of science or technology.

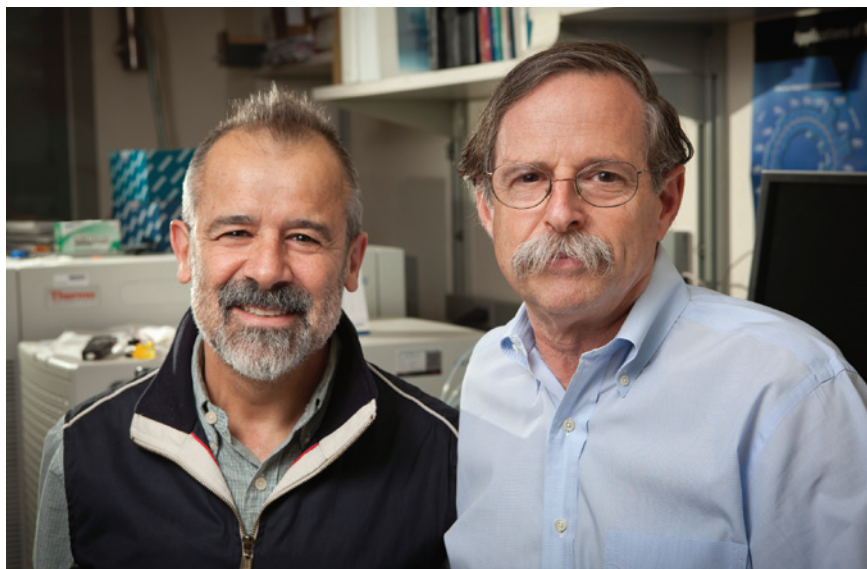
Also elected to the NAS in May was John R. Carlson, PH.D., of the Department of Cellular, Molecular, and Developmental Biology in Yale's Faculty of Arts and Sciences, bringing the total number of NAS members at Yale to 63.

Horwich, an NAS member since 2003, has devoted his career to understanding protein folding—how

chains of amino acids are formed into three-dimensional, functional structures. Misfolded proteins have been implicated in many diseases, including Alzheimer's disease and amyotrophic lateral sclerosis (ALS).

In 1989, Horwich's lab, in collaboration with Hartl and his postdoctoral mentor Walter Neupert M.D., PH.D., discovered a specialized protein in yeast called Hsp60 that acts as a protein-folding machine. Horwich and colleagues went on to elucidate how such machines work by studying a related bacterial protein called GroEL. By 1993, in a collaboration with the late Yale X-ray crystallographer Paul B. Sigler, PH.D., the atomic structure of GroEL—a "beautiful work of nature," in Horwich's words—had been deciphered.

The Shaw Prizes carry a monetary award of \$1 million (U.S.) and are given by the Hong Kong-based Shaw Prize Foundation for achievement in the life sciences, astronomy, and mathematics. Established in 2002 by filmmaker and philanthropist Run Run Shaw, the awards are "dedicated to furthering societal progress, enhancing quality of life, and enriching humanity's spiritual civilization." Horwich and Hartl will receive the award in Hong Kong in September.



Jorge Galán (left), who has studied the molecular basis of infection by *Salmonella* and other food-borne pathogens, was elected to the National Academy of Sciences. Arthur Horwich shares the Shaw Prize in Life Science and Medicine for his contributions to understanding protein folding.

Student research on heart surgery gets a boost from new endowment

In the 1960s, when cardiac surgery was still a young field, Horace C. Stansel Jr., M.D., was already making his mark at Yale as a skillful, innovative pediatric heart surgeon. A member of the School of Medicine faculty until his death in 1994, Stansel built a reputation as a consummate physician, researcher, and educator, and was a mentor to generations of medical students and residents.

Known as "Stan" to friends and colleagues, Stansel trained with Ormand C. Julian, M.D., at Presbyterian St. Luke's Hospital in Chicago and was recruited to Yale by William

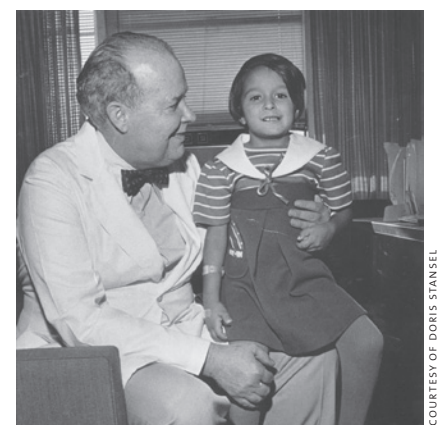
W.L. Glenn, M.D., then chief of the cardiac surgery section.

"As a junior faculty colleague, I learned a great deal from Stan," recalls John E. Fenn, M.D., now clinical professor of surgery at the medical school. "He was a skilled surgeon who could think on his feet. He was a master at knowing how to get out of trouble in the operating room, and colleagues often called on him for assistance."

Stansel also pushed the boundaries of surgical technique—the Damus-Kaye-Stansel procedure is still used by pediatric surgeons to treat congenital

heart defects—and he trained numerous physician-scientists who went on to head surgery departments around the country. "Stan personified the commitment to life-long learning that is so necessary to medicine," says Fenn.

To carry on Stansel's legacy, the Stansel family recently established an endowment that will provide support to Yale medical students conducting research in cardiac surgery. Known as the Horace C. Stansel Jr. Research Fund, the endowment will provide one- and two-year fellowships to students with financial need, allowing them to pursue research // Gift (page 8)



Pediatric heart surgeon Horace Stansel, seen in a 1978 photo with a patient, was a widely admired physician, researcher, and educator.

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Results from a clinical trial show the goal of immunotherapy may be within reach.

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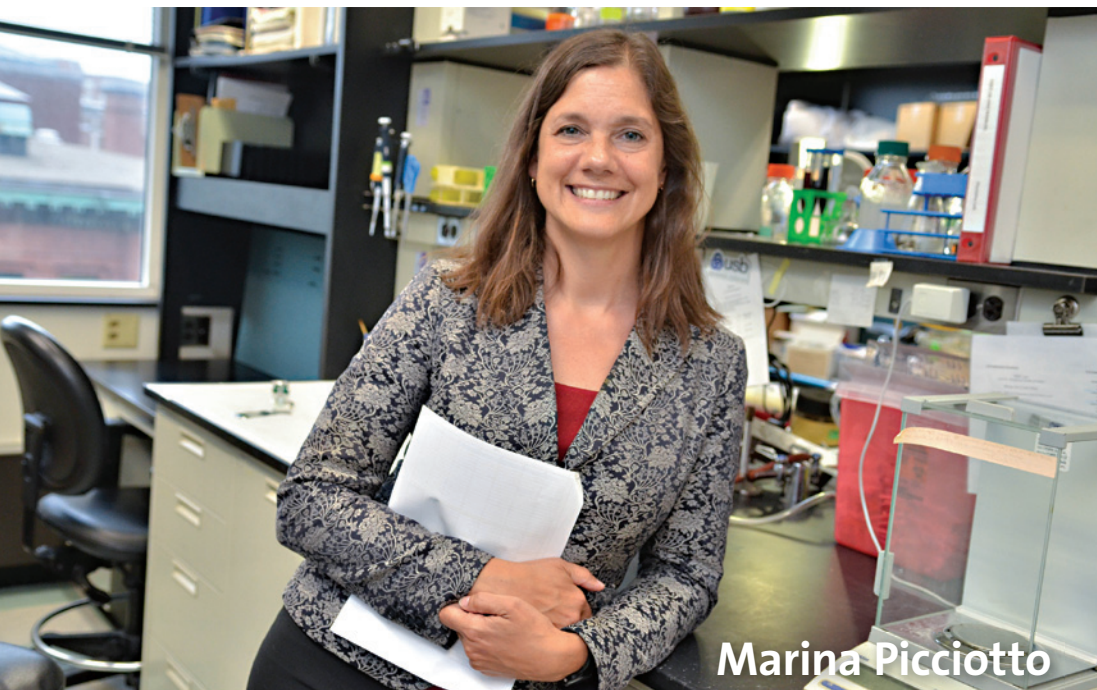
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Marina Picciotto

MICHAEL MARSLAND

Marina Picciotto's research not only sheds light on nicotine's effects on the brain, but also has implications for other important health issues, such as controlling obesity and the development of effective pain medications that do not lead to drug dependence.

Making sense of addiction

Neuroscientist is focused on the brain bases of tobacco dependence

Marina Picciotto, PH.D., says that while she was growing up in Manhattan, she was "one of those scattered people who did well in school but got yelled at by the teachers." In science labs, however, "that was never a problem." At the magnet high school she attended, students completed graduation requirements early, and took on full-time internships as seniors. Somewhat by chance, she came across an opening in a lab at the Rockefeller University, where she worked on studies of feeding behavior in rats that would neatly foreshadow her later career.

After earning a B.S. in biology at Stanford University, Picciotto returned to Rockefeller as a PH.D. student in molecular neuroscience. Her mentor there was Paul Greengard, PH.D., who would later receive the Nobel Prize for his work—a great deal of which he had accomplished while on the Yale School of Medicine faculty—explaining the molecular basis of communication among nerve cells in the brain.

In Greengard's lab, Picciotto studied signal transduction and the

transport of ions across nerve cell membranes. "It was very satisfying, because you could actually say, 'this goes with this' [and make] pictures that made sense. But I was always sneakily trying to get back to [the question], What do those molecules mean for complex behaviors?"

It's a question that has driven Picciotto's research ever since. As a post-doctoral fellow at the Institut Pasteur in Paris, France, she began studying nicotinic acetylcholine receptors (nAChRs), proteins in nerve cells that are activated by the neurotransmitter acetylcholine, but also respond to chemicals like nicotine. She describes this research the way many describe their first cigarette: "Once I started, I was hooked."

In 1995 she joined the School of Medicine's faculty as an assistant professor. Now the Charles B.G. Murphy Professor of Psychiatry and professor of neurobiology and pharmacology, Picciotto studies the links between neurochemical signaling and behavior. Her primary interest is the role of nAChRs in brain development and function, with a special emphasis on behaviors related to nicotine addiction and smoking.

"What's really cool about investigating nicotinic acetylcholine receptors is what happens when you stimulate

them," Picciotto says. For instance, in 2011, she and lab member Yann S. Mineur, PH.D., associate research scientist, teamed up with colleagues in the Section of Comparative Medicine to show that a specific type of nicotinic receptor is the crucial trigger for nicotine's effects on appetite suppression and weight-loss in mice. The study, published in *Science*, could lead to new strategies to treat obesity.

Picciotto also studies galanin, a neuropeptide that works to modulate acetylcholine but also heightens the effects of opiate drugs—many of which are addictive. In 2003, she published research in *Proceedings of the National Academy of Sciences* showing that in addition to increasing the pain-fighting effects of opiates, galanin also decreased their addictive properties. Her lab continues to explore how manipulating galanin might combat addiction and withdrawal symptoms.

"We're never going to understand all the molecules necessary for an entire behavior," Picciotto says, "but the overall philosophy—that you can say something meaningful about molecules in the brain that can inform how we think about the molecular basis of behavior—that's something that's approachable, and it's worth doing."

Class of 2012 urged to give patients 'the best possible existence'

At this year's commencement ceremony, held May 21, graduating medical students were treated to words of wisdom from pediatric neurosurgeon Benjamin S. Carson Sr., M.D., who recounted the story of a dilemma he faced in 1985 as a young doctor.

In his commencement address, Carson said he believed that a hemispherectomy—removal of half of the brain—was the best way to help one of his patients, a girl with severe epilepsy who was suffering constant seizures. But a senior physician, a distinguished neurologist, disagreed. Carson, a 1973 graduate of Yale College, decided to perform the surgery anyway.

"I risked my career because I asked myself why I became a neurosurgeon, and it was to give patients the best possible existence," he told the 100 members of the Class of 2012. "When you tell someone their loved one is doing well," Carson said, "that's the best feeling in the world."

Carson, director of pediatric neurosurgery at Johns Hopkins Medical Institutions, received national attention in 1987 for the first separation of twins joined at the back of the head.

Among his many awards is the Presidential Medal of Freedom, which he received in 2008. Carson's belief in the power of education is



TERRY DAGRAZI

Pediatric neurosurgeon Benjamin Carson delivered the commencement address in May.

such that he and his wife established the Carson Scholars Fund, which has awarded more than \$4.5 million to scholars in 45 states.

New section chief to be appointed for Otolaryngology



Wendell Yarbrough

Wendell G. Yarbrough, M.D., will be named chief of the Section of Otolaryngology at the School of Medicine and Yale-New Haven Hospital (YNHH). He will also be

director of the head and neck cancer program at Smilow Cancer Hospital at Yale-New Haven as well as the co-director of the molecular virology research program at Yale Cancer Center (YCC).

Yarbrough, whose appointment begins August 1, comes to Yale from Vanderbilt University, where he is professor of otolaryngology and cancer biology and director of the Barry Baker Laboratory of Head and Neck Oncology. He is also the Ingram Professor of Cancer Research and co-leader of the thoracic and head and neck program at the Vanderbilt Ingram Cancer Center.

Yarbrough's research concentrates on the identification of tumor suppressors in head and neck cancers and the understanding of tumor growth. Recently, his lab has focused on identifying subtypes of head and neck and salivary cancers and the use of models that the lab has developed to test targeted agents.

"I am confident that Dr. Yarbrough's experience, leadership, and goals for head and neck cancer research and care will strengthen our head and neck cancer program at Smilow Cancer Hospital at Yale-New Haven," said Thomas J. Lynch Jr., M.D., director of YCC and physician-in-chief of Smilow Cancer Hospital at Yale-New Haven.

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The FDA is slow? Not so fast!



Doctors and patients who are impatient for new drugs to hit the market often get the sense that the United States' drug approval process is a long and slow road. But a new study by School of Medicine researchers found that the U.S. Food and Drug Administration (FDA) actually moves faster when reviewing drug applications than its counterparts in Canada and Europe.

The first author of the study, second-year Yale medical student Nicholas Downing, and a team led by Assistant Professor of Internal Medicine Joseph S. Ross, M.D., M.H.S., examined publicly available drug applications from 2001 through 2010 to the FDA, the European Medicines Agency (EMA), and Health Canada.

As reported May 16 in the *New England Journal of Medicine*, for 72 drugs eventually approved by all three agencies, the average review time at the FDA was 90 to 100 days faster than at the other agencies, and most of these drugs hit the U.S. market first. For all drugs reviewed during the nine-year period, the FDA took 322 days on average, while the EMA averaged 366 days and Health Canada took 393 days.

Tight rein on glucose no boon in diabetes

Theories have swirled around the field of diabetes research that aggressively controlling the glucose levels of patients with type 2 diabetes would reduce their risk of impaired kidney function. But a new analysis of the data by Yale researchers has found no evidence that such treatment prevents ultimate kidney failure.

Steven Coca, D.O., M.S., assistant professor of internal medicine, Chirag R. Parikh, M.D., PH.D., associate professor of medicine, and colleagues analyzed seven previous clinical trials that together included 28,065 adult patients monitored for up to 15 years.

When those patients had been treated more aggressively—with higher doses of drugs and a lower target blood glucose level than is standard—certain markers of kidney function did improve over those in patients treated with the standard drugs and glucose targets. But the more aggressive treatment plan did not reduce the patients' risk of impaired kidney function, the need for dialysis, or eventual death from kidney disease, the team reports in the May 28 issue of *Archives of Internal Medicine*.

"Our analysis shows that intensive glycemic control may improve some things about the kidney that we measure, but did not affect patients' outcomes," says Coca.

The medical school's 'hidden treasure'

General Internal Medicine at Yale is a flourishing research powerhouse with a diverse portfolio of projects

As is the case at most medical schools, Yale's Department of Internal Medicine is by far its largest, with over 300 faculty members. These faculty are organized into sections, most of which carry names easily mapped onto familiar medical specialties: Nephrology, Geriatrics, Rheumatology, and so on. But the less descriptive name of the Section of General Internal Medicine (GIM), which claims 91 of the department's faculty as members, makes its role far less obvious, which is perhaps what leads Dean Robert J. Alpern, M.D., to call the section "a hidden treasure of Yale."



Patrick O'Connor

Many of GIM's activities are quite visible: The section is home to the many Yale primary care physicians who work at Yale Internal Medicine Associates (a part of Yale Medical Group), Yale-New Haven Hospital, the VA Connecticut Healthcare System in West Haven, Conn., and clinics and hospitals as far afield as Waterbury, Conn., which together have patient visits in the tens of thousands each year. GIM is also an important educational resource, contributing to three departmental residency programs and numerous medical-student teaching services, which are overseen by some of the medical school's most outstanding clinician-educators.

The more "hidden" aspect of GIM is that the section is a research powerhouse, with a robust and extraordinarily diverse portfolio. The section's physician-scientists study such topics as targeting insulin resistance to prevent stroke and heart attacks, HIV and comorbid disease in aging veterans, occupational asthma and hearing loss, and the effectiveness of health-education video games. They advise the national organizations that judge hospitals. They investigate the diffusion of surgical robot technology and develop office-based treatments for drug addiction and alcohol dependence. They examine the epidemiology and treatment of congestive heart failure, cancer, and stroke. They develop curricular guidelines that are used in internal-medicine residency programs nationwide. And, in keeping with the whole-patient philosophy of general internal medicine, they study the big picture, scrutinizing patient safety, clinical effectiveness, and discrimination in health care.

"In many very good places, the general medicine section is simply a group of clinicians to see primary-care patients," says Jack A. Elias, M.D., Waldemar Von Zedtwitz Professor and chair of the Department of Internal Medicine. By contrast, he says, Yale's GIM physicians, "while providing expert primary care, are also doing things that are going to impact patient care and national policy. They're going to impact how we take care of people from impoverished and affluent backgrounds, alter how we take care of people with heart failure, change how we deal with drug addiction and provide important insights into ways to provide less expensive and safer patient care. They're at a level that almost no other section of general medicine is at."

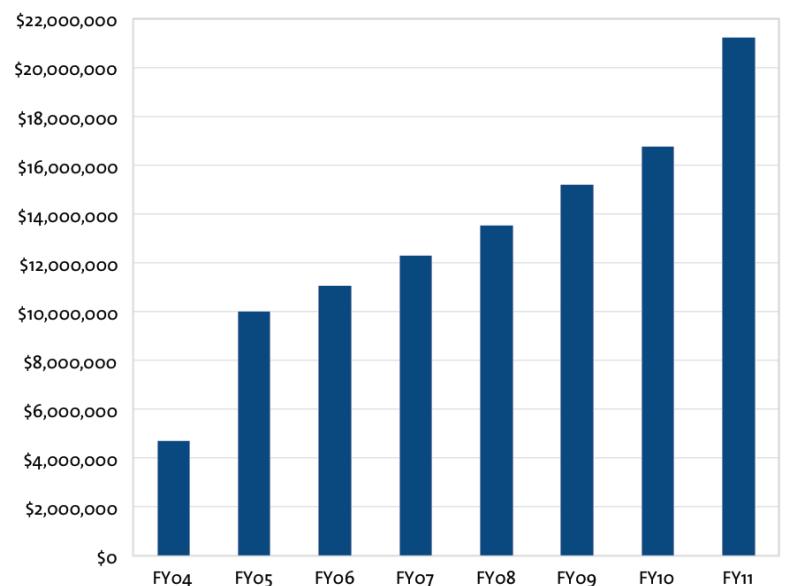
Founded in 1975, the GIM ranks among the highest of the Department of Medicine's sections in research funding. And keeping pace with the department as a whole, it has recently enjoyed meteoric growth. In 2002, it employed 39 full-time faculty; today there are 91. Research funding totaled a healthy \$4 million in 2004, but by 2011 it had zoomed to \$21 million, the vast majority from federal sources (see figure).

"We're spread thick," says GIM Section Chief Patrick G. O'Connor, M.D., M.P.H., of the section's varied research projects. "We approach each of these research areas in a scientifically rigorous manner, and the reputation of the faculty and their success at getting funding in these areas through peer-reviewed federal sources speaks for itself." Some of the most exciting work in the section, he adds, is



The more than 90 faculty members in the Section of General Internal Medicine provide quality primary medical care to patients, but also advance our knowledge and shape national policy through a diverse, well-funded research portfolio.

On the rise



Research funding for investigators in Yale's Section of General Internal Medicine, mostly from federal sources, has seen a steady increase over the past eight years, and is now approaching the \$22 million mark.

being done by up-and-coming junior faculty recruited in the last five or six years.

For example, Joseph S. Ross, M.D., M.H.S., who joined the section in 2008, has already been a co-author of some 70 peer-reviewed original research papers, including some presenting methods to use Medicare data to assess quality and performance at hospitals. Ross did a postdoctoral fellowship at Yale, then worked in New York City before being recruited back to Yale in 2010. "I was really excited to come back, partly because of the community of individuals in the section, some of whom I'd trained with," he recalls. "It just makes it a very stimulating and provocative environment to be around so many good thinkers."

Those thinkers include Marcella Nunez-Smith, M.D., M.H.S., who established the Eastern Caribbean Health Outcomes Research Network (ECHO), which O'Connor calls the "Framingham Study of the Caribbean"—a reference to the landmark Massachusetts heart study that has been providing crucial information on cardiovascular disease // GIM (page 7)

Philanthropy fuels research

The research advances emanating from Yale's Section of General Internal Medicine (GIM) require constant and consistent funding. Private philanthropy often provides critical early support to researchers who wish to pursue creative but untested approaches to important questions, allowing investigators to collect the initial data needed to successfully compete for external funding. Your generosity can fuel research that will lead to tomorrow's treatments and cures. Current-use gifts may be directed for specific projects, while endowments can generate perpetual support for investigators just launching their careers or for a senior professor with a sustained record of accomplishment. To find out more about how to contribute to GIM's research projects, contact Richard Galiette at 203-436-8529 or richard.galiette@yale.edu.

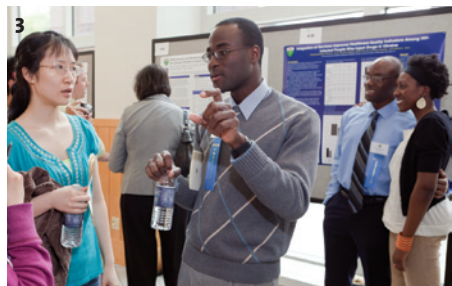
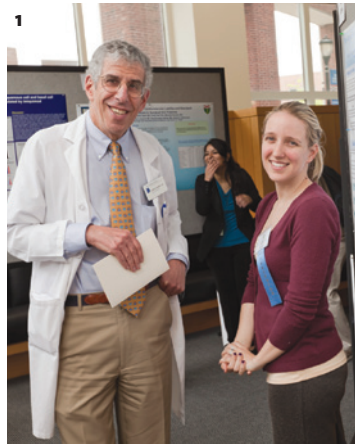
OUT & ABOUT

March 3, 2012 Patients of the Yale Children's Diabetes Program and their families attended the annual **Family Day Symposium** held at the Yale School of Nursing. The half-day symposium included lectures, discussions, and interactive programs for adults and children. 1. **Bryce Ferguson**. 2. **Sasha Averko**, clinical services manager at Massachusetts-based Insulet Corporation, gives a demonstration of an insulin management system. 3. **William V. Tamorlane, M.D.**, professor of pediatrics, speaks to attendees.



CARL KAUFMAN (3)

May 8, 2012 **Student Research Day**, an annual event, showcased medical students' theses, an integral part of the Yale System of medical education, and a requirement for students since 1839. A record 92 students exhibited posters in The Anlyan Center displaying the results of their research. 1. **John M. Leventhal, M.D.**, professor of pediatrics, and **Jennifer Duffy '13**. 2. Students in the Medical Scientist Training Program (MSTP), known informally as the M.D./PH.D. Program, with MSTP Director **James D. Jamieson, M.D., PH.D.**, professor of cell biology (back row, second from left). (Front row, from left) **Nancy Allen '14**, **Ruth Wang'ondu '15**, and **Katherine Uyhazi '12**. (Back row, from left) **Chen Wang '14**, Jamieson, **Corey Frucht '12**, and **Daniel Okin '14**. 3. (From left) **Alice Li '12** and **Kofi-Buaku Atsina, M.D. '11**. 4. (From left) **Kwame Atsina '12** and **Panos Christakis '12**.



TERRY DAGRADI (4)



TERRY DAGRADI

May 11, 2012 A reception was held in the Medical Historical Library marking the election of **Jorge Galán, PH.D., D.V.M.**, chair and the Lucille P. Markey Professor of Microbial Pathogenesis, to the **National Academy of Sciences** (see related story, page 1). (From left) Galán; **Ruslan M. Medzhitov, PH.D.**, the David W. Wallace Professor of Immunobiology and Howard Hughes Medical Institute investigator; **Akiko Iwasaki, PH.D.**, professor of immunobiology and of molecular, cellular, and developmental biology; and **Craig R. Roy, PH.D.**, professor of microbial pathogenesis.



SHANE SEGER

March 31, 2012 The medical school's Department of Psychiatry hosted **Neuroscience 2012**, an annual symposium aimed at mental health professionals and consumers throughout the State of Connecticut. (From left) **John H. Krystal, M.D.**, the Robert L. McNeil Jr. Professor of Translational Research and chair of the Department of Psychiatry; **"Dr. Ruth" Westheimer, ED.D.**, recipient of the department's seventh annual Research Advocacy Award; and **Robert E. Davidson, PH.D.**, president of the Connecticut chapter of the National Alliance on Mental Illness.

May 8, 2012 **Roger Daltrey**, founder and lead singer of English rock band The Who, who has a long record of charitable work for teenagers and young adults with cancer, visited doctors and patients at the medical school and at Smilow Cancer Hospital at Yale-New Haven. 1. Daltrey signs autographs for **Darrel Janis** (left), manager of the medical school's Marigolds Dining Service, and **Joyce Brown**, banquet server for Marigolds. 2. (From left) **Tara Sanft, M.D.**, assistant professor of medicine and medical director of the Survivorship Clinic at Yale Cancer Center; Daltrey; **Stuart E. Seropian, M.D.**, associate professor of medicine; **Hari A. Deshpande, M.D.**, assistant professor of medicine and surgery and assistant clinical professor of nursing; **Michael E. Hurwitz, PH.D., M.D.**, assistant professor of medicine; and **Clifford W. Bogue, M.D.**, interim chair and associate professor of pediatrics, chief of the Section of Pediatric Critical Care Medicine, and physician-in-chief at Yale-New Haven Children's Hospital.



JOHN CURTIS (2)

May 21, 2012 This year's **Commencement** ceremony marked the end of medical school for the Class of 2012, and also set a new record: the class's senior gift campaign raised more than \$1,600 for the Alumni Fund, with 84 percent of graduating students participating. 1. **Mona Sadeghpour** (second from right) with (from left) her mother, **Maryam Dargahi**; her brother, **Mehrad Sadeghpour**; and **Ardavan Akhavan, M.D.** 2. **John Gilbert** (left) and **Whitney Sheen**, who spearheaded the class gift effort. 3. **Michael Ma** (left) and **Henry Park**. 4. (From left) **Richard Belitsky, M.D.**, the Harold W. Jockers Associate Professor of Medical Education, associate professor of psychiatry, and deputy dean for education; and **Matthew Singleton** with his son **Matthew Singleton Jr.**



JOHN CURTIS

TERRY DAGRADI (3)

Tiny genomic change makes big difference



A single regulatory region in the mammalian genome underlies a key difference between mammals' brains and those of other organisms, says a new study by School of Medicine scientists. A hallmark of mammalian brains is the corticospinal system, which, in humans, connects parts of the brain and the spinal cord to make behaviors such as speech and tool-use possible.

In the new work, led by Nenad Sestan, M.D., PH.D., associate professor of neurobiology, Yale researchers discovered that a genomic region called E4 determines whether the corticospinal system emerges during development by exerting regulatory control over the gene *Fezf2*, which directly mediates the system's formation. When the scientists inactivated E4 in mice, the animals lacked corticospinal neurons.

In mammals, the E4 region has changed little over evolutionary time, but varies considerably among other organisms. The team's results, published in the May 31 issue of *Nature*, suggest that just a few small changes in the E4 region marked a crucial turning point in the evolution of mammals.

Probing the cause of diabetes-related pain

Uncontrollable pain and tingling are all-too-familiar sensations for most diabetics. So-called neuropathic pain occurs in more than half of people with diabetes—and the older someone is, and the longer they've had diabetes, the more likely they are to experience it. Though it often plagues the arms, legs, hands, and feet, neuropathic pain can occur in any body part. Doctors have long struggled to understand the source of the pain, let alone treat it.

Now scientists at the School of Medicine and at the VA Connecticut Healthcare System, in West Haven, have proposed a new theory on the origin of neuropathic pain in diabetes.

Previous work by Andrew Tan, PH.D., associate research scientist in neurology, and Stephen G. Waxman, M.D., PH.D., the Bridget Marie Flaherty Professor of Neurology, suggested that alterations in the size, density, and overall distribution of dendritic spines—signal-receiving structures that project from nerve cells—may underlie neuropathic pain that can follow nerve and spinal cord injuries. In the May 16 issue of *The Journal of Neuroscience*, Tan, Waxman, and colleagues report that when they gave diabetic rats a drug that restores dendritic spines to a normal condition, nerve function improved and pain lessened, findings that could lead to new treatments for diabetes-related neuropathic pain.

Turning on immunity to shut off cancer

In multicenter trial, unleashing the immune system's power arrests several forms of late-stage disease

When Lieping Chen, M.D., PH.D., was training to be an oncologist in the 1980s, the lack of effective cancer treatments made it a depressing job. "That's why I quit clinical practice," he says. But Chen soon shifted to research, focusing on the role of the immune system in cancer.

For decades Chen and other scientists have grappled with the mystery of why our immune systems—such brave warriors when it comes to other diseases—mostly sit on the sidelines while cancer invades the body. Though our bodies produce T cells, the immune system's soldiers, in response to cancer, these cells don't seem to have much of an effect. Scientists have yearned to find some way to "switch on" the immune system to attack cancer cells, an approach that could target the disease precisely while sparing normal cells, resulting in greater effectiveness and fewer of the side-effects of conventional treatments. And because the immune system "remembers" invaders it has encountered, the response to immunotherapy should be long-lasting.

On June 2 in the *New England Journal of Medicine*, a multi-center team that included Chen and two Yale colleagues reported that in an early clinical trial of BMS-936558 (a drug developed by Bristol-Myers Squibb) enrolling 296 patients, tumors had regressed significantly in about one in three to one in five patients with non-small-cell lung cancer, kidney cancer, or melanoma. The results, which received wide media coverage, were presented the same day at the annual meeting of the American Society of Clinical Oncology in Chicago, Ill.

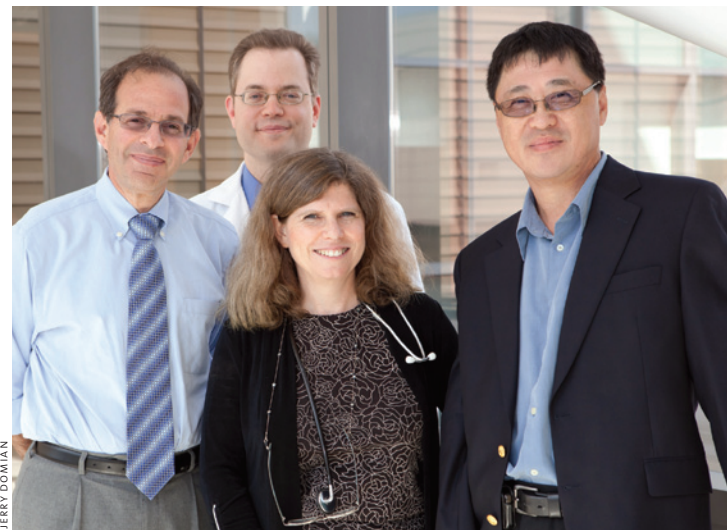
For reasons that are not fully understood, the small number of patients with colorectal or prostate cancer in the trial did not respond to BMS-936558. But the response in lung cancer patients is remarkable, says Professor of Medicine Mario Sznol, M.D., because previously immunotherapies showed effectiveness only in melanoma and kidney cancers. Chen points out that the patients in this trial had all previously been heavily treated with therapies that likely depleted their immune systems; if administered to patients in earlier stages of cancer, the drug should be even more effective, he says.

The other exciting finding of the study, says Sznol, who was instrumental in bringing the trial to Yale, is the consistent, durable regression of cancers: 20 of 31 responses lasted for at least one year, a result only rarely observed with traditional chemotherapy or other forms of therapy that target specific characteristics of tumors.

Since similar results were seen at each of the nine centers participating in the trial, Sznol considers it highly unlikely that the drug's effectiveness is a fluke. Scott N. Gettinger, M.D., associate professor of medicine, who recruited many lung cancer patients for the trial, agrees, saying the response in those patients "opens the door to looking at other solid tumors," such as breast cancer. The majority of his patients experienced few or no side effects, he says, and none of those typical of chemotherapy such as hair loss, a drop in blood-cell counts, and fatigue. "This is probably the best drug I have ever given to patients with lung cancer," Gettinger says.

The long road to these results began in 1991, when Chen, then at the Mayo Clinic, discovered a protein called B7-H1 that had the power to suppress the activity of T cells. He did not know the T cell molecule responsible for this effect, but in 2000, researchers from Harvard Medical School's Dana-Farber Cancer Institute and the University of Kyoto found that B7-H1 binds to another protein called programmed death 1 (PD-1), a "checkpoint" receptor on the surface of T cells that suppresses their activity.

The B7-H1 protein is now usually called PD-L1, to reflect its role as a binding partner, or "ligand," for PD-1. Chen wondered if PD-L1 binding might be one of the mechanisms that allows cancer to evade an immune response, and in experiments with mice lacking the protein, he found that the PD-1 pathway is crucial to the normal functioning of the immune system: a prolonged immune response can be very damaging to the body, so tissues express PD-L1 to turn the response off. Chen dubbed the pathway the "peacekeeper" for its protective role, but he



(From left) Mario Sznol, Scott Gettinger, Harriet Kluger, and Lieping Chen were involved in a nine-center clinical trial of a drug that disarms a molecular defense mechanism mounted by tumors, allowing the immune system to effectively attack cancer.

found that while PD-L1 is expressed in healthy tissue at low levels during an immune response, it is over-expressed in many human tumors.

"Cancer steals this mechanism," Chen, professor of immunobiology and medicine, says. In the presence of cancer, an immune response is triggered properly, and T cells flock to the tumor. But the T cells contribute to their own demise by releasing signaling molecules called cytokines, which induce the tumor to produce PD-L1. When PD-L1 binds to PD-1 on T cells, those cells are either inactivated or die off. BMS-936558 prevents this immune suppression by blocking the PD-1 binding site and keeping PD-L1 at bay.

Tests on tumor samples taken from a subset of patients in the newly published trial revealed that tumors that did not express PD-L1 did not respond to treatment, while 36 percent of PD-L1-positive tumors showed a response, indicating that PD-L1 may be a useful biomarker for identifying patients who will most benefit from anti-PD-1 drugs.

The PD-1 pathway is only one inhibitory strategy tumors may employ to silence the immune system. Last year the FDA approved the drug ipilimumab (marketed as Yervoy), which blocks another checkpoint molecule expressed on the surface of T cells known as CTLA-4, for the treatment of advanced melanoma. Ipilimumab has a response rate of about 11 percent, but anti-PD-1 therapies have been shown to be safer and more efficacious. Chen believes that this is due to limited PD-L1 at sites of inflammation, including tumors. The CTLA-4 ligand, on the other hand, controls an earlier stage of immune system activation, so blocking its receptor has led to severe toxicities. There are side-effects of PD-1 blockage—in the current trial, three patients died of drug-related lung inflammation—but Chen thinks they can generally be successfully managed.

Jedd D. Wolchok, M.D., PH.D., of Memorial Sloan-Kettering Cancer Center, who was not involved in the current trial, says that the new results are important because, along with the success of ipilimumab, they are the second clear demonstration that unleashing the immune system can produce durable regressions in cancer.

Although BMS-936558 was quite effective when used alone, the Yale researchers believe that it will be most useful combined with other therapies. Sznol is currently collaborating with Wolchok on a clinical trial that targets both PD-1 and CTLA-4, and Chen believes that adding drugs that block T cell checkpoints could even reverse the low success rate of cancer vaccines seen thus far.

"We're just at the beginning of a sort of paradigm shift in the treatment of cancer," Sznol says, who believes that immunotherapy will surpass standard treatments like chemotherapy over the next five years. As for BMS-936558, Chen is hoping to see FDA approval in two to three years, but "it should be approved tomorrow," Sznol says: "It's better than the approved agents. I have patients who have benefited enormously from this drug. For some patients it's a home run. For the field it may be a triple." And while current treatments prolong life for months or a couple of years, Sznol says, "these new therapies may eventually offer the possibility of cure."

Grants and contracts awarded to Yale School of Medicine

May–August, 2011

Federal

Serap Aksoy, NIH, *Factors in Emergence of New Sleeping Sickness Foci in Uganda*, 3 years, \$175,077 • **Kevin Behar**, NIH, *Ex Vivo Assay For In Situ Brain-Wide Mapping of Glutamate/GABA Metabolism*, 3.8 years, \$2,076,727 • **Kathleen Belanger**, NIH, *Effects of Fine Particle Composition on Birth Outcomes*, 4.7 years, \$2,610,942 • **Jeffrey Bender**, NIH, *Vascular Research Training*, 5 years, \$2,174,281 • **Anton Bennett**, NIH, *Regulation of Liver by Nuclear Ca2+ Signaling*, 4.7 years, \$516,440 • **Joshua Benoit**, NIH, *Lipid Metabolism During Tsetse Reproduction*, 3 years, \$152,766 • **Megan Bestwick**, NIH, *Direct Regulation of Mitochondrial Transcription by Thyroid Hormone and Receptor*, 2 years, \$98,398 • **Gordon Buchanan**, NIH, *Serotonin Neurons in Arousal, Epilepsy, and SUDER*, 5 years, \$871,290 • **Allison Campbell**, NIH, *The Role of Neutrophil Extracellular Traps and NADPH Oxidase in SLE Pathogenesis*, 2 years, \$93,600 • **Lieping Chen**, NIH, *Molecular Mechanisms of Tumor-Induced Tolerance*, 10 months, \$355,772 • **Anne Colloco**, NIH, *Elucidating the Role of an AP-2 in CTR Endocytosis and Function in the Intestine*, 3 years, \$173,410 • **Joseph Contessa**, NIH, *A Bioluminescent Screen for Inhibitors of N-Linked Glycosylation*, 2 years, \$83,761 • **Deepak D'Souza**, NIH, *Imaging Brain Cannabinoid Receptors in Cannabis Dependence, Withdrawal, and Abstinence*, 1.9 years, \$455,749 • **Nihal deLanerolle**, U.S. Army Medical Research Acquisition Activity (DoD), *Dissection of Macrophage Inhibitory Factor (MIF) in Neuronal Cell Injury after Traumatic Brain Injury (TBI)*, 1.3 years, \$127,473 • **Jonathan Demb**, NIH, *Neural Circuits and Synapses for Early Visual Processing*, 2.4 years, \$931,964 • **James Duncan**, NIH, *Extraction of Functional Subnetworks in Autism Using Multimodal MRI*, 4.8 years, \$1,890,467 • **Marie Egan**, NIH, *The Effects of CTR Dysfunction on Bone Formation*, 1.7 years, \$411,020 • **Barbara Ehrlich**, NIH, *Regulation of Liver by Nuclear Ca2+ Signaling*, 4.7 years, \$339,028 • **Jack Elias**, NIH, *YKL-40 in Idiopathic Pulmonary Fibrosis and Kidney Transplantation*, 3.9 years, \$2,658,000 • **Irina Esterlis**, NIH, *Role of Beta2-nAChR in Bipolar Disorder*, 4.8 years, \$873,523 • **David Feliciano**, NIH, *Role of Perinatal Neuronal Stem Cells in Tuber Formation*, 3 years, \$164,526 • **Erol Fikrig**, NIH, *Training in Investigative Infectious Diseases*, 5 years, \$1,334,334 • **Joanna Fiszdón**, Nat'l Inst. of Mental Health, *Social Cognitive Training for Psychosis: Phase I Treatment Development*, 2.9 years, \$520,575 • **Helen Fox**, NIH, *Chronic Alcohol, Stress Inflammatory Response and Re-lapse Risk*, 5 years, \$1,766,904 • **Liana Fraenkel**, NIH, *Improving Medical Decision Making in Patients with Rheumatic Disease*, 5 years, \$903,176 • **Lisa Fucito**, NIH, *New Approaches to Smoking Cessation in Heavy Drinkers*, 5 years, \$749,483 • **Patrick Gallagher**, NIH, *Research in Perinatal Medicine*, 5 years, \$256,896 • **Joel Gelernter**, NIH, *Center for the Translational Neuroscience of Alcoholism (CTNA)*, 4.9 years, \$90,012 • **Thomas Gill**, NIH, *T32 Training Program in Geriatric Clinical Epidemiology*, 5 years, \$1,200,938 • **Daniel Goldstein**, NIH, *Role of Innate Immunity in Transplantation Tolerance*, 1 year, \$187,000 • **Travis Gould**, NIH, *Realization of TIRF-STED Microscopy and its Application to Fast Nanoscale Imaging of Clathrin-Mediated Endocytosis*, 2 years, \$98,872 • **Elena Grigorenko**, NIH, *The Genetic Bases of Reading and Related Processes in Russian*, 1.9 years, \$432,696 • **Carlos Grilo**, NIH, *Mid-Career Investigator Award in Patient-Oriented Research in Eating and Eating Disorders*, 5 years, \$859,574 • **Nathan Hansen**, NIH, *Reducing Violence and HIV Risk among War-Exposed Liberian Youth*, 1 year, \$708,057 • **Robert Heimer**, NIH, *Training and Research in HIV Prevention in Russia*, 4.9 years, \$2,654,475 • **Erica Herzog**, NIH, *Novel Immunologic Effects of Semaphorin 7a in IPF*, 4.9 years, \$2,099,822 • **Christopher Hickey**, NIH, *Mechanisms of Protein Degradation and Transcriptional Regulation*

by Ubiquitin Modifications, 3 years, \$151,026 • **Michael Hodsdon**, NIH, *A Device for Automating Titration Experiments in High-Resolution NMR Spectroscopy*, 3 years, \$622,500 • **Ralph Hoffman**, NIH, *Pathophysiology of Auditory Hallucinations*, 1.8 years, \$1,713,285 • **Yiyun Huang**, NIH, *Novel PET Tracers for Imaging Kappa Opioid Receptor*, 1.9 years, \$576,162 • **Karl Insogna**, NIH, *Calcitonin for Treating X-Linked Hypophosphatemia*, 2.2 years, \$410,382 • **Sven-Eric Jordt**, NIH, *Targeting Injury Pathways to Counteract Pulmonary Agent and Vesicant Toxicity*, 4.8 years, \$3,369,323 • **Trace Kershaw**, NIH, *A Couple-Based Relationship-Strengthening HIV Intervention for Young Parents*, 2.9 years, \$701,834 • **Haig Keshishian**, NIH, *Interdepartmental Neuroscience Program*, 5 years, \$2,215,556 • **Kaveh Khoshnood**, NIH, *Research Ethics Training and Curriculum Development Program with China*, 5 years, \$1,211,013 • **Dawit Kidane**, NIH, *DNA Polymerase Beta and Gastric Cancer*, 4 years, \$340,223 • **Suchitra Krishnan-Sarin**, NIH, *Center for the Translational Neuroscience of Alcoholism (CTNA)*, 4.9 years, \$214,576 • **John Krystal**, NIH, *Center for the Translational Neuroscience of Alcoholism (CTNA)*, 4.9 years, \$412,107 • **Priti Kumar**, NIH, *Versatile Carriers for Cell-Specific siRNA Delivery*, 2 years, \$446,977 • **Robert LaMotte**, NIH, *Itch Neurons Studied In Vivo*, 2 years, \$456,073 • **Benjamin Land**, NIH, *Control of Cortico-Limbic Feeding Behavior Using Optogenetics*, 2 years, \$103,480 • **Una Makris**, NIH, *Understanding the Impact of Back Pain in Community-Living Older Persons*, 2 years, \$165,750 • **John May**, NIH, *Physiological Roles of Regulated Changes in Membrane Phospholipid Composition*, 2 years, \$98,872 • **Ruslan Medzhitov**, NIH, *Cell Biology of TLR Signal Transduction*, 5 years, \$2,066,182; NIH, *TLRs in Host-Commensal Interactions*, 4 years, \$1,495,149 • **Laura Ment**, NIH, *GABA-Meditated Connectivity in the Preterm Brain*, 2 years, \$474,410 • **Michael Nathanson**, NIH, *Regulation of Liver by Nuclear Ca2+ Signaling*, 4.7 years, \$652,131 • **Antonia Nemec**, NIH, *Targeting Multiple DNA Repair Pathways to Increase Drug Sensitivity*, 1 year, \$51,326 • **Kevin O'Connor**, NIH, *Discovery of Novel Autoantigens in Patients with Inclusion Body Myositis*, 3 years, \$248,917 • **Stephanie O'Malley**, NIH, *Center for the Translational Neuroscience of Alcoholism (CTNA)*, 4.9 years, \$330,642 • **Jullie Pan**, NIH, *7T MR Spectroscopic Imaging for Human Epilepsy*, 3.8 years, \$2,486,071 • **Xenophon Papanemetris**, NIH, *Integration of 3D Slicer and Bioluminescence Suite*, 2 years, \$165,500 • **Marina Picciotto**, NIH, *Antidepressant Effect on Nicotine Receptor Blockade: Neuronal and Biochemical Mechanisms*, 4.8 years, \$2,076,667 • **Katerina Politi**, NIH, *Mutant EGF Receptor-Dependent Lung Cancer in Human Cell Lines and Transgenic Mice*, 4 years, \$1,837,840 • **Godfrey Pearson**, NIH, *Center for the Translational Neuroscience of Alcoholism (CTNA)*, 4.9 years, \$200,237 • **Ismene Petrakis**, NIH, *Center for the Translational Neuroscience of Alcoholism (CTNA)*, 4.9 years, \$252,209; NIH, *Research Training Fellowship in Substance Abuse*, 5 years, \$1,500,592 • **Melinda Pettigrew**, NIH, *Microbial Diversity, Otitis Media, and the Pneumococcal Transcriptome*, 2 years, \$455,750 • **Mohini Ranganathan**, NIH, *Cannabinoid Modulation of Delta-9-THC's Psychotomimetic Effects in Healthy Humans*, 1.9 years, \$359,975 • **Anamika Reed**, NIH, *The Effects of Low pH on Intracellular and Intercellular Communication in the Pancreatic Acinar Cell*, 5 years, \$771,175 • **Scott Rivkees**, NIH, *Yale Pediatric Basic Science Training Program*, 4.9 years, \$1,662,894 • **John Rose**, NIH, *Immune Responses to vsv/HIV/siv Hybrids in Macaques*, 1 year, \$810,993 • **Carolyn Sartor**, NIH, *Genetic and Environmental Contributions to the Course of Alcohol Use in Women*, 4.2 years, \$739,380 • **Richard Schottenfeld**, NIH, *IAS and NIDA Joint Fellowship Program*, 1 year, \$75,000 • **Sheela Shenoj**, NIH, *Community-Based Intensive Case*

Finding for HIV, TB, and MDR/XDR TB in Rural South Africa, 5 years, \$132,770 • **Robert Sherwin**, NIH, *Yale Clinical and Translational Science Award Program*, 5 years, \$12,463,224; NIH, *Yale Clinical and Translational Science Award Program*, 5 years, \$3,902,930; NIH, *Yale Clinical and Translational Science Award Program*, 5 years, \$1,778,895 • **Mark Shlomchik**, NIH, *Transfusion of Donor Effector Memory T Cells for cGV and Immune Reconstitution*, 4.9 years, \$2,201,362 • **Warren Shlomchik**, NIH, *Role of Tissue Antigen Presenting Cells in GVHD*, 5 years, \$2,101,054 • **Michael Simons**, NIH, *Arteriogenesis and Arterial Branching*, 3.9 years, \$2,557,296 • **Jody Sindelar**, NIH, *Yale Training Program in Addiction, Economics, and Policy*, 1 year, \$834,205 • **Sandra Springer**, NIH, *Medication Assisted Therapy as a Conduit to Care for HIV+ cJ5 Populations Transitioning to the Community*, 5 years, \$771,175 • **Joan Steitz**, NIH, *Vertebrate Non-Coding RNAs: Integrating Function, Biogenesis, and Survival*, 3.9 years, \$1,152,954 • **Tami Sullivan**, NIH, *Racial/Ethnic Differences in Daily Dynamics of PTSD, Sexual Risk, and Substance Use*, 4.9 years, \$3,158,932 • **Hameeda Sultana**, NIH, *Human Pathogenic Bacterium Induces Actin Phosphorylation to Selectively Regulate Gene Transcription in the Arthropod Host*, 2 years, \$165,708 • **Hemant Tagare**, NIH, *Cryo-EM 3D Reconstruction of Flexible Particles*, 4 years, \$1,144,906 • **Oyebode Taiwo**, Nat'l Inst. for Occupational Safety and Health/CDC/DHHS, *Yale Occupational Safety and Health Training Grant*, 5 years, \$914,891 • **Jane Taylor**, NIH, *Center for the Translational Neuroscience of Alcoholism (CTNA)*, 4.9 years, \$199,967 • **Mary Torregrossa**, NIH, *Phosphoproteomics of Extinction and Reconsolidation of Drug Memories*, 11 months, \$778,019 • **Jon Vermeire**, NIH, *Defining Target Specificity of Oxadiazole 2-Oxides in Ancylostoma ceylanicum*, 1.9 years, \$269,973 • **Scott Weatherbee**, NIH, *Skin Development Analysis in Mutant Mouse Lines*, 4.8 years, \$1,869,376 • **Carol Weitzman**, Maternal and Child Health Bureau/HRSA/DHHS, *Maternal and Child Health Bureau Collaborative Office Rounds*, 5 years, \$75,000 • **Dianqing Wu**, NIH, *Signaling Mechanisms for Leukocyte Migration Regulation*, 3.9 years, \$2,012,927 • **Yong Xiong**, NIH, *Mechanisms of Enveloped Virus Tethering by Tetherin and Viral Countermeasures*, 5 years, \$2,000,491 • **David Zenisek**, NIH, *Investigating the Role of Ribeye in Retinal Ribbon Function*, 3 years, \$1,120,688 • **Hongyu Zhao**, Nat'l Science Foundation, *Semiparametric Conditional Graphical Model with Application to Gene Network Analysis*, 3 years, \$113,174

Non-federal

Frederick Altice, Fred Hutchinson Cancer Research Center (NIH), *HIV Testing and Treatment to Prevent Onward HIV Transmission among High-Risk MSM*, 10 months, \$62,523 • **Sanjay Aneja**, Radiological Society of North America, *The Role of County-Level Radiology and Radiation Oncology Services in the Management of Breast Cancer*, 1 year, \$6,000 • **Richard Carson**, Research Foundation for Mental Hygiene (NIH), *Characterization of a New Metabotropic Glutamate Receptor Subtype 5 PET Ligand*, 1 year, \$41,826 • **Daniel Colón-Ramos**, March of Dimes, *Molecular Mechanisms of Netrin-Mediated Presynaptic Specificity in the Developing Nervous System*, 3 years, \$375,520; Puerto Rico Science, Technology, and Research Trust, 1.5 years, \$46,000 • **Tichianaa Armah**, American Psychiatric Association, *APA Minority Fellowship Program*, 1 year, \$35,163 • **Christina Azevedo**, Nat'l Multiple Sclerosis Society, *Sylvia Lawry Physician Fellowship Award*, 2 years, \$130,000 • **Titus Boggon**, Connecticut Breast Health Initiative, Inc., *Developing Drugs to Target a Breast Cancer Invasion Control Switch*, 1 year, \$25,000 • **Samuel Buonocore**, Plastic Surgery Educational Foundation, *Altering Tendon Biomechanics after Flexor Tendon Repair*, 1 year, \$10,000 • **Jessica Cardin**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *Distinct Sources of Inhibition Regulate Cortical Function*, 2 years, \$60,000 • **Richard Carson**, Columbia University (NIH), *Novel Mechanisms Underlying Depression: PET Imaging of Kappa Opioid Receptors*, 1 year, \$91,928 • **Owen Chan**, American Diabetes Association, Inc., *CNS Mechanisms of Counter-regulatory Failure*,

3 years, \$339,250 • **Pamela Chang**, Jane Coffin Childs Memorial Fund, *Sensing Gut Microbiota through G-Protein Coupled Receptors*, 1 year, \$149,500 • **Tara Chaplin**, Alcoholic Beverage Medical Research Foundation (ABMRF), *Responses During Parent-Child Interactions and Alcohol Use Behavior in Adolescents*, 2 years, \$100,000 • **Lieping Chen**, Amplimmune, Inc., *The Development of New Immune Modulatory Targets for Therapy*, 3 years, \$500,000 • **Keith Choate**, Doris Duke Charitable Foundation, *Genetics and Pathobiology of Disorders of Keratinization*, 3 years, \$486,000 • **Jaehyuk Choi**, Dermatology Foundation, *Transposon Insertional Mutagenesis Screen for Genes that Confer Resistance to BRAF Inhibitors*, 1 year, \$55,000 • **Sean Christensen**, Dermatology Foundation, *Post-Transcriptional Regulation of Epidermal Stem Cell Homeostasis, Wound Repair, and Carcinogenesis*, 1 year, \$30,000 • **Lawrence Cohen**, Korea Advanced Inst. of Science and Technology, *Collaborative Research and Faculty Support Agreement between Yale and KIST*, 5 years, \$425,054 • **Oscar Colegio**, Dermatology Foundation, *Defining the Role of the Innate Immune System in Tumor Progression and Metastasis*, 1 year, \$55,000 • **Silvia Corbera**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *Decomposing Empathy to Understand Social Skills Deficits in Schizophrenia*, 2 years, \$56,498 • **Chris Cotsapas**, Duke University (NIH), *Mechanisms of B Cell Responses in Autoimmune Disease*, 1 year, \$52,709 • **Jonathan Demb**, Northwestern University (NIH), *CRISPR: Biophysical Properties of Parallel Neural Circuits Serving Night Vision*, 1.2 years, \$131,957 • **Sabrina Diano**, American Diabetes Association, Inc., *Role of Hypothalamic Prolyl Dipeptidase in Glucose Homeostasis*, 3 years, \$339,250 • **Michael DiGiovanna**, Connecticut Breast Health Initiative, Inc., *Combination Targeting of IGF-1 Receptor and HER2 in Breast Cancer*, 1 year, \$50,000 • **Lilangi Ediriwickrema**, Howard Hughes Medical Institute, *Reconstruction of an Outer Retina Using Cells Derived from Human Embryonic Stem Cells*, 1 year, \$39,000 • **Richard Ehrenkranz**, Research Institute at Nationwide Children's Hospital, *Establishing a Biologic Signature for Necrotizing Enterocolitis, Sepsis, and Inflammation in the Neonate*, 2 years, \$139,672 • **Edward Faustino**, Children's Hospital of Philadelphia (NIH), *Impact of Pharmacology on Duration of Ventilation in Patients with Respiratory Failure*, 1 year, \$75,000 • **Romina Fiorotto**, American Liver Foundation, *Dysregulation of TLRU-Dependent Epithelial Innate Immunity on Cystic Fibrosis Cholangiopathy*, 3 years, \$225,000 • **Richard Flavell**, American Diabetes Association, Inc., *Immunity and Diabetes*, 4 years, \$177,750 • **Robert Fulbright**, Haskins Laboratories (NIH), *Neurobiological Predictors of Spoken and Written Language Learning*, 11 months, \$63,665 • **Jeffrey Futterleib**, Howard Hughes Medical Institute, *An Innovative Extracorporeal Photochemotherapy-Derived Dendritic Cell Vaccine For Use In Advanced-Stage Melanoma*, 1 year, \$39,000 • **Aileen Garipey**, Society of Family Planning, *Probability of Pregnancy After Sterilization: A Comparison of Hysteroscopic Versus Laparoscopic Sterilization*, 1.2 years, \$10,094 • **Scott Gleim**, American Heart Association (Founders Affiliate), *Genetic Variants of the Human Thromboxane A2 Receptor*, 2 years, \$85,000 • **Gregg Gonsalves**, Open Society Institute, *The Scale-Up of AIDS Treatment as a Model for Global Health Delivery*, 1 year, \$145,757 • **Elena Grigorenko**, King Faisal University, *Assessment and Genetic and Environmental Etiology of Speech and Language Development*, 2 years, \$151,494 • **Cary Gross**, Sloan-Kettering Institute for Cancer Research, *Cardiotoxic Effects of Chemotherapy*, 1 year, \$62,154; Beckman Research Institute of the City of Hope (NIH), *Clinical and Biological Predictors of Chemotherapy Toxicity in Older Adults*, 1 year, \$21,349 • **Kevan Herold**, University of Michigan (NIH), *Michigan Institute for Clinical and Health Research (MICHR)*, 1 year, \$71,628 • **Jeannette Ickovics**, Connecticut Women's Education And Legal Fund (CDC), *Hartford Teen Pregnancy Prevention Evaluation*, 1.3 year, \$150,000 • **Douglas Guarnieri**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *Novel Genetic Approaches to Investigate the Role of MicroRNAs*

in Depression, 2 years, \$60,000 • **Clayton Halde-man**, Howard Hughes Medical Institute, *The Effect of the Ketogenic Diet on Monocarboxylate Transporter 1 Expression in the Epileptogenic Rat Hippocampus*, 1 year, \$39,000 • **Christopher Hammond**, American Academy of Child and Adolescent Psychiatry, *Stress, Risk-Taking, and Hedonically-Driven Behaviors in Adolescence*, 1.2 years, \$15,000 • **James Hansen**, Radiological Society of North America, *Targeting Cancer with a Cell-Penetrating Anti-DNA Antibody*, 1 year, \$30,000 • **Gretchen Hermes**, American Psychiatric Association, *Post-Weaning Social Isolation: Behavioral and Developmental Neuropsychopathology*, 1 year, \$45,000 • **Michael Higley**, Esther A. & Joseph Klingenstein Fund, *Synaptic Mechanisms and Regulation of Intracortical Feedback Via Long-Range Projections*, 3 years, \$150,000 • **Benjamin Himes**, Howard Hughes Medical Institute, *The Effects of Targeted siRNA Delivery on the Proliferation and Self-Renewal of Glioblastoma Cancer Stem Cells*, 11 months, \$39,000 • **Ellen Hoffman**, American Academy of Child and Adolescent Psychiatry, *A Novel Zebrafish Model for the Functional Analysis of Genes in Autism*, 2 years, \$60,000 • **Melinda Irwin**, Fred Hutchinson Cancer Research Center (NIH), *TREC Coordination Center*, 1 year, \$25,069 • **Akiko Iwasaki**, Washington University in St. Louis (NIH), *Inflammasomes as Innate Link to Antiviral Immunity*, 10 months, \$783,782 • **Ania Jastreboff**, Endocrine Fellows Foundation, *GLP-1 Analogue Effect on Neural Food Reward-Motivation Pathways*, 1 year, \$15,000 • **Jason Johannesen**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *Visual Cortical Neuroplasticity as a Developmental Biomarker in Schizophrenia*, 2 years, \$60,000 • **Shinu John**, Arthritis Foundation, *Cellular and Molecular Mechanisms by which TLR Regulates Lupus Disease*, 2 years, \$100,000 • **Roger Jou**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *The Neural Basis of Weak Central Coherence in Autism Spectrum Disorders*, 2 years, \$52,159 • **Amy Justice**, Johns Hopkins University, *North American AIDS Cohorts on Collaboration and Design (NAACCORD)*, 5 years, \$273,545; University of Pennsylvania (NIH), *Clinical Prediction of Hepatotoxicity and Comparative Hepatic Safety of Medications*, 1 year, \$70,000 • **Gerald Kayingo**, Physician Assistant Foundation, *Capacity Building for Non-Communicable Diseases in Uganda*, 1 year, \$17,200 • **Jun-Dae Kim**, American Heart Association (Founders Affiliate), *Defining the Function of Disabled Homolog 2 (Dab2) Mediating BMP Signaling-Induced Angiogenesis*, 2 years, \$80,000 • **Sang Taek Kim**, American College of Rheumatology, *Characterization of Human Follicular Helper T Cells and Their Clinical Application*, 2 years, \$125,000 • **Megan King**, Searle Scholar Program, *Mechanical Coupling of the Nucleus and Cytoplasm*, 3 years, \$300,000 • **Steven Kleinstein**, Mayo Clinic College of Medicine (NIH), *Bioinformatics Approach to Influenza A/H1N1 Vaccine Immune Profiling*, 1 year, \$28,714 • **Anthony Koleske**, Connecticut Breast Health Initiative, Inc., *Developing Drugs to Target a Breast*

Cancer Invasion Control Switch, 1 year, \$25,000 • **Pradeep Kotapurathu Kurup**, Michael J. Fox Foundation for Parkinson's Research, *Role of Striatal-Enriched Protein Tyrosine Phosphatase 61 (STEP61) in Parkinson's Disease*, 1 year, \$77,541 • **Harlan Krumholz**, Robert Wood Johnson Foundation, *The RWJF Clinical Scholars Program: 3rd Year Cohort 11*, 1 year, \$100,875; Robert Wood Johnson Foundation, *The RWJF Clinical Scholars Program*, 2 years, \$925,998 • **Ivana Kuo**, American Heart Association, *Polycystin 2 Interaction with Ins P3R3 at the Mitochondrial-Associated Membrane Contributes to Cardiovascular Pathologies*, 2 years, \$89,000 • **Gary Kupfer**, St. Baldrick's Foundation, *A Screen for Small Molecules that Activate CDK4 for Chemosensitization*, 1 year, \$100,000 • **Hochang Lee**, Mount Sinai School of Medicine (NIH), *Perioperative Cognitive Protection: Dexmedetomidine and Cognitive Reserve*, 1 year, \$12,353 • **John Leventhal**, State of CT Dept of Children and Family Services, *Child Sexual Abuse Clinic—DCF*, 3 years, \$1,359,843 • **Xiaofeng Li**, American Heart Association (Founders Affiliate), *Structural Studies on Cerebral Cavemous Malformation (CCM) Proteins*, 2 years, \$92,000 • **Janghoo Lim**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *Elucidating the Role of Nemo-Like Kinase in Brain and Psychiatric Disorders*, 2 years, \$60,000 • **Haifan Lin**, G. Harold and Leila Y. Mathers Charitable Foundation, *Toward a Central Question in Epigenetics: A Major Epigenetic Programming Mechanism Guided by piRNAs in Mammals*, 3.3 years, \$1,760,000 • **Catarina M.E. Freitas**, American Heart Association, *Microvascular Plasticity in Aging and Alzheimer's Disease*, 5 months, \$21,663 • **Xiaomei Ma**, Regents University of California, San Francisco (NIH), *Genome-Wide Association Study of Childhood Leukemia by Hispanic Status*, 10 months, \$118,796 • **Stacey MacGrath**, American Heart Association, *The Role of Arg and Nck as a Scaffold for Contract and N-was in Arp 2/3 Complex-Mediated Cell Edge Protrusion*, 2 years, \$44,000 • **Abeel Mangi**, Mount Sinai School of Medicine (NIH), *Network for Cardiothoracic Surgical Investigations in Cardiovascular Medicine*, 1.9 years, \$52,140 • **Alexander Marzuka**, Howard Hughes Medical Institute, *Evaluating the Role of Telomeres in Melanoma Formation and Progression*, 1 year, \$39,000 • **Richard Mattson**, Pfizer Inc., U.S. Pharmaceuticals Group, *Characterization of a Neural Progenitor Cell Biomarker Using Magnetic Resonance Spectroscopy*, 1 year, \$20,000 • **Linda Mayes**, Nat'l Society for the Prevention of Cruelty to Children, *Minding the Baby: NSPCC*, 1 year, \$233,657 • **Wang Min**, Oklahoma Medical Research Foundation (DoD), *Epsin, a Novel Regulator in Prostate Cancer Progression and Metastasis*, 1 year, \$17,831 • **Evan Morris**, Indiana University (NIH), *Dopamine and Unpredicted Alcohol Delivery: Effects of Alcohol Consumption*, 1 year, \$80,190 • **Mary Murphy**, Society for Academic Emergency Medicine, *Alcohol and Tobacco SBIRT for Emergency Department Patients*, 2 years, \$150,000 • **Laura Niklason**, Foundation for Anesthesia Education and Research, *FAER Medical Anesthesia Student Fel-*

lowship, 6 months, \$4,200 • **Ali Ozturk**, Congress of Neurological Surgeons, *The Genetic Basis of Intracranial Aneurysms and the Application of Whole Exome Sequencing to Mendelian Cases*, 1 year, \$12,500 • **Elijah Paintsil**, Brown University (NIH), *Africa-U.S. Higher Education Initiative to Address HIV/AIDS*, 1 year, \$25,937 • **Xenophon Papademetris**, Electrical Geodesics, Inc. (NIH), *Emergency Neurophysical Assessment Bedside Logic Engine*, 5 months, \$22,180 • **Abhijit Patel**, American Society for Therapeutic Radiology and Oncology, *Ultrasensitive Measurement of Tumor DNA in Blood as a Biomarker of Radiation Response*, 2 years, \$200,000 • **Aldo Peixoto**, Internat'l Society of Nephrology, *ISN Sister Renal Center Program*, 7 months, \$17,000 • **John Persing**, Komedypast, *Isolated Sagittal Craniosynostosis Effect on Brain Perfusion, Structure and Function*, 1 year, \$5,000 • **Kitt Petersen**, Pfizer Inc., U.S. Pharmaceuticals Group, *Development of a Novel 13C NMR Method to Assess Rates of Hepatic Mitochondrial Oxidation in Humans*, 2 years, \$990,369 • **Valentina Pirazzoli**, American-Italian Cancer Foundation, *Uncovering Mechanisms of Resistance to New Combinations of Targeted Therapies Using Mouse Models of EGFR Mutant Lung Adenocarcinoma*, 1 year, \$40,000 • **Kurt Roberts**, Foundation for Surgical Fellowships, *MIS Fellowship*, 1 year, \$61,000 • **Robert Rohrbaugh**, Gilead Foundation, *Yale Internat'l Clinical Electives*, 1 year, \$200,500 • **Carla Rothlin**, American Asthma Foundation, *The TAM Tyrosine Kinase Signaling Pathway Prevents Allergic Airway Hyper-Responsiveness*, 3 years, \$450,000 • **James Rothman**, Partner University Fund, *Deciphering Fusion in Intracellular Trafficking*, 3 years, \$390,999 • **Margretta Seashore**, Children's Research Institute (CRI), *Longitudinal Studies for Urea Cycle Disorders*, 6 months, \$23,142 • **Gerald Shadel**, Glenn Foundation for Medical Research, *Biological Mechanisms of Aging*, 2 years, \$60,000 • **Eugene Shapiro**, Children's Memorial Hospital (NIH), *Long-Term Outcome of Childhood-Onset Epilepsy*, 1 year, \$732,326 • **Ruth Sharf**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *Novel Approach to Understanding Atypical Antipsychotic Induced Weight Gain*, 2 years, \$60,000 • **Mark Shlomchik**, Roche Laboratories, Inc., *Investigation of Efficacy and Mechanism of GA101 in Lupus Mice*, 1 year, \$75,122 • **Frederick Sigworth**, Purdue University (NSF), *IDBR: High Throughput Instrumentation for Lipid Bilayers and Patch-Clamp*, 2.9 years, \$290,431 • **Michael Simons**, Fondation Leducq, *Transatlantic Network on Therapeutic Arteriogenesis and Metabolism Modulation*, 1.3 years, \$191,527 • **Brian Smith**, American Society of Hematology, *Clinical and Laboratory Hematology/Hematopathology*, 2 years, \$50,000 • **Megan Smith**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *Effects of Maternal Depression and Antidepressants on Children*, 2 years, \$59,792 • **Serena Spudich**, AIDS Clinical Trial Group, *ACTG Neurology Subcommittee*, 1 year, \$59,299; University of California, San Francisco (NIH), *Long Term CNS Consequences of Treatment*

During Acute Infection, 10 months, \$55,538 • **Bhaskar Srivastava**, Dermatology Foundation, *CD8+ T cell Differentiation to Melanoma: Generating an Effective Cytotoxic Response*, 1 year, \$30,000 • **Till Strowig**, Leukemia and Lymphoma Society, *New In Vivo Model for Multiple Myeloma by Humanization of the Bone Marrow Niche*, 3 years, \$165,000 • **Dewan Syed Fahmeed Hyder**, John B. Pierce Laboratory Inc. (NIH), *Bulbar Maps to Retronasal Smell by Optical Calcium Imaging and fMRI in Acute Rat*, 5 years, \$164,607 • **William Tamborlane**, Case Western Reserve University (NIH), *URO-EDICII: Risk and Progression of Urologic Complication in Type-1 Diabetes*, 1 year, \$1,738 • **Hugh Taylor**, John B. Pierce Laboratory Inc. (NIH), *Phytoestrogens, Insulin Resistance, and Endothelial Function*, 1.9 years, \$48,656 • **Taylor Teplitzky**, Lupus Foundation of America Connecticut Chapter, Inc., *Extrapollicular Helper T Cells in Lupus*, 3 months, \$2,000 • **Mary Tinetti**, John A. Hartford Foundation, Inc., *2012 Competitive Nat'l CoE Program Award Application*, 1 year, \$380,008 • **Kimberly Tsao**, Nat'l Science Foundation, *Dissertation Research: Evaluating Frequency-Dependent Selection on Borrelia burgdorferi*, 1 year, \$15,000 • **Narendra Wajapeyee**, Sidney Kimmel Foundation for Cancer Research, *Deciphering Oncogenic RAS-Directed Alternative Splicing for the Treatment of RAS-Mutant Human Cancers*, 2 years, \$200,000; Leukemia Research Foundation, *Characterization of New Regulators of BCR-ABL+Leukemia*, 1 year, \$115,069 • **Nadia Ward**, United Way of Coastal Fairfield County, *Yale-Bridgeport GEAR UP Partnership*, 1 year, \$70,000 • **Kyle Williams**, Massachusetts General Hospital, *Characterization of the Immune Response to IVIG Treatment in PANDAS Infections*, 1 year, \$74,548; American Academy of Child and Adolescent Psychiatry, *Novel Models of Obsessive Compulsive Disorder in Animals: Microglia and the Neurophysiology of Compulsive Behavior*, 1.2 years, \$15,000 • **Melissa Woolls**, American Heart Association (Founders Affiliate), *Decoding the Molecular and Cellular Mechanisms that Regulate Hemogenic Endothelium*, 2 years, \$44,000 • **Meiyu Xu**, Tourette Syndrome Association, Inc., *Molecular Adaptations to Cholinergic Interneuron Ablation in a Novel Mouse Model of Tourette Syndrome*, 1 year, \$40,000 • **Ke Xu**, American Psychiatric Association, *To Identify Susceptibility Genes for Schizophrenia: Whole Exome Sequencing Using Next-Generation Sequencing for Ketamine Associated Psychosis*, 1 year, \$45,000 • **Bao-Zhu Yang**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *Genetic Basis of Comorbid Depression and Cocaine Dependence*, 2 years, \$60,000 • **Zhong Yun**, American Heart Association, *Adipose Hypoxia Signaling and Cardiomyopathy*, 3 years, \$198,000 • **Hitten Zaveri**, American Epilepsy Society, *Fifth Internat'l Workshop on Seizure Prediction*, 1 year, \$20,000 • **Lingjun Zuo**, Nat'l Alliance for Research on Schizophrenia and Depression (NARSAD), *DNA Methylation of DTNBP1 and Glutamatergic Pathway Genes in Schizophrenia*, 2 years, \$60,000

// **GIM** (from page 3) since 1948. Awarded a five-year, \$5.3 million NIH grant last fall, ECHORN will examine disease burden and conduct capacity-building studies in that region in collaboration with four island universities.

Ross and Nunez-Smith share a special bond with many other GIM faculty members, including O'Connor: they are alumni of Yale's Robert Wood Johnson (RWJ) Clinical Scholars program. The School of Medicine is one of only four sites in the nation that host the program, a prestigious post-residency fellowship for physicians planning careers in policy, leadership, and/or research. In addition to regularly hosting RWJ Scholars, GIM's faculty includes alumni of the Yale program along with alumni of three

other RWJ Scholars programs.

"I think that having that incredible program here has allowed Yale to pick the best graduates each year and get them to stay," says Alpern, who says the RWJ Scholars initiative has been a crucial ingredient in GIM's research excellence. "There's absolutely been a tremendous synergy between the Clinical Scholars program and the section," agrees Associate Professor of Medicine Cary P. Gross, M.D., associate director of the Yale program and an alumnus of Johns Hopkins' RWJ program. "Because the Scholars program is at Yale, we have a home-field advantage when it comes to recruiting talented Clinical Scholars graduates to come and join us," and the example set by internist-scholars makes for a very

supportive environment for all junior faculty, he adds.

Emily Wang, M.D., M.A.S., assistant professor of medicine, cites that environment as key to her work with some of the most vulnerable patients: ex-prisoners. During her internal medicine residency at the University of California-San Francisco, she cared for diabetic patients in the emergency department who had lost access to medical care after serving their sentences.

"It seemed like a frustrating and inefficient way to care for any population," she recalls. She sought parolees' advice, then opened a clinic there in 2006, which has since served 700 patients and provided a model not only for a similar clinic in New Haven, but also for 17 other sites around the

country, including in Boston, Baltimore, and Los Angeles. Mentored by GIM senior faculty member David A. Fiellin, M.D., professor of medicine and public health, and cardiologist Harlan Krumholz, M.D., the Harold H. Hines Jr. Professor of Medicine and director of the Yale RWJ Clinical Scholars program, Wang has received a grant from the National Heart, Lung, and Blood Institute to study cardiovascular disease in the formerly incarcerated.

"What I've always found so refreshing and invigorating here is that people really want to establish new ties and share their ideas and share their resources. Faculty members here really do not want to work in silos," says Gross. "I've been here 10 years. I've never even thought of moving."

Awards & Honors

Jonathan B. Demb, PH.D., associate professor of ophthalmology and visual sciences and of cellular and molecular physiology, has received the **Cogan Award** from the Association for Research in Vision and Ophthalmology. Demb was honored for his “outstanding contributions to vision science in the retina and in the central visual pathways emphasizing three areas of visual science: quantitative psychophysics, retinal microcircuitry, and molecular synaptic mechanisms,” according to the association’s website. Demb joined the Yale faculty in 2011.



Jonathan Demb

Jack A. Elias, M.D., the Waldemar Von Zedtwitz Professor of Medicine and chair of the Department of Internal Medicine, delivered the **J. Burns Amberson Lecture** at the American Thoracic Society International Conference in May. The lecture is given by individuals who have made major lifetime contributions to pulmonary research or clinical practice. Elias studies the cellular and molecular biology of processes related to lung injury and repair. His work established current concepts of the inflammatory mechanisms of lung diseases, including asthma, chronic obstructive pulmonary disease (COPD), acute lung injury, and pulmonary fibrosis.



Jack Elias

Tamas L. Horvath, D.V.M., PH.D., Jean and David W. Wallace Professor of Biomedical Research and chair of the Section of Comparative Medicine, has been honored by the Endocrine Society with the 2012 **Ernst Oppenheimer Award**, one of the society’s Laureate Awards. Horvath, also professor of neurobiology and of obstetrics, gynecology, and reproductive sciences, is director of the Yale Program on Integrative Cell Signaling and Neurobiology of Metabolism. His work has played a key role in the development of the current model of neuroendocrine regulation of energy balance.



Tamas Horvath

Alexandra J. Lansky, M.D., associate professor of medicine and director of the Yale Cardiovascular Research Group and the Yale Valve Program, has received the **Wenger Award for Excellence in Medical Leadership**. Lansky was honored “for her longtime commitment to pursuing gender-based outcomes research and teaching interventional cardiology and prevention,” according to a press release. The Wenger Awards are given by WomenHeart: The National Coalition for Women with Heart Disease to recognize those who have set precedent in advancing women’s heart health.



Alexandra Lansky

Two Yale scientists are inducted into the American Academy of Arts and Sciences

Two Yale scientists have been elected to the American Academy of Arts and Sciences. Richard P. Lifton, M.D., PH.D., chair and Sterling Professor of Genetics and Howard Hughes Medical Institute investigator, and John R. Carlson, PH.D., the Eugene Higgins Professor of Molecular, Cellular, and Developmental Biology, were named fellows of the Academy in April, and will be formally inducted at an October ceremony in Cambridge, Mass.

The Academy was founded in 1780 during the American Revolution by John Adams and other leaders of the new nation, to “cultivate every art and science which may tend to advance the interest, honor, dignity, and happiness



John Carlson



Richard Lifton

of a free, independent, and virtuous people.” Today it is an international society whose 4,600 fellows and 600 foreign honorary members are drawn from multiple disciplines. The current membership includes more than 250 Nobel laureates and more than 260 Pulitzer Prize winners.

Medical school immunobiologist honored for contributions to understanding of antigens

The American Association of Immunologists (AAI) has awarded the 2012 AAI-Life Technologies Meritorious Career Award to Peter Cresswell, PH.D., the Eugene Higgins Professor of Immunobiology, professor of cell biology and dermatology, and Howard Hughes Medical Institute investigator.

Cresswell was honored for “his groundbreaking contributions to the field of immunology in the area of antigen processing and presentation.”

Prior to joining the Yale faculty in 1991, Cresswell was on the faculty at the Duke University Medical Center. His past honors include the 1995 Rose Payne Distinguished



Peter Cresswell

Scientist Award from the American Society for Histocompatibility and Immunogenetics, a MERIT Award from the National Institutes of Health, and the 2010

Buchanan Medal, presented by the Royal Society in the U.K. for distinguished contributions to the medical sciences, among other honors.

He is a member of the U.S. National Academy of Sciences and the American Academy of Arts and Sciences, and is a Fellow of the Royal Society.

explore milestones in our 200-year history on Facebook Timeline

facebook.com/YaleMed

The screenshot shows the Facebook page for the Yale School of Medicine. At the top, there is a banner image of the Yale University building with a flag that says 'Serve'. Below the banner is the profile picture and name 'Yale School of Medicine' with 560 likes and 41 people talking about it. The page is divided into sections: 'Education' (official page for biomedical research, medical education, and clinical care founded in 1810), 'About', 'Photos', 'Likes', and 'Events'. A 'Highlights' section is visible, showing several posts: a link to the Yale Day of Service on Saturday, May 12; a post about the Harvey Cushing/John Hay Whitney Medical Library; a post about the Yale School of Nursing in Nicaragua; a post about the Fund for Yale Cancer Center; and a post about the Yale Day of Service on Saturday, May 12, 2012.

// Gift (from page 1) projects in both laboratory and clinical settings.

“Medical school was a struggle for Stan financially,” says Stansel’s widow, Doris Stansel. “He was very dedicated to his students and would be pleased to know that we are helping to make these opportunities available to them.”

Dean Robert J. Alpern, M.D., says that the new fund provides important backing for the unique “Yale system” of medical education, which places great emphasis on original research by students.

For example, with David D. Yuh, M.D., chief of the Section of Cardiac Surgery, students are working at the frontiers of surgical research. “Advances in mechanical, computational, and biomedical engineering have led to surgical therapies until recently thought unattainable,” Yuh says. “My section is engaged in exploring minimally invasive and even nonsurgical techniques to replace or repair diseased heart valves, and a new generation of devices to replace failing hearts functionally are already in clinical trials.”

Research to advance cardiac surgery is a particularly complex undertaking, explains Yuh, because

the heart is an extremely complex machine. “We need a dynamic model to predict how a heart will behave after a surgical intervention, so we use advanced imaging techniques to build computer models of the beating heart. The many variables, including mechanical and fluid dynamics as well as human tissue properties, require an interdisciplinary research group, with students playing an important role.”

Or students may work with Pramod N. Bonde, M.D., who is developing wireless power supplies for cardiac assist devices. Some patients with failing hearts are outfitted with a mechanical pump, with a power cord routed through the abdomen. To eliminate the cord—a frequent source of infection—Bonde is testing charging technologies that transmit energy to an internal battery via electromagnetic waves.

“Yale faculty break new ground every day, and students in our program engage directly in generating this new knowledge,” Alpern says. “I am grateful that the Stansel family is supporting a program we see as a critical component in the education of tomorrow’s physician-scientists.”