Medicine@Yale

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A boost for research, and a fitting tribute to two strong women

Investing in the future of women's health research, a couple honors their mothers

Norma Weinberg Spungen and the late Joan Lebson Bildner knew each other as loving in-laws: Spungen's daughter Elisa and Bildner's son Robert, both Yale College graduates, married in 1982 and raised a family together. But the two women had more in common than family. Elisa Spungen Bildner describes both as "extremely strong leaders and matriarchs."

Now, the two women have something else in common: their children have chosen to honor them by providing a significant gift to endow a professorship at the School of Medicine in their names. The Bildners' gift, complementing funds donated by an anonymous foundation and others, establishes the Norma Weinberg Spungen and Joan Lebson Bildner Professorship. The endowed chair is intended to support a ladder faculty member whose work is devoted to advancing women's health and studying gender differences in health and disease as director of Women's Health Research at Yale (WHRY).

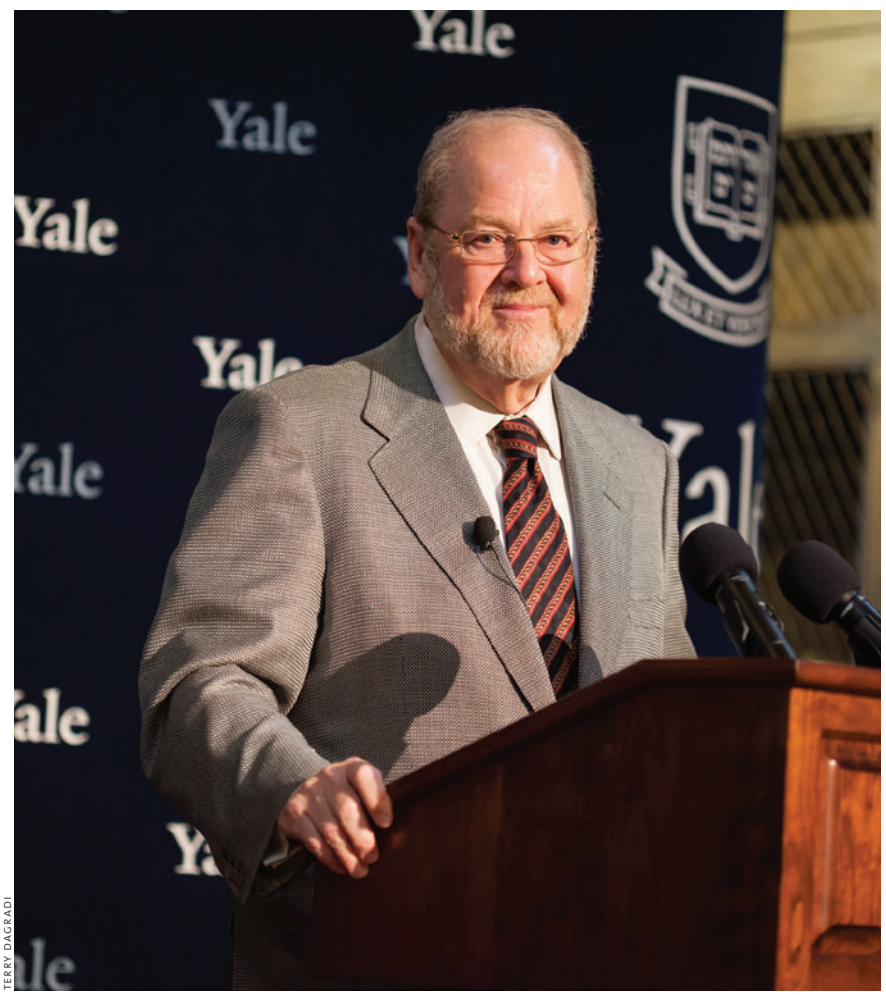
That the professorship honors two strong women is fitting: since its establishment in 1998, WHRY has worked steadfastly to remedy what its founding director, Carolyn M. Mazure, PH.D., sees as one of the largest shortcomings in medical research: "For many years, scientists in almost every area of human disease conducted their research on populations that were largely male," Mazure says. One study in the 1970s, for example, examined the role of estrogen in reducing risks for coronary heart disease: the sample included 8,431 men, but no women. Even after 1993, when the National Institutes of Health began requiring investigators to include women, researchers often have not analyzed results by gender. "The fact is that women and men have different risk factors for disease," Mazure says. "Responses to a given treatment can vary by gender, and prevention strategies often need to be gender-specific."

Joan Lebson Bildner

Norma Weinberg Spungen

The Bildners' gift affirms WHRY's 15-year campaign to change a dominant paradigm in health research. Established to investigate previously unstudied areas // Professorship *(page 7)*

Cell biology chair receives Nobel Prize



TERRY DAGRADI

Nobelist elucidated how information is conveyed in and between cells

James E. Rothman, PH.D., the Fergus F. Wallace Professor of Biomedical Sciences, chair of the Department of Cell Biology, professor of chemistry, and director of the Nanobiology Institute on Yale's West Campus, is one of three winners of the 2013 Nobel Prize in physiology or medicine.

Rothman is one of the world's foremost experts on membrane trafficking, the means by which proteins and other materials are transported within and between cells. The prize highlights his contributions to the understanding of exocytosis, a form of trafficking in which spherical sacs called vesicles fuse with cell membranes to deliver their contents outside the cell.

"This is fitting recognition of Jim Rothman's brave, // Nobel *(page 7)*

The 2013 Nobel Prize in physiology or medicine honors James Rothman's seminal contributions to the understanding of transportation systems within and between cells.

'Love and respect' for library prompt an alumnus's gift

At 85, Stanley Simbonis, M.D., a 1957 graduate of Yale School of Medicine (YSM), can recall his medical school days with enviably sharp precision. Of his experience with the "Yale System" of medical education, which prizes students' independence and their original research, he says: "At Yale, you know what you have to do. They treat you like adults."

But Simbonis fondest words are reserved for YSM's Harvey Cushing/John Hay Whitney Medical Library, an institution that has long played a large role in his life. As a medical student, Simbonis took a year off to do research, and spent a good deal of time in what was then known as the Yale Medical Library. Almost half a century later, in 2003, he became one of the library's 16 elected trustees, a position he still holds.

Now, in a gesture that reflects his debt of gratitude to Yale and his fundamental regard for the library's role in the life of YSM, Simbonis has made a gift of more than $1.1 million in annuities, whose income will be available for use after his death at the discretion of the // Library *(page 6)*

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HAROLD SHAPIRO

Richard Edelson, chair of dermatology at the medical school and director of Yale Cancer Center from 2003 to 2009, has made major strides in treating a once-deadly cancer by pioneering the use of extra-corporeal photochemotherapy. The next step, Edelson says, is to test whether other cancers can be treated similarly.

Coming full circle to beat cancer

Working to curb a fatal cancer, and building on a precursor's work

Richard L. Edelson, M.D., describes the workings of the immune system as "a huge, complex symphony." Though not a musician, Edelson, chair and the Aaron B. and Marguerite R. Lerner Professor of Dermatology, has a conductor's appreciation for the harmonious way the body mounts immune responses to cancer, and the discord that results when these attempts fail.

Edelson's efforts to translate basic research into clinical practice have not only clarified how the immune system's crucial sentinels, T cells, work, but have also helped transform cutaneous T cell lymphoma (CTCL), once a devastatingly fatal disease, into one that now rarely claims patients' lives.

The cancer, which first appears as a simple rash and then spreads from the skin to other organs, used to have a median survival of only five years. Now, due to early diagnosis and new treatments, including a technique developed by Edelson, more than 98 percent of patients survive. Coincidentally, the path to an effective treatment began at Yale School of Medicine (YSM) when the late Aaron B. Lerner, M.D., PH.D., discovered that the naturally occurring chemical 8-MOP was a potent chemotherapeutic. As a member of YSM's Class of 1970, Edelson didn't work with Lerner, but their paths are remarkably intertwined.

After an internship in internal medicine at the University of Chicago's Pritzker School of Medicine, Edelson began a fellowship at the National Institutes of Health (NIH), and was there in 1972, the year human T cells were discovered. At the NIH, Edelson found that a group of seemingly disparate diseases were actually all T cell cancers. "The entity was renamed cutaneous T cell lymphoma. That's when my career began," he says.

Before 1972, doctors encountering CTCL knew they were dealing with a white blood cell cancer, but they didn't know the cell type, or how malignant cells evolved from normal cells. Following the identification of T cells, an understanding of T cell biology and CTCL improved in parallel, and Edelson's research over the years clarified the links between CTCL and the immune system.

In 1982, as a professor of dermatology at Columbia University's College of Physicians and Surgeons, Edelson and colleagues made a new discovery. 8-MOP was known to be effective for psoriasis patients after being activated by ultraviolet (UV) light. After giving CTCL patients 8-MOP and passing their blood through a machine that zapped malignant cells with UV light, Edelson's team found that the light-exposed cells effectively became an anti-cancer vaccine. "In the first patient we treated, the disease disappeared," he says. The team later concluded that the treatment had immunized patients against the cancer.

The light treatment, called extracorporeal photochemotherapy (ECP), became the first FDA-approved cancer immunotherapy in 1988. ECP is now used around the world, not only to treat CTCL, but also in cases of organ transplant rejection and graft-versus-host disease following bone marrow transplants. The advance also introduced a new therapeutic principle: "The immune system is important in initial protection from that cancer, but by the time cancer is clinically evident, the immune system has been silenced," Edelson says.

With Edelson's return to YSM in 1986 to succeed Lerner as chair of the Department of Dermatology, the CTCL success story had come full circle. YSM remains a major center for ECP therapy, as well as research on how UV triggers the immune system. "At Yale, we train doctors to be clinicians who are dynamically involved in pushing their fields forward," Edelson says. "That's the kind of doctor I try to be."

Health literacy expert is new head of Physician Assistant Program

James A. Van Rhee, M.S., PA-C, has joined the School of Medicine as director of the Physician Associate (PA) Program. Van Rhee comes to Yale from Northwestern University Feinberg School of Medicine, where he was founding director of its Physician Assistant Program.

Van Rhee's academic career has also included leadership roles in the PA Programs at Grand Valley State University (GVSU) in Michigan, Western Michigan University, and Wake Forest University, where he was named first chair of the Department of Physician Assistant Studies in 2006.

Throughout his academic career Van Rhee has maintained an active clinical presence, working in internal medicine and oncology. For 10 years he has served as project director for the Physician Assistant Clinical Knowledge and Rating Assessment Tool (PACKRAT) exam, and has been a site visitor for the Accreditation Review Commission on Physician Assistant Education for more than 10 years, and is currently chair of the commission. Among other grants, in 2007 Van Rhee served as co-principal investigator on a three-year Health Resources and Services Administration training grant to develop a health literacy curriculum for PA students.

James Van Rhee

Van Rhee received his B.S. in medical technology from GVSU and his PA-C degree from the University of Iowa's Carver College of Medicine. He holds an M.S. in PA practice from Rosalind Franklin University of Medicine and Science in North Chicago, Ill. He succeeds Interim Director David Brissette, M.S., PA-C, assistant professor in the PA Program.

New transplant chief is champion for organ donation

David Mulligan

David C. Mulligan, M.D., an acclaimed abdominal organ transplant surgeon, has been appointed chief of the Section of Transplantation and Immunology and professor of surgery at the School of Medicine, and director of the Yale-New Haven Transplantation Center (YNHTC) at Yale-New Haven Hospital.

Mulligan comes to Yale from Mayo Clinic in Arizona, where he helped establish the clinic's solid organ transplant program. A champion for organ donations on a national scale, Mulligan is also a liver, kidney, and pancreas transplant specialist with international acclaim for his work in living donor liver transplantation.

Mulligan earned his M.D. at the University of Louisville School of Medicine (ULSM) and completed surgical residencies at ULSM and Case Western Reserve University (CWRU). After a fellowship in multi-organ transplantation at Baylor University Medical Center, he served on the faculty at CWRU, and was director of liver transplantation at University Hospitals of Cleveland before joining Mayo Clinic in Arizona.

Mulligan succeeds Sukru H. Emre, M.D., professor of surgery and pediatrics, a renowned adult and pediatric abdominal organ transplant surgeon credited with transforming Yale's transplant program into a regional leader in the evaluation and treatment of liver disease.

CORRECTION

Our most recent *Grants and contracts* listing should have included Martin Kluger as a co-principal investigator on a four-year NIH grant of $1,369,604 to Jordan Pober entitled *Proteins of the Endothelial Cell Surface*.

Medicine@Yale

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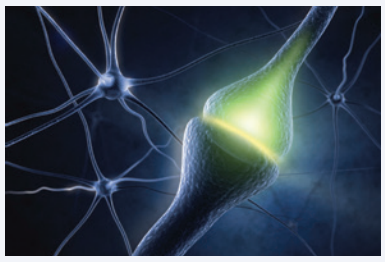
How neurons stay in place during growth



ISTOCKPHOTO

As the *C. elegans* worm grows during its adult life, increasing almost a hundred times in size, the neurons that stretch the length of its body grow, too. Until recently, scientists haven't known what keeps synapses—the junctions between neurons—in their correct positions during this process.

Now, research by Yale scientists offers clues. By screening genetically mutated worms to find animals that maintain synaptic positions incorrectly, a team led by Associate Professor of Cell Biology Daniel A. Colón-Ramos, PH.D., found that the gene *cima-1* is vital for proper synaptic maintenance.

Further experiments revealed that *cima-1* encodes a protein found not in neurons themselves, but in epidermal cells. The protein, the team reported in the July 18 issue of *Cell*, mediates the interactions between epidermal cells and the glial cells that contact neurons at synapses. The finding suggests that glial cell position is vital for maintaining synaptic positions during growth, and could provide clues to how synaptic positions are maintained during growth in humans.

Piecing together the Alzheimer's puzzle

In recent years, scientists in the lab of Stephen M. Strittmatter, M.D., PH.D., Vincent Coates Professor of Neurology, have identified critical steps in the "cascade" of events in which Alzheimer's disease (AD) destroys brain cells. In 2009 they found that amyloid-beta (A-ß) peptides, a hallmark of AD, bind with prion proteins on the surface of neurons in AD.

By an unknown process, the scientists knew, this coupling activates a molecular messenger within the cell called Fyn. To better understand the process, they screened 81 membrane proteins for their ability to stimulate Fyn in the presence of the A-ß-prion complex. In the Sept. 4 issue of *Neuron*, they reported that one protein, metabotropic glutamate receptor 5 (mGluR5), bound to both players simultaneously. They also found that mGluR5 is required for the A-ß-prion complex to signal through Fyn. When they blocked mGluR5 in mice with AD, cutting the connection between the A-ß-prion complex and Fyn, deficits in memory, learning, and synapse density associated with AD were restored.

"Of all the links in this molecular chain, this is the protein that may be most easily targeted by drugs," says Strittmatter, senior author of the study. "This gives us stronger hope that we can find a drug that will work to lessen the burden of Alzheimer's."

Fighting brain cancer with nanomedicine

Scientists with diverse skills joined forces on a cross-campus collaboration that may change the way brain cancer is treated

Brain cancer—a devastating diagnosis in itself—can also be grimly swift in its prognosis. Even with surgery and chemo- and radiotherapy, patients with glioblastoma multiforme (GBM), the primary type of malignant brain tumor that affects 15,000 people in the United States annually, may survive only little over a year, and can suffer tumor recurrence in virtually the same brain region. Now, work combining the unique complementary skills of a neurosurgeon, a bioengineer, and a nanomedicine and stem cell expert has led to a new treatment for GBM that has shown great promise in animal studies. The Yale team reported on their breakthrough online on July 1 in the *Proceedings of the National Academy of Sciences*.

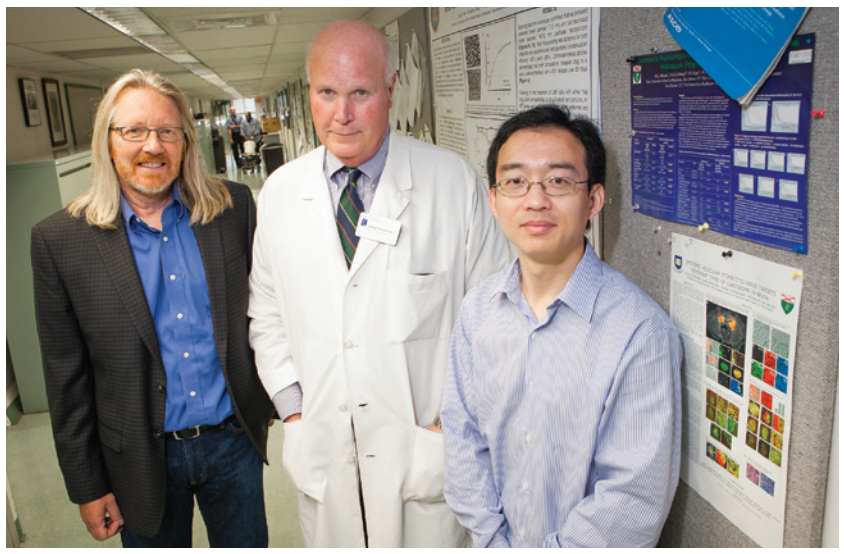
As leader of Yale Cancer Center (YCC)'s Brain Tumor Program, Joseph M. Piepmeier, M.D., Nixdorff-German Professor of Neurosurgery, has devoted years to patient care and research to combat GBM. Recently, he was involved in a clinical trial in which drugs were delivered in solution to tumors by pumping through catheters. "It was a wonderful idea, but it didn't work," Piepmeier says. "The liquid flowed away, into the spinal fluid or blood, and dissipated once we stopped infusion." The delivery problem is central to treating any disease of the organ that is beyond the blood-brain barrier, which protects the sensitive brain tissue from circulating blood. It keeps out bacteria, but also prevents orally or intravenously delivered drugs from getting to where they are needed most, in the case of GBM.

Across campus, W. Mark Saltzman, PH.D., chair and Goizueta Foundation Professor of Biomedical Engineering, had been developing biodegradable materials that could be loaded with chemotherapeutic drugs and placed in the brain after tumor surgery. Saltzman, also professor of cellular and molecular physiology and of chemical engineering, was one of the developers of the Gliadel wafer, a standard-of-care drug delivery system that can extend survival by some months in GBM. The presence of a structure or casing, like the wafer's, is critical because it prevents drugs from dissipating into circulation or being metabolized too quickly. The device's effects, however, are only modest, since drugs fail to diffuse from the wafer into the dense brain tissue. The solution, explains Saltzman, is an engineered nanoparticle about the size of a virus that encapsulates the drug and prevents it from being degraded.

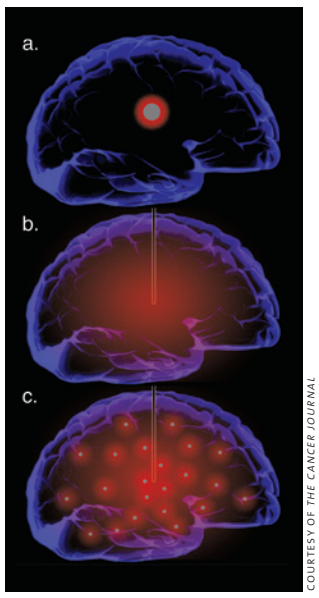
With a well-designed vehicle, the highway into the brain was obvious: Piepmeier's pump infusion system, known as convection-enhanced delivery, or CED. "Our innovation was to combine the two technologies," says Saltzman. "CED can penetrate through tissue, and the nanoparticles control where the drug ends up and ensure its slow release." The particles are small enough to reach interstitial spaces in the brain. Made of the same material as dissolving sutures, they do not aggregate, and eventually degrade.

A novel drug delivery system isn't sufficient by itself in the case of GBM, however. The tumors tend to be infiltrative and particularly resistant to radiotherapy and drugs, in part because of something that wasn't recognized until 2003: even solid tumors have what are called cancer stem cells. "These are the root of tumor development, and the reason we decided to do drug screening in this study," says Jiangbing Zhou PH.D., assistant professor of neurosurgery and biomedical engineering, who studied stem cells and drug screening at the Johns Hopkins University before joining the Yale faculty in 2011. To find the perfect passenger for the nanoparticle vehicle, Zhou screened nearly 2,000 compounds used in various products previously approved by the U.S. Food and Drug Administration. He was looking for anything that would kill or inhibit the self-renewal of brain cancer stem cells, the small fraction of GBM cells that are resistant, and can migrate to cause tumor recurrence. Zhou hit upon dithiazanine iodide (DI), a fungicide that was particularly lethal to brain cancer stem cells in culture.

Step by step, the researchers evaluated the penetration of nanoparticles in both healthy rats and rats grafted with a common tumor cell line. They also investigated how well the nanoparticle system diffused in the brain of a larger animal, a pig. The real test, however, was delivering nanoparticles loaded with DI to rats that had infiltrative tumors very similar to human GBM. Eight of 12 rats were cured. "Normally we don't cure anybody, so this result is pretty great," Piepmeier says.



TERRY DAGRADI



COURTESY OF THE CANCER JOURNAL

(Above, from left) Mark Saltzman, Joseph Piepmeier, and Jiangbing Zhou are pioneering the use of nanoparticles to deliver drugs to treat brain cancer. (At left) representative drug distributions for (a) conventional diffusion-based implant systems, such as the Gliadel wafer; (b) convection-enhanced delivery (CED) of drug solutions; and (c) the Yale team's technique, which involves CED of drug-loaded nanomaterials.

Saltzman, Piepmeier, and colleagues are now preparing for a small human clinical trial, to take place at YCC next year. By monitoring patients with magnetic resonance imaging (MRI), they will be able to observe drug distribution and longevity after delivery. Evaluating the safety and efficacy of the nanoparticle delivery mechanism is critical, they say as is the selection of an optimal drug.

Saltzman commends Yale's "remarkable environment" for enabling the kind of collaborative translational research that led to this new GBM treatment: "In most places, it is not easy for biomedical engineers to work this closely with clinical scientists. What we've done can only happen at a few special places, like Yale," he says.

Creating tomorrow's cures

At the center of Yale School of Medicine (YSM)'s work is the research pursued by faculty and students, including the innovative research in brain cancer described here. YSM faculty members are renowned for their creative approaches to the most vexing biomedical questions, and for their pursuit of answers that will shed light on novel therapies and improve human health.

Funds directed to support research are especially vital to the fulfillment of YSM's mission to expand knowledge in the basic and clinical sciences. These funds stimulate the education of tomorrow's scientific leaders and pave the way for outstanding care and cutting-edge therapies. Endowed gifts are central to YSM's ability to maintain its tradition of academic excellence, its strong programs, and the intellectual diversity of its faculty and students.

Through Professorships, Teaching Funds, Scholarships, and Fellowships, the men and women at YSM sustain the School's vitality, keeping it at the forefront of education, research, and patient care. For more information on creating an endowed fund, contact Zsuzsanna Somogyi, interim director for medical development, at 203-436-8559 or at zsuzsanna.somogyi@yale.edu.

OUT & ABOUT

May 29 Connecticut Mental Health Center (CMHC) faculty and trainees toured the **Connecticut Valley Hospital (CVH)** in Middletown, Conn. (Front) **Frank S.K. Appah Jr.**, M.D., PH.D., public psychiatry fellow. (Center row, from left) **Paul Park**, PSY.D., psychologist at Rutgers Biomedical and Health Sciences; **Brandeis Green**, PH.D., psychologist at the Atlanta VA Medical Center; **Jeanne L. Steiner**, D.O., associate professor of psychiatry and medical director of the CMHC; **Andres B. Barkil-Oteo**, M.D., M.SC., assistant professor of psychiatry; **Jai Shah**, M.D., research fellow in psychiatry at McGill University's Faculty of Medicine. (Rear, from left) **Joseph A. Cherepon**, PH.D., psychologist at CVH; **David Howe**, LCSW, director of recovery and consumer affairs at CVH; **Thomas S. Pisano**, M.D., chief of professional services at CVH; **Ranjit Bhagwat**, PH.D., postdoctoral resident at the Stratton VA Medical Center in Albany, N.Y.; and **Thomas Styron**, PH.D., associate professor of psychiatry.

SHANE SEGER

June 4 As part of a six-week **elective abroad in Chiapas, Mexico**, third-year psychiatry resident **Guillermo Valdés**, M.D., MBA, developed a non-pharmacologic intervention for the treatment of major depressive disorder, lectured to local general practitioners about basic concepts in psychiatric care, and saw patients.

EVA QUESADA

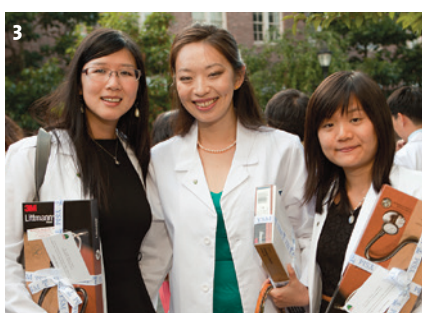
August 6 The Yale-UCL (University College London) Collaborative held its third annual **Yale-UCL Poetry Contest**, open to medical and engineering students at both universities. **Lorenzo Sewanan** '20 (left), a student in the M.D./PH.D. Program who placed first in this year's contest, with Dean and Ensign Professor of Medicine **Robert J. Alpern**, M.D.

JOHN CURTIS

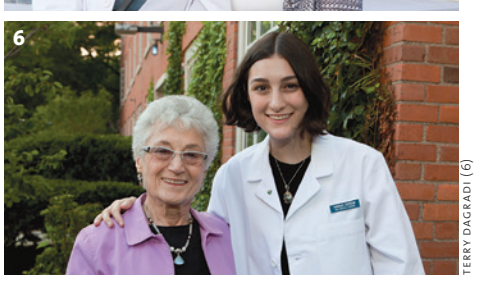
MICHAEL FITZSOUSA

August 12 Friends and colleagues gathered for a **Send-Off Party** to bid fond farewells to **Pete Farley**, the editor of *Medicine@Yale* since its creation in 2005. Pictured with Farley are **Terry Dagradi** (left), photographer with Yale Photo+Design; and Farley's wife, **Kerry L. Falvey**, chief of staff in the School of Medicine Dean's Office and author of *Medicine at Yale: The First 200 Years*, published in 2010 to mark the medical school's Bicentennial.

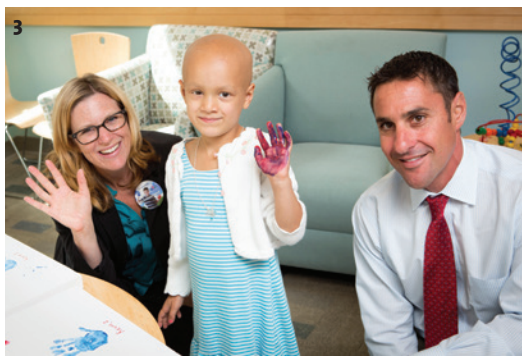
August 15 At the **White Coat Ceremony**, an annual event at which incoming medical students receive physicians' jackets, the School of Medicine formally welcomed the 100 members of the Class of 2017. **1. George Lister**, M.D. '73, chair and Jean McLean Wallace Professor of Pediatrics and physician-in-chief at Yale-New Haven Children's Hospital, delivered this year's keynote speech. **2.** (From left) **Anand Gopal**, Lister, and **Laura R. Ment**, M.D., professor of pediatrics and neurology and associate dean for admissions and financial aid. **3.** (From left) **Heide Kuang**, **Zhenzhen (Jane) Xu**, and **Ava Yap**. **4. Zainab Jaji** (left) and **Nneka Nwachukwu**. **5. Juliana Berk-Krauss** and her mother, **Marlene Krauss**. **6. Jocelyn Malkin**, M.D. '52 (left), and her granddaughter **Hannah Zornow**.



Video "Starting a life in medicine: Yale's 2013 White Coat Ceremony"
Available at youtube.com/yalemedicine



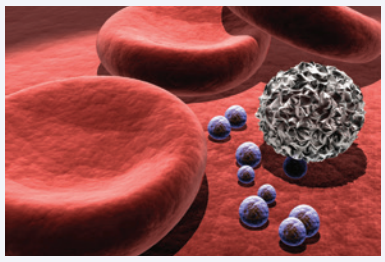
TERRY DAGRADI (6)



HAROLD SHAPIRO (4)

September 9 As part of its **Hope on Wheels** program, which supports pediatric cancer research and treatment programs around the U.S., representatives of Hyundai Car Sales donated $250,000 to the School of Medicine. **1.** (From left) **Kavita Dhodapkar**, MBBS, associate professor of pediatrics; **Gary Kupfer**, M.D., professor of pediatrics and pathology, chief of the Section of Pediatric Hematology and Oncology, and director of the Pediatric Oncology Program at Smilow Cancer Hospital at Yale-New Haven (SCHYNH); and **Thomas J. Lynch**, M.D., Richard Sackler and Jonathan Sackler Professor of Medicine, director of Yale Cancer Center, and physician-in-chief at SCHYNH. **2. Karl Soderlund** (left) and **Jacqueline Soderlund**. **3.** Hyundai representatives **Jill Merriam** and **Jeffrey Merriam** with patient **Annaliese Renker** (center). **4.** (Front, from left) Jeffrey Meriam; Jill Merriam; Kupfer; Lynch; Dhodapkar; Hyundai representatives **Ken Bloech**, **Woody Woodward**, and **Joe Blichfeldt**; and **George Lister**, M.D., chair and Jean McLean Wallace Professor of Pediatrics and physician-in-chief at Yale-New Haven Children's Hospital. (Back, from left) Hyundai representatives **Craig Salera**, **Scott Petty**, **Kim Bucci**, and **Mark Marenzana**.

Discovering immune system's "switch"



ISTOCKPHOTO

When the immune system kicks into action, more immune cells usually mean a faster elimination of the invading bacteria or virus. But when the reaction continues for too long or becomes overblown, excessive inflammation or even autoimmune disease can occur. And scientists may now have a better idea why.

In the July 25 issue of *Immunity*, Carla V. Rothlin, PH.D., assistant professor of immunobiology, and colleagues describe a negative feedback cycle between dendritic cells—early responders to pathogens—and the T cells they activate. Activated T cells, the team showed, produce a molecule called Protein S that then turns down the activity of dendritic cells.

This cycle explains how the immune system is regulated in healthy individuals, and also offers new clues about autoimmune diseases like inflammatory bowel disease (IBD), where activation is more constant. When the team tested patients with IBD, they found less Protein S than in healthy controls, suggesting the cycle may be disrupted in cases of disease.

New metric shows diabetes drug works

In type 1 diabetes (T1D), immune cells gradually attack and kill off the pancreas's insulin-producing ß-cells. Therapies to moderate this autoimmune destruction in recent-onset T1D have shown success, but scientists haven't known whether these therapies were preventing ß-cell killing, or merely restoring some ß-cell function.

When ß-cells die, they release modified versions of the insulin DNA (*INS* DNA) into the blood. Knowing this, Yale researchers recently devised a new method for measuring ß-cell death *in vivo*: directly measuring the modified *INS* DNA in the blood serum. The researchers successfully used this method to study diabetic mice, and more recently measured *INS* DNA in human patients with T1D in a phase 2 clinical trial of the monoclonal antibody drug teplizumab.

Teplizumab, when given in two courses one year apart, significantly reduced ß-cell loss in patients with early-onset T1D, the team reported in the May issue of *Diabetes*. The level of ß-cells at year two was, on average, 75 percent higher in the teplizumab arm of the trial than in the control group.

If approved by the FDA, teplizumab would be "the first drug to change the natural course of T1D since insulin," says Kevan Herold, M.D., professor of immunobiology and medicine and lead author of the study.

For nursing school, westward expansion

Yale's West Campus offers state-of-the-art technology, collaboration-friendly design, and space customized for clinical instruction

Since its acquisition from Bayer Pharmaceuticals in 2007, Yale's West Campus, as the 136-acre facility on the Orange-West Haven border is now known, has buzzed quietly with activity. Gradually, programs have moved there, taking advantage of an abundance of highly configurable space: the West Campus houses several flourishing research centers, core facilities, and art conservation programs. That buzz is now growing louder: over the summer, the Yale School of Nursing (YSN) relocated to the West Campus from 100 Church Street South, on the outskirts of Yale's medical campus.

"The facility at 100 Church Street [South] met our needs for almost 20 years, but would have been difficult to reconfigure to meet our current and future needs," says YSN Dean Margaret Grey, DR.PH., R.N., the Annie Goodrich Professor of Nursing. "Our new building is well equipped for faculty, students, and staff to teach and learn, conduct research, and collaborate with many colleagues here on the West Campus as well as across the University."

YSN's new premises are almost 50 percent bigger than its former headquarters. The new facility, which is airy and filled with natural light, has undergone extensive renovations and has been designed to foster a spirit of collaboration. It contains numerous spaces designed for student-student or student-faculty interaction, including a lounge-like space on the first floor, surrounded by smaller rooms designed for group study. Cushioned benches and whiteboards line the hallways to encourage discussion. State-of-the-art classrooms feature touch-screen controls, multiple monitors, and video conferencing capabilities and outlets for every student.

YSN was founded in 1923 with an initial grant of $150,000 from the Rockefeller Foundation. It was the first independent university-based school for the education of nurses in the U.S., and the first nursing school not subordinate to an existing university department. The school, one of Yale's 10 professional schools, is ranked highly among nursing schools receiving funding from the National Institutes of Health.

As YSN grew, limited room at 100 Church Street South meant that space for clinical instruction activities was often multipurpose and shared. The new facility, in contrast, offers separate rooms designed specifically for assessment labs, task training, exams, and simulation. There is also a section, with its own entrance for patients, devoted to clinical research studies in cardiology and sleep disorders, and to Yale's renowned Minding the Baby program, a community-based intervention that affords underprivileged mothers nursing and mental health services during pregnancy and after childbirth.

MICHAEL MARSLAND

Celebrating the opening of the School of Nursing's new facility on October 4 were (from left) University Chaplain Sharon Kugler; Provost Ben Polak; Stephanie Spangler, deputy provost for health affairs and academic integrity; President Peter Salovey; James Zeoli, first selectman of Orange, Conn.; Margaret Grey, dean of the School of Nursing; West Haven Mayor John Picard; and Scott Strobel, vice president of West Campus planning and program development.

The influx of 450 students, faculty and staff has nearly doubled the population of the West Campus. YSN is the first major educational program to be located there. Says Scott A. Strobel, PH.D., Henry Ford II Professor of Molecular Biophysics and Biochemistry and vice president of West Campus planning and program development: "The addition of YSN to this already thriving community aligns with the vision of Yale's West Campus to strengthen science, medicine, and engineering at Yale. It also means that the School of Nursing will finally have a facility that matches the excellence of its program."

Although students, faculty, and staff began using the new facility in August, the building was formally dedicated on October 4, on the occasion of YSN's 90th anniversary celebration.

Yale physicians lead the way in making CT scans safer for children

Computerized tomography (CT) scanning involves taking X-rays from a rotating camera and feeding the results to a powerful computer to create cross-sectional views of organs in the body. The procedure—simple and painless, taking less than 10 minutes—allows doctors to detect injuries and diseases that don't show up on standard X-rays. CT scans save countless lives and prevent many misdiagnoses and unnecessary surgeries. Given CT's advantages, it's no surprise that its use has surged in the last two decades.

But the technology's diagnostic power carries a cost: a CT scan can expose a patient to 100 to 500 times the amount of radiation she would get in an X-ray, increasing her risk for cancer. Fortunately, that picture may be changing, especially for children, whose smaller, rapidly growing bodies make them even more susceptible than adults to radiation-induced cancer. In data compiled by the American College of Radiology's Dose Index Registry, which tracks and categorizes the radiation given by CT scanners in U.S. hospitals, Yale-New Haven Children's Hospital (YNHCH) recorded the lowest doses of any academic hospital in the country in many age groups and types of pediatric radiation.

ROBERT LISAK

Since his arrival at Yale from Oxford in 2003, T. Rob Goodman has led a successful campaign to reduce patients' exposure to radiation from computerized tomography scans.

"The numbers are very impressive," says T. Rob Goodman, M.B., B.CHIR., interim chair and professor of diagnostic radiology and chief of pediatric diagnostic imaging at YNHCH. "We've more than halved the number of CT scans done on children despite more than doubling the number of scanners in the hospital." In 2003 Yale-New Haven Hospital had three CT scanners and performed 4,844 CT scans on // CT Scans *(page 6)*

Grants and contracts awarded to Yale School of Medicine

July–August 2012

Federal

Clara Abraham, NIH, *IL-23/TH17 Pathways and Inflammatory Bowel Disease*, 1 year, $415,208 **Alan Anticevic**, NIH, *Characterizing Cognitive Impairment in Schizophrenia via Computational Modeling and Pharmacological Neuroimaging*, 4.9 years, $1,773,750 • **Lloyd Cantley**, NIH, *Macrophage Function in Kidney Repair*, 1 year, $200,000 **Michael Cappello**, NIH, *Research Training in Pediatric Infectious Diseases*, 5 years, $623,180 **Tara Chaplin**, NIH, *Parent-Adolescent Interactions and Substance Abuse Risk: Gender Differences*, 4.9 years, $1,872,094 • **Judy Cho**, NIH, *Defining Common and Rare Genetic Associations in Ashkenazi Jewish IBD*, 4.8 years, $2,432,189; NIH, *Yale University Inflammatory Bowel Disease Genetics Research Center*, 4.9 years, $2,050,914; NIH, *Inflammatory Bowel Diseases Genetics Consortium Data Coordinating Center*, 4.9 years, $6,805,195 **Hyung Chun**, NIH, *Role of MicroRNA 424/503 in Pulmonary Arterial Hypertension*, 4.8 years, $2,060,020 • **Steven Coca**, NIH, *Novel Serum and Urinary Biomarkers of Diabetic Kidney Disease*, 4.8 years, $2,946,473 • **Oscar Colegio**, NIH, *Defining the Role of Macrophages in the Progression of Human Cutaneous Squamous Cell Carcinomas*, 4 years, $593,968 • **Joan Cook**, NIH, *Sustained Use of Evidence-Based PTSD Treatment in VA Residential Settings*, 3.8 years, $1,554,618 • **Lynn Cooley**, NIH, *Oocyte Development in* Drosophila, 3.7 years, $2,441,122 • **Joseph Craft**, NIH, *Manipulation of Follicular Helper T Cells in Immunity and Autoimmunity*, 2 years, $411,526; NIH, *Yale Rheumatic Diseases Research Core Center*, 5 years, $2,855,010 • **Thomas Fernandez**, NIH, *Genomic Investigations of Tourette's Disorder*, 4 years, $718,368 • **Gigi Galiana**, NIH, *Narrow Linewidth MRS to Detect Breast Cancer*, 4 years, $658,896 **Alison Galvani**, NSF, *Collaborative Research: Cross-National Differences in Vaccination as Unselfish Behavior*, 3 years, $371,230 • **Antonio Giraldez**, NIH, *Analysis of the Gene Networks Regulating the Maternal to Zygotic Transition*, 4 years, $2,290,078 **Daniel Goldstein**, NIH, *Mechanisms of Dysregulated Immunity with Aging*, 4.9 years, $1,655,771 **Andrew Goodman**, NIH, *Defining the Contribution of Interpersonal Microbial Variation to Drug Metabolism*, 4.8 years, $2,496,000 **Valentina Greco**, NIH, *Live Imaging of Skin Regeneration*, 5 years, $1,853,457 • **Charles Greer**, NIH, *The Olfactory Nerve*, 5 years, $1,829,151 • **Ann Haberman**, NIH, *Yale Rheumatic Diseases Research Core Center*, 5 years, $118,270 • **Ruth Halaban**, NIH, *Yale SPORE in Skin Cancer*, 5 years, $11,217,800 **Michael Henderson**, NIH, *CSP Alpha Regulation of Exo-Endocytic Cycle Enhances Synaptic Stability*, 2 years, $54,488 • **Michael Higley**, NIH, *Cellular Mechanisms of GABAergic Inhibition in Neocortical Dendrites*, 4.9 years, $2,080,208 • **Amber Hromi-Fiedler**, NIH, *Promoting Fruits and Veggies among Pregnant Latinas: Intervention Development*, 1.8 years, $444,655 • **Shuta Ishibe**, NIH, *The Role of Endocytosis and Actin Regulation in Podocytes*, 3.9 years, $1,277,481 • **Sven-Eric Jordt**, NIH, *Accelerating Inflammation Resolution to Counteract Chemical Injury*, 1.9 years, $800,216 **Amy Justice**, NIH, *Translational Research on Alcohol, Immunodeficiency and Aging in COMPAAAS*, 4 years, $2,202,466 • **Arie Kaffman**, NIH, *Defining a Sensitive Period for Socialization in Rodents*, 2 years, $457,250 • **Joan Kaufman**, NIH, *Risk and Resilience in Maltreated Children*, 4 years, $3,034,093 • **Barbara Kazmierczak**, NIH, *Microbiome Acquisition and the Progression of Inflammation and Airway Disease in Infants with Cystic Fibrosis*, 3.8 years, $2,527,626 • **Albert Ko**, NIH, *Ecoepidemiology of Leptospirosis in the Urban Slums of Brazil*, 4.9 years, $2,324,644 • **Diane Krause**, NIH, *Mechanisms of Megakaryocyte Maturation*, 4.9 years, $1,809,783 • **Harlan Krumholz**, DHHS, *Optimizing Medical Device Post-Market Surveillance for Public Value*, 5 years, $749,858 **Kenneth Kwan**, NIH, *Novel Candidate Mechanisms of Fragile X Syndrome*, 2 years, $184,896 **Robert LaMotte**, NIH, *Peripheral Neural Mechanisms of Inflammatory Itch and Pain*, 3.8 years, $1,697,646 • **Robert Malison**, NIH, *Integrated Mentored Patient-Oriented Research Training (IMPORT) in Psychiatry*, 4.7 years, $1,202,202 **Steven Marans**, SAMHSA, *Childhood Violent Trauma Center*, 4 years, $2,319,336 • **Andres Martin**, NIH, *Research Training for Medical Students & Physician-Scientists in Child Psychiatry*, 5 years, $841,889 • **Sherry McKee**, NIH, *Does Doxazosin Attenuate Stress-Induced Smoking and Improve Clinical Outcomes?*, 2 years, $457,250 **Evan Morris**, NIH, *Dynamic Dopamine Images: A New View of Neurochemistry of Smoking*, 1.7 years, $437,323 • **Don Nguyen**, NIH, *A Novel Lineage Specific Metastasis Suppressor Pathway in Lung Cancer*, 4.8 years, $1,855,775 • **Elijah Paintsil**, NIH, *A Bioecological Pediatric HIV Disclosure Intervention in Ghana – "SANKOFA"*, 5 years, $1,848,090 • **Kevin Pelphrey**, NIH, *Multimodal Developmental Neurogenetics of Females with ASD*, 4.8 years, $13,952,100 • **Joao Pereira**, NIH, *Control of B-Lineage Cell Migration During Differentiation in Bone Marrow*, 1 year, $415,209 **David Schatz**, NIH, *Interdisciplinary Immunology Training Program*, 5 years, $2,389,365 • **Mark Schlesinger**, DHHS, *Eliciting Patient Experiences to Augment Public Reports on Health Care Quality*, 2.9 years, $929,434 • **Mark Shlomchik**, NIH, *Yale Rheumatic Diseases Research Core Center*, 5 years, $166,131 • **Warren Shlomchik**, NIH, *Yale Rheumatic Diseases Research Core Center*, 5 years, $99,678 **Rajita Sinha**, NIH, *Prazosin to Decrease Alcohol Craving, Anxiety, Stress Dysregulation and Alcohol Relapse*, 5 years, $2,602,106 • **Robert Tigelaar**, NIH, *Yale SPORE in Skin Cancer*, 5 years, $282,200 **Christian Tschudi**, NIH, *Training in Parasitology and Vector Biology*, 5 years, $1,223,093 • **David Zenisek**, NIH, *Retinal Synaptic Transmission*, 4 years, $1,664,062

Non-federal

Jessica Cardin, Alfred P. Sloan Foundation, *Sloan Research Fellowship Cardin Lab*, 2 years, $50,000 **Paul Cleary**, RAND, *Hospice Experience of Care Survey*, 2 years, $17,124 • **Gary Cline**, Georgia Health Sciences University (NIH), *MMPC Metabolic Imaging Symposium*, 1 year, $28,567 • **Daniel Colon-Ramos**, Sloan-Kettering Institute for Cancer Research (NIH), *An Integrated System to Monitor Complex Tissues at Single-Cell Resolution*, 1.4 years, $157,740 • **Eve Colson**, Boston University (NIH), *Social Media and Risk-Reduction Training for Infant Care Practices (SMART)*, 1.7 years, $71,275 **Joseph Craft**, L2 Diagnostics (NIH), *Therapeutic Inhibition of MIF in Rheumatoid Arthritis*, 1 year, $53,494 • **Robert Dubrow**, Kaiser Permanente

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// CT Scans *(from page 5)* children. In 2012, with seven scanners, the hospital performed 2,344.

The lower numbers are partly due to a greater awareness among physicians of CT's risks. Says Lei Chen, M.D., associate professor of pediatrics, "We have really started thinking critically about the risks and benefits of CT scans. We often elect alternative strategies, either watchful waiting—in cases of suspected head trauma—or ultrasound and MRI [magnetic resonance imaging]."

In January 2008, the Alliance for Radiation Safety in Pediatric Imaging launched a campaign to educate doctors and the public about cumulative radiation exposure. Manufacturers began building scanners that automatically adjusted doses based on a patient's age and weight and the sensitivity of the area to be scanned.

Goodman became concerned about CT scan radiation even earlier, in 2003, when he left Oxford University to join the School of Medicine's faculty and realized that Americans were receiving three times more medical radiation than Europeans. He began conducting grand rounds for pediatricians on reducing radiation doses, and urged them to consider alternatives to CT scans such as ultrasound. He worked with YNHCH's medical physicists to adjust CT scanning practices to give children the least possible dose while still making images useful for diagnosis.

Not all imaging centers have changed their approach. A study published in June in the journal *JAMA Pediatrics* reported that of the estimated 4 million CT scans given every year to U.S. children under age 15, a third are unnecessary and may lead to 5,000 cases of cancer.

Still, doctors say that in some cases a CT scan is the best test. "If we can get the necessary information from a plain X-ray or an MRI, we forego the CT scan," says Cordelia W. Carter, M.D., assistant professor of orthopaedics and rehabilitation. However, for certain fracture patterns, such as a common ankle "triplane" fracture, a CT scan provides the amount of detail a surgeon needs. Still, Carter adds, "we are very aware of the increased radiation associated with CT scans, and we do whatever we can to minimize the patient's exposure."

Goodman expects the use of CT to drop further as MRI, which emits no radiation, becomes the standard tool for many diagnoses. His campaign to lower radiation doses at YNHCH has been so successful that he now sometimes finds himself urging clinicians and parents not to avoid CT in the correct clinical setting.

"If the suspicion is high that a child may have a significant lesion in the lung," says Goodman, "parents should be reassured that the CT radiation doses at Yale are the lowest in the country and doing the scan is what's best for the patient."

// Library *(from page 1)* library's director.

"It was an easy gift to make, because I have great respect and love for the library," Simbonis says. "A library is the guts of any university. Without a library, you don't have a university."

Says R. Kenny Marone, MLS, director of the Cushing/Whitney Medical Library, "Great libraries are not made, they're nurtured. Stan is proud of the work the library is doing. He is able to remember the help he needed from the library [as a student], and he can see that the library is continuing its good work with students."

The library's recent innovations include its "personal librarian" program, in which medical students are paired with one of its librarians, giving them personalized research support; and efforts to keep apace with today's sweep toward digitalization. The digitalization of medical journals, in particular, has resulted in new subscription models that mean substantially higher subscription costs for the library.

"Stan understands the importance of collections from a student perspective. I think he could see that by giving to the library, he wasn't only giving for right now, but he was giving to future generations of students," says Marone, also associate university librarian for research support and collections at the Yale University Library. In a display of appreciation for Simbonis support, on April 25 the Medical Library staff dedicated a conference room to Simbonis, naming it the Dr. Stanley Simbonis Conference Room.

In addition to supporting an institution whose history is intertwined with his own, the gift is "one way of paying Yale back," Simbonis says.

Born in Manhattan in 1928 to emigrants from Greece, Simbonis grew up in a tenement apartment in the Bronx with his mother and brother.

TERRY DAGRADI

Stanley Simbonis's support helps usher the medical school's library into the digital era.

He had not heard of Yale, he says, until his mother married and moved to New Haven. After four years in the U.S. Marine Corps, he was admitted to Yale College, which he attended with support from the G.I. Bill and scholarships.

Following his graduation in 1953, Simbonis entered YSM, where his tuition was covered entirely by scholarships. "Out of pocket I may have spent $100. They were very good to me," he says. After graduating he worked in the New York University lab of biochemist Severo Ochoa, M.D., who won the 1959 Nobel Prize for medicine or physiology for his discovery of an enzyme that can synthesize RNA.

Following stops at Columbia University and Holy Name Hospital in Teaneck, N.J., Simbonis settled down at St. Joseph's Hospital in Paterson, N.J., where he became chair of pathology. He retired in 1992 but remains an associate clinical professor of pathology at Columbia University's College of Physicians and Surgeons.

Since 1975 Simbonis has lived in a historic brownstone in Greenwich Village, New York City, where he is active in neighborhood preservation. For many years he also owned a vacation home on Fire Island, N.Y., which he has recently donated to the medical school. The home will be sold and the proceeds divided between the library and a scholarship to be set up in his name.

Northern California (NIH), *Antiretroviral Therapy Strategies to Lower Cancer Risk in HIV-Infected Persons*, 1.3 years, $225,768 • **Peter Ellis**, American Psychiatric Foundation, *HAVEN Free Clinic Mental Health Advocacy Program*, 1 year, $4,799 • **John Forrest**, Doris Duke Charitable Foundation, *International Clinical Research Fellowships for Medical Students*, 5 years, $864,000 • **Jorge Galán**, Rockefeller University (NIH), *Mechanical Analysis of Flavonoids on Bacterial Virulence*, 1.7 years, $249,002 **Nicolas Gaspard**, Epilepsy Foundation of America, *Multimodality Functional Mapping of Language: Comparison of Available Methods*, 1 year, $45,000 **Mark Gerstein**, University of Massachusetts (NIH), *Data Analysis and Coordination Center for the Encyclopedia of DNA Elements (ENCODE)*, 3.9 years, $622,427 • **David Glahn**, Texas Biomedical Research Institute, (NIH), *Characterization of a Mendelian Form of Psychosis in a Population Isolate*, 1.4 years, $169,622 • **Mihaly Hajos**, Envivo Pharmaceuticals, *Evaluation of an α7 Nicotinic AChR Agonist on Hippocampal Neurophsyiological Activity in Control and Aβ Overproducing Mice: A Translational* In Vivo *Efficacy Assay Predicting Cognitive Outcome*, 1 year, $363,669; Biogen Idec, Inc., *Abnormal Neurophysiological Markers in Tau Transgenic Mice: Development of a Functional* In Vivo *Efficacy Assay*, 1 year, $253,500 • **Kevan Herold**, Juvenile Diabetes Research Foundation International, *Assessment of Beta Cell Stress and Death by Epigenetic Changes of Insulin*, 2 years, $423,857 • **Karen Hirschi**, Columbia University (NIH), *Integrated Heart-Liver-Vascular Systems for Drug Testing in Human Health and Disease*, 1.3 years, $136,614 • **Arthur Horwich**, Ellison Medical Foundation, *Lipofuscin Production in Motor Neurons of Normal and ALS Mice*, 4 years, $797,737 • **Natalia Ivanova**, Connecticut Innovations, Inc., *Transcriptional Control of Pluripotency in Human Embryonic Stem Cells*, 4 years, $750,000 • **Samuel Katz**, Lymphoma Research Foundation, *Reactivating Apoptosis in Mantle Cell Lymphoma by Peptide Replacement of the Tumor Suppressor BIM*, 1 year, $81,432 • **Steven Kleinstein**, Mayo Clinic of Rochester (NIH), *Shared HIPC Resources for Network Analysis of Vaccine Immune Response*, 9 months, $62,844 • **Jeffery Kocsis**, Connecticut Innovations, Inc., *Remyelination Potential of Human ES Cell-Derived OPCs Transplanted into the Demyelinated Nonhuman Primate Spinal Cord*, 4 years, $750,000 • **Diane Krause**, Connecticut Innovations, Inc., *Stem Cells for Cell Therapy of Hypoparathyroidism*, 2 years, $200,000 • **John Leventhal**, State of CT Dept of Social Services/Disability Determination, *Nurturing Families Network*, 3 years, $2,512,806 • **Richard Lifton**, Columbia University (NIH), *Discovery and Fine Mapping of Susceptibility Loci for IgA Nephropathy*, 11 months, $311,670 • **Janghoo Lim**, Alfred P.Sloan Foundation, *Molecular Mechanisms of Neural Development and Neurological Disorders*, 2 years, $50,000 • **Haifan Lin**, Connecticut Innovations, Inc., *Continued Service and Technology Development at the Yale Stem Cell Center Cores*, 1 year, $500,000 • **Brett Lindenbach**, Columbia University (NIH), *Targeting an Essential Cellular Protease for Flavivirus Replication*, 1.5 years, $290,526 • **Heather Lipkind**, HealthPartners Research Foundation, *Vaccine Safety Datalink*, 3 years, $59,197 • **Paul Lombroso**, Simons Foundation, *The Role of MVP and STEP in Autism*, 1 year, $59,972 • **Steven Marans**, International Association of Chiefs of Police, *Enhancing Law Enforcement Response to Children Exposed to Violence*, 1.9 years, $155,016 • **In-Hyun Park**, Connecticut Innovations, Inc., *Molecular Regulation of the Neuronal Development by MeCP2*, 4 years, $750,000 • **Kevin Pelphrey**, Binational Science Foundation, *Translational Research in Human Social Dysfunction: Can Oxytocin Improve Core Brain, Neuroendocrine, and Behavioral Features of ASD in Children?*, 4 years, $89,758; Simons Foundation, *Multimodal Developmental Neurogenetics of ssc Adolescents*, 2 years, $499,205 • **Lajos Pusztai**, Breast Cancer Research Foundation, *Characterization of Intratumor Heterogeneity in Breast Cancer and its Clinical Implications*, 1 year, $239,448 **Yibing Qyang**, Connecticut Innovations, Inc., *Human Tissue-Engineered Blood Vessels Using Induced Pluripotent Stem Cells*, 4 years, $750,000; University of Pennsylvania, *Determinants of Right Ventricular Failure in Idiopathic Pulmonary Arterial Hypertension*, 1 year, $100,000 • **Peter Rabinowitz**, Mary Imogene Bassett Hospital (*DHHS*), *Molecular Approaches to Zoonotic Infection Risk and Control in Dairy Workers*, 1 year, $15,000 **D. Redmond Jr.**, Connecticut Innovations, Inc., *Are Dopaminergic Neurons Derived from Human Embryonic Stem Cells or from Fibroblasts the Best Candidates for Treatment for Parkinson's Disease as Studied in the Best Primate Model?*, 4 years, $1,800,000 • **Valerie Reinke**, University of Washington, Seattle (NIH), *Comprehensive Identification of Worm and Fly Transcription Factor Binding Sites*, 11 months, $402,500 • **Yongming Ren**, Connecticut Innovations, Inc., *Modeling Hypertrophic Cardiomyopathy (HCM) Using Human Induced Pluripotent Stem Cells*, 2 years, $200,000 • **David Rimm**, Breast Cancer Research Foundation, *NeoALTTO: Whole Exome Sequencing of Pre-treatment, Day-14 and Residual Cancer Samples, Correlative Science for the Breast International Group (BIG)*, 1 year, $240,000 • **Martin Schwartz**, U.S.-Israel Binational Science Foundation, *The Role of Mechanical Force on Integrin and Chemokine Bonds in Lymphocyte Motility and Arrest*, 1 year, $21,500 • **Satinder Singh**, Alfred P. Sloan Foundation, *Alfred P. Sloan Research Fellowship*, 2 years, $50,000 **Steven Southwick**, Mount Sinai School of Medicine (*DHHS*), *Biomarkers of Psychological Risk and Resilience in World Trade Center Responders*, 1 year, $62,623; Dartmouth College (NIH), *National Center for Disaster Mental Health Research*, 1 year, $21,005 • **Matthew State**, Simons Foundation, *Functional Analysis of Patient Mutations in EPHB2m and ASD Candidate Gene*, 3 years, $268,929 • **William Tamborlane**, Case Western Reserve University (NIH), *Epidemiology of Diabetes Interventions and Complications*, 1.3 years, $181,183; University of Connecticut Health Center (NIH), *A Reinforcement Approach to Improve Diabetes Management*, 3.9 years, $503,804 • **Janet Tate**, New York University (NIH), *The Operations Research Collaboration for Alcohol Abuse and AIDS: ORCAAA*, 5 years, $47,822 • **Elisabetta Ullu**, U.S.-Israel Binational Science Foundation, *RNomics in* Trypanosoma Brucei *Bioinformatics and Functional Approaches*, 4 years, $62,869 • **Zheng Wang**, Connecticut Innovations, Inc., *Genome-wide shRNA Screen Identifies Novel Regulatory Pathways in Human ES Cells*, 2 years, $200,000 **Stephen Waxman**, University of Michigan (NIH), *Functional Genetics of the Neuronal Sodium Channel Gene SCN8A*, 10 months, $50,428 **Sherman Weissman**, Stanford University (NIH), *Production Center for Mapping Regulatory Regions of the Human Genome*, 1.4 years, $166,761 • **John Wysolmerski**, George Mason University, *Preventing Breast Cancer by Killing Premalignant Lesions*, 3 years, $180,625 • **Xiao Xu**, University of Michigan (NIH), *Testing a Latino Web-Based Parent Adolescent Sexual Communication Intervention*, 9 months, $11,504 • **Jing Zhou**, Connecticut Innovations, Inc., *Evaluation of Mechanical Impact on Lung and Endoderm Development*, 2 years, $200,000

// Professorship *(from page 1)* of women's health, today the initiative supports pilot studies, original research, training of women's health researchers, and outreach to practitioners and the public.

"Dr. Mazure has made this program a catalyst for meaningful research and better health care, advancing medicine for women and men alike," says Robert Bildner.

A true "Yale family," the Bildners have a long history of service to the University. Elisa Spungen Bildner, a 1975 graduate of Yale College and a graduate of Columbia Law School, is a longtime WHRY board member. Robert Bildner, a 1972 graduate of Yale College and a graduate of the University of Pennsylvania Law School and the Jewish Theological Seminary in New York, is a member of the University Council, an advisory body to the University's president. The parents of three Yale College alumni, Elana '06, Ari '09, and Eli '10, and current student Rafi '16, the Bildners have served on numerous University committees. Among other roles, they are trustees and founders of the Joseph Slifka Center for Jewish Life at Yale, where they have endowed travel grants and fellowships.

Through their efforts, the Bildners carry on the generosity of spirit and mindfulness of community that has characterized their mothers' lives. A firm and forceful believer in the importance of education and scholarship, Norma Spungen received postgraduate degrees in both education and history and taught grade school for a number of years in her native Chicago. Later, she became a lecturer on history, and until her retirement headed the Chicago Jewish Archives, a center for research and scholarship. "She values the kind of scholarship that a chair exemplifies," says Elisa Spungen Bildner, herself a former journalism and law professor.

PHIL CANTOR

A gift from Yale College alumni Elisa Spungen Bildner and Robert Bildner has endowed a professorship in women's health research.

Joan Lebson Bildner, Robert Bildner says, "was regarded as a visionary and a leader who got things done." A resident of Jupiter, Fla., she was a devoted philanthropist who worked to advance the missions and resources of numerous health-related and cultural organizations, supporting both Jewish and civic causes. Among these is the Allen and Joan Bildner Center for the Study of Jewish Life at Rutgers University, which she co-founded with her husband, Allen. "She made things happen, in the same way that Carolyn Mazure makes things happen at WHRY," says Robert Bildner.

Says Elisa, "We could think of no better way to honor our mothers."

// Nobel *(from page 1)* important, creative scientific research," said Yale University President Peter Salovey, PH.D., the Chris Argyris Professor of Psychology. "Yale is absolutely thrilled to have one of our most distinguished faculty—who is also one of our most distinguished alumni—receive this great honor."

Exocytosis is ubiquitous in biology—it is essential to cell division and insulin secretion, for example—but it plays a particularly crucial role in the nervous system. In neurons, vesicles carrying neurotransmitters fuse with cell membranes at synapses, emptying their cargo to pass on the chemical messages that govern movement, perception, cognition, memory, and mood. For three decades, Rothman has performed biochemical and cell biology experiments that have revealed the molecular machinery of membrane trafficking in fine detail. Much of this work was done using a "cell-free" approach, in which Rothman sidestepped the complexities of working with complete cells by isolating the intracellular components crucial to membrane trafficking. This strategy allowed him to propose that complexes of membrane-associated proteins called SNAREs are required for vesicles to fuse with membranes.

"Jim Rothman is one of the most brilliant researchers of our time," says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. "When he started his career, a number of successful biochemists were recognizing the importance of studying molecular processes in cell-free systems, but no one imagined that you could study vesicle trafficking in a cell-free system. Jim had the courage to try and the skills to succeed, and this bold approach revolutionized the field."

Rothman shares the prize with Randy W. Schekman, PH.D., of the University of California–Berkeley, and Thomas Südhof, M.D., of Stanford University. While at the University of Texas Southwestern Medical Center, Südhof discovered synaptotagmin, a protein in vesicle membranes that senses intracellular calcium levels. When a neuron is stimulated, calcium binds to synaptotagmin, which prompts the vesicle to release its contents by interacting with SNARE complexes and fusing with the cell membrane. Schekman discovered a set of genes required for vesicle traffic.

In 2002 Rothman and Schekman received the Albert Lasker Award for Basic Medical Research and the Louise Gross Horwitz Prize of Columbia University. In 2010 Rothman, Südhof, and Richard H. Scheller, PH.D., were jointly awarded the Kavli Prize in Neuroscience.

In addition to grants from federal agencies, Rothman's research has benefited from the long-term support of the G. Harold and Leila Y. Mathers Charitable Foundation.

Rothman graduated summa cum laude from Yale College in 1971, and earned a PH.D. in biological chemistry from Harvard Medical School in 1976. After a postdoctoral fellowship in the lab of biochemist Harvey F. Lodish, PH.D., at the Massachusetts Institute of Technology, he served on the faculties at Stanford School of Medicine, Princeton University, Memorial Sloan-Kettering Cancer Center and the Sloan-Kettering Institute in New York, and, most recently, Columbia University's College of Physicians and Surgeons, where he was professor of physiology and biophysics, the Clyde and Helen Wu Professor of Chemical Biology, and director of the Columbia Genome Center.

Pioneering RNA researcher is elected a member of the National Academy of Sciences

Over and over in his 19-year career at Yale, Ronald R. Breaker, PH.D., chair and Henry Ford II Professor of Molecular, Cellular and Developmental Biology, has transformed our understanding of RNA. Far from playing second fiddle to proteins in cellular machinery, Breaker has found, RNA can play an array of exotic biochemical roles—and may have even been in charge of cellular functions during the dawn of evolution. Breaker's extensive contributions to our understanding of RNA biology have now garnered him a new honor: On April 30, he was elected to the National Academy of Sciences (NAS), a body representing the nation's most prominent and productive researchers.

"Ron has always done outstanding science," says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. "He's a pioneer in defining new RNA functions within the cell."

Science had long held that RNA simply carries information between DNA and protein-manufacturing ribosomes. Breaker, also professor of molecular biophysics and biochemistry, suspected early on that nucleic acids like RNA might be capable of more than we gave them credit for.

Ronald Breaker

In 1998 Breaker opened a new era of molecular biology when he synthesized the first RNA sequences that work as molecular switches. Soon afterward, he found the first such structures in nature, where they respond to metabolites and help determine which genes will be expressed. Some of these so-called "riboswitches" behave like enzymes, while others help bacteria process vitamins or even fend off fluoride—a great surprise, given that fluoride was not previously known to play much of a role in biological systems.

RNA may also behave like an antibody or a complex machine. One RNA "machine" Breaker's lab discovered demands the presence of two specific chemical signals before it removes itself from a messenger RNA; another unusual RNA is essential for cells to tolerate high doses of alcohol. While organisms today mostly rely on proteins to do such things, some still use RNA. Breaker's research suggests this may be a holdover from billions of years ago, before DNA existed, when RNA was the dominant machinery inside cells. If true, this notion would help clarify how life could have arisen without proteins, which require DNA instructions to build.

Breaker has also co-founded two biotech startups, Archemix and BioRelix, to explore RNA's therapeutic and diagnostic capabilities, including novel antibiotics that target bacterial riboswitches.

Breaker earned his B.S. at the University of Wisconsin–Stevens Point, and his PH.D. at Purdue University. As a postdoctoral fellow at the Scripps Research Institute, he helped develop methods of driving evolution in the lab to find RNA enzymes. It was there that he and his colleagues created the first enzymes made of DNA.

A Howard Hughes Medical Institute investigator, Breaker has received fellowships from the Arnold and Mabel Beckman Foundation, the David and Lucile Packard Foundation, and the Hellman Family Trust, and has won the Arthur Greer Memorial Prize, the Eli Lilly Award in Microbiology, and the Molecular Biology Award from the NAS. He was named a fellow of the American Association for the Advancement of Science in 2004.

Founded during the Civil War in 1863 by an Act of Congress that was signed by Abraham Lincoln, the NAS is a non-profit organization whose goal is to advance science, technology, and medicine and serve as an independent advisor to the nation.

The 105 new members and foreign affiliates named to the NAS this year include two other Yale faculty members: Xing-Wang Deng, PH.D., Daniel C. Eaton Professor of Plant Biology in the department of molecular, cellular, and developmental biology; and David R. Mayhew, PH.D., Sterling Professor of Political Science. All three will be inducted into the Academy during its April 2014 meeting in Washington, D.C.

Expert in human polycystic diseases receives American Society of Nephrology's top honor

Stefan Somlo, M.D., the C.N.H. Long Professor of Medicine, professor of genetics, and chief of the Section of Nephrology in the Department of Medicine, has been named the 2013 recipient of the Homer W. Smith Award from the American Society of Nephrology. The award is presented annually to an individual whose achievements have fundamentally affected the science of nephrology.

Stefan Somlo

Somlo's laboratory studies the human polycystic diseases of the kidney and liver, with the goal of achieving understanding of basic mechanisms that will translate to development of specific treatments. Polycystic kidney disease affects more than 12 million individuals worldwide and causes progressive disruption of the normal structure and function of the kidney through growth of fluid-filled cysts. The most significant clinical consequence to patients is the loss of kidney function, necessitating renal replacement by dialysis or transplantation.

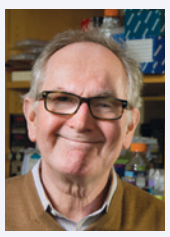
Somlo's team has identified four of the genes responsible for these human diseases, and studied the functions of the protein products of these genes in cells and animal models. They have discovered the mechanisms by which mutations in these genes result in cyst formation, and have also defined the way in which these protein products work together to maintain normal kidney structure and function.

Somlo earned his B.A. at Harvard University and his M.D. at Columbia University's College of Physicians and Surgeons. He completed his internship and residency in internal medicine at Albert Einstein College of Medicine, and a fellowship in nephrology at Yale School of Medicine (YSM).

The Homer W. Smith Award, established in 1964, is named for one of the major intellectual forces in renal physiology. Smith spent most of his career at New York University, where he developed and refined his concepts of glomerular filtration and tubular absorption and secretion of solutes. His findings and insights form the cornerstones of current understanding of renal function. His use of comparative approaches to explain normal human physiology stands as a model for students of biology and scientists attempting to unravel the mysteries of normal and disordered renal function.

Somlo joins a distinguished group of Yale faculty who have received the award. The previous Yale awardees include Peter S. Aronson, M.D., the C.N.H. Long Professor of Medicine and professor of cellular and molecular physiology; Walter F. Boron, M.D., PH.D., professor of cellular and molecular physiology; pathologist and cellular biologist Marilyn Farquhar, PH.D., who was on the YSM faculty from 1973 to 1990; Richard P. Lifton, M.D., PH.D., chair and Sterling Professor of Genetics, professor of medicine, and a Howard Hughes Medical Institute investigator; the late Steven C. Hebert, M.D., chair and C.N.H. Long Professor of Cellular and Molecular Physiology and professor of medicine; Emile Boulpaep, M.D., professor of cellular and molecular physiology; Gerhard H. Giebisch, M.D., professor emeritus of and senior research scientist in cellular and molecular physiology; and the late Robert W. Berliner, M.D., professor of cellular and molecular physiology and dean of YSM from 1973 to 1984.

Awards & Honors



Richard A. Flavell, PH.D., chair and Sterling Professor of Immunobiology and a Howard Hughes Medical Institute investigator, has been elected the first president of the newly formed International Cytokine and Interferon Society (ICIS). The ICIS is a non-profit organization of more than 600 scientists who study interferon, cytokine, and chemokine cell biology, molecular biology, biochemistry, and the clinical use of these biological response modifiers. The society was formed this year through the merger of two existing organizations, the International Society for Interferon and Cytokine Research (ISICR), and the International Cytokine Society.

Flavell received the Vilcek Prize in Biomedical Science from the ISICR in 2013. He and colleagues have discovered several important receptors of the innate immune system, and he has made major contributions to our understanding of how activation of the innate system triggers the adaptive immune system's more specialized responses.

Joan A. Steitz, PH.D., Sterling Professor of Molecular Biophysics and Biochemistry and a Howard Hughes Medical Institute investigator, has been named the 2013 Grand Medal winner by the French Academy of Sciences. Each year, the Grand Medal, the Academy's highest honor, is awarded to a French national or to a foreign scientist who has made "remarkable and decisive" contributions to his or her field.

Steitz is best known for her pioneering work with non-coding RNA. With her student Michael Lerner, she discovered and later defined the contribution of small ribonucleoproteins (snRNPs) to the cellular process of making proteins. She is also recognized for her work encouraging women to pursue careers in science. Her honors include the National Medal of Science, the Gairdner Foundation International Award, the Lewis S. Rosenstiel Award for Distinguished Work in Basic Medical Research, and the E.B. Wilson Medal from the American Society for Cell Biology.