Medicine@Yale

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New Yale Institute of Global Health to address worldwide issues

Health sciences schools take the lead on an initiative that aspires to have global impact

The Schools of Medicine, Public Health, and Nursing have come together to launch the Yale Institute of Global Health (YIGH), a university-wide effort that will address worldwide health issues. The initial focus of YIGH will be on research aimed at improving the health of individuals and populations around the world.

The creation of YIGH reflects a growing interest by students, faculty, and advanced trainees across the university in conducting global health research, along with the need for a centralized resource for faculty to collaborate on these projects. The recent arrivals of Sten H. Vermund, M.D., Ph.D., dean and Anna M.R. Lauder Professor of Public Health, and professor of epidemiology (microbial diseases) and of pediatrics; and of Ann E. Kurth, Ph.D., C.N.M., M.P.H., dean and Linda Koch Lorimer Professor of Nursing—both of whom bring a wealth of expertise in global health research—was another driving factor.

"There are complicated regulatory, legal, and logistical challenges to doing research in international locations," says Robert M. Rohrbaugh, M.D., professor of psychiatry and director of the Office of International Medical Student Education at the School of Medicine, where more than 40 faculty members conduct global health research. "A centralized group with this type of expertise is helpful, especially for junior faculty."

ROBERT A. LISAK

The Yale Institute of Global Health officially came into existence in December, with its approval by the Yale Corporation. (Left to right): Deans Robert Alpern of the School of Medicine, Sten Vermund of the School of Public Health, and Ann Kurth of the School of Nursing marked the occasion, along with Robert Rohrbaugh, the School of Medicine's faculty lead for the institute.

"Yale has examples of amazing work being done in multiple schools from which the experience, expertise, and findings can be harnessed and further developed within larger-scale, higher-impact,

// YIGH *(page 4)*

Slayman professorship is established

Endowment is created to honor the memory of beloved deputy dean and mentor

The School of Medicine has established an endowed professorship to honor the memory of the late Carolyn Walch Slayman, Ph.D., a distinguished scientist and visionary academic leader who graced the School of Medicine with her inimitable presence for almost 50 years. At the time of her death at age 79 in December 2016, Slayman was deputy dean for academic and scientific affairs, Sterling Professor of Genetics, and professor of cellular and molecular physiology.

"We continue to feel Carolyn's absence, and her influence will be with us for many years to come," says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. "I am delighted that this professorship has been created to honor her legacy."

Slayman joined the School of Medicine faculty in 1967 as an assistant professor in the Department of Physiology and Microbiology. After spending her initial years at Yale as a bench scientist, she went on to assume administrative responsibilities through which she influenced scores of students, trainees, and colleagues, and kept the School of Medicine at the forefront in countless areas. She was a trailblazer on many fronts. When named chair of the Department of Human Genetics (now Genetics) in 1984, she became the first woman to head a department at Yale School of Medicine. In 1995, she became the school's first deputy dean for academic and scientific affairs, and the first woman to hold a deputy deanship. Shortly after her appointment as deputy dean she said that her job was to be a catalyst, bringing people together to foster active discussion that would guide the school. By all accounts, she succeeded admirably in this endeavor. Many sought

TERRY DAGRADI

A professorship at the School of Medicine has been endowed in memory of Carolyn Walch Slayman (1937-2016), to be occupied by a faculty member who embodies qualities for which Slayman was revered during her nearly 50 years at the school.

// Endowment *(page 5)*

David W. Wallace, 1924-2017, generous and loyal benefactor

David W. Wallace, a former corporate attorney, businessman, and philanthropist who was a longtime supporter of the School of Medicine and Yale University, died at home in Greenwich, Connecticut, on Dec. 24, 2017. He was 93.

David Wallace and his wife, Jean McLean Wallace, have donated more than $33 million to Yale, about half of which—$16.5 million—was used to endow six professorships at the School of Medicine. Their generous gifts place them among a select group of supporters of the school.

"David has a special place of honor because he was such an enthusiastic and committed donor to the medical school, says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. "David was proud of the fact that he had given so many endowed chairs to the medical school, which have enabled us to attract outstanding faculty and to provide

// Benefactor *(page 7)*

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ROBERT A. LISAK

Gary Desir has served the School of Medicine with distinction as a researcher, clinician, educator, and administrator. His discovery and further investigation of the flavoprotein renalase are milestones in the understanding of renal and cardiovascular function.

A stalwart in laboratory and clinic

Internal Medicine chair discovered a protein with kidney, heart, cancer roles

On a spring day in New York, Gary V. Desir, M.D. '80, now chair of Internal Medicine, and Paul B. Beeson Professor of Medicine, answered a phone call from his father back home in Port-au-Prince, Haiti. Desir had planned to enjoy his first vacation to the United States, while staying at his cousin's apartment in Queens, and return in a couple of weeks. "My father said, 'You probably should stay in the U.S. and go to college,'" Desir recalls. "So, I stayed."

Desir's father, a cardiologist, had trained in Canada and Chicago and wanted his children to earn their degrees from U.S. schools. So, Desir applied, and was accepted at New York University, where he would major in biology. When the time came to follow his father, paternal grandfather, and great grandfather into medicine, he considered Johns Hopkins, Cornell, and others, but chose Yale because of its system of medical education, which promotes independent learning.

As a first-year, Desir shared a cadaver with a classmate, and soon decided he wanted to share his life with her. He and the then Deborah Dyett pursued internal medicine residencies at Yale New Haven Hospital, a decision heavily influenced by Samuel O. Thier, M.D., then Yale's chair of internal medicine, who made sure the couple had similar on-call schedules so they could enjoy days off together. "Also, at the time, I wanted to do research in renal physiology, and Yale was top-rated in this area," Desir says. That, along with mentors such as Thomas P. Duffy, M.D., professor emeritus of medicine (hematology), persuaded the two to stay.

Desir finished a nephrology fellowship at Yale in 1987 and joined the faculty as an assistant professor in 1988. At first, he dedicated himself to research, seeking to better understand ion channel function in kidneys and searching for ways to advance clinical care.

Major success came in 2005. "A renal fellow and I were caring for patients suffering from kidney disease, and he was lamenting that, in spite of our best efforts, many of our patients ended up dying of cardiovascular-related complications," Desir says. "That was the inspiration for looking into the connection between kidney and heart disease. And that search, which took several years, led us to discovery of renalase, a flavoprotein, synthesized in the kidney and secreted in blood, that enhances various cells' ability to survive. The renalase protein is approximately 3 billion years old, and is encoded by a single, highly conserved gene."

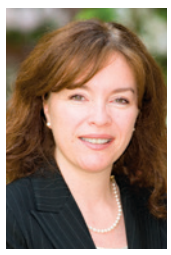
Desir and his team hypothesized that renalase could be used to protect patients from kidney injury and heart attacks, and minimize cardiac cell damage. More recently, Desir and others have also found that dysregulated renalase signaling alters the immune response to tumors and can contribute to the development of certain cancers. His laboratory is developing agents that block renalase signaling as first-in-class therapeutic agents for cancer. Desir holds several renalase-related patents and is scientific founder of two biotech companies.

Over time, Desir has taken on added clinical and administrative roles. He was appointed internal medicine chair at the West Haven VA hospital in 2003. A decade later, he became interim chair of Yale's Department of Internal Medicine, and then its chair and chief in 2016. Desir also is board chair for Yale Medicine, the school's clinical practice, where he is working toward making electronic-health-record software less intrusive in physican-patient interactions. In addition, he co-founded the Minority Organization for Retention and Expansion (MORE), with the goal of recruiting—and keeping—more minority faculty and students.

He also has a dual teaching appointment with the School of Forestry & Environmental Studies, where he co-led a graduate course called "Sustainable Development in a Post-Disaster Context," in collaboration with the Albert Schweitzer Hospital in Deschapelles, Haiti, and continues to host visiting Haitian doctors and nurses in an exchange program.

What at first was going to be a temporary stay for Desir at Yale has now turned into four decades, and he says he has never questioned his original decision to stay. He and Deborah Dyett Desir, M.D. '80, a rheumatologist in private practice, have raised four children during 38 years of marriage. And, within the medical school, he is thankful "to have found collaborators and people at Yale willing to help even though they were not benefiting from what they were helping me with. Even when I was a junior faculty member researching ion channels, I had people willing to help me." Now, as a senior leader, and by personal example, it is that kind medical school he is dedicated to maintaining.

Garino is appointed director of the Physician Associate Program



Alexandria Garino

Alexandria (Xandi) Garino, Ph.D., PA-C, assistant professor of medicine, has been appointed director of the Yale School of Medicine Physician Associate (PA) Program, after serving as interim director since July 2016. Garino joined the PA Program faculty in 2006, and has worked clinically for 10 years as a physician assistant at Yale Cancer Center.

Garino, who places a high value on the program's research focus, received her Ph.D. in learning science in January 2018 from Fordham University's Contemporary Learning and Interdisciplinary Research program. Her doctoral work explored the non-cognitive factors that explain how students in the health professions react to, interpret, and use feedback.

She graduated from Catholic Medical Center's PA program in 1999, and earned her M.S. in biostatistics and clinical research design from Columbia University's Mailman School of Public Health in 2004.

Geirsson is named chief of cardiac surgery section

Arnar Geirsson

Arnar Geirsson, M.D., associate professor of surgery (cardiac surgery), has accepted the position of chief of the Section of Cardiac Surgery at the School of Medicine, after serving as interim chief since October 2016. Geirsson also will serve as co-surgical director of the Heart and Vascular Center (HVC) at Yale New Haven Hospital and medical director of the Bridgeport Hospital Cardiac Surgery program.

Since he first joined the faculty of the School of Medicine in 2007, his clinical focus has been on minimally invasive surgery and valve surgery. He has a busy mitral valve repair practice done by minimally invasive right thoracotomy. Geirsson performed the first valve-sparing root replacement at Yale (2008); the first hybrid revascularization at the West Haven Veterans Affairs Hospital (2008); the first right thoracotomy mitral valve repair at Yale (2009); and the first robotic heart operation at Yale (2011).

His research interests include investigating the biological changes and pathways involved in pathogenesis of mitral valve prolapse and thoracic aortic aneurysm. He has published various research articles in both basic and clinical science, and serves as an editorial reviewer for *Annals of Thoracic Surgery*, *Journal of Thoracic and Cardiovascular Surgery*, *Journal of Heart and Lung Transplantation*, and *Circulation*.

Geirsson is an active member of the Society of Thoracic Surgeons and the American Heart Association (AHA), serving on various committees of the AHA.

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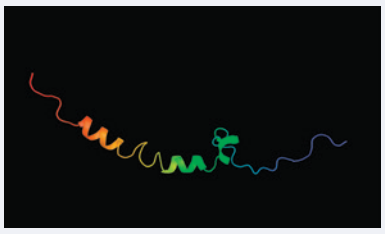
Potential new type 2 approach identified



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The protein apelin, previously known to improve glucose metabolism, could become the focus of diabetes treatments, suggests a new study led by Hyung J. Chun, M.D., associate professor of medicine (cardiology).

The study, published in *Science Translational Medicine* on September 13, reports apelin's receptors are located specifically on the endothelial cells that line the blood vessels and that apelin binding of its receptor prevents another protein—endothelial fatty-acid binding protein 4 (FABP4)—from importing fatty acids into the tissues. Excess fatty-acid accumulation can result in insulin resistance and poor glucose metabolism—the hallmarks of diabetes.

Chun's team fed mice high-fat chow, which led them to gain weight and develop insulin resistance. Those mice also produced less apelin. Injecting those same mice with apelin improved their glucose metabolism.

Chun believes drugs that activate apelin receptors or inhibit FABP4 might be potential diabetes treatments. Further, since apelin prevents atherosclerosis in mice, such treatments could also address diabetes-associated cardiovascular problems.

A path toward drug synthesis in cells

A Yale-led research team has described the structure of pyrrolysyl-tRNA synthetase (PylRS), a protein that synthetic biologists rely upon to add new letters to the genetic code.

In the past, most biology textbooks have described 20 amino acids—the building blocks of all proteins— and 20 tRNA synthetases, responsible for matching the amino acids with the correct genetic molecules. Recently, however, researchers have uncovered additional rare amino acids, including the so-called "22nd amino acid" pyrrolysine, found in bacteria and single-celled organisms.

To help advance efforts to integrate pyrrolysine into the genomes of other types of cells, Dieter Söll, Ph.D., Sterling Professor of Molecular Biophysics and Biochemistry, and professor of chemistry, and colleagues determined the three-dimensional structure of PylRS—the tRNA synthetase required for pyrrolysine.

As published October 16 in *Nature Chemical Biology*, Söll's team not only described the structure of a unique section of PylRS, but also evolved new variants of the protein using a standard lab setup that is both simpler and faster than prior techniques that need specialized equipment. Söll foresees "the exciting prospect of synthesizing new drugs inside living cells."

Clinical trials take innovative approach

Frequent consultation between bench and clinic enhances the effectiveness and impact of Yale Cancer Center's Phase I Program

It is a simple concept: bench investigators who identify potential cancer therapies, and clinicians who evaluate experimental drugs in patient trials, sitting down together to figure out how each can make the others' work more effective. And yet, until just the past few years, the two groups often worked separately from one another at many institutions. The thought process at the bench seldom extended to therapeutic practice, and clinical trial physicians developed their protocols with limited input from the basic scientists who made the initial discoveries.

Because of that, Ranjit S. Bindra, M.D., Ph.D., associate professor of therapeutic radiology, says extraordinary lab work frequently went unnoticed. "There are so many great discoveries in journals like *Science Translational Medicine*, *Science*, and *Nature*, from many institutions, where the clinical implications are so profound, and yet they never made it into the clinic." Some work, Bindra says, was just not translatable, but in other instances, he says, "they probably also just never had a feasible mechanism to drive them into the clinic."

Such a mechanism is now the organizing principle of the Phase I Program at Yale Cancer Center (YCC), one of the few academic programs in the country where regular contact between bench scientists and clinicians is standard practice.

"There is a special drug development seminar once a month," says Joseph Paul Eder, M.D., professor of medicine (medical oncology) and clinical leader of the Phase I Research Group. "There's another that's called clinical cancer colloquium, where basic scientists from Science Hill come talk to us, or we go to them, and say, 'Here are great targets.' What is special about Yale is that the clinicians and translational scientists talk almost daily. The clinicians attend the science lectures, we pass each other in the hall, and I hope that every scientist knows our doors are always open and our cell phones are always on."

One project enhanced by these frequent interactions was a paper published in February 2017, whose senior authors were Bindra and Peter M. Glazer, M.D., Ph.D., chair and Robert E. Hunter Professor of Therapeutic Radiology and professor of genetics.

Their research, in *Science Translational Medicine*, demonstrated the sensitivity of tumor cells with mutations in two metabolism genes, *IDH1* and *IDH2*, to targeted drugs called PARP inhibitors. In the discussion section of the manuscript, the authors wrote that their findings could form "the basis for a possible therapeutic strategy." They could say that confidently because before the paper was even published, Bindra began a series of discussions about how to translate this discovery directly into the clinic with Patricia M. LoRusso, D.O., director of the early therapeutics clinical trials program and associate center director of experimental therapeutics at YCC, who leads the Phase I Program's Disease Aligned Research Team.

Bindra recalls, "She raised her hand in a research seminar and said "I'm not impressed with your animal data. You're showing these curves that are barely separating in a flank model, you're not going to be able to convince clinicians to bring this into the clinic.'" Bindra went back to the lab to "look at the different PARP inhibitors and to find one that had the biggest difference." They ended up selecting an FDA-approved PARP inhibitor, olaparib, which demonstrated marked activity in vivo.

That choice is helping patients already. Eder quickly plugged the findings into an existing protocol designed to thwart cancer cells' ability to repair their own disease-promoting DNA. "Yale had set up a clinical trial to be reactive to potentially important new information in the area of DNA repair," says Eder. "Yale investigators took that basic information and brought it immediately into the clinic. Yale enrolled *IDH1/2*-mutant patients into the study, and already months later we know at least in some patients this really works."

LoRusso and Bindra have even more ambitious plans. "Pat and I are writing a series of trials together, really testing [the findings] in rigorous Phase II studies," says Bindra. LoRusso says trialists will go a step beyond standard safety-related protocols and send samples obtained from their patients back to the bench scientists, "to try to understand why it's working or why it's not working and in what patients it's working."

"You can't often do that by just looking at the patients," she adds. "You need to take the tumor and the patient information and go back into the lab. That's one of the beauties of having the science and the clinic here."

Another development seen as beautiful by those involved is the clinic itself, a dedicated trial facility significantly funded by Yale New Haven Hospital that opened in 2016. "Instead of being a sort of designated corner of a general medical oncology unit," says Eder, "it's now a specified place." LoRusso says the new facility has accelerated the Phase I Program, which served roughly 25 patients per year when she came to Yale three years ago, and now is on target to enroll at least 150 patients in 2018. "I think it's done wonders," she says, "There's nothing like working in an extremely pleasant environment. It's a state-of-the-art facility."

Those comforts matter to patients who struggle to follow the strict protocols of a clinical trial, according to Joseph W. Kim, M.D., assistant professor of medicine (medical oncology). Kim designs many of the trials. His role also includes explaining both the pros and cons of trial participation to his Yale Medicine patients. "These trials are quite involved with research blood draws and biopsies," Kim says. "The patients need a lot of attention." While cautioning against false hope, Kim can also describe the encouraging longevity certain patients have enjoyed thanks to recent research advances. "We have patients from 2014 who remain on treatment without any evidence of disease," he notes. "An average life expectancy of patients coming to the Phase I clinic is 3 to 6 months. So, they are well beyond life expectancy. It's amazing."

ROBERT A. LISAK

Since their arrivals at Yale within the past six years, Patricia LoRusso (right) and Joseph Paul Eder (center)—shown conferring with Clinical Research Coordinator Alexandra Minnella—have overseen a sharp increase in the number of clinical trials conducted by the Phase I Program at Yale Cancer Center. Bench investigators and the clinicians who design and conduct early-phase trials interact regularly, each sharing knowledge with the other that both strengthens the basic science and brings new discoveries to patients more quickly and effectively.

Kim has adapted other work by Glazer and Bindra for a current trial to treat patients with advanced prostate cancer. "We sat down and talked about how hypoxia could suppress DNA repair," Bindra says. "He clearly looked at the papers and was thinking deeply about it." Their close cooperation mirrors that of many other bench researchers and clinicians at Yale.

For Eder, the program puts Yale in a place where it wants to be. "I don't think you can find any of the original papers on immuno-oncology drugs like ipilimumab and nivolumab where Yale investigators were not first or last authors on those papers."

Now, he says, investigators have the optimal outlet for their work. "It's not just great scientists at the bench. It's not just great docs in the clinic. We can bring these two things together and bridge that for a clinical trial that will benefit [patients] now." And, he enthusiastically tells patients, "You can be among the first."

OUT & ABOUT

May 3 **Cheryl Henson** (front left), Yale College '84, president of the Jim Henson Foundation founded by her late father, who created the Muppets, helped film a segment for the **Yale Early Social Cognition Lab**, with puppeteers **Lindsey "Z." Briggs** (front, second from left) and **Stephanie D'Abruzzo** (front right). **Katarzyna Chawarska**, Ph.D., (center rear), lab director and professor in the Yale Child Study Center, is surrounded by her lab team, which analyzes responses of children with autism to videos of puppets interacting with live actors.

COURTESY OF KATARZYNA CHAWARSKA

October 1 The inaugural **First Sunday** was held at the home of **Darin A. Latimore**, M.D. (front, center), deputy dean for diversity and inclusion and chief diversity officer. More than 45 medical, graduate, and postdoctoral students attended the community-building event, with plans to hold similar gatherings each month.

COURTESY OF DARIN LATIMORE

HAROLD SHAPIRO

October 6 On **National PA Day**, New Haven **Mayor Toni Harp** (center) helped celebrate the 50th anniversary of the Physician Assistant (PA) profession with Yale leaders. From left, **Rita A. Rienzo**, M.Sc., PA-C, assistant professor in Yale's PA Program; **Michael Devanney**, MHS, PA-C, current vice president of Connecticut Academy of Physician Assistants; **Courtney Fankhanel**, MM.Sc., PA-C, assistant professor in Yale's PA Program; **James Van Rhee**, M.S., PA-C, director of Yale's PA Online Program; **Alexandria Garino**, Ph.D., PA-C, director of the Yale PA Program; **David Brissette**, MMS, PA-C, assistant professor in Yale's PA Program.

COURTESY OF GARY DESIR

September 9 Gary V. Desir, M.D. '80, chair of internal medicine and Paul B. Beeson Professor of Medicine, and his wife, Deborah Dyett Desir, M.D. '80, a rheumatologist, hosted the annual **Minority Organization for Retention and Expansion (MORE)** reception at their home. Nearly 50 medical school faculty, students, fellows, and residents attended the event.

JUDY SIROTA ROSENTHAL

September 28 **Harriet M. Kluger**, M.D., professor of medicine (medical oncology), and **Veronica L.S. Chiang** , M.D., professor of neurosurgery and radiation oncology, presented **"The Highlights of Brain Metastasis and Melanoma Research,"** in Wilton, Connecticut, and thanked friends and donors to the Brain Metastasis Research Fund and Melanoma Research Fund for their support. **Richard Metz** (left) and **Stephen Connor** (right), both melanoma survivors and leaders of the Brain Metastasis Research Fund, stand with Kluger (second from left) and Chiang.

ERIN SHREVE

October 9 Brothers **Srinivas Seela**, M.D., (second from left), and **Harinath Sheela**, M.D., (right), recently gifted funds to support the Department of Internal Medicine's **Section of Digestive Diseases**. This includes research led by **James L. Boyer**, M.D. (second from right), Ensign Professor of Medicine (Digestive Diseases) and emeritus director of the Yale Liver Center, who was the brothers' mentor when they worked in the section as postdoctoral fellows. Srinivas Seela's son **Rithvik Seela** (left) worked last summer in Boyer's lab.

HAROLD SHAPIRO (2)

Nov 14–16 The inaugural **National Clinician Scholars Program (NCSP)** national meeting brought clinician scholars to the Omni Hotel in New Haven to explore themes around "Advancing Health Through Scholarship and Action." **1.** From left, scholars—and postdoctoral fellows—**Raymond Jean**, M.D., M.A.; **Katie Piwnica-Worms**, M.D.; **Kathleen O'Neill**, M.D.; **Shelli Feder**, Ph.D., APRN; and **Paul Joudrey**, M.D., M.P.H. **2.** (Left to right): Co-directors **Sarwat I. Chaudhry**, M.D., associate professor of medicine (general medicine), and **Robin Whittemore**, Ph.D., APRN, professor of nursing; as well as Yale's NCSP director, **Cary P. Gross**, M.D., professor of medicine (general medicine) and of epidemiology (chronic diseases); made opening remarks.

// YIGH *(page 1)* sustainable global partnerships," says Vermund. Current programs across the university address such areas as infectious diseases, maternal and childhood health, noncommunicable diseases, and health systems and research capacity. YIGH will build upon this foundation to address such global challenges as pandemic preparedness, refugee health, urbanization, and climate change and health. Researchers at the health sciences schools will collaborate with experts from the Schools of Forestry & Environmental Studies, Law, and Management to expand the institute's interdisciplinary agenda.

It is a sign of increasing demand for what YIGH plans to do that about a third of each year's School of Medicine class travels abroad for an international clinical elective. Rohrbaugh notes that many of these students also want experience conducting research in international settings; one challenge this trend presents has been student access to mentors. By bolstering opportunities for international projects, YIGH is expected to develop new mentorship capacity to support student research at the health professions schools and across the university.

A search is underway for a faculty director and YIGH is already ramping up its activities. Initiatives include a program to provide consultation to faculty who are developing new grant proposals or exploring potential collaborations based on geographic or topical areas of interest, and seed grants for faculty to pursue new research opportunities.

"We want to harvest all the talent and the distinct assets we have across the university, to make a deeper impact with our global initiatives," says Kurth. "YIGH will provide a catalyzing center for these collaborations."

ADVANCES
Health & Science News

Major brain impact arises from few cells

SHUTTERSTOCK.COM

Neurons called vasoactive intestinal peptide (VIP) cells make up just 1 percent of all brain cells, but their disruption in mice causes symptoms that mimic those of humans with schizophrenia, reports a study by Jessica A. Cardin, Ph.D., associate professor of neuroscience, published on August 16 in *Neuron*.

Cardin and her team mutated VIP cells in young mice, then observed the consequences in the visual cortex.

VIP cells usually fire when mice start to walk, but they did not do so in the mutant mice. The mutant mice also had reduced synchrony of neuronal firing and impaired vision. The failure of neurons to respond to changes in behavioral state, of which walking is one example, is characteristic of neurodevelopmental disorders such as autism and schizophrenia, as are reduced firing synchrony and perception problems.

In the mice, all of these symptoms emerged by adolescence, the time when, in humans, schizophrenia typically begins. These correspondences between mice with mutated VIP neurons and conditions of neurodevelopmental disease suggest to Cardin that VIP neurons may represent a therapeutic target.

Seeing more nuance for a cancer therapy

A growing number of cancer drugs are designed to shut off epidermal growth factor receptor (EGFR), a protein known to be involved in a wide array of cellular processes including proliferation. Now, Yale researchers have answered a long-standing question about how EGFR can mediate so many diverse processes.

Scientists already knew that seven different growth factors bind to the receptor portion of the EGFR protein, each causing two receptor molecules to come together, turning on the active portion of the proteins. But researchers had been puzzled by how the binding of each growth factor causes different actions within the cell.

Mark A. Lemmon, Ph.D., David A. Sackler Professor of Pharmacology and co-director of the Cancer Biology Institute at Yale Cancer Center, and colleagues formed crystals of the EGFR protein to study its structure under different conditions. Different growth factors, they showed, cause EGFR's receptor portions to assemble in slightly different ways, with variations in the timing and strength of the association—which the cell 'reads out' as different signals.

The discovery, published online in *Cell* on October 12, may lead to drugs that target EGFR in more nuanced ways, rather than simply shutting it off.

Gift supports work on a stubborn cancer

Non-smoker's lung cancer, and associated gene mutations, are among the priorities for Yale scientists in both the lab and the clinic

For a quarter century, Ginny Grunley, her husband Ken Grunley, president and chief executive officer of Grunley Construction, Inc., and their family have been enthusiastic philanthropists. Their determination to help others has included Ginny volunteering as a court-appointed special advocate for disadvantaged children.

"Writing a check is not enough," Ginny declares as a firm statement of family philosophy. "You need to be involved in the process."

In 2017 the Grunleys became supporters of Yale School of Medicine, with a million-dollar gift to fund lung cancer research led by Roy S. Herbst, M.D., Ph.D., Ensign Professor of Medicine and professor of pharmacology, associate director for translational research at Yale Cancer Center (YCC), and chief of medical oncology at YCC and Smilow Cancer Hospital. Their involvement, however, is something they would not have imagined just a few years ago. Ginny came to learn about Herbst's research because she had become one of his patients, after being diagnosed with a form of lung cancer associated with the *EGFR* gene mutation—a condition commonly known as non-smoker's lung cancer.

COURTESY OF ROY HERBST

Ginny Grunley (left) became a patient of Roy Herbst (center) after being diagnosed with a form of lung cancer associated with the *EGFR* gene mutation, also known as non-smoker's lung cancer. Grunley and her husband Ken (right) have given a million-dollar gift to support Herbst's research.

She considers herself lucky that the cancer was discovered so early—many lung cancers are not—and also that Ellen V. Sigal, Ph.D., founder and chair of the organization Friends of Cancer Research, and the wife of one of Ken Grunley's business acquaintances, knows Herbst well because of his basic and clinical-trials work in the field. Sigal, whom Ginny now calls "my guardian angel, my best friend, my sister," is well-connected in the cancer community, and "she brought Roy in from the very beginning."

The Grunleys flew to New Haven, where Herbst introduced them to his clinical and research teams, including Katerina Politi, Ph.D., associate professor of pathology. Grunley says Politi, whom she calls "an amazing young woman, so brilliant," examined her tumor in extraordinary detail. Based on that analysis, Politi and Herbst recommended that Grunley switch from her prior medication to afatinib, a targeted medication that she says kept her cancer at bay with just minimal side effects for two joy-filled years. "To be able to see these brilliant minds at work," says Grunley, "you're just in awe." Herbst agrees. "My proudest achievement is the team I've built here at Yale, and the way they work together," he says. "They're committed, and they're caring, from the lab to the clinic."

As for the Grunleys' gift, Herbst says, "It has allowed us to expand our sequencing work in lung cancer to look for new mutations that might result in patients becoming resistant to some of these target drugs while building new animal models to test new therapies. It's allowed us to explore new approaches of how to study brain metastases, and target them in lung cancer research."

The resistance to drugs that Herbst notes has now caught up with Ginny Grunley. The two good years the afatinib gave her have run their course. So, Herbst and the Grunleys are teaming up, along with other top cancer experts, to determine the next treatment solutions together. "The thing Roy does is he gives me hope that there's so much coming down the road, that this isn't by far the last thing to try," says Grunley. "I just want to make it for my daughter's wedding and my grandson's bar mitzvah, and he knows how important that is to me. He gets it. There are not enough adjectives to describe Roy. He's the best."

Yale as an institution also impresses Grunley, from Herbst's lab to the University Art Gallery, which Ken and Ginny—an amateur artist—toured with Herbst after a challenging day of treatment and consultation. "I went from discussing all these really tough issues to this museum full of beauty and history and it was wonderful," she says with admiration. "Yale has something to offer everyone, and to feel like you've been taken into their community is just very kind." A Yale hoodie is now a frequent part of her wardrobe.

The Grunleys' generous philanthropy, in sum, is one part for Roy Herbst, a physician-scientist they admire; one part for Yale, an institution that Ginny has come to love; and one part for future patients affected by the *EGFR* mutation. "I did not know about this form of cancer," Ginny says. "But now that I do, I want [Herbst and his team] to understand that I'm not just doing this for a cure for me. I think that they can eventually find a cure for this. Whether I'm there or not I'm not sure, but I know they can do it, and I will never stop supporting it."

// Endowment *(page 1)* her counsel, benefiting from her wise judgment and enthusiastic leadership.

The $3 million endowment to create the Carolyn Walch Slayman, Ph.D., Professorship came to be thanks to the generosity of Dan Adams, executive chair and head of global business development at Protein Sciences in Meriden, Connecticut; Thomas Israel, chair and chief executive officer of Ingleside Investors; Richard S. Sackler, M.D., of Greenwich, Connecticut; Jonathan M. Rothberg, Ph.D. '91, professor (adjunct) of genetics and a pioneer of next-generation gene sequencing; Bonnie E. Gould Rothberg, M.D. '94, M.P.H. '05, Ph.D. '09, assistant professor of medicine (medical oncology); and Clifford L. Slayman, Ph.D., emeritus professor of cellular and molecular physiology, who was married to Slayman for 57 years.

Carolyn Slayman was an exceptional mentor who was committed to nurturing the next generation of scientists. In 2012, for example, she was instrumental in establishing a Junior PI (Principal Investigator) Retreat—now an annual event—aimed at helping junior investigators navigate the complexities of establishing a research program. Early career investigators often sought her advice, which she readily dispensed, and she would periodically check in with them to learn if she could be of further assistance. The yet-to-be-named holder of the professorship will be a preeminent scientist at the School of Medicine who embodies the attributes and character Slayman displayed in her scientific and administrative roles, is committed to mentoring young investigators, and is supportive of advancement opportunities for women.

"Carolyn was an outstanding role model and a beloved figure," says Alpern. "She had the rare ability to motivate, inspire, and engage individual faculty at every level while at the same time carrying out a broader vision. This professorship is a fitting tribute to the indelible imprint she left upon the school and its community."

Grants and contracts awarded to Yale School of Medicine

December 2016–February 2017

Federal

Alan Anticevic, NIH, *Mapping the Longitudinal Neurobiology of Early-course Schizophrenia*, 4.8 years, $938,515 • **Sviatoslav Bagriantsev**, NIH, *Role of Piezo2 and Nav Channels in Rapidly Adapting Neuronal Mechanoreceptors*, 5 years, $1,832,030 • **Choukri Ben Mamoun**, NIH, *Development of Endochin-like Quinolones for Babesiosis Therapy*, 4 years, $2,673,329 • **Titus Boggon**, NIH, *Specificity and Regulation in a Protein Kinase Cascade Affecting the Actin Cytoskeleton*, 4 years, $1,306,492 • **Susan Busch**, NIH, *Causes and Consequences of Out-of-Network Mental Health Care Use*, 1.9 years, $478,706 • **John Carlson**, NIH, *Analysis of a Large Family of Taste Receptors*, 5 years, $1,739,466 • **Luke Davis**, NIH, *International Research Training on TB and Other Pulmonary Complications of HIV*, 1 year, $271,296 **Naomi Driesen**, NIH, *Assessing the Relationship between Cortical Oxidative Metabolism and Working Memory Deficits Under NMDA Receptor Blockade*, 2 years, $404,250 • **Deepak D'Souza**, NIH, *Characterization of Cannabinoid Induced Acute Persistent Psychosis (CIAPP)*, 2 years, $374,180 • **Carlos Fernandez-Hernando**, NIH, *Novel Insights into the Molecular and Cellular Mechanism Regulating Lipid Metabolism and Atherosclerosis*, 7 years, $5,950,413 • **Charles Fuchs**, NIH, *Dietary and Lifestyle Determinants of Colon Cancer Recurrence and Survival*, 3 years, $1,648,992 • **Nicola Hawley**, NIH, *Development of a Group Prenatal Care Intervention to Address Maternal and Child NCD Risk in American Samoa*, 2 years, $470,679 • **Ansel Hillmer**, NIH, *Multimodal Neuroimaging of Alcohol Withdrawal: The Role of Glutamate in Neural Reorganization*, 5 years, $894,401 • **Tamas Horvath**, NIH, *Feeding Driven by POMC Neurons*, 4 years, $1,944,525 • **Fahmeed Hyder**, NIH, *MRS Validation of Computational Metabolic Modeling of Human Brain Function to Determine Energetic Disruptions Underlying fMRI-derived Functional Connectivity in Degenerative or Psychiatric Disorders*, 5 years, $958,512 • **Akiko Iwasaki**, NIH, *Innate Antiviral Defense Against Vaginal Transmission of ZIKA Virus*, 2 years, $460,625 • **Daniel Jane-Wit**, NIH, *Mechanisms of Non-Canonical NF-kB Activation in Transplant Arteriosclerosis*, 3 years, $731,879 **Lucia Jilaveanu**, NIH, *Inherent Tropism and/or Immune Modulation in Melanoma Brain Metastasis*, 5 years, $1,915,780 • **Amy Justice**, NIH, *21st International Workshop on HIV and Hepatitis Observational Databases (IWHOD)*, 11 months, $58,000 • **Susan Kaech**, NIH, *Discovery of NR4A1/2 Ligands Controlling Tissue-resident Memory T (Trm) Cells*, 2 years, $460,625 • **Samuel Katz**, NIH, *Multifactor mRNA Mediated T Cell Reprogramming for Systemic Lupus Erythematosus*, 2 years, $460,625 • **Kenneth Kidd**, DOJ, *Enhancing and Sustaining the ALFRED-FROG-kb Forensic Resource*, 2 years, $1,062,736 • **Alex Kwan**, NIH, *Frontal Cortical Neural Dynamics and Chronic Social Stress*, 4.8 years, $2,093,750 **Francis Lee**, NIH, *Bone and Breast Cancer Molecular Interactions*, 4 years, $2,153,394; NIH, *Mechanobiological Mechanism for Inflammatory Bone Loss*, 1.2 years, $30,118 • **Haifan Lin**, NIH, *Translational Regulation of Embryonic Stem Cell Self-Renewal by Pumlio Proteins*, 4 years, $1,474,000 • **Arya Mani**, NIH, *The Identification and Characterization of Genetic Variants Underlying Cardiovascular Diseases*, 6.9 years, $7,035,000 • **David McCormick**, NIH, *Cortical Dynamics and Neural/Behavioral Performance*, 8 years, $4,055,354; NIH, *Mechanisms of Rapid Modulation of Auditory Responsiveness*, 5 years, $1,779,690 • **Wang Min**, NIH, *CCM3-mediated Exocytosis in Pathogenesis of Cerebral Cavernous Malformation*, 4 years, $1,934,049; NIH, *Stress Signaling Pathways Linking Endothelial Injury to Graft Arteriosclerosis*, 4 years, $1,675,000 • **Christopher Pittenger**, NIH, *Histamine Regulation of the Basal Ganglia and the Pathophysiology of Tics*, 5 years, $2,056,000 **Aleksander Rebane**, NIH, *Direct Single-molecule Observation of Regulated Snare Assembly*, 2 years, $56,478 • **Lynne Regan**, NIH, *Designed Proteins to Study and Modulate Cellular Processes*, 4 years, $1,198,993 • **David Reiss**, NIH, *IPA: David Reiss*, 9 months, $76,882 • **Matthew Rodeheffer**, NIH, *Cellular and Molecular Mechanisms of White Adipose Tissue Regulation in Development and Disease*, 4 years, $1,790,651 • **Yasmmyn Salinas**, NIH, *Identification of Pleiotropic loci for Asthma and Obesity*, 3 years, $100,108 • **Maor Sauler**, NIH, *MIF and DNA Repair in the Emphysematous Lung*, 5 years, $842,400 • **Martin Schwartz**, NIH, *Endothelial-to-Mesenchyma Transition and Atherosclerosis*, 4 years, $3,253,161 • **Mitchel Stacy**, NIH, *Radiotracer-based Imaging for Quantitative Assessment of Angiosome Perfusion Following Lower Extremity Revascularization*, 5 years, $2,093,750 • **Stephen Strittmatter**, NIH, *Genome-wide Discovery and Translational Research for Neural Repair*, 8 years, $8,135,644 • **Jane Taylor**, NIH, *Decision-making Dysfunction and Chronic Cocaine*, 5 years, $1,653,750 • **Rebecca Treger**, NIH, *Cell-intrinsic Mechanisms of Endogenous Retroviral Control*, 3 years, $105,108 • **Alda Tufro**, NIH, *Molecular Characterization of a Novel Cause of Human FSGS*, 4 years, $2,019,771 • **Andrew Wang**, NIH, *Regulation of Metabolic Programs for Host Tolerance to Inflammation*, 5 years, $783,965 **Dan Wu**, NIH, *Signaling Mechanisms and Functions Related to Patho-physiology of Vascular, Lung and Blood Systems*, 7 years, $6,386,198

Non-federal

Fuad Abujarad, Michigan State University, *An Integrated Model for Personal Assistants Research and Training (IMPART)*, 2 years, $106,394 **Anahita Amiri**, Brain & Behavior Research Foundation (formerly NARSAD), *High-throughput Quantitative Analysis of Enhancer Elements Associated with ASD*, 2 years, $70,000 • **Gustavo Angarita-Africano**, Brain & Behavior Research Foundation (formerly NARSAD), *Vitamin D as a Therapeutic Adjunct in the Stimulant Treatment of ADHD: A Proof-of-Concept Study of Stimulant-Induced Dopamine Release Using [11C]-PHNO PET in Healthy Humans*, 2 years, $70,000 • **Nancy Angoff**, Arnold P. Gold Foundation for Humanism in Medicine, *2017 Leonard Tow Humanism in Medicine Award*, 10 months, $2,000 • **Lynnette Averill**, Robert Leet and Clara Guthrie Patterson Trust, *Connectivity Networks Underlying Ketamine-induced Improvements in Suicidal Ideation*, 2 years, $90,000 • **Helene Benveniste**, Fondation Leducq, *Understanding the Role of the Perivascular Space in Cerebral Small Vessel Disease*, 5 years, $703,330 **Jonathan Bogan**, American Diabetes Association, *Regulation of Energy Expenditure by Proteolysis of TUG Protein*, 1 year, $115,000 • **Amanda Brewster**, Commonwealth Fund, *Partnerships and Performance: The Role of Health Care and Social Service Networks in Reducing Health Care Utilization and Costs*, 1.5 years, $296,720; AcademyHealth, *Linking Health Care and Social Services for Older Adults: Which Strategies Reduce Avoidable Utilization and Contain Costs?*, 1 year, $10,000 **Clemente Britto-Leon**, American Thoracic Society, *SPLUNC1: A Sputum Biomarker of Future Exacerbations in Cystic Fibrosis*, 1 year, $40,000 **Martina Brueckner**, **Daniella Teape**, American Thoracic Society, *Novel PCD Genes in Congenital Heart Disease*, 2 years, $80,000 • **Martina Brueckner**, Cincinnati Children's Hospital (NIH), *Administrative Coordinating Center: Cardiovascular Development and Pediatric Cardiac Genomics Consortia. Steering Committee Chair for the PCG*, 1 year, $40,647; Cincinnati Children's Hospital (NIH), *Administrative Coordinating Center: Cardiovascular Development and Pediatric Cardiac Genomics Consortia- CHD Brain and Genes Protocol*, 1 year, $96,866 • **Joaquin Camara-Quintana**, DePuy Synthes, *AOSpine North America: Complex Cervical Spine Surgery and Complication Management*, 3 months, $1,518 • **Lloyd Cantley**, University of Southern California, (NIH), *(Re)Building a Kidney Partnership Project Program*, 2 years, $149,999 **Michael Caplan**, GlaxoSmithKline, *Proof of Principle Experiments to Explore the Potential Applicability of Compounds Directed Against BRD4 in the Treatment of Autosomal Dominant Polycystic Kidney Disease*, 1 year, $138,816; GlaxoSmithKline, *Proof of Principle Experiments to Explore the Potential Applicability of Gene Therapy Animal Study for the Treatment of ADPKD (Autosomal Dominant Polycystic Kidney Disease)*, 1 year, $154,139 • **Manavi Chatterjee**, Brain & Behavior Research Foundation (formerly NARSAD), *Inhibitors of STEP in the Treatment of Fragile X Syndrome*, 2 years, $70,000 • **Sidi Chen**, Breast Cancer Alliance, *Discovering Inhibitory Factors of T Cell Function in Metastatic Breast Cancer Immunotherapy*, 1 year, $100,000 • **Youngsun Cho**, Brain & Behavior Research Foundation (formerly NARSAD), *Characterizing Shared Mechanisms of Cognitive and Motivational Deficits in Schizophrenia*, 2 years, $69,006 • **Stephen Collins**, Louisville Institute, *Childlessness in the Church: Exploring How Clergy Guide and Support Congregants through Infertility*, 1.5 years, $16,342 • **Zack Cooper**, National Institute for Health Care Management Foundation, *Identifying The Scope for Shopping and the Limits of Price Transparency*, 1 year, $18,000 • **Kumar Dharmarajan**, Robert Leet and Clara Guthrie Patterson Trust, *Recovery After Cardiopulmonary Hospitalization: The REACH Study*, 2 years, $90,000 • **Ronald Duman**, Allergan (inclusive of Allergan Sales LLC), *Contract # RAP-PH-02*, 2 years, $82,230; Allergan (inclusive of Allergan Sales LLC), *Contract # RAP-PH-03*, 2 years, $246,960 • **Thomas Durant**, College of American Pathologists Foundation, *Moving Averages and Machine Learning for Reducing Medical Error in the Clinical Laboratory*, 1 year, $4,960 **Jennifer Dwyer**, Thrasher Research Fund, *Efficacy of Rapid-Acting NMDA Antagonist for Treatment of Adolescent Depression*, 2 years, $25,000 **Marie Egan**, **Jonathan Koff**, Cystic Fibrosis Foundation Therapeutics (CFFT), *Yale Cystic Fibrosis Therapeutic Development Center*, 1 year, $72,549 **Barbara Ehrlich**, ILSI Health and Environmental Sciences Institute, *Optimizing Treatment for Breast Cancer Patients*, 2 years, $50,000 • **Ayman El-Guindy**, American Cancer Society, *Regulation of Epstein-Barr Virus Late Gene Expression*, 4 years, $792,000 • **Shawn Ferguson**, The Bluefield Project to Cure Frontotemoporal Dementia, *Role of Lysosomes in Progranulin-linked Frontotemporal Dementia*, 1 year, $170,000 • **Sjoerd Finnema**, Brain & Behavior Research Foundation (formerly NARSAD), *PET Measurement of Ketamine-induced Changes in Synaptic Density in Patients with Depression*, 2 years, $70,000 • **Richard Flavell**, Washington University in St. Louis (NIH), *Towards True Precision Oncology: Validation of a Comprehensively Humanized, Autologous Mouse Model*, 3 years, $277,428 • **John Forrest**, **Sheela Shenoi**, Doris Duke Charitable Foundation, *International Clinical Research Fellowships for Medical Students*, 2.5 years, $462,000 • **Patrick Gallagher**, Jackson Laboratory (NIH), *Comprehensive Mapping of Long-range Chromatin Interactions in Human and Mouse Genomes*, 1 year, $121,709 **Mark Gerstein**, University of Massachusetts (NIH), *EDAC: ENCODE Data Analysis Center*, 1 year, $392,000 • **Emily Gilmore**, University of Southern California (NIH), *The Epilepsy Bioinformatics Study for Antiepileptogenic Therapy (EpiBioS4Rx)*, 4.9 years, $38,800 • **Peter Glazer**, **Marie Egan**, **W. Mark Saltzman**, PNA Innovations (PNAI), *Modified PNAs to Develop Gene Editing Therapeutics for Hematopoietic Blood Disorders and Cystic Fibrosis*, 2 years, $3,000,000 • **Melissa Grafe**, University of Massachusetts Medical School (NIH), *Rethinking Early Neurosurgery: The Harvey Cushing Collection*, 5 months, $7,689 • **David Hafler**, Broad Institute (NIH), *A Catalog of Cell Types and Genomic Elements in Tissues, Organoids and Disease*, 4 years, $134,000; Benaroya Research Institute, *Transcriptional Profiling of Fat-resident Regulatory T Cells in MS*, 1 year, $125,556 **Tamas Horvath**, Monash University, *The Dorsomedial Hypothalamic Leptin Receptor Expressing Neurons in the Control of Metabolism, Glucose Tolerance and Cardiovascular Control*, 1 year, $18,833; Biogen MA, *Modulation of AB Pathology by TREM2*, 4 months, $77,834 • **Janice Hwang**, American Diabetes Association, *Investigating Brain Responses to Hyperglycemia*, 3 years, $595,317 • **Lucia Jilaveanu**, American Cancer Society, *Inherent Tropism and/or Immune Modulation in Melanoma Brain Metastasis*, 1 months, $14,650 • **Ayana Jordan**, University of California, San Francisco (NIH), *Mentoring Early-Career Scientists for Drug Abuse Research Careers*, 10 months, $27,000 • **Leonard Kaczmarek**, Autifony Therapeutic, *Development of Kv3 Channel Modulators for Treatment of Tinnitus*, 1 year, $159,039 • **Kristopher Kahle**, Hydrocephalus Association, *Innate Immunity and CSF Production in Post-hemorrhagic Hydrocephalus*, 1 year, $50,000 • **Benjamin Kelmendi**, Brain & Behavior Research Foundation (formerly NARSAD), *The Effects of MDMA on Functional Connectivity in Posttraumatic Stress Disorder*, 2 years, $69,089 **Richard Kibbey**, Monash University, *The Role of PEPCK-M in Hepatic and Extra-hepatic Glucose Production*, 1 year, $3,826 • **Anthony Koleske**, Breast Cancer Alliance, *Profiling of Circulating Tumor Cells to Identify Targets for Adjuvant Therapy in Metastatic Triple Negative Breast Cancer*, 1 year, $100,000 • **Priti Kumar**, American Foundation for AIDS Research (amfAR), *Targeted Inactivation of Integrated HIV through Host Cell DNA Repair Pathways*, 1 year, $200,000 • **Gary Kupfer**, Hyundai Motor America, *Yale Phase 1 Clinical Trial Program*, 1 year, $50,000 • **Gary Kupfer**, **Peter Glazer**, Fanconi Anemia Research Fund, *Use of Triplex-forming PNAs as a Strategy for Correction of the FA Phenotype*, 1 year, $112,500 • **Alex Kwan**, Simons Foundation, *Learning-related Activity in the Autistic Brain*, 1 year, $70,000 • **Francis Lee**, Musculoskeletal Transplant Foundation, *Biological Modification of Structural Bone Allografts*, 6 months, $100,139 • **Rafael Lefkowitz**, Association of Occupational and Environmental Clinics, *Development of Flood Health Hazard Educational Resources Addressing Needs of Gulf Coast Community*, 9 months, $25,000; Association of Occupational and Environmental Clinics, *Development of a Continuing Education Module in Environmental Medicine on Possible Flood Related Health Concerns in the Gulf Coast*, 9 months, $25,000 **Judith Lichtman**, American Heart Association (Founders Affiliate), *Post-Acute Care Services and Outcomes Among Elderly Stroke Patients*, 2 years, $154,000 • **Janghoo Lim**, Kennedy's Disease Association, *The Role of VCP in the Pathogenesis of Kennedy's Disease*, 1 year, $50,000 • **Yi-Hwa Liu**, Connecticut Innovations, *Development and Integration of Novel SPECT and PET Quantitative Analysis Tools for Sympathetic and Molecular Nuclear Cardiac Imaging*, 3 years, $500,000 **Robert Makuch**, Boehringer Ingelheim International GmbH, *CFDA Drug Registration and Regulatory Affairs Course for Boehringer*, 3 years, $225,000 • **Nikhil Malvankar**, Charles H. Hood Foundation, *Targeting Bacterial Infections by Imaging Electrical Interactions Between Host Surface and a Pathogen*, 2 years, $150,000 **Jessica Mariani**, Brain & Behavior Research Foundation (formerly NARSAD), *Exploring Trideimensional Chromatin Interactions in ASD-derived Brain Organoids*, 2 years, $70,000 • **Scott Miller**, University of Utah, *Using Numerical Analysis Tools to Design and Study Chiral Catalysts*, 4 years, $255,532 • **Pramod Mistry**, Laboratorio Chamoles, *Biomarkers and Genetic Mutations in Gaucher Disease Population in Argentina*, 1 year, $173,713 **Dennis Moledina**, Robert Leet and Clara Guthrie Patterson Trust, *Early Non-invasive Diagnosis of Human Acute Tubulo-Interstitial Nephritis (AIN) with Cytokines Representing T-helper Cell Pathway*, 2 years, $90,000 • **Janitza Montalvo-Ortiz**, Brain & Behavior Research Foundation (formerly NARSAD), *Epigenetics of Depression in Early Sexually Abused Females*, 2 years, $70,000 • **Don Nguyen**, AstraZeneca UK Limited, *Therapies for Brain Metastasis in Lung Cancer*, 3 years, $1,726,595 • **Linda Niccolai**, State of CT Dept. of Public Health (DHHS), *Connecticut Emerging Infections Program*, 5 years, $2,847,156 • **Noah Palm**, Artizan Biosciences, *Exploiting the Host Immune Response to Identify and Treat Microbiota-Driven Inflammatory Diseases*, 11 months, $603,757; Richard & Susan Smith Family Foundation, *A Universal Genetic Toolkit to Illuminate Host-Microbiota Interactions*, 3 years, $300,000 **Abhijit Patel**, **Alessandro Santin**, Honorable Tina Brozman Foundation, *Early Detection of Ovarian Cancer via Analysis of Genomic Alterations in DNA and RNA from Multiple Sources in Blood*, 2 years, $200,000 • **Jordan Peccia**, University of Tulsa, *Research to Practice: Translating the Science of the Microbiology of the Built Environment Program*, 1.5 years, $23,530; University of Tulsa, *Development, Calibration, and Validation of a Simple Tool for Guiding Mold Inspection and Remediation in U.S. Homes*, 3 years, $324,876 **Rachel Perry**, **Gerald Shulman**, Augusta University (Formerly Georgia Regents University) (NIH), *Developing a Stable Isotope Tracer Method to Measure All Key Hepatic Fluxes in Mice*, 8 months, $75,000 • **Rachel Perry**, Augusta University (Formerly Georgia Regents University), *Development of a Stable Isotope Tracer Method to Measure all Key Hepatic Flux Rates in Mice*, 8 months, $75,000 **Zorana Pringle**, **Marc Brackett**, Fundacion Marcelino Botin, *Creativity, Emotion, and the Arts*, 1 year, $167,799 • **Asghar Rastegar**, Brigham and Women's Hospital (DHHS), *Resilient and Responsive Health Systems Initiative*, 1 year, $330,518 **David Reiss**, University of Oregon (NIH), *The Early Growth and Development Study Pediatric Cohort*, 6 months, $22,681 • **David Rimm**, AstraZeneca, L.P., *Standardization of PD-L1 Assays*, 4 months, $406,768 • **Matthew Rodeheffer**, Monash University, *Identification of Novel Human Adipocyte Progenitor Cell Populations*, 1 year, $15,941 • **Helena Rutherford**, Bial Foundation, A *Psychophysiological Perspective of the Transformative Experience of Pregnancy*, 2 years, $45,484 • **Nicholas Ryan**, Harvard University, *Decreasing Children's Exposure to Indoor Air Pollution through Modern Cookstoves: A Proposed Evaluation of India's Landmark Gas-stove Subsidy Program*, 1.1 years, $59,323 **Emmanuelle Schindler**, Heffter Research Institute, *Safety and Efficacy of Psilocybin for the Treatment of Cluster Headache*, 3 years, $68,200 • **Dongju Seo**, Brain & Behavior Research Foundation (formerly NARSAD), *Neurobiology of Stress, Depression, and Comorbid Alcohol Abuse*, 2 years, $70,000; Peter F. McManus Charitable Trust, *Neural Circuits for Stress Resilient Coping and Hazardous Drinking*, 1 year, $50,000 • **Nikhil Singh**, Robert Leet and Clara Guthrie Patterson Trust, *Cellular and Molecular Characterization of Human Acute Kidney Injury*, 2 years, $90,000 • **Megan Smith**, Ford Foundation, *MOMS Evaluation on Maternal Depression*, 1 year, $250,000 • **Derek Steinbacher**, DePuy Synthes, *Craniomaxillofacial/Orthognathic Research Fellowship*, 1.5 years, $70,000 • **Michael Strambler**, Spencer Foundation, *Partnering to Support Early Childhood Dual Language Learners*, 3 years, $399,989 • **Toral Surti**, Brain & Behavior Research Foundation (formerly NARSAD), *Sleep-Dependent Learning and Sleep Spindles in Schizophrenia*, 2 years, $70,000 **Seyedtaghi Takyar**, American Thoracic Society, *A Cell-specific Endothelial MicroRNA Adenylation Pathway Regulates Th2 Inflammation in Asthma*, 2 years, $80,000 • **Mary Tinetti**, Institute for Healthcare Improvement, *Creating Age-Friendly Health Systems Prototype*, 11 months, $45,628 **Jeffrey Turner**, University of Washington, Seattle (NIH), *Biological Determinants of Peritoneal Dialysis Outcomes*, 1.4 years, $8,983 • **Michael Van der Linden**, University of Hartford, (*Michael Van Der*

Linden) *CubeSat Project*, 7 months, $1,000 • **Sten Vermund**, FHI 360 (NIH), *International Research Training on TB and Other Pulmonary Complication of HIV*, 10 months, $98,101; Harvard School of Public Health (NIH), *New Methods for the Design and Evaluation of Large HIV Prevention Interventions*, 4 months, $13,988 • **Noemi Vila**, American Heart Association, *Functional and Physiological Role of ANGPTL4 During Atherosclerosis*, 3 years, $231,000 • **Lisa Walke**, University of Colorado Denver, *Practice Change Leaders for Aging and Health*, 1 year, $5,000 • **Shiyi Wang**, **Cary Gross**, Patient-Centered Outcomes Research Institute, *Comparative Effectiveness Analyses Among Conservative Treatment Strategies For Ductal Carcinoma In Situ*, 2.1 years, $438,751 • **Stephen Waxman**, European Commission, *Pain-NET*, 4 years, $279,705 • **Samuel Wilkinson**, Brain & Behavior Research Foundation (formerly NARSAD), *Cognitive Behavior Therapy to Sustain the Antidepressant Effects of Ketamine: A Randomized Controlled Trial*, 2 years, $69,804; Robert Leet and Clara Guthrie Patterson Trust, *Examining the Efficacy of Cognitive Behavior Therapy to Sustain the Antidepressant Effects of Intravenous Ketamine*, 2 years, $90,000 • **Kuanlin Wu**, American Heart Association (Founders Affiliate), *PDGF Signaling Regulates Integrin Activation Through Arg*, 2 years, $51,900 • **Yang Yang**, Colleen's Dream Foundation, *Dissecting Mitochondrial Function in Ovarian Cancer Cells by Super-Resolution Microscopy*, 1 year, $10,000 • **Gihyun Yoon**, Brain & Behavior Research Foundation (formerly NARSAD), *Intranasal Insulin for Treating PTSD: A Double-blind, Placebo-controlled Crossover fMRI Study*, 2 years, $60,000

// Benefactor *(page 1)* them with the resources and intellectual freedom to pursue innovative research."

Wallace understood the financial challenges that research entails and the need for philanthropic support to fuel scientific discovery. "To have medical progress, you have to feed it money. It's the nature of the beast. Running labs, doing surveys, it's all expensive," Wallace said in 2006. "But I think we're at a point in medicine where we're making leaps and bounds."

For Hugh S. Taylor, M.D., chair of the Department of Obstetrics, Gynecology & Reproductive Sciences, this includes developing a new test and therapies for endometriosis, discovering environmental agents that can affect fetal development, understanding the effects of cross-gender hormone therapy, and demonstrating the benefits of transdermal estrogens on sexual function in menopausal women. Taylor, who holds the Anita O'Keeffe Young Professorship, established in honor of a friend of the Wallaces to promote women's health, says, "The Wallaces' support enabled me to devote time to all aspects of women's health, not only delivering care to patients but also being an advocate and doing novel research that I wouldn't have been able to do otherwise, bringing new understanding of women's health diseases."

Lucian V. Del Priore, M.D., Ph.D., chair of the Department of Ophthalmology & Visual Science, who joined Yale in 2016, says that the Robert R. Young Professorship endowed by the Wallaces was instrumental in his recruitment, allowing for protected research time, as well as time to mentor medical students who are interested in ophthalmology. "We need a generation of physicians who can push the envelope," he says, noting that the vast majority of his patients benefit from advances that have been developed during the course of his career. "We have to train people who can think outside the box and approach problems in a new way." Medical students under his guidance have conducted research on the thinning of the retina and the generation of stem cells from skin biopsies in patients with macular degeneration, and the use of medical marijuana in patients with poorly controlled glaucoma.

Wallace's ties with Yale date back to his undergraduate days, when he resided at Branford College. His studies were interrupted by World War II, during which he served as an officer in the 1st Infantry Division and was awarded the Purple Heart. He received his bachelor's degree from Yale's School of Engineering in 1948, but quickly decided he was more suited to the law, graduating from Harvard Law School in 1951.

(Left to right): Yale benefactors David Wallace and Jean McLean Wallace, who endowed six School of Medicine professorships, are shown with Dean Robert J. Alpern, who says innovative research has sprung from their generosity.

Reflecting back on a career that included stints at Allegheny Corporation, United Brands (now Chiquita Banana), Piper Aircraft, Bangor-Punta, and Todd Shipyards, Wallace put his time at Yale above them all, calling it his greatest achievement. Just prior to his 50th year reunion, Wallace and his wife donated $9 million to renovate Branford College, whose Gothic-style York Street wing is now called Wallace Hall. In 2004, he was awarded a Yale Medal, the highest award presented by the Association of Yale Alumni. "David loved Yale from the moment he arrived as an undergraduate," says Jean Wallace. "It was his pleasure and honor to be able to support both the university at large and the School of Medicine."

PROFESSORSHIPS ENDOWED BY THE WALLACE FAMILY

Jean and David W. Wallace Professor of Comparative Medicine
Tamas L. Horvath, D.V.M., Ph.D., chair, Department of Comparative Medicine; professor of neuroscience and of obstetrics, gynecology & reproductive sciences

David W. Wallace Professorship
Now vacant. Most recently held, until 2016, by Ruslan M. Medzhitov, Ph.D., Sterling Professor of Immunobiology

Fergus F. Wallace Professor of Genetics
Antonio J. Giraldez, Ph.D., chair, Department of Genetics

Jean McLean Wallace Professor of Pediatrics
George Lister, M.D., professor of cellular and molecular physiology

Robert R. Young Professor of Ophthalmology and Visual Science
Lucian V. Del Priore, M.D., Ph.D., chair, Department of Ophthalmology & Visual Science

Anita O'Keeffe Young Professor of Women's Health
Hugh S. Taylor, M.D., chair, Department of Obstetrics, Gynecology & Reproductive Sciences

Yale researcher is a new member of National Academy of Medicine

Arnsten is recognized for work including mechanisms of brain vulnerabilities

Amy F.T. Arnsten, Ph.D., professor of neuroscience, psychiatry, and psychology, and at the Yale Child Study Center, has been elected to the National Academy of Medicine (NAM), which recognizes individuals who have demonstrated outstanding professional achievements and commitment to service. NAM membership is widely considered one of the highest honors in the fields of health and medicine.

Arnsten's lab discovered molecular mechanisms that govern activity in the brain's highest-order circuits and helped explain why neurons are vulnerable to disorders such as schizophrenia and Alzheimer's disease. Her research has led to two treatments now in widespread clinical use: guanfacine (Intuniv®) for treating childhood cognitive disorders such as attention deficit hyperactivity disorder (ADHD) and autism, and prazosin for the treatment of post-traumatic stress disorder (PTSD).

"It is a great honor and a personal pleasure to be elected to the National Academy of Medicine," Arnsten says. "As my lab does research that is quite different from many neuroscientists, it is particularly moving to be recognized by one's peers."

Amy Arnsten

Arnsten received her Ph.D. in neuroscience from the University of California, San Diego, in 1981. She did postdoctoral research with Susan D. Iversen, Ph.D., at Cambridge University in the UK, and at Yale with the late Patricia Goldman-Rakic, Ph.D., Eugene Higgins Professor of Neuroscience. She joined the School of Medicine faculty in 1986.

The National Academy of Medicine, established in 1970 as the Institute of Medicine, is an independent organization of eminent professionals from diverse fields including health and medicine; the natural, social, and behavioral sciences; and beyond. It serves alongside the National Academy of Sciences and the National Academy of Engineering as an adviser to the nation and the international community.

Yale Cancer Center director led trials for FDA-approved drug

The first immunotherapy treatment approved to treat advanced stomach cancer

A drug whose clinical testing was led by Charles S. Fuchs, M.D., M.P.H., Richard Sackler and Jonathan Sackler Professor of Medicine (Medical Oncology) and director of Yale Cancer Center, has become the first approved immunotherapy treatment for advanced stomach cancer.

The drug, pembrolizumab (Keytruda®), was approved by the U.S. Food and Drug Administration (FDA) for adult patients diagnosed with advanced stomach cancer or gastroesophageal junction cancer showing PD-L1 positive tumors, in cases where the cancer has progressed despite two or more prior lines of treatment with standard therapies. Pembrolizumab works by increasing the ability of the body's immune system to help detect and fight tumor cells.

The FDA made its approval on an accelerated basis, deciding to forego Phase III clinical trials after a Fuchs-led Phase II trial of pembrolizumab had demonstrated the value of the drug for patients with the PD-L1 mutation.

Persuasive data from the trial, called KEYNOTE-059, were presented last September at the European Society for Medical Oncology (ESMO) annual meeting. Sixteen percent of PD-L1-positive patients had achieved at least a partial response to the treatment, including several patients whose tumors completely disappeared. Some of those responses lasted for what were considered long periods of time, ranging from several months to more than a year.

Charles Fuchs

"The responses really are quite robust and far longer than you would see with any cytotoxic chemotherapy agent," says Fuchs.

Prior to pembrolizumab, the only FDA-approved drug for non-responsive stomach cancer was ramucirumab (Cyramza®), a monoclonal antibody whose benefits to patients have been classified as "modest" by the National Cancer Institute.

Fuchs says progress against advanced stomach cancer has been less robust than he would like because very few drugs have been developed to address the particular biology of the cancer. "Most commonly," he explains, "we use anticancer drugs that are used to treat other cancers and apply them to patients with stomach cancer because we just don't have dedicated efforts to develop drugs specific for stomach cancer." That is a deficit he hopes to continue to rectify.

Chair named for Radiology & Biomedical Imaging

Extensive experience in the US and UK shapes plans for research and clinical care

Rob Goodman

Rob Goodman, MB BChir, M.B.A., has been appointed chair of the Department of Radiology & Biomedical Imaging and chief of Radiology and Biomedical Imaging at Yale New Haven Hospital. Goodman, professor and section chief of pediatric radiology served for six years as vice chair for clinical affairs for the department and recently completed two years as its executive vice chair. Before his appointment took effect on Jan. 1, he had served as interim chair.

"As chair, Rob will build upon his many experiences in radiology to enhance and integrate the department's world-class research and clinical strengths," says Robert J. Alpern M.D., dean and Ensign Professor of Medicine. "I'm delighted that he will lead the department and look forward to working with him."

Research areas on which Goodman plans to focus include such areas as novel MR pulse sequences, functional MRI, MR spectroscopy, novel PET tracers, and 3D image manipulation. By including industry partners, he is eager to expand the department's translational research program to help convert basic science discoveries into clinical applications that improve patient care.

Goodman joined Yale in 2004 from the John Radcliffe Hospital in Oxford, UK, where he was lead clinician for its radiology department. When he came to the United States, he was struck by the marked differences in radiation awareness between the two countries, which is especially relevant in pediatric radiology due to children's susceptibility to the effects of radiation. He has since played a major role in the movement to reduce radiation exposure from CT scans in children, as well as adults.

During his tenure at Yale, Goodman has overseen the expansion of pediatric radiology services, spearheaded the installation of a dedicated pediatric MRI scanner at Yale New Haven Children's Hospital, implemented a critical test result reporting system, and identified mechanisms to improve the radiology peer review process. Building upon his experience implementing a Picture Archive and Communication System (PACS) in the UK, he now will be involved in the implementation of a new enterprise PACS across Yale New Haven Health. As well as improving clinical efficiency, this cutting-edge tool will have the potential to augment departmental machine learning/artificial intelligence research.

"What I find inspiring about radiology is that we touch every medical and surgical specialty," says Goodman. "Any improvements we make have a trickle-down effect throughout the entire medical enterprise."

Goodman obtained his medical degree from Cambridge University in 1988 and an M.B.A. in health care from Yale in 2017. Upon completing his residency at the Central Oxford Hospitals in the UK, he did a fellowship in pediatric radiology at the Hospital for Sick Children in Toronto. He is the Pediatric Community of Practice President for the American Institute for Ultrasound in Medicine, which recently elected him to its Board of Governors.

New program makes the addiction crisis a priority

A collaboration to treat patients, train practitioners, and investigate addiction

ROBERT A. LISAK

David Fiellin has been put in charge of the multidisciplinary Yale Program in Addiction Medicine, established to serve clinical, educational, and research needs as the United States faces rising levels of substance abuse and addiction.

The School of Medicine's Section of General Internal Medicine has established the Yale Program in Addiction Medicine, a multidisciplinary clinical, educational, and research program. The program is intended to enhance Yale's portfolio of state-of-the-art addiction research and patient care, while increasing the pipeline of physicians trained in evidence-based strategies to tackle the opioid crisis and other addiction-related health issues.

The program will emphasize research on topics that include improving the recognition of, and access to treatment for, substance use disorders in primary care, emergency departments, and hospitals; addressing the quality of addiction treatment; and technology-based prevention in youth.

The Yale Program in Addiction Medicine includes collaborations with Yale School of Public Health and the Departments of Emergency Medicine and Psychiatry. Its director is David A. Fiellin, M.D., professor of medicine (general medicine), of emergency medicine, and of public health.

"Since the use of opioid, tobacco, alcohol, marijuana, and other substances is common in general medical settings, and often goes undetected and untreated, we need a medical system that does a better job of making sure that all health care professionals implement effective prevention, screening, treatment, or referral practices, and treat addiction as they do other medical conditions," Fiellin says.

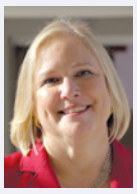
The establishment of the program comes at a time when addiction to opioids and other substances is widely seen as a crisis. Drug overdose deaths nearly tripled during 1999–2014, according to the Centers for Disease Control and Prevention. From 2014 to 2015, the death rate from synthetic opioids increased by 72.2 percent, and heroin death rates increased by 20.6 percent. Death rates rose across all demographic groups and regions, and in many states.

Yale School of Medicine was one of the first medical institutions to establish an accredited fellowship program in addiction medicine. It began accepting trainees in 2015.

In addition, Patrick G. O'Connor, M.D., the Dan Adams and Amanda Adams Professor of General Medicine and chief of general internal medicine, and Gail D'Onofrio, M.D., chair and professor of emergency medicine, led the effort to make addiction medicine an official medical subspecialty in 2016. This landmark change will increase the number of physicians in a variety of primary care and other medical specialties, including psychiatry, to be trained and certified as specialists in addiction prevention and treatment.

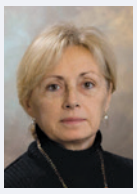
"The current opioid epidemic, along with the high prevalence of a variety of substance use disorders, demands innovative and creative approaches in prevention, treatment, and medical education," says O'Connor. "Yale is uniquely positioned to provide national leadership in this critical area."

Awards & Honors



Hilary P. Blumberg, M.D., John and Hope Furth Professor of Psychiatric Neuroscience and professor of psychiatry, in the Child Study Center, and of radiology and biomedical imaging, has been awarded the Colvin Prize for Outstanding Achievement in Mood Disorders Research, by the Brain & Behavior Research Foundation.

Hal Blumenfeld, M.D., Ph.D., the Mark Loughridge and Michele Williams Professor of Neurology and professor of neuroscience and of neurosurgery, has received a Jacob Javits Neuroscience Investigator Award from the National Institute of Neurological Disorders and Stroke, recognizing him as a scientist with "superior competence and outstanding productivity." Blumenfeld also has received the American Epilepsy Society's 2017 Clinical Scientist Research Recognition Award.



Sonia Caprio, M.D., professor of pediatrics (endocrinology) has received the Samuel J. Fomon Nutrition award from the American Academy of Pediatrics, for outstanding achievement in research relating to the nutrition of infants and children.

Lieping Chen, M.D., Ph.D., United Technologies Corporation Professor in Cancer Research and professor of immunobiology, of dermatology, and of medicine (medical oncology), has received the Warren Alpert Foundation Prize for transformative discoveries of anti-PD-1/PD-L1 cancer immunotherapy.

Roberta L. Hines, M.D., chair and Nicholas M. Greene Professor of Anesthesiology, has received the SEA/Duke Award for Excellence and Innovation in Anesthesia Education, from the Society for Education in Anesthesia.

Kevin N. Sheth, M.D., associate professor of neurology and of neurosurgery, has received the Derek Denny-Brown Young Neurological Scholar Award from the American Neurological Association.