

New year brings a new Yale Cancer Center director

Incoming leader plans to direct advances in research as well as clinical practice

Charles S. Fuchs, M.D., M.P.H., an internationally renowned expert in gastrointestinal cancers and cancer epidemiology, has been named director of Yale Cancer Center (YCC), one of just 47 National Cancer Institute-designated comprehensive cancer centers in the nation and the only one in Connecticut, and physician-in-chief of Smilow Cancer Hospital at Yale New Haven.

Known for his research that spans the prevention, biology, and

treatment of gastrointestinal cancers, Fuchs has spearheaded clinical trials that have resulted in FDA approval of new drugs for patients. He established one of the first large-scale molecular epidemiology laboratories, characterizing an array of molecular events in thousands of tumors. This ongoing project, which has yielded valuable information about patients both before and after cancer diagnosis, led to the finding that healthy individuals who took aspirin had a significantly lower risk of developing colorectal cancer. It also led to the identification of a molecular tumor profile that is connected to better patient outcomes with aspirin use

after diagnosis, uncovered energy balance pathways that contribute to the development and progression of cancer, and identified new potential targets for cancer therapy.

“Charlie’s scientific renown and contributions, which include discoveries about the underpinnings of cancer, insights into prevention, and developing new therapies, speak for themselves,” says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. “His considerable experience will be an asset to the cancer center as we build upon the solid foundation that already is in place.”

Fuchs received his medical degree from Harvard Medical School in 1986.



Charles Fuchs

He completed his medical residency at Brigham and Women’s Hospital, where he also served as chief medical resident, and completed his medical oncology fellowship at Dana-Farber Cancer

Institute. In 1994, he received his M.P.H. from Harvard School of Public Health. He has been professor of medicine at Harvard Medical School and chief of the gastrointestinal oncology division and the Robert T. and Judith B. Hale Chair in Pancreatic Cancer at // **Cancer Center** (page 5)

In memoriam: Carolyn Walch Slayman, Ph.D.

Renowned geneticist and administrator was a pioneer among women in science

Carolyn Walch Slayman, Ph.D., deputy dean for academic and scientific affairs at the School of Medicine, Sterling Professor of Genetics, and professor of cellular and molecular physiology, died on December 27 at Yale New Haven Hospital. She was 79, and had been undergoing treatment for recurrent breast cancer.

Slayman was a faculty member and leader at the medical school for almost 50 years. While she was steadfastly humble about her accomplishments, her career was characterized by a series of firsts. She was the first woman to head a department at Yale School of Medicine when she was named chair of the Department of Human Genetics (now Genetics) in 1984. In 1995, she became the school’s first deputy dean for academic and scientific affairs, and the first woman to hold a deputy deanship.

“It is difficult to overstate Carolyn’s influence on the School of Medicine and the many individuals



TERRY DAGRAZI

who have passed through our doors,” says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. “We depended on her judgment and wisdom to help guide every major decision.”

After graduating from Swarthmore College in 1958 with highest honors in biology and chemistry, Slayman earned a Ph.D. in biochemical genetics under Nobel Laureate E.L. Tatum at Rockefeller University, where she was the only woman in her class. As a National Science Foundation Fellow, Slayman

Carolyn W. Slayman, a member of the Yale School of Medicine faculty for nearly 50 years, is warmly remembered as a pioneering woman of science, skilled administrator, and mentor to young scientists.

did postdoctoral work in membrane biochemistry at Cambridge University.

Following a brief stint as assistant professor of biology at Western Reserve University (now Case Western Reserve), she joined Yale as assistant professor in the departments of microbiology and physiology in 1967. She helped to // **Slayman** (page 7)

School of Public Health welcomes a new dean



Sten Vermund

Sten H. Vermund, M.D., Ph.D., an expert on HIV/HPV science and cervical cancer prevention, has been named dean of the School of Public Health.

Vermund comes to Yale in February

after serving since 2005 on the faculty of Vanderbilt University School of Medicine, where he was professor of pediatrics, medicine, health policy, and obstetrics and gynecology; the Amos Christie Chair in Global Health; director of the university-wide Vanderbilt Institute for Global Health; and vice president for global health of the Vanderbilt University Medical Center.

“In the mid-1980s, Dr. Vermund helped establish an adolescent health clinic that provided some of the earliest care to HIV-infected youth in New York City,” noted Yale President Peter Salovey, Ph.D. ’86, and Dean and Ensign Professor of Medicine Robert J. Alpern, M.D., // **Public Health** (page 7)

2 Lifelines

William C. Sessa demonstrates that the veins and arteries of the cardiovascular system are far more than passive plumbing.

3 Cancer as a complex system

A multidisciplinary team at West Campus has begun intensive study of the biological systems that govern the spread of cancers.

5 An alumnus shows his gratitude

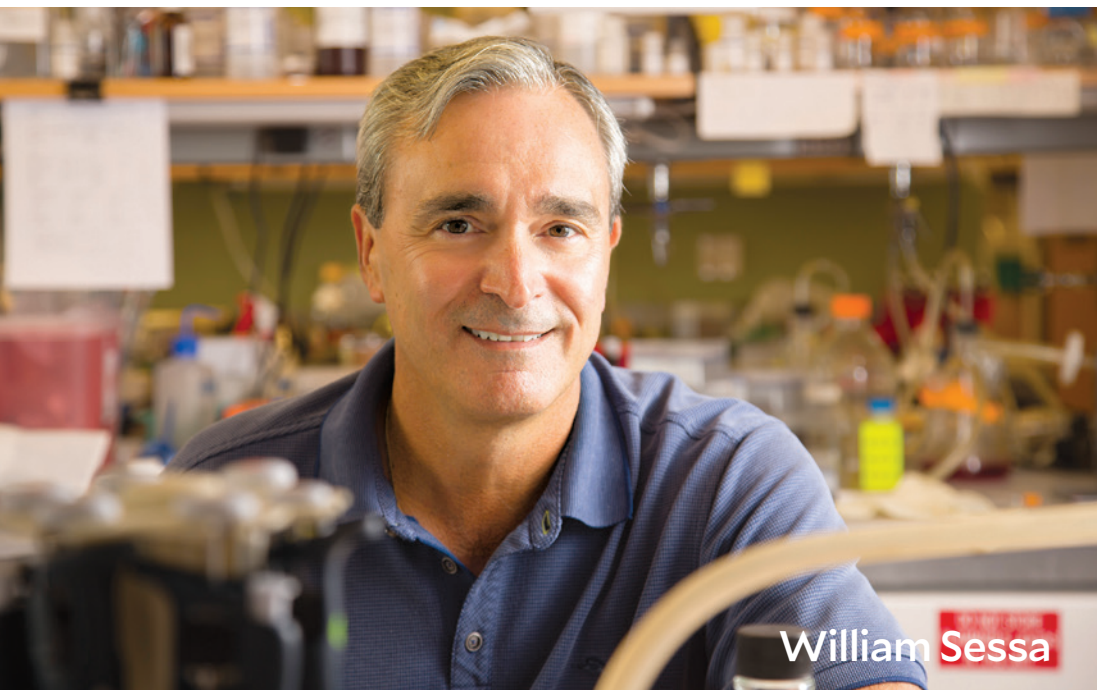
Michael Singer, M.D. ’02, Ph.D. ’00, says Yale was the catalyst for much success. His gift honors a mentor and a classmate.

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William Sessa

HAROLD SHAPIRO

William C. Sessa has been a leading figure in the transformation of vascular biology from a near-afterthought to an essential aspect of biomedical research. Sessa's discoveries have added to the understanding of the role of veins and arteries in numerous biological functions, especially their contribution to this country's leading cause of death, cardiovascular disease.

Revealing the vascular system

Investigator demonstrates that veins and arteries are far more than passive plumbing

In the late 1980s, William C. Sessa, PH.D., then a doctoral candidate in pharmacology, read an editorial by Nobel Laureate George E. Palade, M.D., professor, chair, and founder of Yale's then-named section of cell biology. Palade argued that long-held assumptions about the biology of the endothelium, or inner lining, of blood vessels, had become questionable, and he urged investigators to probe more deeply into the unknowns of the vascular system.

Sessa, now Alfred Gilman Professor of Pharmacology and professor of medicine, took Palade's words to heart. He wanted to know how particles of LDL (low-density lipoprotein) cholesterol morphed from floating hitchhikers in the bloodstream to permanent lodgers in artery walls, where their effect on health can be profound.

Blood vessels had first caught Sessa's attention when he was an undergraduate at Philadelphia College of Pharmacy and Sciences. As part of a research lab course, Sessa measured how the brain controls blood pressure, and he came away full of curiosity.

During that era, he says, science characterized the body's vasculature as a network of passive garden hoses that merely shuttled blood and nutrients throughout the body. Three decades of inquiry have broadened that view.

"Vascular biology in the present world is really how blood vessels control different aspects of organs—particularly the brain, heart, and kidney," says Sessa, director of the Vascular Biology and Therapeutics Program since 2007. The control, he explains, starts with biochemical changes within endothelial cells that protect blood vessels against potential antagonists, especially lipids.

While completing his doctorate in pharmacology at New York Medical College, Sessa crossed paths with Sir John R. Vane, D.PHIL., who had won the 1982 Nobel Prize in physiology or medicine for discovering how aspirin works. "I wrote to him and said I would love to do a postdoc in your lab," Sessa recalls. Soon the New Jersey native was working under Vane in London, studying the enzymatic pathway through which endothelial cells produce nitric oxide, which relaxes blood vessel walls.

"All endothelial cells make nitric oxide, and we know that with almost every cardiovascular disease, they stop making it to some degree," Sessa says. During his second postdoctoral fellowship, at the University of Virginia, Sessa cloned the gene for the enzyme that makes nitric oxide. "It was very competitive," he says. "Within three months, three papers came out from major institutions and I was the lone postdoc working on it."

When he started his lab at Yale in 1993, Sessa wanted to learn which molecule regulates the gene and enzyme responsible for generating nitric oxide via the endothelial lining of vessels.

More recently, based on his initial curiosity provoked by the Palade article, he has worked to identify undiscovered pathways through which LDL can damage blood vessels beyond those on which statins act. In June, Sessa received a \$1 million Merit Award from the American Heart Association that will help him pursue that line of inquiry. On Nov. 21, *Nature Communications* published his first report of progress, in which he described the protein ALK1 as a promising target for reducing atherosclerosis, which remains this country's leading cause of death.

Sessa also took a recent sabbatical, the first in his more than 20 years at Yale. In the fall of 2015, he went to Cambridge, Mass., where Pfizer made him interim director of its global cardiovascular and metabolism unit. The role forced Sessa to think in a new way about pharmaceutical development, involving him in decisions to initiate, augment, or terminate research projects. "It is more complex than you think it is," Sessa says. "There are so many moving parts and very tight timelines in drug development."

He will apply lessons he took from industry to CavtherRx, a biotech company he founded in 2014 to develop a drug for the orphan disease uveitis, inflammation of the eye wall. "I've sharpened what we need to do to be successful therapeutically," he says. He also says he has renewed appreciation for the freedom of inquiry he enjoys at his true professional home—his lab at Yale.

A new executive chair for Yale institutional review boards is chosen

John D. Roberts, M.D., professor of medicine and medical director of the Yale New Haven Hospital Adult Sickle Cell Program, has been selected as executive chair of Yale University's Institutional Review Boards (IRBs), the committees that work to ensure that all Yale human subjects research is conducted ethically and according to governmental and university requirements. His new role begins as of the new year, with the retirement of his predecessor Maurice Jeremiah Mahoney, M.D., J.D.

Roberts assumes the executive chair position as changes in IRB procedures are occurring nationwide. "Clinical research has moved from predominantly single center studies, with oversight from a local IRB, to multicenter studies, often involving scores of institutions," he says. Many organizations involved in human subjects research, including the National Institutes of Health and industry sponsors, are advocating use of central IRBs, which can oversee research at many sites. "This offers opportunities



John Roberts

for increased efficiency for sponsors and researchers, and creates challenges in terms of maintaining awareness of local context research oversight," he says.

"I look forward to working with all of the IRB chairs and with Linda M. Coleman, J.D., the recently arrived director of the Yale Human Research Protection Program, as Yale // IRBs (page 7)

Appointments to ongoing endowed professorships



Gary Desir



Joann Sweasy



Susan Kaech



Lucian Del Priore

Gary V. Desir, M.D., becomes Paul B. Beeson Professor of Internal Medicine. He also is professor and chair of medicine, and holds a secondary appointment at Yale School of Forestry & Environmental Studies.

Joann B. Sweasy, PH.D., becomes Ensign Professor of Therapeutic Radiology. She also is professor of genetics; vice chair of basic research, therapeutic radiology; and associate director, basic science, Yale Cancer Center.

Susan M. Kaech, PH.D., has been named Waldemar Von Zedtwitz Professor of Immunobiology. Kaech joined the School

of Medicine faculty in 2004 as an assistant professor of immunobiology, and became a professor of immunobiology in 2015.

Lucian V. Del Priore, M.D., has been named Robert R. Young Professor of Ophthalmology and Visual Science, in addition to his appointment as chair of ophthalmology and visual science. Del Priore arrived at the medical school in July from the Storm Eye Institute at the Medical University of South Carolina.

Medicine@Yale

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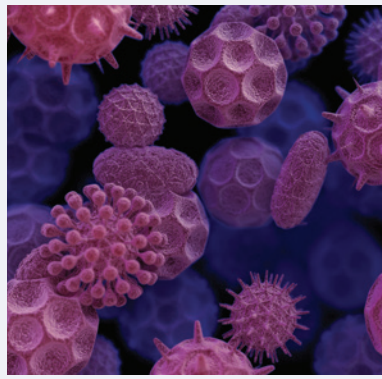
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Infections' varying reactions to foods



Many organisms experience a lack of appetite or avoid certain foods when they catch a virus or acquire harmful bacteria. A study led by Ruslan Medzhitov, PH.D., the David W. Wallace Professor of Immunobiology, published Sept. 8 in *Cell*, suggests that nutrition has different effects on viral versus bacterial infections.

"When animals are infected, they stop eating and switch to a fasting metabolic mode," Medzhitov says. "The question was whether fasting metabolism is protective or detrimental."

Fasting proved helpful for recovery from fevers brought on by, for example, bacterial sepsis. However, eating food, which provides glucose, aided the mice's ability to recuperate from a viral infection. The findings suggest that various diet preferences may correlate with different types of infections. Still, the authors note, the old adage, "Starve a fever, feed a cold," might not apply because the effect likely depends on specific infections.

The findings of this study may inform clinicians' decisions on nutrition for intensive care patients who suffer from acute infections.

New type 2 diabetes protein target named

Insulin resistance in type 2 diabetes is linked to defects in the insulin receptor in numerous organs, including the liver. The search for better drug targets is an ongoing effort. Narendra Wajapeyee, PH.D., associate professor of pathology, and Gerald I. Shulman, M.D., PH.D., the George R. Cowgill Professor of Medicine (Endocrinology) and professor of cellular and molecular physiology, have led a study that identifies a promising protein target.

After a large-scale RNA interference screen of more than 600 proteins that interact with E3 ubiquitin ligase, another protein that is involved in many cellular processes, the team found MARCH1 to be a highly influential protein that degrades the surface of the insulin receptor—thus thwarting the normal function of insulin, which is to keep glucose levels from rising in the bloodstream. To the researchers' surprise, they found that obese people had noticeably higher levels of MARCH1 expression than non-obese people. Their study was published Aug. 31 in *Nature Communications*.

According to Wajapeyee, patients need more treatment options because they face a catch-22. "Type 2 diabetes cannot initially be treated with insulin because the glucose signaling is disrupted," he says. The team now will work to find a small molecule drug to target MARCH1.

Major grant accelerates cancer research

West Campus becomes a multidisciplinary center to explore how biological systems can aid—or block—aggressive cancer spread

A \$9.5 million, five-year grant from the National Cancer Institute (NCI) will fund an intensive multidisciplinary research effort that seeks to better understand how cancer cells reach an aggressive state and begin to damage surrounding tissue. The initiative, called Cancer Systems Biology at Yale (CaSB@Yale), is one of four new research centers in NCI's Cancer Systems Biology Consortium, and is directed by Andre Levchenko, PH.D., the John C. Malone Professor of Biomedical Engineering and director of the Yale Systems Biology Institute.

CaSB@Yale is based at the university's West Campus and brings together investigators with varying research backgrounds from three schools and seven departments at the university, and a variety of other institutes and programs. In particular, at the core of CaSB@Yale, the Yale Systems Biology Institute on West Campus will join forces with the Yale Cancer Biology Institute, the Raymond and Beverley Sackler Institute for Biological, Physical and Engineering Sciences, the Yale Cancer Center, and Emory University to address fundamental questions at the core of cancer biology. Four of the 12 principal and primary investigators are members of the School of Medicine faculty.

The program will address the specific problem of phenotypic plasticity of invasive cancers. Cancer cells with the same genomic makeup can adopt different phenotypes, or characteristics, switching from rapid division and growth to invasive migration and metastatic spread through unknown mechanisms. Furthermore, different phenotypes may co-exist in the same tumor, with cells exchanging signals among themselves and with surrounding normal tissues. CaSB@Yale will explore this complexity of invasive cancer through a range of novel techniques and approaches.

CaSB@Yale will also be devoted to understanding and manipulating the complex molecular networks governing complex cell behaviors. A key focus of the research will be on translational applications aimed at identifying new targets for therapeutic intervention and the development of new drugs targeting invading cells.

Says Levchenko, "Our approach will vary from the use of synthetic biology to evolutionary approaches, and will rely heavily on advances in engineering, mathematics, and physics, in addition to breaking new ground in biology and chemistry."

"The next important goal in cancer therapeutics will be to control or correct signaling networks rather than targeting individual molecules, and CaSB@Yale brings unique sets of expertise and perspective together to do this," says Mark A. Lemmon, PH.D., co-director of the Yale Cancer Biology Institute and the David A. Sackler Professor of Pharmacology at the medical school.

Other School of Medicine investigators who plan to take full advantage of CaSB@Yale's advanced resources and collaborative approach include Jesse Rinehart, PH.D., associate professor of cellular and molecular physiology. Rinehart says a portion of the grant will support a project that he and Farren J. Isaacs, PH.D., an assistant professor of molecular, cellular, and developmental biology in the Yale Combined Program in the Biological and Biomedical Sciences, have developed.

"We've combined our expertise in an area called synthetic biology and molecular biology, to build very, very unique bacterial cells," says Rinehart. "They're unique because they allow us to encode human genes and then endow those human genes with the same physiological function that you might find in human cells. We recently demonstrated that we could bring in genes that are responsible for small protein networks or genetic networks in cancer, and that we could accurately model their properties in these bacterial cells."

Rinehart, whose primary expertise is in signaling networks, says that as the work proceeds, the presence of additional disciplines such as mathematical modeling will be

invaluable. "Mathematical models can combine real terms and real quantities with unknown variables, giving us a model that has flexibility and outcomes that are both predictable and testable." Says Rinehart of CaSB@Yale colleagues who have expertise beyond the biological sciences, "I really want to learn from them."

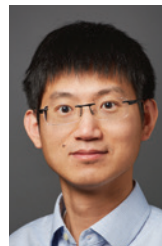
Gunter P. Wagner, PH.D., Alison Richard Professor of Ecology and Evolutionary Biology, is looking for ways to use the knowledge of normal physiological aggressive cell growth to understand and thwart the often-fatal metastasis of cancers in humans. He hopes to find clues in certain mammals for which the skin cancer melanoma has become a chronic, non-malignant condition. "Given all the molecular biology tools we have at our disposal it would not be surprising if we could find the gene regulatory differences



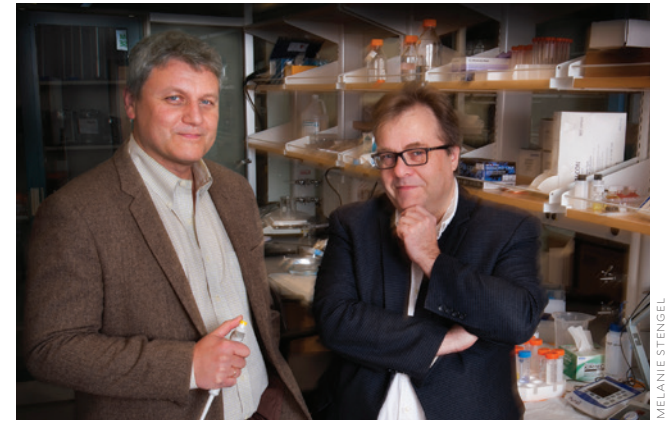
Jesse Rinehart



Gunter Wagner



Sidi Chen



Andre Levchenko (left), director of Cancer Systems Biology at Yale, and Mark A. Lemmon say a large National Cancer Institute grant will spur far-reaching multidisciplinary research on the role of biological systems in the spread, or potential containment, of malignant cells. Yale is one of four institutions in the country where major research centers have been established.

that make the difference between cows and pigs on the one hand, and humans," Wagner says.

Wagner will draw from Levchenko's expertise in examining aggressive cancers in the context of surrounding biological matrix and normal stromal (connective tissue) cells. Levchenko views metastatic disease in military terms. "If you think about an invading army, it can be welcomed by the population or resisted. A lot depends on the country that is being invaded and the population that lives there. Very similarly in cancer you can think about what happens with the cells that are normal and experience the invasion of cancer cells. Are they going to resist? Or are they going to promote the invasive spread?"

Sidi Chen, PH.D., assistant professor of genetics and systems biology, will use his lab's expertise in designing experimental models to benefit CaSB and the field. "My role in this grant is to build a platform to study cancer in animal models," says Chen. "We have previously developed the CRISPR/Cas gene editing technology in vivo in Cas9 transgenic mice. We want to utilize this platform to build new mouse models to better study cancer."

A hallmark of CaSB@Yale will be the opportunity for speed, efficiency, and new ways of attacking problems that collaboration brings. The moment any lab makes tangible progress, other investigators will know it. "We typically get to interact with ideas and progress from other labs after it's been published," says Rinehart. "Even when it's a breakthrough, it's something that the lab was working on in the past. Sometimes that may be five years ago. You really need to know what they are doing now, and that's exactly what we have."

Levchenko compares this approach to a famous precedent—the Manhattan Project—which brought together scientists from many disciplines with the urgent goal of developing an atomic bomb that could win World War II. "I don't think a lot of people thought it was possible to do what is already happening here, including identification of new lead compounds that have the potential to become anti-cancer drugs, in just a few years of our active work. We are dealing with one of the most difficult problems in medicine and the hope was that with harnessing all the interdisciplinary approaches, this problem can be solved—and the progress has been very impressive."

Lemmon believes the benefits of collaboration, with an emphasis on systems biology over studying components of cancer in isolation, may bring progress that is "beyond exponential." Argues Lemmon, "The emergent properties won't emerge—you'll never know what they are—unless you take a systems approach. So, if you're actually trying to understand the properties of the system, you will never understand it by looking at the parts."



June 8 **The Precision Paradigm**, held in New York City’s Hearst Tower, recognized how genomics research at Yale School of Medicine is helping to unravel the mysteries of perinatal loss, birth defects, and cancer. **1. Mary Lake Polan, M.D. ’75, PH.D. ’70, M.P.H.**, clinical professor in obstetrics, gynecology, and reproductive sciences, and her



husband, **Frank A. Bennack Jr.**, executive vice chair and former CEO of the Hearst Corporation, hosted the event. **2. Susan Barber** (left), a 1963 graduate of Yale School of Drama, talks with **Cathy Sokil Milnikiewicz**, a 1979 graduate of Yale College, and **Alessandro D. Santin, M.D.**, professor of obstetrics, gynecology, and reproductive sciences and co-chief of the section of gynecologic oncology.



August 11 At the Class of 2020 **White Coat Ceremony**, **Lillian Oshva, M.D. ’96**, the newly appointed chair of the Yale School of Medicine Alumni Fund, gave personal stethoscopes to all first-year students, including **Maryam Ige** (foreground) and **Daniel Jacobs**.

September 12 Leadership and staff gathered for the Long Ridge Medical Center’s **Center for Musculoskeletal Care Grand Opening** in Stamford. From left to



right, **Heather Eastman**, interim facilities director of Greenwich Hospital; **Sue Brown, R.N., M.S.N.**, chief nursing officer and executive vice president of Greenwich Hospital’s operations and patient care services; **Margie Guglin**, vice president of clinical project management at Yale New Haven Health System (YNHHS); **Marc Kosak**, Greenwich Hospital’s senior vice president of administration; **Marna Borgstrom**, YNHHS CEO and president; **Norman Roth**, Greenwich Hospital president; **Paul Taheri, M.D., M.B.A.**, Yale Medicine CEO; **Mary O’Connor, M.D.**, director of the Center for Musculoskeletal Care; **Marie Follo**, YNHHS director of practice management; **Kimberly Moriarty**, chief strategy officer of YNHHS; **Prathibha Varkey, M.B.B.S.**, Northeast Medical Group CEO; and **Thomas Madden**, director of economic development for the City of Stamford.



September 16 In a panel discussion entitled **Compassion, Meaning, and Joy in the Practice of Medicine**, sponsored by the Yale Program on Medicine, Spirituality, and Religion, **Benjamin R. Doolittle, M.D., MA, DIV.**, associate professor of medicine (general medicine) and of pediatrics hosted **Sadhguru Jaggi Vasudev**, a prominent yogi, visionary, and author from India, and discussed how physicians can combat stress and depression.



October 10 To celebrate the **John and Hope Furth Professorship in Psychiatric Neuroscience**, a dinner was held at the Yale Club in New York City. **1.** On the far left, Dean **Robert J. Alpern, M.D.**, joins the Furths, along with (second from right) **Hilary Blumberg, M.D.**, recipient of the Furth professorship and professor of psychiatry, and (far right) **John Krystal, M.D.**, Robert L. McNeil, Jr. Professor of Translational Research and professor of psychiatry. **2. Hope Furth**, and her husband, **John**, hold replica wooden chairs that symbolize their gift.



November 10 A large crowd turned out for a public symposium that celebrated the **10th anniversary of the Yale Stem Cell Center**. From left, **Na Liu, PH.D.**, associate research scientist in cell biology; **Lauren Gonzalez**, a doctoral student in genetics at Yale University; **Haifan Lin, PH.D.**, director of the Yale Stem Cell Center; **Hongying Qi, PH.D.**, associate research scientist in cell biology; and **Suping Peng, PH.D.**, a postdoctoral associate at the Yale Stem Cell Center.

New endowed professorship established in experimental pathology

In the 1980s, Joseph A. Madri, M.D., PH.D., professor of pathology; and Leonard Bell, M.D. ’84, then a post-doctoral fellow; enjoyed lingering in Madri’s lab after work and cooking up plans to launch a biotech company one day. “We had a folder on the Mac called ‘Fantasy,’” Madri recalls. Fantasy would become reality when Madri, Bell, and four colleagues met in 1991 at the Omni Hotel in New Haven, and set a course that would bring a startup called Alexion to life the following year.

Today Alexion is a global biopharmaceutical company that employs 3,000 people. It is a world leader in developing life-extending therapies for people with rare, devastating, and potentially fatal diseases of the blood and bone.

The success of the company he helped to found has inspired Madri and his wife Lucille to endow a new professorship at the School of Medicine—the Joseph A. and Lucille K. Madri Professor of Experimental Pathology.

Madri says he owes many professional achievements to the faculty, postdocs, and students in his lab and the medical school’s Department

of Pathology, who have informed and inspired his work.

“We felt strongly that we should give back now that we have the ability,” Madri says. “I am a strong proponent of doing that through research that benefits the department’s research enterprise, so we came up with a professorship for an experimental pathologist.”

The professorship’s first occupant is Gerald S. Shadel, PH.D., who also is professor of pathology and of genetics, and director of the Yale Center for Research on Aging (Y-Age).

“Gerry Shadel is an ideal person to be the inaugural Madri professor, an outstanding scientist who is committed to understanding the cellular and molecular mechanisms of aging,” says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine.

Shadel, who became a member of the faculty in 2004, researches the role of mitochondria—energy generators within cells—in disease, aging, and the immune system. Shadel’s laboratory has contributed crucial



Joseph Madri



Gerald Shadel

knowledge to the understanding of mitochondrial gene regulation and metabolic stress signaling pathways. The lab’s groundbreaking aging studies have shown that mitochondrial respiration and reactive oxygen species signaling are key components of conserved longevity pathways.

Madri notes that in making his gift, he had a particular desire to support a mid-career researcher, and he is confident Shadel is the right choice. “He is an outstanding investigator,” says Madri. “He has a true and abiding interest in developing the department, its research, and its educational mission.”

Madri also continues to pursue his own abiding goal—to help people worldwide whose health needs are often forgotten. The company he launched has worked hard to achieve that vision.

Alexion Pharmaceuticals extends the lives of people who are afflicted with two rare blood diseases: atypical hemolytic-uremic syndrome and paroxysmal nocturnal hemoglobinuria.

“We treat people who have paroxysmal nocturnal hemoglobinuria in 50 countries, and now they have a life expectancy that parallels the average person in their particular country, and they are productive members of society,” says Madri.

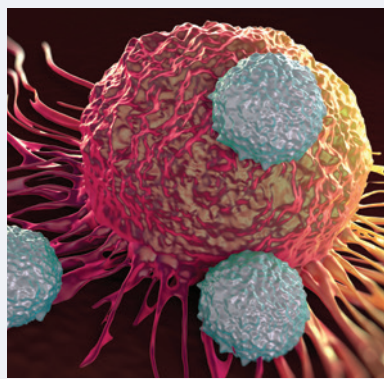
The company makes therapies that also treat the bone-softening disease hypophosphatasia, as well as lysosomal acid lipase deficiency, a condition in which uncontrolled accumulation of cholesterol and triglycerides leads to organ damage and early death.

“If I do nothing else in science, having helped thousands of people live a long, productive life is more than enough reward for me,” he says.

The Madris have spent their entire professional lives at Yale. Joseph Madri arrived as a postdoc in 1975. Lucille Madri held administrative roles at the university for 25 years.

It is rare for a faculty member to endow a professorship, but Madri says Yale and the Department of Pathology deserve such a special gift. “Yale is a unique place and the postdocs and students who’ve cycled through the lab have been outstanding,” he says.

Durable immune cells may protect for years



Yale researchers have discovered a population of cells that may help explain how the human immune system can provide protection against pathogens for decades after a person is first exposed.

The cells, a subset of tissue-resident memory T (Trm) cells, are found throughout the body—including in the blood, bone marrow, gut, and skin—rather than just the lymphatic system where many immune cells reside.

A team led by Madhav Dhodapkar, M.B.B.S., professor of medicine (hematology) and of immunobiology, found that some Trm cells in all these tissues remain in a static resting state, the G0 phase of the cell cycle, where they are neither dividing nor preparing to divide.

This quiescent cell population, the researchers reported in their Sept. 12 *Journal of Clinical Investigation* paper, has the ability to be mobilized into circulation when needed.

The new cells, because they are so long lasting and tend to localize in tissues, may be an attractive candidate for use in immune-based therapies such as those designed to shrink tumors, they suggested.

Copycat proteins may trigger type 1 diabetes

Despite the fact that it appears in childhood and has several genetic risk factors, autoimmune type 1 diabetes cannot be entirely predicted by genetics. Only one identical twin may get the disease, for instance. New research suggests how an environmental factor—gut bacteria—could play a role.

According to the study, led by Li Wen, M.D., Ph.D., senior research scientist in medicine (endocrinology), *Fusobacteria* in the guts of mice produce proteins that mimic the structure of molecules in insulin producing pancreatic beta cells, the same cells that are destroyed in type 1 diabetes.

As the number of *Fusobacteria* in mice increases, the immune system produces more T cells that recognize these molecules, spurring immune activity not only against the bacteria, but also against the pancreatic cells.

In mice with a genetic risk factor for type 1 diabetes, having excess *Fusobacteria* in their guts accelerated the onset of disease. Moreover, altering their guts to decrease *Fusobacteria* reversed the development of type 1 diabetes, the researchers reported Sept. 12 in *Journal of Experimental Medicine*.

The new findings could eventually provide targets for new therapies in humans with type 1 diabetes.

Alumnus Singer '02 funds Yale programs

Serial entrepreneur and physician honors a faculty mentor and a classmate as he salutes Yale for inspiring his personal achievements

The School of Medicine will receive support for cardiac research, a neuroscience lectureship, and a global health fellowship; and a Yale College scholarship will honor a medical school faculty member, thanks to a large gift to Yale University by self-described “serial entrepreneur” Michael Singer, M.D. '02, Ph.D. '00, and his wife Baharak Asefzadeh, O.D., M.S. The gift is in thanks to Yale for the role it played in shaping Singer's success.

Singer's professional life is centered in Boston, where he has lived since he began a residency in ophthalmology at Harvard. He has founded a series of health-related companies there and also teaches at Harvard Medical School. Topokine, which produces a topical treatment that acts on fat cells to contour the face, was one of Singer's privately held companies. In 2015, Singer and Asefzadeh donated to Yale Topokine shares then valued at over \$1 million. This past spring, the multinational pharmaceutical company Allergan purchased Topokine, providing Yale with immediate cash and rights to future milestone payments.

Yale University is “kind of where I grew up,” says Singer, who also attended Yale as an undergraduate, earning a Bachelor of Science degree in 1995. “Everything positive that has happened to me since depended on my arriving at Yale back in 1991.” Singer credits Yale with fostering his creativity and encouraging him to pursue a wide array of ideas and habits of thinking that led him to become the entrepreneur he is today.

Faculty, and fellow students alike, made a big impression on Singer. “The most important part of the Yale experience is the people you meet,” he says. Accordingly, each facet of the gift will recognize individuals who made Singer's time at Yale the formative experience it was.

As an undergraduate work-study student and then as a Ph.D. candidate, Singer studied the olfactory system in the lab of Gordon M. Shepherd, M.D., D.Phil., professor of neuroscience. Shepherd was more than a scientific mentor. “We also formed a very nice personal bond,” Shepherd recalls, noting that Singer was often a guest at his home. “My wife [Grethe Shepherd] enjoyed having him; she always enjoys having students come out, as they do from time to time.” The Shepherds were a “home-away-from-home” for him and for many Yale students, Singer says. In honor of the Shepherds, part of the gift will endow an undergraduate scholarship, the Gordon and Grethe Shepherd Scholarship Fund.

Also in honor of Singer's mentor, the donation will endow a School of Medicine lectureship in integrative neuroscience, which Singer describes as “the hallmark of [Shepherd's] long and distinguished career as a neuroscientist.” That field, Shepherd says, is concerned with synthesizing different kinds of data that scientists gather about the nervous system into a greater understanding of the system as a whole. The Department of Neuroscience,

headed by Pietro De Camilli, M.D., the John Klingenstein Professor of Neuroscience and professor of cell biology, will administer the lectureship.

Singer's gift also memorializes a classmate and friend, Joshua “Josh” Gibson, M.D. '01, who died in 2005 due to an unrecognized heart condition. The Joshua C. Gibson, M.D., Memorial Fund for Heart Research will sponsor work in the laboratory of Daniel L. Jacoby, M.D. '00, another contemporary and director of the Advanced Heart



Michael Singer and his wife Baharak Asefzadeh have donated to Yale in thanks for the university's role in what Singer says is “everything positive that has happened to me” since he first arrived at Yale more than 25 years ago. They are funding a lectureship in integrative neuroscience at the School of Medicine, heart research, sponsorship for scholars from around the world to visit Yale, and scholarships for Yale College undergraduates.

Failure and Cardiomyopathy and General Heart Failure programs. Singer and Gibson shared an interest in travel and global health, and during medical school both traveled to less-developed countries to do health research through Yale's Downs Fellowship program. Another portion of the gift, also in Gibson's name, will endow what Singer thinks of as a “reverse Downs fellowship” to sponsor scholars from less-developed countries to visit Yale School of Medicine.

Singer's next venture is Cartesian Therapeutics, a company developing novel cancer therapies, and philanthropy is an ongoing priority. “I would like to begin a movement to encourage more entrepreneurs and early-stage investors to donate their privately held stock to support charity and institutes of higher learning,” he says.

“[Singer] was thrilled and excited by every opportunity that was presented to him here,” says Charles A. Greer, Ph.D., professor of neurosurgery and of neuroscience, and director of the Interdepartmental Neuroscience Graduate Program. Greer, who will co-administer the Shepherd lectures, says the donations reflect Singer's character. “You know, sometimes people can become rather indifferent about opportunities being presented,” says Greer. “As they have a series of successes, they come to think that they maybe deserve them in some way. Michael never exhibited that trait. Michael always treated any success, any gesture or effort that was extended on his part with the greatest of gratitude and continues to do so.”

// **Cancer Center** (page 1) Dana-Farber Cancer Institute.

After spending his entire career in Boston, where he has led a clinical enterprise as well as research programs, Fuchs says he is now ready to bring his work to an even higher level in his new role at Yale. “The opportunity to lead such an extraordinary center as Yale Cancer Center and Smilow will allow me to do that,” he says. Fuchs plans to continue to expand clinical trials

and science at the cancer center and will coordinate these efforts with discoveries that emerge across Yale's research enterprise. His vision is to advance Yale's capacity to do innovative clinical, translational, population, and basic science research to further enhance the cancer center's position as a leader in cancer prevention, biology, and treatment.

“The cancer center and Smilow have had impressive growth over the past five years,” he says. “I am excited

about the opportunity to continue to expand the breadth and depth of the clinical practice as well as the extraordinary cancer research ongoing at Yale to meaningfully improve the outcome of patients.”

With the start of the new year, Fuchs succeeds Peter G. Schulam, M.D., who served as interim director of the Cancer Center for the past year, Schulam remains chair of the Department of Urology and chief of urology at Yale New Haven Hospital.

Early career recognition goes to five Yale investigators

A highly competitive new program identifies and funds the most promising young scientists in the United States

Five School of Medicine scientists have been named Howard Hughes Medical Institute (HHMI) Faculty Scholars in recognition of their potential to make unique contributions to their fields.

This newly established program—a joint endeavor of HHMI, the Bill & Melinda Gates Foundation, and the Simons Foundation—supports early career basic researchers with more than four and up to 10 years of experience. The investigators were chosen based on their innovative approaches to solving biology-related problems that are relevant to human health.

Daniel A. Colón-Ramos, PH.D., associate professor of cell biology and neuroscience, is using *Caenorhabditis elegans*, also known as roundworms, to explore the cellular mechanisms used to create, maintain, and modify synapses in order to further understanding of their role in producing behaviors and storing memories.

Antonio J. Giraldez, PH.D., professor of genetics, seeks to understand how the cellular codes that shape gene expression are used to turn a fertilized egg into a complex multicellular embryo. Using zebrafish as a model system, he aims to shed light on the mechanisms that initiate embryonic development and specify different cell types in vertebrates.

Andrew Goodman, PH.D., associate professor of microbial pathogenesis, is exploring the mechanisms that human commensal microbes—those normally found in the body—use to cooperate, compete, and antagonize each other in the gut and how manipulating these communities could improve drug responses in patients.

Valentina Greco, PH.D., associate professor of genetics, is investigating how stem cells initiate and coordinate tissue regeneration to maintain healthy tissues and restore damaged tissue after injury, and how tissues respond to cells with cancer-promoting mutations, which will shed light on the earliest events that lead to cancer.

Carla V. Rothlin, PH.D., associate professor of immunobiology and of pharmacology, is studying the biochemical mechanisms that control the immune response and lead to inflammation that can trigger autoimmune disorders or fuel cancer.

“Promising young faculty members are the backbone of our ability to continue to conduct groundbreaking research,” says Dean Robert J. Alpern, M.D., Ensign Professor of Medicine. “I am proud



In the first year of a program designed to identify and fund promising young investigators, (left to right) Valentina Greco, Andrew Goodman, Carla V. Rothlin, Daniel A. Colón-Ramos, and Antonio J. Giraldez have been named Howard Hughes Medical Institute Faculty Scholars. No medical school in the United States had a larger group chosen.

that HHMI has chosen to support five of our most accomplished investigators.” Yale’s five awardees, as many as were chosen from any medical school, are among just 84 Faculty Scholars selected from a pool of more than 1,400 applicants.

// **IRBs** (page 2) addresses these issues.”

Prior to joining the Yale faculty in 2012, Roberts was professor of internal medicine at Virginia Commonwealth University (VCU), where he was an IRB member for nearly 20 years. At VCU he also taught human subjects protection at the graduate level. Shortly after his arrival at Yale, he was appointed co-chair of the Yale IRB Cancer Panel (Human Investigations Committee I). Roberts

has extensive experience in clinical trials, and was a co-investigator in a landmark study that demonstrated that chronic pain is common in adults with sickle cell disease.

Roberts earned his M.D. at the University of Pennsylvania. In 2012, he received the Principal Investigator of the Year (Harry Hines Award) from the Community Clinical Oncology Program of the National Cancer Institute.

// **Slayman** (page 1) establish the graduate program in the nascent Department of Human Genetics in 1972 and served as director of graduate studies in genetics from 1972 to 1984. In 1984, she was named chair of the Department of Genetics, serving in that position for 11 years. In 1991, she was named Sterling Professor of Genetics in recognition of her academic excellence.

As deputy dean for academic and scientific affairs, she focused her attention on faculty recruitment and development, and the creation and advancement of research programs and core facilities—including the Yale Center for Genome Analysis at the West Campus—and was instrumental in Yale’s applications for many institutional grants, such as the National Institutes of Health (NIH) Clinical and Translational Science Award. Slayman spearheaded the renovation and modernization of the medical school’s laboratory space in an effort to create a collaborative environment that fosters the sharing of ideas.

“One of Carolyn’s strengths was that she never had any personal ego stake in an outcome, other than what was going to be the very best for the institution,” says Richard P. Lifton, M.D., PH.D., president of Rockefeller University and former chair of the Department of Genetics at the School of Medicine.

A renowned scientist, Slayman was elected to the Institute of Medicine (now the National Academy of Medicine) in 1995. She was recognized for her research on the proteins that transport nutrients across cell membranes and the genes that code for those proteins. She served on numerous scientific boards and panels, including the Howard Hughes Medical Institute Scientific Review Board and the NIH Panel on Scientific Review.

Slayman, who was passionately committed to the training and education of young scientists, became a mentor to many, relishing the opportunity to guide their research and careers. Megan C. King, PH.D., associate professor of cell biology, notes that Slayman was instrumental in her earning an Early Outstanding Investigator Award, which sustained King between grants, enabling her to move from yeast to animal model systems in her work on the role of a mechano-transduction pathway in cardiomyopathies and generate data that will allow her to continue this research. “She gave advice,” King says, “which is a skill that most of us don’t have but which is increasingly important.”

The School of Medicine plans to hold a public memorial for Slayman in the coming weeks.

// **Public Health** (page 1) in a joint statement announcing Vermund’s appointment. “His work showed that HIV was a risk factor for cervical cancer, which motivated routine cervical cancer screening for HIV-infected women worldwide.”

Vermund received his medical degree from Albert Einstein College of Medicine in 1977. During his training in pediatrics at Columbia University, he was exposed to many cases of preventable illness in underserved minority populations. “The more preventable illness I saw, the more my passion for a public-health based orientation grew,” he says.

He pursued this interest by completing a master’s degree in community health in developing countries at the London School of Hygiene and Tropical Medicine, a diploma in public health at the Royal Institute of Public Health and Hygiene, and a Mellon Foundation-supported fellowship in clinical epidemiology at Columbia-Presbyterian Medical Center. He received his PH.D. in epidemiology from Columbia in 1990.

Vermund served as chief of the Vaccine Trials & Epidemiology Branch in the Division of AIDS at the National Institute of Allergy and Infectious Diseases from 1988 to 1994, a time when AIDS activism had a major influence on government policy. Recognizing the need for prevention approaches, his branch launched HIVNET (HIV Network for Prevention Trials), a major international research network that evolved into several NIH-sponsored networks focused on prevention.

For the past two decades, Vermund, who is a member of the National Academy of Medicine (formerly the Institute of Medicine), has focused on global health issues. In developing countries, where Pap smears are not routine, his team promulgated a

simple technique to visually detect cervical lesions and built a major screening program in Zambia that has become a global training center.

In 2000, he founded the Centre for Infectious Disease Research, now one of Zambia’s largest NGOs, which currently supports more than 330 clinics that play an instrumental role in the prevention of maternal-fetal HIV transmission and the implementation of antiretroviral therapy. He also founded Friends in Global Health, an NGO in Mozambique and Nigeria that has provided HIV-related care to over 140,000 individuals.

Vermund has been a mentor to scores of individuals who have gone on to distinguished careers heading major programs, including Ann E. Kurth, PH.D., C.N.M., M.P.H., dean of Yale School of Nursing. He has also written many grants through which hundreds of individuals have received training in public health science. He plans to draw upon this experience to work closely with interested faculty to help increase the number of Yale’s public health doctoral trainees.

He adds that he plans to work tirelessly to expand Yale’s research enterprise for highly relevant discovery and to support faculty who are at the leading edge of health policy and reform. He also looks forward to spearheading larger collaborative initiatives across the entire university, including climate change and population projects with the School of Forestry & Environmental Studies, strengthening global health care systems with the School of Management, and collaborations on health ethics with Yale Divinity School.

“At Yale,” Vermund says, “the opportunities are immense to get involved with a variety of enterprises.”

School welcomes chief diversity officer

Deputy dean arrives with long experience in areas of recruitment and inclusion

Darin A. Latimore, M.D., has been appointed deputy dean for diversity and inclusion, beginning in January as the School of Medicine's inaugural chief diversity officer.

Latimore obtained his medical degree at University of California, Davis School of Medicine and completed his residency in internal medicine at University of California, Davis Medical Center. He specialized in HIV care as a physician with the Permanente Medical Group in South Sacramento, Calif., where he also trained medical students and residents before joining UC Davis as a volunteer clinical faculty member in 2002.

His passion for promoting diversity and inclusion stems from his own experiences. As an undergraduate at University of California, Berkeley, he felt isolated on a campus where there



Darin Latimore

were few African-Americans and even fewer students from his modest socioeconomic background.

While serving as associate program director for the UC Davis internal medicine program,

he noted that many of the students and residents with whom he worked shared his experiences of isolation and discrimination, prompting him to write a job description that led to his inaugural position as director of medical student diversity at UC Davis in 2008. He later became associate dean for student and resident diversity, developing initiatives to increase the pipeline of socioeconomically disadvantaged students, residents, and faculty and spearheading programs to support and empower underrepresented students interested in attending medical school.

"The School of Medicine is strongly committed to promoting

racial, gender, ethnic, and socioeconomic diversity," says Robert J. Alpern, M.D., dean and Ensign Professor of Medicine. "I am pleased that we have recruited such an exceptional candidate to head our efforts at promoting a culture in which all members of our community feel respected and included."

At Yale, Latimore will coordinate with such groups as the Office of Multicultural Affairs, the Minority Organization for Retention and Expansion (MORE), the Committee on the Status of Women in Medicine (SWIM), the Committee on Diversity, Inclusion, and Social Justice, and the newly formed Dean's Advisory Council on LGBTQ Affairs.

Latimore will aid with recruitment efforts to increase diversity within School of Medicine faculty. In addition, he says, "I am looking forward to working with Yale's student body to develop programming that is more inclusive and to help underserved communities around the Yale campus."

Albany Prize is awarded to investigator of proteins

Arthur L. Horwich, M.D., Sterling Professor of Genetics, professor of pediatrics, and a Howard Hughes Medical Institute investigator, is one of three recipients of the 2016 Albany Medical Center Prize in Medicine and Biomedical Research, one of the most prestigious honors in medicine.

Horwich, F. Ulrich Hartl, M.D., of the Max Planck Institute, and Susan Lindquist, Ph.D., at the Massachusetts Institute of Technology will share the \$500,000 prize for their discoveries about the biology of protein folding.

Proteins must be folded into a proper three-dimensional structure to carry out their functions, which are crucial to all life. The scientists have shown that protein folding inside cells does not occur spontaneously as previously believed but depends upon molecular "assistants"



Arthur Horwich

in a process called "chaperone-mediated protein folding."

"Protein folding is a concept considered revolutionary in modern biology, with important implications for the treatment or delay

of Parkinson's disease, Alzheimer's disease, Huntington's disease, and other neurodegenerative conditions, as well as cancer and drug resistance," says Vincent Verdile, M.D., the Lynne and Mark Groban, M.D. '69, Distinguished Dean of Albany Medical College and chair of the Albany Prize National Selection Committee.

A Chicago native, Horwich received both his undergraduate and medical degrees from Brown University, and then came to Yale

for his internship and residency in pediatrics. He served as a postdoctoral fellow first at Salk Institute in the Tumor Virology Laboratory and then in the genetics department at the School of Medicine, before joining the medical school faculty in 1984.

He has received numerous honors including the Lasker Award for Basic Medical Research in 2011 and the Shaw Prize in Life Science and Medicine in 2012. He is a member of the National Academy of Sciences and the National Academy of Medicine (formerly the Institute of Medicine).

Horwich has studied ALS for several years, focusing on aspects that include protein quality control mechanisms, in an effort to understand exactly what causes the motor failure and paralysis that are hallmarks of the disease.

Taylor is elected to National Academy of Medicine

Hugh S. Taylor, M.D., Anita O'Keefe Young Professor and chair of the Department of Obstetrics, Gynecology, and Reproductive Sciences; professor of molecular, cellular and developmental biology; and chief of obstetrics and gynecology at Yale New Haven Hospital is one of 79 individuals elected in October to the National Academy of Medicine (NAM).

Taylor's clinical research centers on implantation, endometriosis, and menopause. His basic science research focuses on uterine development, the regulation of developmental gene expression by sex steroids, endocrine disruption, and stem cells. Taylor's work has led to, among other insights, a better understanding of endometriosis, including its genetic cause and the role of stem cells in the disease.

Taylor earned a Bachelor of Arts from Yale College in 1983, and his M.D. degree from the University of Connecticut School of Medicine in 1988. He then returned to Yale for his residency in obstetrics and gynecology. His postdoctoral training at Yale included a fellowship in reproductive endocrinology and infertility as well as a fellowship in molecular biology. He became an associate research scientist in 1992 and joined the ladder track faculty in 1998.

In 2015-2016, he served as president of the Society for Reproductive Investigation, the leading academic society in the field of obstetrics and gynecology, and presided over its 2016 annual meeting. In 2013, he was awarded the IVI Foundation International Award for the impact of his

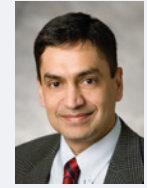


Hugh Taylor

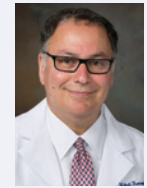
research in reproductive medicine, and was named Mentor of the Year by the American College of Obstetricians and Gynecologists. In 2012, he was named Honoree of the Year by the Endometriosis Association.

The NAM (originally the Institute of Medicine) was established in 1970 under the charter of the National Academy of Sciences to advise the nation on medical and health issues. Members are elected by their peers for distinguished contributions to medicine and health. At its annual meeting, NAM announced 70 new members from the United States and nine international members.

Awards & Honors



Madhav V. Dhodapkar, M.B.B.S., Arthur H. Bunker and Isabel Bunker Professor of Medicine (Hematology) and professor of immunology, has been named an Outstanding Investigator by the National Cancer Institute. Dhodapkar is also chief, section of hematology, department of internal medicine; and Disease Aligned Research Team leader, Hematology Program, Yale Cancer Center.



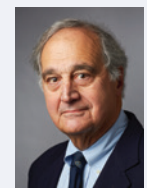
Naftali Kaminski, M.D., Boehringer Ingelheim Pharmaceuticals, Inc., Professor of Medicine (Pulmonary), professor

of pharmacology; and chief of pulmonary, critical care, and sleep medicine, has received the European Respiratory Society Gold Medal in Interstitial Lung Disease, and been elected a Society fellow.



Stefania Nicoli, Ph.D., assistant professor of medicine (cardiology) and of pharmacology, has received the 2016 Springer Junior

Investigator Award from the North American Vascular Biology Organization. Nicoli is the first woman ever to receive this award, which was inaugurated in 2011.



Robert J. Touloukian, M.D., professor emeritus of surgery (pediatrics), has been named the next president of the New England

Surgical Society. His term begins in September 2017.



Richard E. Carson, Ph.D., professor of radiology and biomedical imaging, and of biomedical engineering; director, Yale PET Center; and director of



graduate studies, biomedical engineering; and D.S. Fahmeed Hyder, Ph.D., professor of radiology and

biomedical imaging and of biomedical engineering; technical director, Magnetic Resonance Research Center; and program director, Core Center for Quantitative Neuroscience with Magnetic Resonance; have been named Distinguished Investigators of the Academy of Radiology Research.