Medicine@Yale

february/march 2019
volume 15, issue 1
Advancing Biomedical Science, Education, and Health Care

Alpern will not seek a fourth term as School of Medicine dean

Will continue to serve until successor is installed, and then remain on the faculty

Robert J. Alpern, MD, dean and Ensign Professor of Medicine, informed the Yale School of Medicine (YSM) community in December that he will not seek to serve a fourth five-year term as dean when his current term expires later this year. Alpern said he will remain as dean until his successor is appointed, and then plans to continue on the Yale faculty and pursue a number of academic interests.

Alpern, who arrived in 2004 after serving since 1998 as dean of the University of Texas Southwestern Medical School, calls the change "bittersweet" after 21 years as a dean. "I will especially miss the many colleagues I have worked with so closely over these years." But, he says, he is looking forward to what will come next. "I'm really excited about going back to my pre-dean years and being able to focus on the latest advances in medicine and the biomedical sciences. Right now, my time is entirely consumed with responsibilities associated with the dean's job."

After he steps down, Alpern expects to devote more time addressing his varied academic interests, some of which are related to renal physiology and kidney disease. He wants to focus more on the development of a drug that has the potential to transform the care of kidney patients. He also hopes to pursue other areas of interest related to biomedical science, clinical medicine, teaching, and issues of national and international importance in medicine.

First, there is a deanship to complete. Alpern looks back with satisfaction at achievements that include recruiting outstanding researchers—scientists at the top of their fields—along with young investigators whose accomplishments and personal development have been a source of particular pride; a much-enhanced relationship with Yale New Haven Health System (YNHHS) and a clinical practice that he says has been transformed; a curriculum revision in 2015 (for which he credits Richard Belitsky, MD, Harold W. Jockers Associate Professor of Medical Education and associate professor of psychiatry, and deputy dean for education) as well as the YSM Teaching and Learning Center; enhanced financial aid for students; and huge strides by a cancer center that was in

// Dean *(page 8)*

ROBERT A. LISAK

Robert Alpern, who arrived in 2004 as dean of Yale School of Medicine, has announced that he will not seek to serve a fourth five-year term. He will remain as dean until a successor takes office, and then continue on the medical school faculty.

Endowment to support student research

Medical students receive a summertime opportunity to do research at Woods Hole

Roughly 170 miles up the highway from New Haven, at the southwest tip of Cape Cod, lies Woods Hole, Mass. Nestled in this seaside village, between Eel Pond and the Atlantic coast, is the Marine Biological Laboratory (MBL), founded in 1888.

A dozen or so Yale scientists head to the MBL every summer, joining some 500 other researchers and trainees from institutions around the world who also spend their summers making use of the MBL's unique resources and collegial environment. Discoveries by investigators at or affiliated with the MBL have produced more than 50 Nobel prizes since 1920.

Hematologist Jack Levin, MD '57, took full advantage of what Woods Hole offers. During a research fellowship at the Johns Hopkins Hospital in the early 1960s, which had immersed him in research on platelets—the cells in blood that contribute to blood coagulation—Levin spent a summer at the MBL. Hopkins professor Frederik Bang, MD, was there working on *Limulus polyphemus*, the Atlantic horseshoe crab. Their collaboration led to a major scientific discovery about blood coagulation in *Limulus*, and also to the use of *Limulus* as a model organism to provide new insights into the non-hemostatic

// MBL *(page 4)*

DEE SULLIVAN

Shobana Subramanian (center) became the medical school's first Levin Fellow when she joined faculty members Elizabeth Jonas (left) and Leonard Kaczmarek at Woods Hole's Marine Biological Laboratory during the summer of 2018.

Foundation endows directorship of the MD-PhD program

A new gift from the Gustavus and Louise Pfeiffer Research Foundation will create an endowed directorship for Yale School of Medicine's MD-PhD Program. The foundation has a long-standing relationship with Yale, having generously supported the Yale Combined Program in the Biological and Biomedical Sciences and made grants to bolster research ranging from cancer to prosthetics to psychiatry.

The new gift builds on a $1 million endowed gift made by the foundation in 2015 that provides long-term support to current students in the program, especially those with an interest in neurological and psychiatric diseases.

The inaugural Gustavus and Louise Pfeiffer Research Foundation MD-PhD Program Director is Barbara Kazmierczak, MD, PhD, professor of medicine (infectious diseases) and of microbial pathogenesis, a School of

// MD-PhD *(page 8)*

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ROBERT A. LISAK

Valentina Greco has made singular contributions to knowledge about long-hidden functions of skin cells. She and members of her lab have explored the epithelium's role in guiding stem cell regeneration, and in containing cells that might become cancers. She also has worked forcefully to advance women in science.

Scientist finds skin deep is very deep

Reveals skin properties that may limit cancer and aid stem cell regeneration

Two images published in a *Cell Stem Cell* paper in September 2018 summarize years of relentless questioning on how skin stem cells regenerate, which has driven much of the research of Valentina Greco, PhD, Carolyn Walch Slayman Professor of Genetics and professor of cell biology and of dermatology, and her lab members.

The side-by-side images feature individual mouse cells in grayscale microscopy and those same cells rendered in a pastel, color-by-numbers image that illustrates skin stem cells' self-renewal process. Greco and her team shattered dogma, which held that skin stem cells decide when to renew themselves. Instead, they found that neighboring epidermal cells create a niche environment that drives the timing of stem cell regeneration.

Greco's personal journey toward making these discoveries was filled with twists and turns, punctuated by one transformative moment as she considered pursuing her doctorate in the late 1990s. After earning an undergraduate degree in molecular biology at the University of Palermo in her native Italy, Greco stayed on for two years as an unpaid researcher, a typical practice at the time, in a lab with meager resources. The bleak research environment was all Greco knew and it felt normal to her, until—fortuitously—her alma mater turned down her doctoral application. That rejection became her catalyst to look elsewhere.

She landed at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, which felt a world away. "When I interviewed there, I saw that science was a world of fun," Greco says. "It was essentially the difference between having resources that allow you to really move your ideas forward, as opposed to having to be creative, but for survival."

After studying principles of tissue growth under Suzanne Eaton, PhD, at EMBL, a supportive and "powerful" experience that she cherishes, she took a postdoctoral fellowship in the lab of Elaine Fuchs, PhD, at the Rockefeller University. That is where she first delved into epidermal stem cells and the epithelium itself, which have been her focus since she arrived at Yale in 2009.

The Greco lab has observed that, aside from their interplay with stem cells, epidermal cells in mice perform roles usually left to the immune system, such as the clearing of dead cells and correction of tissue defects including tumor-like growths. "We are fascinated by the idea that the epithelium can take care of many housekeeping functions in the skin," Greco says. In particular, she suggests, a better understanding of how epidermal cells address microinjuries or mutations may lead to new ways of approaching cancer treatment.

The goal of many current therapies is to prevent malignant cells from proliferating. Greco and her team hope to validate a different approach, by developing knowledge of how epidermal cells tolerate, and then contain within the epithelium, aberrant cells that have not yet developed into cancers.

Greco also finds it important to contemplate the environment of her own laboratory, to ensure that her team members can thrive. "I am continuously scrutinizing myself and our lab to be as free from codes that society gives for determining talent," Greco says. "We make a special effort to think carefully about the biases we hold that affect the way we hear and respond to ideas from others." This philosophy, in turn, "creates a space where these people can conceptualize the best idea ever, and shape it in a way that, as they approach science within my lab, they are independent."

She credits her dedication to younger colleagues' success to that of her own mentor at Yale, the late Carolyn W. Slayman, PhD, deputy dean for academic and scientific affairs, Sterling Professor of Genetics, and professor of cellular and molecular biology. Greco says Slayman set a standard for developing opportunities for junior faculty. "The fact that I carry her endowed professorship is particularly touching to me."

Greco says she wants her mentees to feel deep respect, so they can share any idea, no matter how unusual it might seem, through conversations that are often difficult, but necessary. "That's how you create an environment for learning and creative thinking and pushing forward, rather than something that needs to fit a very narrow filter."

Her desire for a positive environment also extends to women throughout the medical school. Greco is deeply involved with the Committee on the Status of Women in Medicine (SWIM), which has worked to provide a more favorable balance of power and of opportunity for women faculty since 1979. Says Greco, mindful of her own growth since her postdoc years: "If you give people a voice and empower them and invest in individual quality, then people could do so much better and the organization that they are part of will have more impactful outcomes."

Role of humanities in treating the seriously ill is a new fund's focus

The Max Ritvo '13 and Alan B. Slifka '51 Program Fund for the Medical Humanities has been established at the Yale Child Study Center to explore the interface between children's illness experiences—particularly of psychiatric conditions and of chronic or terminal illnesses—and the humanities.

The multidisciplinary program aims to improve the clinical experience of those affected by illness, and to strengthen the ability of providers to deliver compassionate care. It will include a guest speaker and visiting scholar component, as well as the presence of an artist-in-residence.

Riva Ariella Ritvo, PhD, and the Alan B. Slifka Foundation have endowed the initiative, in memory of Ritvo's husband and son.

A program at the Child Study Center honors (l to r): Max Ritvo (1990-2016) and Alan Slifka (1929-2011).

Institute for Global Health names its inaugural director

Saad Omer

Saad B. Omer, MBBS, MPH, PhD, has been named the inaugural director of the Yale Institute for Global Health (YIGH). Omer is currently the William H. Foege Professor of Global Health, Epidemiology, and Pediatrics at Emory University's schools of public health and medicine. He will hold joint appointments at Yale School of Public Health and Yale School of Medicine and a secondary appointment at Yale School of Nursing, effective July 1.

"Some of the most pressing problems of our time are related to global health," says Omer. "Addressing them will require us to bring our 'A game.' Therefore, global health needs and deserves the involvement of an institution such as Yale."

Omer plans to tap Yale's preeminence in research, teaching, and clinical care. His vision for YIGH is to support faculty and trainees in developing transformative initiatives that cross disciplines and have an impact on people's lives across the globe.

Omer has published widely in peer-reviewed journals, has multiple awards, and has served on several advisory panels including the National Vaccine Advisory Committee, the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria—Incentives for Vaccine Working Group, and the WHO Expert Advisory Group for Healthcare Worker Vaccination.

He received his PhD and MPH degrees from Johns Hopkins University, and his MBBS from the Aga Khan University Medical College.

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Medicine@Yale is published four times each year by:
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1 Church Street, Suite 300, New Haven, CT 06510-3330
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Email medicine@yale.edu

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Postal permit held by Yale University,
155 Whitney Avenue, New Haven, CT 06520

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Promising path seen to a malaria vaccine

A vaccine targeting a protein that malaria parasites use to evade the immune system protects mice from malaria infection, a new study reports. It raises hope for humans, for whom surviving malaria infection can reduce later susceptibility to the disease's worst symptoms, but does not rule out reinfection.

Richard Bucala, MD, PhD, professor of medicine, epidemiology, and pathology, and colleagues hypothesized that PMIF, a Plasmodium version of the mammalian protein MIF—which interferes with immunological memory—might be the parasite's key to reinfection success. To find out, Bucala's group gave an RNA-based vaccine against PMIF to mice with a rodent equivalent of malaria. The vaccinated mice combated initial and repeat malaria infections better than mice that received a control vaccine.

The results tell the authors that an MIF-based vaccine could provide a new tool to fight malaria in humans. Further, since such other parasites as hookworm also have MIF-like molecules, similar vaccines might also work against other parasite-caused diseases. This collaboration between Bucala's team and Novartis appeared July 13 in *Nature Communications*.

Parkinson's function uncovered in genes

The function of a gene family associated with Parkinson's and other inherited diseases has been elucidated by Yale scientists. Mutations in human VPS13 genes were known to cause neurodevelopmental and neurodegenerative diseases, but the mechanisms were unknown.

In a new study, the labs of Pietro De Camilli, MD, chair and John Klingenstein Professor of Neuroscience and professor of cell biology, and Karin Reinisch, PhD, Jean and David W. Wallace Professor of Cell Biology and professor of molecular biophysics and biochemistry, probed the locations and roles of VPS13 proteins.

The proteins, they found, tether different organelles in cells to each other and help move organelle-defining lipids between them. VPS13C—associated with Parkinson's—works at the junctions between the endoplasmic reticulum (ER) and endosomes and lysosomes, while VPS13A—associated with a Huntington's-like syndrome—functions at contacts between the ER and mitochondria.

The findings, published Aug. 9 in the *Journal of Cell Biology*, imply that these diseases arise from defects in lipid dynamics and could suggest new therapeutic strategies to treat them.

New center to harness burgeoning data

School of Medicine joins universitywide move toward using advanced data science to enhance research, scholarship, and education

Data have become an essential ingredient for investigators pursuing advanced biomedical science. James Noonan, PhD, associate professor of genetics, says the time has long passed when his lab could do its work on the human phenotype without the insights that abundant data provide. "To really understand these complex biological systems, we need data," Noonan says. "We need a lot of data and a lot of different kinds of data."

This reality for labs throughout the School of Medicine, and for the school's clinical researchers and providers, led to the recent establishment of the Center for Biomedical Data Science (CBDS), which is one part clearinghouse for the newest data-related ideas; one part incubator for ways to educate students, trainees, and faculty on what data can offer; and, one part an innovator of data techniques to advance biomedical science and data science. As CBDS matures, additional pursuits are sure to follow.

Xinxin (Katie) Zhu, MD, PhD, arrived last August from the IBM Watson Research Center to take primary responsibility for moving CBDS forward. "People don't necessarily consider biomedicine as a big data field, or health care as a big data field, but we are," says Zhu. One of her first jobs has been to identify and connect Yale experts who can enhance each other's work. "You could have a biologist working on things s/he's been doing before," Zhu says, "but s/he may not have the data science knowledge; or may not have a computer scientist to help with some computational models. That's where we come in." In turn, there are quantitative experts throughout Yale whose methods could help shape biomedical science, but have not been introduced to potential collaborators.

Ruth R. Montgomery, PhD, associate dean for scientific affairs and professor of internal medicine, who helped establish CBDS, says connections such as those Zhu describes have greatly helped her own science. "I have really found it fascinating to work with my bioinformatics colleagues when they analyze my data in a way that is not from my own background," she says. "We go back and forth several times until we have each understood what the other was looking for and really find new things."

One-to-one matchmaking is just an early step. CBDS already has enlisted more than 100 faculty members, and expects to welcome even more, to facilitate broader exchanges of ideas that can boost the scientific enterprise exponentially. Yale is the ideal place for it, according to Harlan M. Krumholz, MD, Harold H. Hines, Jr. Professor of Medicine, who is a member of the CBDS faculty steering committee. "We have a small-town atmosphere here," says Krumholz. "People are not worried about turf in general. They are open to people from different sectors of the university coming together and thinking about how we might best do things together."

Zhu foresees experts sharing insights with each other as never before. "Data science is quite new, a quite different discipline in the academic world," she explains. "This is one of the areas where the more you share, the more you have, instead of holding something very tight to your chest, and you become very good."

An essential task for CBDS will be figuring out how to manage ever-expanding datasets from multiple sources that Yale both generates and receives, so as not to drown in a sea of numbers without knowing how to make sense of them. "With all the technological advances we have seen, such as imaging, sequencing, wearable devices, hospital databases, and cloud computing," says Hongyu Zhao, PhD, chair and Ira V. Hiscock Professor of Biostatistics, professor of genetics and of statistics and data science, and co-director of CBDS, "there is a great need to develop efficient ways to collect, store, manage, analyze, visualize, and interpret the results."

It is a kind of "data fusion," adds Mark B. Gerstein, PhD, Albert L. Williams Professor of Biomedical Informatics, professor of molecular biophysics and biochemistry, of computer science, and of statistics and data science, and CBDS co-director. "We're integrating all the different types of data together, and that's just something that is hard to do in a completely generic, automated way. You need to think about what you're putting together."

That includes gathering insights that enhance clinical care. Krumholz says that one of CBDS's great advantages is the presence and participation of Yale clinicians, who can help steer data-driven science toward its greatest possible impact. "We have a medical center and actual patients being seen and care being delivered," he explains, "and so we have the opportunity to go end to end, where we're thinking at first about the end users." That, Krumholz says, could lead to new discoveries, quicker paths toward better treatment decisions by clinicians, and even insights into how the broader health care system can be redesigned for the better.

The center also has a vital educational mission, giving Yale scientists at all levels—including accomplished investigators whose training preceded the "big data" era—a greater familiarity with data science and what it can do for them. That will require detailed planning, and extensive listening to various constituencies' needs. "It's easy to expose graduate students to it because you can just make a course," says Noonan, who also is on the CBDS steering committee. "But you can't do that with postdocs and faculty. What we have to do through the center is get people in place who know how to teach these concepts to a diverse group of people with diverse backgrounds and help them understand what they need to know to function in this new world because they're going to need to know it." Gerstein adds that having more data expertise in the Yale community will be a catalyst toward another essential goal—attracting future recruits in the field at all levels, from students to expert faculty.

ROBERT A. LISAK

Xinxin (Katie) Zhu came to Yale last August, to take primary responsibility for growing the Center for Biomedical Data Science, whose goals include bringing together biomedical scientists and quantitative experts to bolster each other's research, adding to data science expertise throughout the medical school and university, and exploring how to manage rapidly expanding sources of data.

CBDS is part of a constellation of data science activity exploding throughout the university, from a new undergraduate major to the recruitment of theoreticians at the most advanced levels of the field. "Integrative data science and its mathematical foundations" is on the University Science Strategy Committee's suggested list of the most promising opportunities for investment across the sciences, which President Peter Salovey, PhD '86, endorsed in November. "CBDS fits perfectly into this new emphasis," says Zhao. "This center really serves at the interface of mathematics, statistics, computer science, biology, medicine, and public health."

"We're poised to do good work. We're positioned to be successful," says Krumholz, who credits the late Carolyn W. Slayman, PhD, deputy dean for academic and scientific affairs, Sterling Professor of Genetics, and professor of cellular and molecular physiology, for having the early sense that a center was needed, and considers CBDS to be part of her legacy. "I think Yale has a unique opportunity to lead and inspire and produce tools that will take us into that next era, and I'm excited to be part of it."

OUT & ABOUT

May 29 Colleagues, friends, family, students, and former patients packed into Harkness Hall for a **Retirement Party**, to celebrate the widespread impact of **Margaret Bia**, MD, professor emerita of medicine (nephrology) and senior transplant nephrologist, on the medical school community. **1.** From right to left, former patient **James Silvertrini**; **Shin Lin**, MD, a nephrologist in West Haven; Bia; and **Sharon Silvestrini**, wife of James. **2.** From left, **Janylet Dopico**, RN, transplant coordinator at Yale New Haven Hospital (YNHH); Bia; **Debbie Patton**, RN, transplant coordinator at YNHH; **Cindy Banuelos-Blessing,** associate transplant coordinator; and **Kelly Flynn**, RN, transplant coordinator.

1.

ROBERT A. LISAK (2)

2.

September 30 Researchers, cancer doctors, and community leaders kicked off the **6th annual Discovery to Cure Beverly Levy Walk**, with a ribbon-cutting at Yale's Payne-Whitney Gymnasium. The Discovery to Cure program raises money for research projects for the early detection and treatment of women's reproductive cancers. The walk is named in honor of Beverly Levy, who started the walk to raise awareness and lost her battle to ovarian cancer in 2014.

HAROLD SHAPIRO

1.

October 18 Stephen and Margery Riker hosted a **Dinner Party**, at the Lotus Club in New York City to highlight recent advances by the Yale Cancer Center (YCC). **1.** From left, **Joel E. Smilow,** YC '54, philanthropist and former CEO of Playtex Products, Inc., **Charles S. Fuchs,** MD, MPH, director of YCC and physician-in-chief of Smilow Cancer Hospital; and **Nick Makes**, senior vice president of Turner Construction Company and YCC board member. **2.** From left, **Stephen Riker**, YC '58, vice chair of Cushman & Wakefield, and YCC board member; and **Iris Morse**, wife of Andrew Morse, YC '68, share a laugh.

2.

JULIE BROWN (2)

October 9 On Yale Founders Day, university staff members celebrated **Service Milestones**. **Lena Smith Parker** (second from right), director of operations at the School of Medicine's Office of Communications, planted a tree at Phelps Gate to mark 15 years at Yale. Celebrating from the Office of Communications were (l-r) **Justin Navarro**, operations deputy director; **Maya Szatai**, visual design specialist; **Mary Hu**, MBA, associate dean for communications and chief communications officer; **Liz Pantani**, web support specialist; Parker; and **Claudia Davis**, business systems analyst and web producer.

ROBERT A. LISAK

TONY FIORINI

October 8 Recipients of the **Wilbur Lucius Cross Medal**, the highest award given by Yale's Graduate School Alumni Association (GSAA) included **Kelsey Martin**, MD '92, PhD '91, a graduate of the medical school's MD-PhD program. Martin, dean of the David Geffen School of Medicine at the University of California, Los Angeles, is a celebrated neuroscientist. From left, **Anna Barry**, PhD '98, chair of GSAA; **Lynn Cooley**, PhD, dean of Yale's Graduate School of Arts and Sciences; Martin; and President **Peter Salovey**, PhD, at a dinner Salovey hosted at the Yale Center for British Art.

// MBL *(page 1)* functions of human platelets. The discovery's significance was such that a resulting product was later commercialized.

In recognition of MBL's influence on Levin's career and the opportunities it can offer to Yale medical students, he and his wife Francine have made a philanthropic commitment to establish the Jack and Francine Levin Yale-at-MBL Initiative for Student Research.

Second-year medical student Shobana Subramanian was selected as the first Levin Fellow in 2018 and spent this past summer at the MBL conducting research on synaptic conditions alongside Leonard Kaczmarek, PhD, professor of pharmacology and of cellular and molecular biology, and Elizabeth A. Jonas, MD, professor of medicine (endocrinology) and of neuroscience.

The MBL, an affiliate of the University of Chicago, provides access to, and training in, super-resolution and high-resolution microscopy. The necessary instrumentation is offered at no cost by such specialty manufacturers as Zeiss and Olympus. Subramanian became adept with these imaging techniques and used them to examine the structural dynamics of synapses in rodent brains, studying how the synapses' cytoskeletal structure changes under various conditions.

Jack Levin

Subramanian "was of course so brilliant and was able to learn this really complex super-resolution microscopy, and she learned how to process the images," Jonas says. "She got amazing data by the end of the summer." Jonas and Subramanian are working together to prepare their results for publication.

The Levin Fellowship will support up to five Yale medical students next summer and possibly a greater number in future years. Its aim is to enable YSM students to engage in biomedical research related to human health at the MBL and encourage them to consider careers that include original biomedical research. The Levins hope that over time their initiative will encourage the formation of a self-renewing community of YSM students and faculty at the MBL.

Kaczmarek has been a summer regular at the MBL since 1986. "When medical students hear 'marine biology' they initially think it may not be related to their interests," he says, "but the fact is that the world's top scientists go to the MBL to meet and collaborate on key questions in medical science and basic biology."

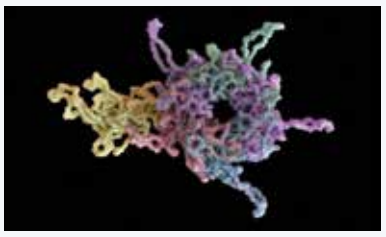
Levin's experience at the MBL in the 1960s epitomized this rich scientific atmosphere. During their work on *Limulus*, anticoagulants that he and Bang had expected to prevent coagulation had no effect on the crab's blood, which continued to clot. In what he calls "an act of scientific desperation," Levin prepared glassware that was free of endotoxin, which is a component of Gram-negative bacteria like *E. coli*. When he collected *Limulus* blood using the endotoxin-free glassware, the blood did not clot, and so Levin and Bang established that the blood coagulation mechanism in *Limulus* was sensitive to bacterial endotoxin.

This observation paved the way for the development of what is known as the *Limulus* amebocyte lysate (LAL) test for bacterial endotoxin, which was commercialized in the U.S. in the '70s and makes it possible for drug companies to detect minute concentrations of potentially deadly endotoxin during the manufacturing process and thereby prevent contamination.

Levin subsequently spent more than 20 summers doing research at the MBL. He was a faculty member at the Johns Hopkins University School of Medicine for 17 years and then moved to the University of California, San Francisco School of Medicine, where he remains a member of the faculty of the departments of Laboratory Medicine and Medicine. Francine Levin was an important scientific collaborator and a co-author of many of his papers.

Jack Levin sees medical school as a formative period in which scientific exploration can yield tremendous payoffs. His advice: "One should never hesitate to tackle a new unusual project because you're unfamiliar with it." He hopes that future Levin Fellows will also have the experience of serendipity that he encountered at Woods Hole more than five decades ago and shaped an important component of his life's work.

Behavior of cervical cancer virus is seen



Human papillomavirus (HPV), the virus that causes cervical cancer, enters the cells it infects inside a membrane-bound sac called the endosome, a new Yale study has found.

A team led by Daniel DiMaio, MD, PhD, deputy director of Yale Cancer Center and Waldemar Von Zedtwitz Professor of Genetics, and professor of molecular biophysics and biochemistry, and of therapeutic radiology, had previously found that the retromer protein shepherds HPV from the endosome to the nucleus by grabbing onto an HPV protein called L2. But it was unclear in what way the retromer, in the cytoplasm, could access L2, within the endosome.

In a study published Aug. 16 in *Cell*, DiMaio and his team reveal that a short portion of L2, a cell-penetrating peptide (CPP), protrudes from the endosome into the cytoplasm. When the CPP, which is next to L2's retromer binding site, enters the cytoplasm, it brings along the retromer binding site and exposes it to the retromer, the researchers found. Drugs that target the CPP or retromer binding could potentially block HPV infection, DiMaio says, and his lab is testing that possibility.

Labs visualize cell "skeleton" structure

The protein filamin and its close relatives help assemble filaments of the protein actin into a kind of cellular skeleton. A number of genetic diseases result from defects in this cytoskeleton. Researchers led by Charles V. Sindelar, PhD, associate professor of molecular biophysics and biochemistry, and David A. Calderwood, PhD, associate professor of pharmacology and of cell biology, have used cryo-EM to visualize the 3D structure of filamin's actin-binding section as it attaches to actin.

The protein, they found, has three actin binding sites. Each has slight nuances in how it binds to actin and which part of the actin structure it interacts with. They then showed how slight changes in filamin's actin-binding section, or domain, can interrupt its connection to actin.

The findings, published Sept. 16 in *Nature Structural Molecular Biology*, explain why mutations linked to genetic diseases are so detrimental. The actin-binding domain must open and close to bind actin, and some disease mutations apparently enhance this opening, leading to increasing binding, while others more directly disrupt the interactions between one of filamin's actin-binding sites and actin, leading to an entirely separate disease.

Patient's bequest supports research by her physician

Posthumous gift adds to years of generous support for the Department of Medicine

Shortly after Walter Newberry Kernan, MD, professor of medicine (general medicine) joined the School of Medicine faculty in 1989, he became Liesa Bing Allen's primary care physician. Their doctor-patient relationship would last nearly three decades until her death on July 19, 2017, six days shy of her 87th birthday.

Throughout her time as Kernan's patient, Allen, a successful attorney and corporate officer during her career, took an interest in his research, which focused on education in primary care and secondary stroke prevention. "They had a relationship of mutual respect," says Allen's stepdaughter, Jane Allen.

Early in that relationship, Allen donated money to the medical school to support education in the Department of Medicine. The gift was directed toward improving the training of students and residents at the school. "This funding was instrumental in several studies that used novel databases at Yale to examine and improve emerging practices in office-based education," says Kernan.

As her final years approached, Allen wanted her financial support of Yale School of Medicine to continue after her death. She shared this wish with Kernan. "She invited me to help with the language for a gift so that the funds could be used to support ideas and purposes that we had discussed over the years, particularly education and stroke prevention," he says.

Nearly nine months after Liesa's death, her husband of 35 years, Milton Allen, and Jane Allen presented Kernan with the final installment of this bequest, a check for $1 million. When Allen's family learned about the bequest and her previous donations, which Liesa—who kept her philanthropy private—had not disclosed to them, they say they were not surprised. Milton Allen describes his wife as a principled person with a long, though quiet, history of giving, including completely funding the educations of several children she had encountered through the years. "Dr. Kernan was another person that she ran into that she wanted to do something for," says Milton Allen. "So, she did it."

Her principles grew from a personal history of adversity. When she was a young girl, Allen and her parents fled Nazi Germany in 1938 for the United States. "Those experiences as a refugee affected her character and how she dealt with people for the rest of her life," says Milton Allen. "She was always very concerned people were treated fairly," says Jane Allen, which motivated her philanthropy.

As Kernan learned more about Allen through the years, he came to know her concerns with fairness and equity. Occasionally, Allen would tell him stories that, Kernan says,

COURTESY OF JANE ALLEN

Liesa Bing Allen (above) and her primary care physician at Yale, Walter Newberry Kernan, developed a long doctor-patient relationship that inspired Allen to give financial support to education in the Department of Medicine during her lifetime, and then to make a $1 million bequest that continues to support Kernan's research into preventing stroke, as well as targeting health care disparities that may adversely affect medical education.

"gave me an insight into her brilliance, her moral compass and the sensibilities that underlaid her grace, strength, and generosity. She would tell stories about her life which affected my awareness of bigotry and the opportunities we all have to treat each other with respect and care. I learned a lot from her. I am sure many other people can say the same."

Kernan plans to use some of her funds to explore how health care payment disparities may affect primary care education among medical students and residents. Some teaching institutions establish separate clinics or care pathways for patients who are uninsured or underinsured. Research has not yet demonstrated how widespread this practice is or its consequences. However, Kernan says, "We risk conveying the message to students and residents that it's okay to treat different patients differently. I think Mrs. Allen would be interested in this issue because she had a very strong interest in helping those with limited resources to have a fair opportunity."

Liesa Allen's final gift also helped Kernan complete secondary analyses of data from the Insulin Resistance Intervention after Stroke (IRIS) trial, leading to publication in the journal *Circulation*, among others. The main IRIS trial showed that a medication lowering cellular resistance to insulin reduces the risk of subsequent stroke in insulin-resistant, nondiabetic patients who have previously experienced a stroke. He plans to devote more of the funds to studying novel stroke prevention methods.

Kernan says he is grateful that Allen entrusted him with her bequest. "My job," he says, "is to be sure that the good that comes out of this opportunity is commensurate with her intentions and the goodwill in her heart."

Leducq Transatlantic Network makes Schwartz a team leader

It is rare for science to identify one key protein that determines a cell's behavior in health and disease. KLF2 is one such protein. Among other functions, "it is the principal transcriptional pathway that keeps your arteries open and healthy," says Martin A. Schwartz, PhD, Robert W. Berliner Professor of Medicine (Cardiology) and professor of biomedical engineering and of cell biology. Because it performs this essential role, Schwartz takes particular interest in anomalies in KLF2 expression that underlie multiple vascular diseases.

Fondation Leducq's Transatlantic Networks of Excellence program has awarded Schwartz and a network of five other researchers, from North America and Europe, a five-year, $6 million grant to study the KLF2 transcription factor. Schwartz will oversee the North American researchers of the network, marking the fourth time a Yale professor has played such a role.

Two years ago, a postdoctoral researcher in the Schwartz Lab, Brian G. Coon, PhD, used the gene-editing tool

Martin Schwartz

CRISPR to perform a genome-wide screen in endothelial cells, the cells that line blood vessels. The friction generated by blood flow past these cells induces KLF2 expression, and Schwartz and Coon wanted to know which genes mediate this process. "What we got out of it was astounding," says Schwartz. The screen produced a hit list of 500 possible genes. "The trouble is, to really exploit this amount of data, you need a team," he says.

Schwartz began reaching out to other investigators. After talking to a colleague about possible experiments and funding, "we decided that Leducq would be a good way to do it," he says. They forged a team from both sides of the Atlantic and took their plan to Leducq, which endorsed it.

Based in Paris, Fondation Leducq was founded by the late Jean and Sylviane Leducq in 1996 to fund cardiovascular and neurovascular research. In 2003, the organization established the Transatlantic Networks of Excellence program to foster collaborative research in these domains. According to its mission statement, the fight against vascular disease is a battle that "should be waged at the international level." Including the five 2018 grants, the foundation has supported 62 of these networks.

During the early stages of this project, Schwartz and his network will develop tools to test the hit list's genetic targets. The Schwartz Lab will receive $1.16 million of the grant to unravel the signaling network that allows blood flow to influence KLF2 expression. Other investigators will test these genes in vitro in endothelial cells as well as in vivo in mice. At the end of the grant period, Schwartz says, "we will have realistic drug targets."

Schwartz projects confidence in his team's ability to push vascular research forward. "I think it's a problem that is ripe to be solved." he says.

Grants and contracts awarded to Yale School of Medicine

September 2017–December 2017

Federal

Syed Ali, NIH, *Function of Slack Potassium Channels in Early Onset Epilepsy and Intellectual Disabilities,* 3 years, $176,906 • **Susan Baserga**, NIH, *A New Role for the PAX9 Protein in Ribosome Biogenesis,* 4 years, $1,260,397 • **Jeffrey Bender**, NIH, *Competitive Macrophage microRNA-RNA Binding Protein Interactions in Wound Repair,* 3.9 years, $1,289,752 **Steven Bernstein**, NIH, *Yale Scholars in Implementation Science (YSIS),* 4.8 years, $2,975,435 • **Linda Bockenstedt**, NIH, *Pathogenesis of* Borrelia miyamotoi *Infection and Lyme Coinfection in Mice,* 5 years, $2,093,750 • **Douglas Brash**, NIH, *Chemiexcitation: A New Mode of Skin Disease,* 3.9 years, $1,670,093 • **Christopher Burd**, NIH, *Lipid Dynamics in the Golgi Apparatus,* 4.3 years, $1,638,320 **Jason Cai**, NIH, *Synthesis and Evaluation of an 18F Labeled SV2A Ligand as a Novel Biomarker for Alzheimer's Disease,* 6 months, $170,629 • **Sreeganga Chandra**, **Charles Greer**, DoD, *Mechanisms of Olfactory Deficits in Parkinson's Disease,* 3 years, $586,250 • **Sandy Chang**, NIH, *Role of BRIT1 in Telomere Dysfunctional Triple Negative Breast Cancer,* 2 years, $167,500 • **Katarzyna Chawarska**, **Joseph Chang**, **Todd Constable**, **Laura Ment**, **Kelly Powell**, **Flora Vaccarino**, **Fred Volkmar**, NIH, *Cellular, Molecular, and Functional Imaging Approaches to Understanding Early Neurodevelopment in Autism,* 4.9 years, $4,810,051 • **Xi Chen**, NIH, *Social Pension, Health, and Healthy Aging,* 4 years, $513,518 **Hyung Joon Chun**, NIH, *Molecular Mechanisms of Neonatal Pulmonary Hemorrhage,* 1.9 years, $631,803 • **Daniel Colon-Ramos**, NIH, *Cellular and Molecular Mechanisms that Modulate Synaptic Function and Plasticity,* 5 years, $2,191,560 • **Daniel Colon-Ramos**, **Zhirong Bao**, **William Mohler**, NIH, *WormGUIDES: A Resource for Global Understanding in Dynamic Embryonic Systems,* 3.7 years, $3,242,190 • **Edward Courchaine**, NIH, *Cajal Body Assembly Mechanisms in Vitro and in the Context of Neurodegenerative Disease,* 3 years, $73,300 **Joseph Craft**, **Richard Flavell**, NIH, *An in Vivo CRISPR-Cas9 Genetic Screen in Murine Primary T Cells to Discover Metabolic Regulators of Follicular B Helper T (Tfh) Cell Differentiation,* 2 years, $809,597 • **Amy Davidoff**, NIH, *Patterns of Medication Therapy and Patient-Reported among Older Adults with Cancer: SEER-MHOS Part D Linkage,* 1.2 years, $99,932 • **Pietro De Camilli**, **Katherine Bownes**, NIH, *Lipid Transfer at Membrane Contact Sites in Neuronal Function,* 4.8 years, $1,825,240 **Pietro De Camilli**, **Xinran Liu**, **Derek Toomre**, NSF, *MRI: Acquisition of a Focused Ion Beam Scanning Electron Microscope (FIB-SEM) for Large Volume 3-Dimensional Imaging of Whole Cells,* 3 years, $698,558 • **Robin de Graaf**, NIH, *Robust 3D MR Spectroscopic Imaging through Multi-Coil Magnetic Field Shaping,* 3.7 years, $1,882,538 • **Nicole Deziel**, **James Saiers**, Environmental Protection Agency, *Drinking Water Vulnerability and Neonatal Health Outcomes in Relation to Oil and Gas Production in the Appalachian Basin,* 3 years, $1,998,515 **George Dragoi**, NIH, *Development of Predictive Coding Networks for Spatial Navigation,* 5 years, $2,093,750 • **Deepak D'Souza**, NIH, *Fatty Acid Amide Hydrolase (FAAH) Inhibitor Treatment for Cannabis Use Disorder (CUD),* 2.8 years, $8,633,637; NIH, *Synaptic Vesicle Density in Cannabis Dependence,* 2 years, $460,625 • **Thomas Fernandez**, NIH, *Neurogenetic Investigations of Obsessive-Compulsive Disorder,* 5 years, $2,760,879 • **Carlos Fragoso**, NIH, *COPD Pharmacotherapy in Aging Populations,* 2 years, $167,500 • **Gigi Galiana**, NIH, *Practical Nonlinear Gradient Encoding for Enhanced Accelerated Imaging,* 4.8 years, $1,507,500 • **Mark Gerstein**, NSF, *Collaborative Proposal: ABI Innovation: A Graph Based Approach for the Genome Wide Prediction of Conditionally Essential Genes,* 3 years, $1,203,514 • **Leigh Goedeke**, NIH, *Effect of Liver-Specific Acetyl-CoA Carboxylase Inhibition on Hepatic Steatosis and Insulin Resistance,* 2 years, $116,832 • **Carlos Grilo**, **Sherry McKee**, NIH, *Efficacy and Mechanisms of Naltrexone & Bupropion for Binge Eating Disorder,* 4.8 years, $3,615,287 • **Jaime Grutzendler**, NIH, *Biological Basis of Post-Delirium Cognitive Decline,* 4.8 years, $2,853,240 • **Ruth Halaban**, NIH, *Integrative Genomic Biomarkers for Predicting Response to Immunotherapy in Melanoma Patients,* 2 years, $400,744 • **Marc Hammarlund**, **Oliver Hobert**, **David Miller**, **Nenad Sestan**, NIH, *Discovery and Analysis of the* C. elegans *Neuronal Gene Expression Network (CENGEN),* 4.8 years, $6,081,264 **Alicia Heapy**, **Christopher Ruser**, NIH, *Cooperative Pain Education and Self-management: Expanding Treatment for Real-world Access (COPES ExTRA),* 1.9 years, $1,090,947 • **Michael Higley**, NIH, *Cellular Mechanisms of GABAergic Inhibition in Neocortical Dendrites,* 4.9 years, $2,091,810 • **Tamas Horvath**, NIH, *AgRP Neurons Promote the Effects of Calorie Restriction on Lifespan,* 3.7 years, $1,733,964 **Tamas Horvath**, **Matthew Lawrence**, NIH, *In Vivo and in Vitro Systems to Validate Geronic Proteins and Their Mechanisms of Action,* 3.7 years, $2,093,519 • **Henry Huang**, NIH, *Novel PET Radiotracer for Muscarinic M1 Receptor,* 2.8 years, $2,357,664 • **Shuta Ishibe**, NIH, *Role of Clathrin Mediated Endocytosis in Podocyte Biology,* 5 years, $1,884,375; DoD, *Targeting Histone Deacetylase in Focal Segmental Glomerulosclerosis—From Mice to Patients,* 3 years, $1,195,342 • **Yasuko Iwakiri**, NIH, *The Role of Kupffer Cells in Alcohol-Induced Liver Disease,* 5 years, $1,895,974 • **Monika Jadi**, NIH, *Cholinergic Modulation of Cortical Visual Processing,* 2.9 years, $722,629 • **Elizabeth Jonas**, NIH, *Requirement for Enhanced Metabolic Efficiency in Hippocampal LTP,* 1.9 years, $399,879 • **Amy Justice**, NIH, *3/3 COMpAAAS Tripartite: ART-CC, KP, and VA,* 4.9 years, $2,908,542 • **Robert Kerns**, **Cynthia Brandt**, **Peter Peduzzi**, NIH, *Pain Management Collaboratory Coordinating Center (PMC3),* 5.9 years, $9,755,798 • **Trace Kershaw**, **Nathan Hansen**, NIH, *Using Smart Phones to Understand the Link Between Social and Geographical Context and HIV Risk Behavior Among MSM,* 4.7 years, $4,143,253 **Daryl Klein**, NIH, *Harnessing Receptor Pleiotropy to Control Cancer,* 3 years, $430,314 • **Diane Krause**, NIH, *Megakaryocyte Erythroid Progenitor Fate Specification,* 4 years, $2,061,936 • **Maria Lara-Tejero**, **Joerg Bewersdorf**, NIH, *Structural and Functional Characterization of the* Salmonella Typhimurium *Type III Secretion System Sorting Platform,* 1.9 years, $460,625 • **Francis Lee**, NIH, *ERK Signaling in Inflammatory Bone Loss,* 2 years, $767,890; NIH, *Modification of Bone Grafts for Orthopaedic Procedures,* 4 years, $2,157,614 **Morgan Levine**, **Gerald Shadel**, NIH, *Molecular Mechanisms and Social Constructs: How Genes and Environment Regulate the Rate of Aging,* 2.7 years, $772,656 • **Morgan Levine**, **Gerald Shadel**, **Christopher Van Dyck**, NIH, *Molecular Networks Underlying Resilience To Alzheimer's Disease Among Apoe4 Carriers,* 4.7 years, $4,542,145 • **Don Li**, NIH, *Mechanistically Linking Insulin Action and the Thermic Effect of Food,* 3 years, $106, • **Judith Lichtman**, NIH, *Patterns of Recurrent Stroke in the Elderly,* 1.9 years, $834,672 **Jun Liu**, NIH, *Structural Basis of Phage Infection and DNA Ejection,* 1.5 years, $311,515; NIH, *Structural Basis of Signaling Between Bacterial Chemoreceptors and Flagella,* 2 years, $524,375; NIH, *Structure-Function Relationships in the Spirochetal Flagellar Motor,* 2.7 years, $1,372,082 • **Naila Makhani**, NIH, *The Radiologically Isolated Syndrome in Children,* 5 years, $791,856 • **Robert Malison**, NIH, *Assessing Glutamate Homeostasis in Cocaine Addiction Using 7T 1H-MRS,* 2 years $460,625; NIH, *Imaging Complement Component 4 Gene Effects on Human Synaptic Density in Vivo Using 11C-UCB-J PET,* 2 years, $404,250 • **Nikhil Malvankar**, NIH, *Targeting Bacterial Infections by Imaging Electrical Interactions Between Host Surface Pathogens,* 4.8 years, $2,479,145 • **Gilbert Moeckel**, DoD, *MIF as Preventive Drug Against Combat Injury-Related Acute Renal Failure,* 3 years, $1,218,967 • **Gil Mor**, NIH, *Discovery to Cure Summer Program,* 4.8 years, $540,000 • **Kristen Morie**, NIH, *Development of Reward Processing in Prenatally Exposed Adolescents and Young Adults,* 5 years, $907,145 **Rebecca Muhle**, NIH, *Mapping Regulatory Networks of Autism Risk at Cellular Resolution during Neurodevelopment,* 4 years, $616,340 • **John Murray**, NIH, *Linking Large-Scale Dysconnectivity in Schizophrenia to Cortical Circuit Function at the Individual Level through Computational Modeling and Multimodal Neuroimaging,* 4 years, $1,660,406 **Mandar Muzumdar**, NIH, *Elucidating KRAS-Specific Vulnerabilities in Pancreatic Cancer,* 3.7 years, $702,675 • **Xenophon Papademetris**, **Dustin Scheinost**, NIH, *Multi-context Software for Robust and Reproducible Neuroscience Image Analysis,* 2.8 years, $1,223,156 • **Chirag Parikh**, NIH, *AKI Matched Phenotype Linked Evaluation with Tissue (AMPLE-Tissue),* 9 months, $377,001 • **Katerina Politi**, DoD, *Functional Characterization and Modeling of Acquired Resistance to Immune Modulation in Lung Cancer,* 2 years, $586,250 • **Lajos Pusztai**, NIH, *Immune Biological Differences between Triple Negative Breast Cancer in African American and non-African American Women and Potential Immunotherapy Opportunities to Improve Treatment Outcome,* 4 years, $1,974,200 • **Elizabeth Ralevski**, NIH, *Effect of Allopregnanolone on Stress-induced Craving,* 3 years, $343,613 • **Jesse Rinehart**, NIH, *Expanding the Genetic Code with Phosphotyrosine and Phosphothreonine,* 4 years, $1,084,289 • **Marc Rosen**, **Steve Martino**, NIH, *Engaging Veterans Seeking Service-Connection Payments in Pain Treatment,* 1.9 years, $1,176,868 **Craig Roy**, NIH, *Functional and Structural Analysis of the* Legionella Pneumophila *Dot/Icm Apparatus,* 2 years, $460,625 • **Santiago Salazar**, NIH, *Investigating the Role of Pyk2 in Alzheimer's Disease Pathophysiology,* 9 months, $38,083 **David Schatz**, NIH, *Interdisciplinary Immunology Training Program,* 5 years, $3,314,619; NIH, *Mechanism and Targeting of V(D)J Recombination,* 5 years, $2,301,595 • **Christian Schlieker**, NIH, *Defining the Nuclear Envelope-resident Protein Turnover Machinery Implicated in Diseases Affecting Cholesterol Metabolism,* 3.3 years, $1,265,581 • **Martin Schwartz**, **Gaudenz Danuser**, **Mark Ginsberg**, NIH, *Mechanisms of Mechanosensing through Integrins,* 3.7 years, $1,648,200 • **Gerald Shulman**, NIH, *Effects of Hepatic Acetyl-CoA Carboxylase Inhibition on NAFLD and Hepatic Insulin Resistance,* 4.9 years, $3,656,218 • **Justin Shyer**, NIH, *Metabolic Regulation of Follicular B Helper T (Tfh) Cell Development,* 3 years, $132,612 • **Michael Simons**, NIH, *Syndecan Function in Endothelial Cells,* 4 years, $2,022,285 • **Albert Sinusas**, **James Duncan**, NIH, *Image Guided Delivery of Bioresponsive Hydrogels,* 4 years, $3,069,279 • **Dana Small**, **Sonia Caprio**, NIH, *Neurocognition in Youth with Prediabetes,* 4.9 years, $3,795,286 • **Dieter Soll**, **Jeffrey Townsend**, NSF, *CCI Phase I: Center for Genetically Encoded Chemical Materials (C-GEM),* 3 years, $1,800,001 **Yajaira Suarez**, NIH, *MicroRNAs in Vascular Diseases,* 4 years, $1,687,412 • **Zhaoxia Sun**, NIH, *Role of Cilia in Renal Fibrosis,* 4.7 years $1,884,375 • **Carson Thoreen**, NIH, *Translational Control of Gene Expression by the mTOR Pathway,* 5 years, $1,758,750 • **Susumu Tomita**, NIH, *Mechanisms for Synaptic Localization of Ionotropic GABA Receptors in the Brain,* 5 years, $2,093,750 • **Anthony Van den Pol**, NIH, *Zona Incerta GABA Neurons Modulate Energy Homeostasis,* 4.8 years, $2,009,140 **Tiara Willie**, NIH, *She's PrEPared: The Impact of Intimate Partner Violence on Women's Engagement in the PrEP Care Continuum,* 2.2 years, $88,568 **Frederick Wilson**, NIH, *Mechanistic Dissection of an Arginine Methyltransferase Dependency in Cancer,* 5 years, $876,420 • **Francis Wilson**, DoD, *Targeting Histone Deacetylase in Focal Segmental Glomerulosclerosis - From Mice to Patients,* 3 years, $1,295,599 • **Dan Wu**, NIH, *DKK2 Regulates NK Activation and Tumor Immunity,* 5 years, $2,566,560 **Xiaoyu Xue**, NIH, *Functions of the DNA/RNA Motor Protein AQR in R-loop Resolution,* 9 months, $209,375 • **Yang Yang-Hartwich**, NIH, *A New Ovarian Cancer Mouse Model Based on Nanoparticle Gene Delivery,* 1.9 years, $160,750 • **Jessica Ye**, NIH, *Insulin Signaling in Tissue Resident Macrophages,* 3 years, $107,052 • **Laura Yockey**, NIH, *Immune Control of Zika Virus after Vaginal Infection,* 3 years, $109,708 • **Z. Jimmy Zhou**, NIH, *Visual Science Training Grant,* 5 years, $681,929

Non-federal

Clara Abraham, Icahn School of Medicine at Mount Sinai (ISMMS) (NIH), *Mount Sinai School of Medicine Inflammatory Bowel Disease Genetics Research Center,* 11 months, $103,947 • **Thomas Adams**, International Obsessive Compulsive Foundation, *Non-Invasive Brain Stimulation to Improve Consolidation of Therapeutic Learning Memories,* 2 years, $48,646 **Jean Adnopoz**, Child Health & Development Inst. of Connecticut, *Singh CONNECT FY18 Agreement,* 1 year, $98,471 • **Kathleen Akgun**, University of Colorado Denver, Duke University, *Refinement and Expansion of the Palliative Care Research Cooperative Group (PCRC),* 10 months, $28,000 • **Frederick Altice**, University of Connecticut (NIH), *Testing a Bio-Behavioral Primary HIV Prevention Intervention Among High-Risk People Who Use Drugs,* 1.3 years, $78,720 • **Kumar Ashtekar**, Arnold and Mable Beckman Foundation, *Development of Novel Platforms Toward Expanding the Druggable Kinome,* 2 years, $139,673 • **Lynnette Averill**, American Foundation for Suicide Prevention, *Brain Connectivity Networks and Predictors of Rapid Improvement in Suicidal Ideation Among Veterans,* 1.5 years, $85,000 • **William Becker**, Northern California Institute for Research & Education (NIH), *Implementation of a Pragmatic Trial of Whole Health Team vs. Primary Care Group Education to Promote Non-Pharmacological Strategies to Improve Pain, Functioning, and Quality of Life in Veterans,* 1.9 years, $66,148 • **Morris Bell**, University of Texas at Arlington (NSF), *PFI:BIC: iWork, a Smart Robot-Based Service for Vocational Assessment, Personalized Training and Rehabilitation,* 3 years, $383,822 **Helene Benveniste**, SUNY Stony Brook (NIH), *Nitric Oxide-Mediated Changes in Glymphatic and CSF Systems in Aging and Alzheimer's Disease,* 5 years, $1,170,561 • **Ranjit Bindra**, **Stephanie Halene**, Leukemia and Lymphoma Society, *Exploiting Mutant IDH1/2-induced BRCAness with PARP Inhibitors as a Novel AML/MDS Therapy,* 3 years, $600,000 **Ranjit Bindra**, **W. Mark Saltzman**, Alex's Lemonade Stand, *Development of Nanoparticle-encapsulated Chemo/Radio-Sensitizers for Intrathecal Delivery,* 2 years, $250,000 • **Marc Brackett**, University of Tennessee, *UT RULER Training,* 1 year, $12,000 **Demetrios Braddock**, Texas Children's Hospital (NIH), *Novel Pathways in Ischemic Stroke in Sickle Cell Anemia,* 11 months, $10,162 • **Christina Camell**, American Federation for Aging Research, *Macrophage Inflammasome Activation and the Mechanism of Lipolysis Resistance in Aged Adipose,* 2 years, $120,000 • **Lloyd Cantley**, Augusta University (Formerly Georgia Regents University) (NIH), *Simultaneous Spatially Preserved Protein and mRNA Expression Profiling of the Hum,* 1 year, $99,538 **Jessica Cerdena**, **Richard Bribiescas**, Robert Wood Johnson Foundation, Health Policy Research Scholars Program, *Health Policy Research Scholars - Minor,* 5 years, $120,000 • **Sidi Chen**, V Foundation for Cancer Research, *Tackling Epigenetic Drivers of Medulloblastoma in Vivo,* 2 years, $200,000 • **Christian Connell**, State of Rhode Island Dept. of Children, Youth & Families (DHHS), *Evaluation of RI TIPS-MAPP Curriculum,* 1.2 years, $65,000 • **Philip Corlett**, University of Maryland (NIH), *Predictive Coding as a Framework for Understanding Psychosis,* 11 months, $294,770 • **Kelly Cosgrove**, Brain & Behavior Research Foundation (formerly NARSAD), *Imaging Glucocorticoid and Neuronal Dysfunction in PTSD,* 2 years, $99,986 • **Nicholas Dainiak**, **Joseph Albanese**, Oak Ridge Assoc. Universities, *Interlaboratory Comparison of Procedures, Calibration Curves and Results for Cytogenetic Biodosimetry Laboratories Located at Yale and the Radiation Emergency Assistance Center/Training Site (REACTS),* 1.6 years, $218,999 • **Amy Davidoff**, Lung Cancer Research Foundation, *Patterns of Palliative Care and Concurrent Therapy for Lung Cancer at End-of-Life: Implications for Quality,* 2 years, $149,270 • **Henk De Feyter**, James S. McDonnell Foundation, *21st Century Science Initiative-Planning Grant: Explore Opportunities to use Magnetic Resonance Spectroscopy (MRS) Together with Metabolic Perturbations to Study Effects on Brain Functional-Neuroenergetic Networks,* 1 year, $50,000 **Robin de Graaf**, University of Minnesota (NIH), *Imaging Human Brain Function with Minimal Mobility Restrictions,* 1.2 years, $769,181 • **Enrique De La Cruz**, University of California, Davis (NIH), *Function and Regulation of a DEAD-box Protein in mRNA Export,* 4.7 years, $251,250 • **Gail D'Onofrio**, State of CT Dept. of Public Health (DHHS), *CT DPH Prescription Drug Overdose Prevention for States,* 1.8 years, $728,538 • **James Duncan**, **Pamela Ventola**, George Washington University (NIH), *Multimodal Developmental Neurogenetics of Females with ASD,* 4.9 years, $1,674,159 • **Tore Eid**, University of Connecticut Health Center, *UConn Health Personal Service,* 1 month, $4,369 • **Stephanie Eisenbarth**, Bloodworks Northwest (NIH), *Immunobiology of Transfusion,* 1.3 years, $420,844 • **Carrie Epstein**, National Children's Alliance, *Introducing, Implementing and Evaluating CFTSI in Children's Advocacy Centers in the Northwestern U.S.,* 1.9 years, $110,000; National Children's Alliance, *Spreading and Sustaining Child and Family Traumatic Stress Intervention (CFTSI) in Child Advocacy Centers in the Carolinas,* 2 years, $198,373 • **Thomas Fernandez**, University of Sao Paulo, *Sao Paulo Sequencing Agreement,* 1 year, $16,000 • **Alfonso Galderisi**, Robert Leet and Clara Guthrie Patterson Trust, *Pathogenesis of Youth Onset Pre-diabetes and Type 2 Diabetes: Effect of TCF7L2 on Beta Cell Function and Incretin Response,* 2 years, $100,000 • **Patrick Gallagher**, New York Blood Center (NIH), *Red Cell Membrane Studies (Project),* 1.4 years, $320,288; New York Blood Center (NIH), *Red Cell Membrane Studies (Core),* 1.4 years, $169,538 • **Alison Galvani**, Oxford University, *ATF: Projections on Eliminating NTDs (Integrating Mapping with Modelling),* 1 year, $63,698 • **Guadalupe Garcia-Tsao**, University of Pittsburgh (NIH), *Molecular Subtypes for Targeted Therapies in Alcoholic Hepatitis,* 1.3 years, $30,004 **Evan Geller**, Autism Speaks, *High-throughput Screens to Discover Regulatory Mechanisms Contributing to Autism Spectrum Disorder,* 2 years, $64,000 • **Mark Gerstein**, University of Chicago (NIH), *Center for Functional Validation and Evaluation of ENCODE Enhancer Regions,* 1.3 years, $48,146 • **Antonio Giraldez**, University of Utah (NIH), *Initial Formation of 3D Chromatin Domains in Early Vertebrate Embryos,* 1.5 years, $226,681; Simons Foundation, *Effect of Autism Risk Genes in Neural Cell Identity Using Single Cell Seq.,* 3 years, $825,000 • **Valentina Greco**, Glenn Foundation for Medical Research, *Glenn Foundation Unsolicited Award,* 2 years, $60,000 • **Abigail Greene**, American Psychiatric Association, *Health ACT: Toward Improved Integration of Primary and Behavioral Health Care,* 1 year, $4,579 • **Jeffrey Gruen**, Lafayette College (NIH), *Genes to Behavior: Unlocking the Code for Early Detection of Reading Disorder,* 3 years, $38,733 • **David Hafler**, The Saudi Arabian Cultural Mission, *Multiple Sclerosis and Neuroimmunology Fellowship (Saudi Arabia),* 1 year, $75,807; The *Nancy Taylor Foundation for Chronic Diseases, Inc., Longitudinal, Single-cell Assessment to Define the Mechanism of B Cell Depletion Therapy in Autoimmunity,* 2 years, $216,000 • **Kassandra Harding**, International Society for Research in Human Milk and Lactation, *Will #Breastfeeding4Ghana Go Viral? Evaluating the Impact and Potential of the First Breastfeeding Social Media Marketing Campaign in Ghana,* 1.4 years, $99,215 • **Jeanne Hendrickson**, Bloodworks Northwest (NIH), *Immunobiology of Transfusion,* 1.3 years, $404,764 • **Kevan Herold**, Albert Einstein College of Medicine (NIH), *Mechanisms Underlying the HIV-HSV-2 Syndemic,* 1 year, $267,053; University of California, San Francisco, *Identification of Antigen-specific Responses in Patients with Autoimmune Endocrinopathies Following Checkpoint Inhibition in Cancer Immunotherapy,* 1 year, $110,000; L2 Diagnostics (NIH), *Novel Diagnostic for Autoimmunity from Checkpoint Inhibitor Immune Therapy,* 1 year, $98,663

Developing more resilience in children and communities

Joint program to counteract life-diminishing hardships in families and communities

Physicians, in their often-limited time with patients, try their best to zero in on a person's deficits—his or her physical and emotional vulnerabilities—and find a way to shore them up. But it often is a person's strength, an area on which physicians cannot always afford the time to focus, that can make the difference between sickness and health. That is especially true in children's mental health.

"How do you foster that resilience in children, their ability to bend and not break in the face of challenging stressors?" asks Linda C. Mayes, MD, Arnold Gesell Professor of Child Psychiatry, Pediatrics, and Psychology, and chair of the Yale Child Study Center.

The new Yale Child Study Center-Scholastic Collaborative for Child and Family Resilience aims to answer that question. The two organizations anticipate a long-term alliance that will yield numerous methods to cultivate resilience in children, families, and communities that face ongoing adversity.

The Collaborative is not a program with a fixed endpoint. Instead, Scholastic, the global children's publishing, education, and media company, and the Child Study Center expect the partnership to operate like a think tank, to which both will contribute and from which ideas will emerge organically and become concrete products and practices. Both groups see their individual differences as their collective strength. "We're bringing together people who are immersed in the development of children's literature with people who are immersed in the care of children's mental health," says Mayes. "In a partnership between a for-profit and a not-for-profit, there are interesting and different ways of thinking that come together, too."

The Child Study Center and Scholastic started their work together in 2012 when they teamed up to pilot Discover Together in rural Grundy County, Tennessee. The literacy and place-based educational program aims to build community pride and strengthen relationships in order to develop family and community resilience.

"One of the biggest predictors of resilience is social connectedness, so our initial research question was, 'Can literacy be used to foster those connections that build resilience?'" says Karen Baicker, publisher for family and community engagement curriculum at Scholastic.

AMANDA M. DETTMER

The collaboration between the Yale Child Study Center (CSC) and Scholastic includes (l-r): Greg Worrell, president, Scholastic Education; Fay Brown (CSC), Karen Baicker, publisher for family and community engagement, Scholastic; Linda Mayes, chair of CSC; Janelle Cherrington, SVP and publisher, Scholastic Education, and Megan Smith (CSC).

Through the Discover Together program, parents and children learn storytelling. Parents can use the skills to instill in their children the sense of security they need in order to be resilient. Stories about family origins help children feel grounded. Stories about others overcoming adversity help children feel safe. "The single most developmentally nurturing condition is relationships," says Mayes. "Having people around who can put adversity into context, help children come back to the baseline, and say, 'You're going to be ok.'"

For children who live in the shadow of poverty, addiction, or violence, stories are a vehicle for changing their circumstances. "If kids understand the idea of story, they can craft their own narratives and imagine different futures," says Baicker.

Scholastic and the Child Study Center agree that education and well-being are inextricably linked. They expect their collaboration to result in numerous materials that will promote the two simultaneously. Among the ideas already on the table are to adapt Discover Together for other locations; to create classroom materials that destigmatize childhood mental health problems; and to develop a tool to assess the skills inherent in resilience.

Scholastic is the ideal partner for this work, says Mayes. "It stands out as a company that truly cares about children."

Joy Hirsch, Haskins Laboratories (NIH), *Tracking Neurocognitive Changes During Computer-Aided Reading Instruction in Typically and Atypically Developing Children*, 1.8 years, $291,301 • **Karen Hirschi**, Columbia University (NIH), *Multi-tissue Platform for Modeling Systemic Pathologies*, 10 months, $83,750 • **Michael Hoge**, Southern Connecticut State University, *Southern Connecticut University, Department of Social Work*, 10 months, $37,210 • **Melinda Irwin**, Breast Cancer Research Foundation, *Biological and Biochemical Effects of Exercise and Diet on Breast Tissue*, 1 year, $250,000; Oregon Health Sciences University (NIH), *SWOG NCORP Research Base*, 1.7 years, $52,232 • **Nikhil Joshi**, Lung Cancer Research Foundation, *Investigating Anti-tumor T Cell Function in Autochthonous Models of Lung Adenocarcinoma*, 2 years, $150,000 • **Kellie Ann Jurado**, L'Oréal USA, American Association for the Advancement of Science, *Type I Interferon-mediated Zika Virus Neuroimmuno Protection*, 1 year, $60,000 • **Benjamin Kelmendi**, Heffter Research Institute, *Neural Correlates of the Effects of Psilocybin in Obsessive-compulsive Disorder: a Double-blind, Placebo-controlled Study*, 1 year, $139,142 • **Babar Khokhar**, Amyotrophic Lateral Sclerosis Association (ALS Association), *Memorandum of Understanding (MOU) ALS Association CT Chapter (ALSACT) and Yale Department of Neurology (YDN)*, 1 year, $40,000 • **Anthony Koleske**, Broad Institute, *Trio Haploinsufficiency as a Therapeutic Target in Schizophrenia*, 1 year, $100,247 • **Alex Koral**, Nasphan Foundation, *Unsedated Transnasal Endoscopy in Monitoring of Eosinophilic Esophagitis and Diagnosis of* Helicobacter pylori, 1 year, $5,000 **Priti Kumar**, University of Utah (NIH), *Center for the Structural Biology of Cellular Host Elements in Egress, Trafficking, and Assembly of HIV (Cheetah Center)*, 1.7 years, $75,000 • **Gary Kupfer**, Boston Children's Hospital, *Community Counts CDC Public Health Surveillance for Bleeding Disorders Program*, 3 years, $93,452 • **Heather Lipkind**, HealthPartners Institute (DHHS), *Evaluating the Risk of Spontaneous Abortion Following 4vHPV and 9vHPV*, 1 year, $28,453; HealthPartners Institute (DHHS), *HealthPartners Institute Response to VSD Infrastructure Recompete (RFTOP# 07607)*, 5 years, $56,427 • **Anthony Lisi**, **Lori Anne Bastian**, **Cynthia Brandt**, Palmer College of Chiropractic (NIH), *Chiropractic Care for Veterans: A Pragmatic Randomized Trial Addressing Dose Effects for cLBP*, 1.9 years, $205,208 • **Jun Liu**, University of Texas at Austin (NIH), *Initiation of Phage Infection*, 3.7 years, $396,976; University of Kansas (NIH), *Assembly/function of the Sorting Platform of the Shigella Type III Secretion Apparatus*, 3.4 years, $589,701 • **Aug Liu**, University of Texas Health Science at Houston (NIH), *Virulence Determinants of Fusobacterium Nucleatum*, 10 months, $41,034 **Johanna Madera**, Miriam Hospital-The Center for Behavioral & Preventive Med. (NIH), *Care Utilization Among Justice-Involved Men in a Specialized Primary Care Setting: The Role of Trauma in Patient Engagement*, 1 year, $16,200 • **Steven Marans**, New Alliance Foundation, *Child Development-Community Policing Program*, 1 year, $5,000; National Children's Alliance, *Introducing, Implementing, and Evaluating Child and Family Traumatic Stress Intervention in the Carolinas*, 4 months, $5,000 • **Carolyn Mazure**, **Jennifer Culhane**, **Michelle Silasi**, Eppley Foundation, *Viral Infections During Pregnancy: Enhancing Detection and Reducing Adverse Outcomes*, 1 year, $25,000 • **Wajahat Mehal**, Gilead Sciences, *Cellular Mechanism of Action of ASK1 Specific Inhibitors in Reducing Hepatocyte Steatosis and HSC Activation*, 1.4 years, $52,300 • **Kofi Mensah**, Robert Leet and Clara Guthrie Patterson Trust, *Erosive Rheumatoid Arthritis Correlates with Defective B Cell Expression of Ataxia-telangiectasia Mutated Protein*, 11 months, $95,000 • **Walther Mothes**, Duke University (NIH), *The Conformational State of Immunogens Assessed by smFRET*, 8 months, $199,650 **Linda Niccolai**, American University (NIH), *Social Determinants of HIV/AIDS: The Intersecting Impacts of Mass Incarceration, Housing Policy and Housing Instability*, 3.5 years, $698,052 • **James Noonan**, Simons Foundation, *Mapping ASD Regulatory Networks at Cellular Resolution in Neurodevelopment*, 3 years, $825,000 • **Elaine O'Keefe**, State of CT Dept. of Public Health (DHHS), *Basic Infection Control Training Project*, 1.6 years, $137,162 **Stephanie O'Malley**, Columbia University (NIH), *Multi-site Study: Varenicline Treatment of Alcohol Dependent Smokers*, 1 year, $23,320 • **Manoj Pillai**, **Stephanie Halene**, Fox Chase Cancer Center (NIH), *Robust Rational Design of Chemical Tools to Inhibit RNA-binding Proteins*, 10 months, $52,032 • **David Pitt**, University of Michigan (NIH), *Arginase-1 and iNOS Expressing CNS Myeloid Cell Subsets in EAE and MS*, 1.8 years, $142,924 • **Renato Polimanti**, Simons Foundation, *Cognitive and Brain Imaging Study of Autism Spectrum Disorder Risk Alleles Under Positive Selection in Affected and Unaffected Individuals*, 1 year, $69,984 • **Lajos Pusztai**, Regents University of California, San Francisco, *I-SPY2 +: Evolving the I-SPY 2 TRIAL to Include MRI-directed, Adaptive Sequential Treatment to Optimize Breast Cancer Outcomes*, 1 year, $12,194; Regents University of California, San Francisco, *I-SPY2 +: Evolving the I-SPY 2 TRIAL to Include MRI-directed, Adaptive Sequential Treatment to Optimize-Project 4*, 1 year, $12,194 • **Chin Reyes**, Champlain Valley Head Start, *CHILD Training—Vermont Head Start*, 2 months, $7,500; The Theresa and Frank Caplan Foundation, *Closing the Achievement Gap without Closing the School Door: Addressing Implicit Biases and Preschool Expulsions by Nurturing the Mental Health Climate of Classrooms*, 1.5 years, $82,001; The New York City Dept. of Health and Mental Hygiene, *Exploring Classroom Factors Relating to Preschool Expulsions & Disciplinary Practices*, 4 months, $20,000 • **David Rimm**, Breast Cancer Research Foundation, *Targeted and Immune Therapies in Breast Cancer*, 1 year, $250,000; University of Michigan, *Financial Support for the Breast Cancer Intergroup Correlative Science Studies*, 1 year, $19,399 • **Marjorie Rosenthal**, Child Health & Development Inst. of Connecticut, *Healthy Eating through Group Well Child Care*, 2 years, $59,903 • **Joseph Ross**, Regents of the University of Minnesota (DHHS), *Medical Reversals: De-implementing Ineffective and Unsafe Treatments*, 10 months, $30,184; New York University School of Medicine (DHHS), *Understanding Hospital Readmission Rates: Patients, Hospital and Community Effects*, 1 year, $12,432 • **Douglas Rothman**, Columbia University, *Services Contract between Columbia University and Yale University*, 1 year, $33,926 • **Michael Rowe**, Hospital Authority Hong Kong, *Program for Allied Health Professionals in Recovery of People Experiencing Psychiatric Disability*, 3 months, $27,500 • **Julia Rozanova**, Robert Leet and Clara Guthrie Patterson Trust, *Improving HIV Prevention and Treatment in Prisons*, 2 years, $95,000 • **Joel Rozowsky**, Beth Israel Deaconess Medical Center (NIH), *The Impact of Circadian Rhythm in Obtaining Reference Profiles of exRNAs in Healthy Individuals*, 7 months, $20,062 **Helena Rutherford**, Massage Therapy Foundation, *Massage Therapy as an Adjunct Intervention to Decrease Tobacco Use in Pregnancy*, 2 years, $29,757 • **Basmah Safdar**, American Medical Association Foundation, *Does Stereotyping of a Physician by Gender and Race Affect Patient Satisfaction? Evidence from a Patient Analog Experiment*, 1 year, $10,000 • **Tara Sanft**, University of Connecticut (NIH), *Multilevel Resilience Trajectories in the Transition to Cancer Survivorship*, 11 months, $29,540 • **Kurt Schalper**, Institut De Recherche Pierre Fabre, *Localized Measurement and Significance of Vista (PD-1H) Pathway in Lung and Colorectal Tumors*, 1 year, $269,675 • **Curt Scharfe**, Cystic Fibrosis Foundation (CFF), *Implementing Rapid and Comprehensive Molecular Testing for Cystic Fibrosis*, 2 years, $216,000 • **Michael Schilsky**, Wilson Disease Association, *Wilson Disease Registry Study*, 1 year, $174,389; Wilson Disease Association, *Wilson Disease Registry*, 1 year, $76,346 • **Dena Simmons**, Aspire Public Schools, *Aspire Public Schools Anchor Tools Training*, 1 year, $178,000; Hawaii Association of Independent Schools, *Hawaii (HAIS) RULER Training*, 1 year, $36,000; Hawaii Community Foundation, *Hawaii (HCF) RULER Training*, 1 year, $96,000 • **Albert Sinusas**, Children's Hospital Corporation, (formerly CHB) (NIH), *A Novel F-18 PET Myocardial Perfusion Radiopharmaceutical based on Rhodamine Dyes*, 1.3 years, $148,157 • **Patrick Skosnik**, Brain & Behavior Research Foundation (formerly NARSAD), *An Electrophysiologcial Examination of CB1 and NMDA Receptors: Relationship to Psychosis*, 2 years, $100,001 • **Arietta Slade**, Florida State University, *FSU Minding the Baby FY18*, 3 months, $11,550 • **Robin Stern**, The Lower Eastside Girls Club, *RULER Training The Island School*, 7 months, $15,000 • **David Stitelman**, Cystic Fibrosis Foundation (CFF), *Fetal Gene Editing for Treatment of Cystic Fibrosis*, 2.7 years, $216,000 • **Carla Stover**, University of South Florida (NIH), *IPV and Fatherhood Intervention in Residential Substance Abuse Treatment*, 9 months, $94,468 • **Carla Stover**, **Belinda Oliver**, University of South Florida (NIH), *Randomized Controlled Trial of Prenatal Co-parenting Intervention for African American Fragile Families*, 1.3 years, $48,870 • **Stephen Strittmatter**, Dr. Ralph & Marian Falk Med. Res. Trust, *Fyn Kinase Inhibition for the Tauopathy in Fronto-Temporal Dementia and Glaucoma*, 1 year, $300,000 **William Tamborlane**, George Washington University (NIH), *Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study (GRADE)*, 1.4 years, $737,117 • **Hugh Taylor**, **Lubna Pal**, Mayo Clinic of Rochester (NIH), *Prevention of Alzheimer's Disease in Women: Risks and Benefits of Hormone Therapy*, 1 year, $273,037 • **Janis Tondora**, Via Hope Texas Mental Health Resource, *VIA HOPE Professional Service Agreement*, 1.2 years, $34,931 • **Christopher Van Dyck**, University of Southern California (NIH), *Alzheimer's Clinical Trials Consortium (ACTC)*, 1 year, $182,725 **Arjun Venkatesh**, Addiction Policy Forum, *Rapid Implementation and Assessment of Emergency Department Interventions to Reduce Opioid Associated Harm*, 3.2 years, $1,406,589 • **Pamela Ventola**, Children's Hospital of Philadelphia (DHHS), *Autism Intervention Research Networks: Online Parenting Training in Pivotal Response Treatment: Increasing Access to Care*, 1 year, $21,529 **Pamela Ventola**, **Kevin Pelphrey**, Simons Foundation, *Translating Neuroprediction into Precision Medicine via Brain Priming*, 6 months, $194,450 **Jacob Wallace**, Harvard University, *Health Care Markets and Regulation Lab*, 1 year, $37,316 • **Carol Weitzman**, Boston University (NIH), *Early Identification and Service Linkage for Urban Children with Autism*, 1.8 years, $53,612 • **Li Wen**, National Multiple Sclerosis Society, *The Role of IgA-bound Gut Bacteria in MS*, 1 year, $44,000 • **Travis Whitfill**, Indiana University, *Implementation of a Pediatric Community Outreach Mobile Education (PCOME) Program*, 8 months, $22,050 • **Joseph Woolston**, Lorain County Board of Mental Health, *IICAPS Training and Consultation*, 7 months, $2,000 • **Qin Yan**, Meharry Medical College (NIH), *Mechanism and Oncogenic Role of Lysine Demethylase Kdm5b in Prostate Cancer*, 4.8 years, $167,500 • **Amer Zeidan**, Dana Farber Cancer Institute, *A New Paradigm of Transfusion Support for Patients with Myelodyplastic Syndromes*, 2 years, $99,244 • **Yu Zhang**, William O. Seery Foundation, *Evaluating the Effect of Anti-program Death Immune Therapy on Anti-Tumor T Cell Responses in Non-Small Cell Lung Cancer Patients*, 2 years, $90,000

David Hafler elected to National Academy of Medicine

Physician-scientist is widely recognized for his work to unravel multiple sclerosis

David A. Hafler, MD, chair and William S. and Lois Stiles Edgerly Professor of Neurology, and professor of immunobiology, has been elected to the National Academy of Medicine, in recognition of his outstanding achievements in medicine. Hafler is among 75 inductees from the United States and 10 international newly elected members.

Hafler, who also is neurologist-in-chief at Yale New Haven Hospital, is widely recognized for his contributions in identifying the underlying causes of multiple sclerosis (MS). Early on, he demonstrated that the disease begins in the blood, as opposed to the brain, a discovery that led eventually to the development of natalizumab, which blocks the migration of immune cells from the blood to the brain. He was the first to identify myelin-reactive T cells in MS, showing that it is an autoimmune disorder, as well as the first to identify regulatory T cells in humans

David Hafler

and to demonstrate their dysfunctional state in MS.

As a founding member of the Broad Institute of MIT and Harvard prior to arriving at Yale in 2009, Hafler identified the genes that cause MS. He also identified the key transcription factors and signaling pathways associated with MS genes that are potential treatment targets, and went on to discover that salt plays a role in inducing pathogenic immune responses in such autoimmune diseases as MS.

Robert J. Alpern, MD, dean and Ensign Professor of Medicine, noted at a reception celebrating Hafler's election that when he recruited Hafler to be chair of neurology nearly a decade ago, Hafler's goal was to elevate the department's research, clinical practice, and teaching. "David has hit all of the missions and truly personifies the visionary physician-scientist and department leader," Alpern said.

Hafler thanked everyone in his department "for making me look good," and Alpern for the opportunity to come to Yale. "You didn't know how passionate I would be about building a clinical department. You put trust in me. You've created an incredible milieu for us to be physician-scientists, educators, and clinicians, and I thank you for everything you've done," said Hafler. "I wouldn't have made it into the National Academy without the help of Yale and thank you for that."

Hafler earned his medical degree from the University of Miami School of Medicine, and completed an internship in internal medicine at Johns Hopkins and a neurology residency at New York Hospital-Cornell Medical Center. He received training in immunology at the Rockefeller University and Harvard, where he joined the faculty and was one of the executive directors of the Program in Immunology and the Breakstone Professor of Neuroscience. He has received numerous honors, including the National Institutes of Health Javits Investigator Award, the Raymond Adams Prize from the American Neurologic Association, and the Dystel Prize from the American Academy of Neurology.

// Dean *(page 1)* danger of losing its National Cancer Institute funding when he arrived but now does stellar research and provides unsurpassed clinical care at Smilow Cancer Hospital, which Yale New Haven Hospital opened in 2009.

Alpern also points to a school that ran annual deficits when he arrived, but where surpluses are now the norm. "It's those surpluses," he says, "that have allowed us to recruit top faculty, build the school's new research and education programs, and attain so many other important goals."

In the time that remains before the search for a new dean concludes and his successor takes office, there are several things Alpern still wants to accomplish. One is bringing the school and YNHHS even closer. "I think we have developed a great relationship," he says, "but we still function as two organizations." He wants to come closer to operating "virtually as one."

Another priority is continuing to work on issues related to climate at the school, which range from physician burnout, to faculty engagement, to creating an environment free of all forms of bullying, harassment, and racial and gender disparities, as well as broader issues of inclusion. "It's probably going to take some time to address these issues," he says. "But I will continue to focus on them as long as I am the dean and hope to accomplish as much as I can."

Alpern says his time at the helm of the School of Medicine has been incredibly rewarding and credits a team effort by YSM deans, chairs, faculty, students, and staff alike for making it so. "It's a wonderful place," he says, "because you are continually surrounded by the best."

The same atmosphere of cooperation and excellence that is so characteristic of Yale will greet his successor, Alpern predicts, paving the way for even greater achievements ahead.

// MD-PhD *(page 1)* Medicine faculty member since 2001 who has led the program since 2014.

Kazmierczak strongly embodies the program's dual-degree ethos. She is an accomplished physician-scientist who works on infectious diseases in clinical settings and also studies host-pathogen interactions in her lab. "The most obvious reason to have both degrees is to carry out the practice of medicine and through that, to see what the limitations of our current practice are," Kazmierczak says. "A person trained in this way can see what we actually don't know, what we can't treat—and then has the skills to turn those questions into opportunities to do basic fundamental research that leads to new ways of treating patients and understanding disease."

"We are honored to endow the directorship of Yale's MD-PhD Program and to support Yale's work in training a new generation of physician-scientists under the leadership of Barbara Kazmierczak," says Kimberly Alvarez, president of the foundation. "We are confident that graduates of the program will continue to be leaders in medicine and biological research and to make the most of the unique preparation that the MD-PhD Program offers them."

The Yale MD-PhD program trains students to be both versatile physicians treating human disease and adept basic scientists who conduct research at the cellular and molecular levels. Brian R. Smith, MD, deputy dean for scientific affairs (clinical departments), chair and professor of laboratory medicine, and professor of biomedical engineering, of medicine (hematology), and of pediatrics, says that equipping tomorrow's leading investigators with both an MD and a PhD unlocks tremendous potential. "It is particularly powerful when you can invest the knowledge of the bench and the knowledge of the bedside in the same person," Smith explains. "Today's physician-scientists are helping define diseases with new diagnostics and developing targeted therapeutics against cancer and other diseases. We are grateful to the Gustavus and Louise Pfeiffer Research Foundation for its investment in this vital program."

ROBERT A. LISAK

The directorship of the School of Medicine's MD-PhD program is now an endowed position. Barbara Kazmierczak (above), who has run the program since 2014, is the inaugural Gustavus and Louise Pfeiffer Research Foundation MD-PhD Program Director. The program trains students to be both versatile physicians treating human disease and adept basic scientists who conduct research at the cellular and molecular levels.

"We desperately need physician-scientists for the advancement of medicine," adds Pietro De Camilli, MD, chair and the John Klingenstein Professor of Neuroscience and professor of cell biology, who works routinely with MD-PhD students in his lab. "They are some of the best students we have at Yale."

Awards & Honors

Gregg Gonsalves, PhD, assistant professor of epidemiology (microbial diseases) and associate (adjunct) professor of law, has been named a MacArthur Fellow, an award commonly known as a "genius grant," honoring his advocacy in the early years of HIV/AIDS and how that informed his later epidemiology work which serves poor and marginalized communities.

Peggy S. Myung, MD, PhD, assistant professor of dermatology and pathology, has received a Clinical Scientist Development Award for early-career physician-scientists from the Doris Duke Charitable Foundation. Myung's research focuses on tissue generation in the skin that can be orderly, as in hair follicle formation, or uncontrolled as in the development of cancers.

Harvey Risch, MD, PhD, professor of epidemiology (chronic diseases), has received a Ruth Leff Siegel Award for Excellence in Pancreatic Cancer Research, for "novel, sustained, and substantial contributions to understanding the etiology and early diagnosis of pancreatic cancer," such as associating colonization by *Helicobacter pylori* with the disease.

Lauren Sansing, MD, associate professor of neurology, has received the American Neurological Association's highest award, the Derek Denny-Brown Young Neurological Scholar Award. Sansing's work focuses on mechanisms by which inflammation contributes to secondary injury after acute brain injury, and the modulation of inflammation to promote brain recovery.

Hugh S. Taylor, MD, chair and Anita O'Keeffe Young Professor of Obstetrics, Gynecology, and Reproductive Sciences, has been elevated to the top leadership of the American Society of Reproductive Medicine. Taylor is vice president during 2018–19, president-elect in 2019–20, and president of the society in 2020–21.

Stephen G. Waxman, MD, PhD, Bridget M. Flaherty Professor of Neurology and professor of neurobiology and pharmacology, has received the Julius Axelrod Prize from the Society for Neuroscience, for providing "a model of rigorous laboratory studies coupled with application to human patients in studying the role of ion channels in diseases of the brain and spinal cord."