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

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 (YNHH) 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

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

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 Karmireczak, MD, PhD, professor of medicine (infectious diseases) and of microbial pathogenesis, a School of
scientist finds skin deep is very deep

Valentina Greco

Scientists find 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 Walsh 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 shuttered 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 division.

Greco’s personal journey toward making these discoveries was filled with twists and turns, punctuated by one particularly formative 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 maager 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 only epithelial cells 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 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 address microinjuries or mutations may lead to new ways of approaching cancer treatment.

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 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. Slika ’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 illness—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. Slika Foundation have endowed the initiative, in memory of Ritvo’s husband and son.

Institute for Global Health names its inaugural director

Saad B. Omer, MMBS, MPH, PhD, has been named the inaugural director of the Yale Institute for Global Health (YIGH). Omer is currently 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 MMBS from the Aga Khan University Medical College.

Slika ’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 illness—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. Slika Foundation have endowed the initiative, in memory of Ritvo’s husband and son.

Institute for Global Health names its inaugural director

Saad 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 MMBS from the Aga Khan University Medical College.

Slika ’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 illness—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. Slika Foundation have endowed the initiative, in memory of Ritvo’s husband and son.

Institute for Global Health names its inaugural director

Saad 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 MMBS from the Aga Khan University Medical College.

Slika ’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 illness—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. Slika Foundation have endowed the initiative, in memory of Ritvo’s husband and son.
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-Stain 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—which is associated with Parkinson’s—works at the junctions between the endoplasmic reticulum (ER) and endosomes and lysosomes, while VPS13A—which is associated with Huntington’s-like syndrome—functions at contacts between the ER and endosomes 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 HARNESSE BURGEONING DATA

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 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 to 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. This 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.

CBDS is part of a constellation of data science activity exploding throughout the university, from a new under-graduate 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 empha-sis,” 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. Slattery, 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.”

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.

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-Stain 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—which is associated with Parkinson’s—works at the junctions between the endoplasmic reticulum (ER) and endosomes and lysosomes, while VPS13A—which is associated with Huntington’s-like syndrome—functions at contacts between the ER and endosomes 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.

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 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 to 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. This 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.

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. Slattery, 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.”
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, MD, professor emerita of medicine (nephrology) and senior transplant coordinator; and former patient James Silvertrini, wife of James. 2. From left, Janyjet 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.

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.

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.

October 18  Stephen and Margery Riker hosted a Dinner Party, at the Lotus Club in New York City to highlight recent advances at the Yale Cancer Center (YCC). 1. From left, Joel E. Smillow, YC ’54, philanthropist and former CEO of Playtex Products, Inc., Charles S. Fuchs, MD, MPH, director of YCC and physician-in-chief of Smillow 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.

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; Mayza Szatal, 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.

October 18  Stephen and Margery Riker hosted a Dinner Party, at the Lotus Club in New York City to highlight recent advances at the Yale Cancer Center (YCC).
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 shepherders 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 its 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 pharmacology and of molecular biophysics and biochemistry, and of therapeutic radiology, had previously identified 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 pharmacology and of molecular biophysics and biochemistry, and of therapeutic radiology, had previously identified that actin-binding sites and actin, leading to opening, leading to increasing binding, and some disease geneticists have suggested that 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.

Posthumous gift adds years to 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 21, 2017, six months after her 90th 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 work with her to help with this expenditure, and she thought 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, 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 were surprised. Milton Allen describes his wife as a philanthropist, “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 at Yale School of Medicine and healthy, says Martin A. Schwartz, Robert W. Berliner Professor of Medicine at Yale School of Medicine.

It is rare for science to identify one key protein that determines a cell’s behavior in health and disease. KL2 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 forms this essential cell-cell connection, KL2 can help cells communicate, which is critical for cell movement, differentiation, and tissue homeostasis. KL2 mediates the formation of circulating blood vessels. The friction generated by blood flow past these cells induces KL2 expression, and Schwartz and Coon wanted which genes mediate this process. “What we got out of it was astounding,” says Schwartz. The screen produced a hit list of 300 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 their plan to Leducq, which endorsed it.

Based in Paris, Fondation Leducq was created 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 network against vascular disease is a battle that “should be waged at the international level.” Including the five previous 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 $116 million of the grant to unravel the signaling network that allows blood flow to influence KL2 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 a good handle on 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.

Leducq Transatlantic Network makes Schwartz a team leader

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 KL2 expression, and Schwartz and Coon wanted which genes mediate this process. “What we got out of it was astounding,” says Schwartz. The screen produced a hit list of 300 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 their plan to Leducq, which endorsed it.

Based in Paris, Fondation Leducq was created 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 network against vascular disease is a battle that “should be waged at the international level.” Including the five previous 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 $116 million of the grant to unravel the signaling network that allows blood flow to influence KL2 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 a good handle on 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.
Developing more resilience in children 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 if we really want to foster resilience, 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 we foster that resilience in children, their ability to bend and break, to recover from adversity? We need to develop 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 Grandy 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 curricula at Scholastic.

Through the Discover Together program, parents and children learn storytelling. Parents can use the skills to instill in their children the need for resilience, but also the 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. “If you can put someone up in adversity, help them 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 you can’t change 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 Original Stories for other locations; to create classroom materials that destigmatize childhood mental health problems; and to develop a resilience program aimed at 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.”
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 internationally newly elected members.

Until Hafler, who also is neuroimmunologist-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 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 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 physi- cian 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) 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 surprises are now the norm. “It’s those surprises,” he says, “that have allowed us to recruit top faculty, build the school’s new research and education programs, and retain so many other important goals.”

“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. Karmierczak strongly endorses 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,” Karmierczak says. “A person trained in this way can see that we really 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.”

“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.

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 particularly powersafely, 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 foundation in this vital program.”

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.

The directorship of the School of Medicine’s MD-PhD program is now an endowed position. Barbara Kaminetzky (abover), who has run the program since 2014, is the inaugural Gustavus and Louise Pfeiffer Research Foundation Flaherty Professor of 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.”

The directorship of the School of Medicine’s MD-PhD program is now an endowed position. Barbara Kaminetzky (above), who has run the program since 2014, is the inaugural Gustavus and Louise Pfeiffer Research Foundation Flaherty Professor of 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 (professor) of law, has been named a MacArthur Fellow, an award commonly known as a “genius grant,” honoring his leadership in 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 L. Kirschstein National Research Service 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 cigarette smoking by Helicobacter pylori with the disease.

Lauren Sappington, MD, associate professor of neurology, has received the American Neurological Association’s highest award, the Derek Denny-Brown Young Neurological Scholar Award. Sappington’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’Keefe Young Professor of Obstetrics, Gynecology and Reproductive Sciences, has been elevated to the top leadership of the American Society of Reproductive Medicine. Taylor is president during 2018–19, president-elect in 2019–20, and president of the society in 2020–21.

Stephen G. Waxman, MD, Flaherty Professor of Neurology and professor of neurology 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.”