Medicine@Yale

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School of Medicine holds "100 Years of Women" celebration

Symposium highlights a century of achievements in all facets of science and medicine

Hundreds of faculty, students, alumni, staff, and friends of the School of Medicine gathered on June 1 for *Celebration and Reflection*, a symposium to commemorate 100 years of women at YSM.

Sponsored by the Committee on the Status of Women in Medicine (SWIM), the Minority Organization for Retention & Expansion (MORE), and the Dean's Office, the daylong program kicked off Alumni Weekend. Included were presentations by faculty and alumnae on the history of women in medicine, basic science, clinical science and practice, and current issues facing women. "The breadth and depth of the accomplishments of this impressive group of clinicians and scientists, as well as their deep commitment to improving health, was inspiring," says Robert J. Alpern, MD, dean and Ensign Professor of Medicine.

In addition to discussing their contributions to their respective fields, speakers addressed the struggles that women in medicine have faced: how choosing medicine was seen as a rejection of social and family life, the paucity of women role models in leadership positions, the exclusion of women from committees and conversations, and the challenges of working in systems and practices defined by men.

"We wanted this symposium to highlight all the expertise, talent, and resourcefulness of Yale faculty and alumnae, but we also wanted each speaker to share her own special story—something that does not routinely occur at most symposia," says Margaret J. Bia, MD, professor of medicine (nephrology), who led the planning committee together with Elizabeth A. Jonas, MD, professor of medicine (endocrinology).

In her science session keynote address, Juanita L. Merchant, MD '81, PhD '84, H. Marvin Pollard Professor

// 100 Years *(photo gallery, page 6; text, page 7)*

ROBERT LISAK

Juanita Merchant, an alumna who now is a professor at the University of Michigan Medical School, was keynote speaker at a science session that was part of ***Celebration and Reflection***, the symposium on June 1 that marked 100 years of women at Yale School of Medicine.

A new gift will spur stem cell research

Financial support for work on epigenetic foundations of essential cellular activity

Luye Life Sciences Group, a Chinese medical conglomerate, has given the Yale Stem Cell Center (YSCC) $1 million in support of basic stem cell research. The gift "will allow my lab to explore cutting-edge questions that are high-risk and unlikely to be funded by mainstream funding mechanisms," says Haifan Lin, PhD, YSCC's director, Eugene Higgins Professor of Cell Biology, and professor of genetics and of obstetrics, gynecology, and reproductive sciences.

With the gift, Lin and his lab team will continue to investigate a class of genes he discovered called the Argonaute/Piwi gene family, which is linked to human fertility. Lin has researched these genes' potential role in the division of cancer cells—gaining knowledge that might lead to new anti-cancer treatments.

HAROLD SHAPIRO

At the signing ceremony that made Luye Life Sciences Group's gift official, (l–r): Peter Schiffer, Yale vice provost for research; Tim Maguire, director of business development, Luye Boston R&D, LLC; Sean Fu, president of Luye Boston R&D, LLC; Dean Robert J. Alpern, and Haifan Lin.

The boost from Luye Life Sciences will help Lin focus on "epigenetic mechanisms mediated by the Piwi-piRNA pathway in defining a cell's fate," he says. "I am very grateful to Luye Group's leadership for their friendship and trust in my research. I look forward to a wonderful relationship with Luye colleagues in years to come," Lin says.

The donation comes from Luye's new Boston area-based research and development center, which opened in July 2017. "As one of the world's largest stem cell research organizations, YSCC has made significant contributions to advancing the development of stem cell technology," says Dianbo Liu, executive chair of Luye Life Sciences Group, which is comprised of three divisions that are spread globally: Luye Pharma, Luye Medical, and Luye

// Luye *(page 4)*

Devastating disease of the lung is a new research gift's focus

The lungs are made up of some 30 to 40 different types of cells. "When you get sick, these cells can change. New cells can come in and resident cells can change over," says Naftali Kaminski, MD, Boehringer Ingelheim Pharmaceuticals, Inc., Endowed Professor of Medicine (Pulmonary), and chief of the Section of Pulmonary, Critical Care, and Sleep Medicine (Yale PCCSM) at the School of Medicine. If researchers understood the interactions that take place between cells as disease takes hold in the lungs, he says, they might be able to develop targeted treatments to block crucial steps in the disease process.

A particular priority is idiopathic pulmonary fibrosis (IPF), a disorder where debilitating scarring develops on the lungs for unknown reasons. An estimated 132,000 to 200,000 Americans have IPF, and 50,000 new cases are diagnosed each year according to the Pulmonary

// Lung *(page 5)*

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ROBERT A. LISAK

Marcella Nunez-Smith learned through experiences during her training that delivering the best health care is not possible where inequality reigns. Through research, patient care, and teaching, she has been dedicated to investigating the health system's inequalities and using data-driven insights to correct them.

A champion of health care fairness

Uncovering inequalities and striving to improve both care and education

Medicine permeated the youth of Marcella Nunez-Smith, MD, MHS '06, associate professor of medicine (general medicine) and of epidemiology (chronic diseases/social and behavioral sciences). Her godfather, a surgeon, practiced it. Her mother, a nursing professor, taught community health. Etched in family lore, and recorded somewhere, is Nunez-Smith's confident declaration, at age 6, of her plans to become a reproductive endocrinologist. Her devotion to medicine has never wavered.

At 16, she matriculated at Swarthmore College in Pennsylvania, and double-majored in biological anthropology and psychology. She took a year after graduation to help care for her ailing grandmother, and teach at her former high school in St. Thomas, U.S. Virgin Islands, and then began medical school at Thomas Jefferson University Medical College in Philadelphia in 1997.

Eventually, internal medicine would supplant reproductive endocrinology as her primary interest. It became the focus of her residency at Brigham and Women's Hospital in Boston. One day, a close colleague mentioned a fellowship program that provided skills and resources for physicians to affect the health of whole populations, rather than one patient at a time. "I immediately thought—I want to do that!" Nunez-Smith says. She applied to what was then the Robert Wood Johnson Foundation Clinical Scholars Program at Yale, and learned of her acceptance from Harlan M. Krumholz, MD, Harold H. Hines, Jr. Professor of Medicine (Cardiology) and professor of investigative medicine and of public health (health policy), who would be her program director.

Inspired by the work of one of her mentors, JudyAnn Bigby, MD, former secretary of Massachusetts' Executive Office of Health and Human Services, Nunez-Smith knew she would pursue fellowship research on health disparities and inequities. Her first project grew out of her own residency experience as a woman of color. "We had a very supportive environment there," Nunez-Smith says. "We also had some medical staff who, for the length of the residency, confused me with another resident, who is 6 feet tall, and many shades darker than myself. We laughed it off at the time, but I began to think, 'What does it look like for our profession to support diversity?'"

"People of color in hospitals and practices are often invisible and must deal with climate and culture issues all the time," says Nunez-Smith. "For example, patients might refuse to accept that a person of color is a physician, even with data they have—like seeing a stethoscope."

She led a group that approached Krumholz and her fellowship program advisor, Elizabeth H. Bradley, PhD, now president of Vassar College, with a plan to investigate workforce diversity in health care—a topic so nascent that neither had heard of it. That qualitative research would lead to work on patient health care inequity, and, with pilot data supported through a Yale Center for Clinical Investigation (YCCI) Scholar Project Award in 2006, Nunez-Smith became principal investigator of a National Institutes of Health (NIH)-funded grant to develop a Patient-Reported Experiences of Discrimination in Care Tool (PreDict). She became assistant professor of medicine at Yale a year later.

Nunez-Smith would soon develop the Eastern Caribbean Health Outcomes Research Network (ECHORN), a collaborative, multimillion dollar research study funded by the National Institute for Minority Health Disparities. Among other NIH and foundation-funded projects, she would found the Equity Research and Innovation Center (ERIC), which turns five this year. All ongoing projects at ERIC—from population migration, to cardiovascular disease, to pediatric obesity—are examined through a health-equity lens, she explains.

During her 14 years in the field, Nunez-Smith has found that a participatory research approach is the most important tool she has in translating health equity research to tangible results. "At its core, participatory research means that researchers cede some power to community members who have the expertise necessary for the scientific success of a project," she says. In 2016, Nunez-Smith and colleagues were awarded nearly $10 million in funding over five years to launch the Yale Transdisciplinary Collaborative Center for health disparities research (Yale-TCC), within ERIC, which aims to improve early identification of individuals at risk for hypertension and type 2 diabetes.

No matter which research project Nunez-Smith works on, the immense impact she felt during her initial Yale fellowship, now called the National Clinical Scholars Program (NCSP), is never far from her mind. "I learned to take risks. Build good teams. To not take 'no' easily," she says. Now, as a core NCSP faculty member, she impresses these lessons on the next generation of clinician-scholars.

A collaborative immuno-oncology center is launched

Charles Fuchs

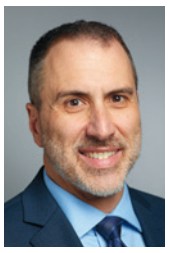
Yale Cancer Center (YCC) has launched the Yale Center for Immuno-Oncology (YCIO), which will build on YCC's international leadership in immunobiology, cancer immunology, and development of novel cancer immunotherapies. It is a partnership between YCC and immunobiology at Yale University.

"This new center gives us the chance to work more collaboratively and efficiently with our world-renowned scientists and faculty to address scientific questions in immuno-oncology," says Roy S. Herbst, MD, PhD, Ensign Professor of Medicine and professor of pharmacology, associate director for translational research at YCC, and chief of medical oncology at YCC and Smilow Cancer Hospital. "We hope we can transform the way we treat people affected by cancer by generating research advances more quickly." Herbst will serve as interim director until a search for a permanent director is completed.

"The addition of YCIO continues our goal to expand the depth and breadth of our science, including the broadening of our translational research infrastructure," said Charles S. Fuchs, MD, MPH, Richard Sackler and Jonathan Sackler Professor of Medicine (Medical Oncology) and director of YCC.

Goals for YCIO include building upon Yale's leadership in immunobiology and immunotherapy drug development, developing the next generation of immune-based therapies, and genetically engineering immune cells to target cancers.

Medical director is named for Yale New Haven Psychiatric Hospital



Frank Fortunati

Frank Fortunati, MD, JD, assistant professor of psychiatry, has been named medical director for Yale New Haven Psychiatric Hospital and associate chief of psychiatry for Yale New Haven Hospital (YNHH). He served in an interim capacity for more than two years.

Fortunati earned his JD from Rutgers University School of Law—Camden and then his MD from UMDNJ (now Rutgers) New Jersey Medical School. He completed a psychiatry residency and fellowships in child and adolescent psychiatry and forensic psychiatry at Yale School of Medicine.

"We are thrilled to conclude our very competitive national search with the appointment of Dr. Fortunati, someone we know, respect, and rely on as a psychiatrist and a leader," says John H. Krystal, MD, Robert L. McNeil, Jr. Professor of Translational Research, chair and professor of psychiatry, and professor of neuroscience, and chief of psychiatry at YNHH.

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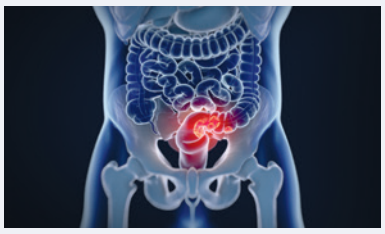
A new colorectal cancer discovery



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Immune checkpoint inhibitors are drugs designed to turn the immune system into a cancer-destroying weapon. However it appears that certain tumors, such as those associated with colorectal cancers, possess immune-suppressive mechanisms that thwart such therapies. Dianqing (Dan) Wu, PhD, professor of pharmacology, and colleagues have identified what might become a more effective approach to colorectal cancer immunotherapy, described on Feb. 12 in *Nature Medicine*.

Normally when the immune system detects cancer, it releases cytokine IL-15, which stimulates natural killer and cytotoxic T cells to attack tumors. Wu's team found that the protein DKK2, present in high levels in colorectal cancers, impairs the IL-15 signaling pathway, thereby weakening the tumor-destroying cells. The potential therapy is an antibody against DKK2, which would act, in Wu's words, to "inhibit the inhibitor." Wu's team found that the anti-DKK2 antibody kept the immune cells active and reduced tumor numbers in mice with colorectal cancer.

Wu is working with Just China, licensor of the technology, to develop anti-DKK2 antibodies into immunotherapies against colorectal cancers and potentially certain melanomas.

Lung disease may respond to hormone

Thyroid hormone, or drugs based on the hormone, may be effective against pulmonary fibrosis—a chronic and progressive lung disease—according to a new study. Researchers led by Naftali Kaminski, MD, chief of pulmonary critical care and sleep medicine and the Boehringer Ingelheim Pharmaceuticals, Inc., Endowed Professor of Medicine (Pulmonary), first found that a protein involved in activating thyroid hormone was increased in the lungs of people with a severe form of pulmonary fibrosis. This led the investigators to try the effects of aerosolized delivery of thyroid hormone in two different mouse models of lung fibrosis.

Mice treated with aerosolized thyroid hormone, as well as a small molecule that mimics the effect of the hormone, showed significant resolution of the fibrosis in their lungs and survived longer compared to untreated mice. The hormone, the team discovered, improved the function of energy-generating mitochondria in the cells that line the lungs. This effect, which may shield the cells from damage, may be important in the resolution of fibrosis. The results, reported on Dec. 4 in *Nature Medicine*, suggest that aerosolized thyroid hormone should be developed for pulmonary fibrosis in people.

Seeing how cells work as never before

Yale is adding microscopy that provides an unprecedented view of specimens whose thickness had thwarted close inspection

Biological structures exist and function in three dimensions, but the limitations of imaging technology have long meant that scientists could examine only two dimensions in fine detail. The traditional practice of analyzing specimens one thin slice at a time, even if the structure being investigated is considerably thicker, can only get a researcher so far, says Derek K. Toomre, PhD, associate professor of cell biology, and director of the Yale "CINEMA" (Cellular Imaging using New Microscopy Approaches) laboratory. "Imagine if I had to recognize your face if I had just a slice through your skull," he says. "It would be very hard."

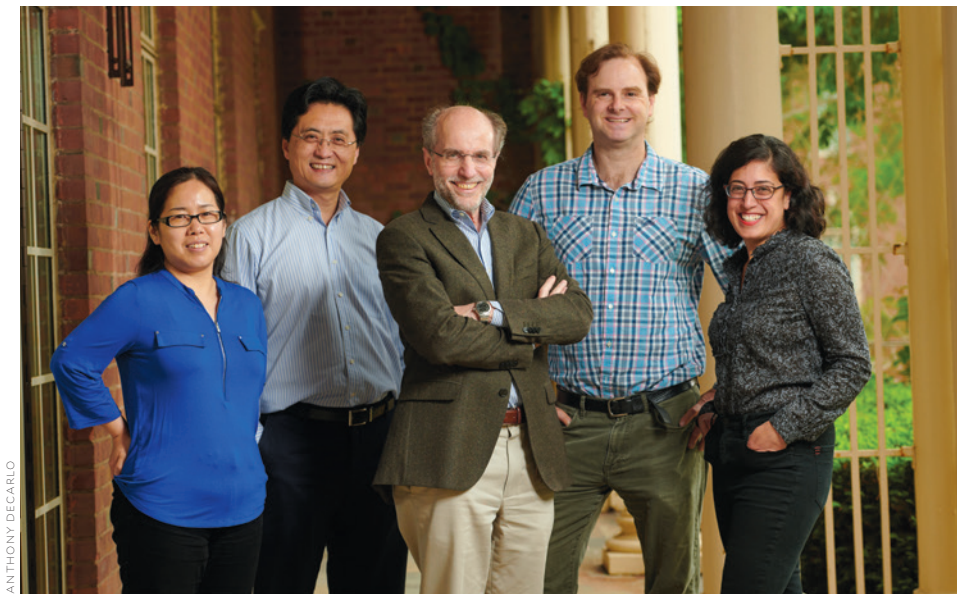
This summer, Yale is on track to install what for Toomre and his colleagues is a major advance: the focused ion beam-scanning electron microscope (FIB-SEM), which acquires tomography data from biological specimens. "There are relatively few of these microscopes around," he notes. "There is not one in the region. It's new and it's something we've been wanting for a while, and I think it plays to an inherent strength of Yale, which has been in imaging." For the first time, the z axis, which represents a specimen's thickness, appears with resolutions that match those of two-dimensional x and y. FIB-SEM accomplishes this by imaging the surface of a thick cellular specimen (typically cells or tissue embedded in plastic or vitrified), and then using its ion beam to mill and etch away a very thin layer of the specimen while not damaging the remaining tissue. That exposes a new surface to be scanned. The process repeats, a few nanometers at a time. "And you can do that, drill down, as deep as you want," says Toomre.

What emerges, layer by layer, is a computer-generated 3D image of the entire cell and all of its structures, which can be rotated to show views of the cell's working parts from any angle. Pietro De Camilli, MD, chair and John Klingenstein Professor of Neuroscience and professor of cell biology, says FIB-SEM gives him unprecedented views of large volumes of neuronal cells and their specialized compartments, such as dendritic spines and axon terminals, including subtle details of the endoplasmic reticulum (ER), mitochondria, synaptic vesicles, and other organelles. "There is not a technique that allowed us to reconstruct with such a degree of precision the intracellular structure of a neuron, or any cell for that matter," De Camilli says. "This technique is a fantastic tool for a cell biologist."

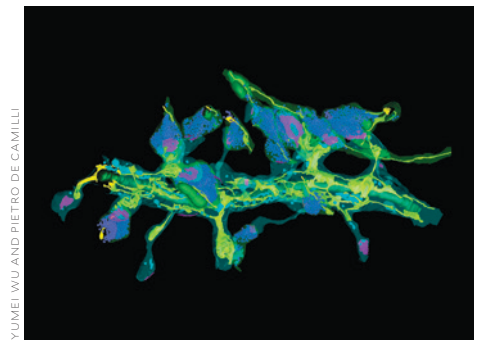
Shirin Bahmanyar, PhD, assistant professor of molecular, cellular, and developmental biology, is one such scientist. Her work on cells' nuclear envelope pockets was one example cited when De Camilli, Toomre, and Xinran Liu, MD, PhD, director of the electron microscopy facility in the Center for Cellular & Molecular Imaging, secured National Science Foundation funding to bring FIB-SEM to Yale. Bahmanyar is investigating how the DNA housed in the nuclear envelope of every cell in a living organism is accurately replicated, with the copy then safely encased when cells divide. It is an intricate process through which the ER—a complex network of membranes that generate the nuclear envelope—changes shape, opens and closes, and even appears to change its biochemical composition as division occurs, all for the purpose of preserving and propagating an organism's most fundamental feature, its genetic code.

Bahmanyar wants to know what happens both when the process works well and when things go wrong. "If this process goes awry, and you don't generate a single nuclear compartment, and you have chromosomes that are not enclosed in the single compartment, the genome is misregulated." Resulting mutations, she says, can create malignant "supercells" that propagate better and faster than healthy cells and give cancers a biological advantage. She explains that with FIB-SEM, "we can see at an ultrastructure level how these compartments are wrapping around the nucleus, and how the chromosomes are stacked so that they stay together and generate this high-fidelity process that is essential to life. Essentially it would be impossible to look at this process given the large volume of a mitotic [dividing] cell, without this sort of microscopy."

FIB-SEM can streamline the imaging process, letting investigators obtain fine structural detail of whole cells all within one imaging session. Liu, who will host and oversee the operation of the system, says a researcher can set various resolutions for different parts of the cell, and the system will be able to etch with the ion beam and then scan with electrons to form images automatically. "You can just set it up, and the process can be continued from a few hours to several days until a 3D dataset is obtained." With FIB-SEM physically on campus, Yale investigators will be able to test far more of their hypotheses as well. The handful of similar instruments elsewhere, such as the Howard Hughes Medical Institute's setup at its Janelia Research Campus in Virginia, are heavily subscribed. De Camilli says he has obtained striking images in Virginia,



ANTHONY DECARLO



YUMEI WU AND PIETRO DE CAMILLI

Above (l–r): Yumei Wu, Xinran Liu, Pietro De Camilli, Derek Toomre, and Shirin Bahmanyar.

Left: A neuronal dendrite captured by Yumei Wu, associate research scientist. Detail from FIB-SEM includes endoplasmic reticulum (yellow), mitochondria (green), and synaptic clefts (magenta).

but at the same time, "these machines are terribly overbooked. We have been able to view a few specimens, but there is no way we can do something systematic without an instrument at Yale."

Bahmanyar relishes the access she will have to Yale's FIB-SEM while still a junior investigator. "Proximity, availability, all of those things just lower the barrier to new discoveries," she says. "You can try things. You can get the people in your lab to go there and get trained themselves. To use the newest technologies is just so much faster and easily achievable if you have it at home."

The technological strides represented at Yale by FIB-SEM and other modern imaging systems inspire Toomre to recall how prolific a giant of the past was with more primitive tools. The late George E. Palade, MD, Nobel Laureate and longtime School of Medicine faculty member, is widely considered the father of modern cell biology. One extraordinary aspect of Palade's work, Toomre notes, is that he managed to define organelles and structures in cells despite seeing less than 1 percent of the volume of an individual cell in any given image. Just imagine today's possibilities, Toomre says. "To see the cell in its entirety, to see tissues in three dimensions, in physiological and pathological conditions, the insights are much more profound. That is the revolution that we've been seeing with these volumetric approaches as will now be enabled at the medical school. They will be cutting edge with FIB-SEM."

OUT & ABOUT

November 7 At **A More Unified Yale**, a reunion event in San Diego, a group of rheumatologists visited and shared advances in the field. (Left to right): The event was hosted by **Matthew Browne**, YC '90, and his wife, **Juli Oh**; and included **Gary V. Desir**, MD '80, chair of internal medicine; and **Joseph E. Craft**, MD, section chief of rheumatology.

DAVE SICCARDI

HAROLD SHAPIRO (3)

March 16 On the annual **Match Day**, all 123 medical students in the Class of 2018 who sought residencies learned which programs they will be joining. **1. Marcella Nunez-Smith**, MD, MPH '06, associate professor of medicine (general medicine) and of epidemiology, and **Darin A. Latimore**, MD, deputy dean and chief diversity officer, give congratulations to **Marquita Nicole Kilgore.** **2. Andrew Loza** (left) and **John Andrews** are all smiles. **3.** From left, **Alyssa Zupon**, **Blair McNamara**, **Alyssa Thomas**, **Rachel Klausner**, **Andi Shahu**, and **Hadley Bloomhardt** hold up their match letters after opening them at noon in Harkness Hall.

CHRISTOPHER S. GARDNER

February 2 At the inaugural **Sidney Blatt Lecture**, **Paul L. Wachtel**, MA '63, PhD '65, (center), distinguished professor of psychology at City College of New York, gave a lecture titled, "Revisiting the Dynamics of Personality: Beyond Diagnostic Categories, Developmental Levels, and Linear Formulations." Sidney J. Blatt, PhD, died in 2014 and served a 50-year career in Yale's department of psychiatry. Wachtel was a mentee of Blatt. From left, **John Casey**, YC '79, and his wife, **Judy Casey**, YC '81, a daughter of Blatt; **David Blatt**, YC '85, Law '88, his son; Wachtel; **Lisa Blatt**, David's wife; and **Susan Goetsch**, MFA '76, daughter of Blatt, and her husband, **Charles Goetsch**.

HAROLD SHAPIRO

February 9 Yale Law School's Solomon Center for Health Law and Policy hosted **The Policy, Politics & Law of Cancer** conference in collaboration with Smilow Cancer Hospital and Yale Cancer Center. Featured speakers at the two-day event included, from left, **Norman E. Sharpless**, MD, director of the National Cancer Institute; **Otis W. Brawley**, MD, chief medical and scientific officer for the American Cancer Society; and **Roy S. Herbst**, MD, PhD, Ensign Professor of Medicine, professor of pharmacology, and chief of medical oncology at Yale Cancer Center and Smilow Cancer Hospital.

March 1 **1. Richard A. Silverman** (center) with his wife Nancy and surrounded by family at his **Retirement Party**, was the School of Medicine's director of admissions for 18 years, capping four decades of service to Yale University. His career began at Yale College, where he was associate director of admissions from 1977 to 1983, and continued at the School of Management, where he served as director of admissions from 1983 to 1999. **2.** A farewell card filled with best wishes.

HAROLD SHAPIRO (2)

DAVID SUROWIECKI

April 4 The **Section of the History of Medicine** hosted a screening of *Thank You for Coming*, a documentary about the years-long search by filmmaker **Sara Lamm** (right) for her sperm-donor biological father, **Patrick Mullen**, MD, (second from right). Also fielding—and asking—questions after the screening were (from left) **Rene Almeling**, PhD, associate professor of sociology, and **Joanna Radin**, PhD, associate professor in the history of medicine, of anthropology, and of history.

// Luye *(page 1)* Investment. "I am glad to see the cooperation between them and Luye Life Sciences Group, and look forward to more progress coming out."

The proximity of Luye's Boston office is an added advantage for continued collaboration with Yale, says Liu. "We believe these connections will lead to the launch of innovative drugs as well as technologies with real clinical value, thereby contributing to the health of all humankind."

"This generous support from Luye Life Sciences will allow Dr. Lin and the Stem Cell Center to continue to work at the edge of what we know about basic stem cell biology. This kind of research remains crucial to the field of stem cells in general and regenerative medicine in particular," says Robert J. Alpern, MD, dean and Ensign Professor of Medicine.

The timing of Luye's gift is especially opportune, Lin notes, because a frequent source of funding for the center's basic research, the state of Connecticut, has more limited ability to provide support this year than in the past because it faces significant budget constraints.

Targeting vaccines more effectively

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Migratory type 2 conventional dendritic cells (cDC2s) appear to induce an especially robust immune response to vaccination, making vaccines more effective. Stephanie C. Eisenbarth, MD, PhD, associate professor of laboratory medicine, of immunobiology, and of medicine, and colleagues investigated the process by which dendritic cells convey vaccine-delivered antigens to T cells in the lymph nodes, which in turn spur antibody production. Their findings appeared Dec. 1 in *Science Immunology*.

In mouse models engineered to prevent cDC2 cells from migrating to lymph nodes, antibody production in response to a vaccine-like virus was impaired. Inhibiting migration of a different form of dendritic cell (cDC1) did not impair response.

Therefore, to ensure maximum antibody production from a given vaccine dose, Eisenbarth suggests inoculation in ways that maximize vaccine interaction with cDC2. That could mean fewer injections into muscle, where dendritic cells are scarce, and more focus on the top layer of skin, where cDC2 cells are common.

Eisenbarth says maximum efficacy from the smallest possible vaccine dose may be especially valuable during flu pandemics, when vaccine production might lag during a surge in demand.

Fetal mutations may start immediately

Immediately after conception, the cells in a fetus can begin to accumulate tiny genetic mutations—the kinds of changes that occur throughout life and may lead to diseases such as cancer. So conclude researchers who analyzed differences among fetal human brain cells, as published Dec. 7 in *Science*.

Brain precursor cells isolated from a single fetus, they found, already had genetic differences. Overall, each cell had accumulated 200 to 400 small genetic mutations—an average of one mutation per cell division beginning at fertilization. The mutation rate increases dramatically during neurogenesis. Some mutations were found to arise so early in development that a fetus' sex cells have not yet fully formed, suggesting that the mutations could be passed along to future offspring.

"This opens up a larger perspective on human development," says co-corresponding author Flora M. Vaccarino, MD, Harris Professor in the Yale Child Study Center and professor of neuroscience. "Some of our genome does not come from our parents." It explains one reason identical twins can have different physical traits, and may point toward new explanations for childhood neurodevelopmental disorders.

First online physician assistant class gets to work

Goal is to train primary care providers for their own underserved communities

MARA LAVITT

The first class enrolled in the School of Medicine's inaugural physician assistant online program came to Yale in March and received their ceremonial white coats at Battell Chapel. They also participated in a week of immersion that included faculty lectures and work in Yale's simulation lab. The program's goal is to train primary caregivers who are equipped to serve populations in often-underserved regions of the country.

The launch in January of the medical school's inaugural physician assistant online program (PA Online) marked the first time that students not on campus could work toward a Yale degree. Forty-two students are enrolled in the initial class, in a program designed to let talented aspiring physician assistants from across the country benefit from a Yale education while staying in their home communities.

Those communities, which often are underserved, also stand to benefit because their own home-grown health professionals are considered more likely to remain and provide primary care locally.

"The goal is to contribute to the health care needs of the country," says Robert J. Alpern, MD, dean and Ensign Professor of Medicine, "and to give more qualified applicants the opportunity to earn a Yale School of Medicine Master of Medical Science degree."

PA Online provides 12 months of online didactic work, with cohorts of 11 to 15 students engaging frequently with each other and a School of Medicine faculty member through an interactive "Online Campus." Sixteen months of clinical rotations then follow, predominantly in students' home areas, including a month-long capstone research project. Mixed in are three separate weeks of on-campus immersion that include work in Yale's simulation lab and in-person faculty lectures. During the first such week, in March, students received their ceremonial white coats.

The physician assistant field is expanding rapidly across the country, expected to grow by 37 percent between 2016 and 2026, according to the U.S. Bureau of Labor Statistics. Yale's Physician Associate Program, based on the Yale campus, has contributed to the profession since its first students arrived in 1971. By adding PA Online, the School of Medicine now extends that reach more broadly.

PA Online's director, James Van Rhee, MS, PA-C, associate professor of medicine, praises the quality of the inaugural students in his program, including their health care experience, which averages just over 8,000 hours of patient care.

"Compared to the national data from the Physician Assistant Education Association," says Van Rhee, "the first cohort of online students, on average, had twice the health care experience and was five years older than the average PA program matriculating student." Their past roles range from PharmD, to work at a clinic for homeless people, to two decades' service as a medic on a Native American reservation in Arizona. The inaugural class includes three military veterans.

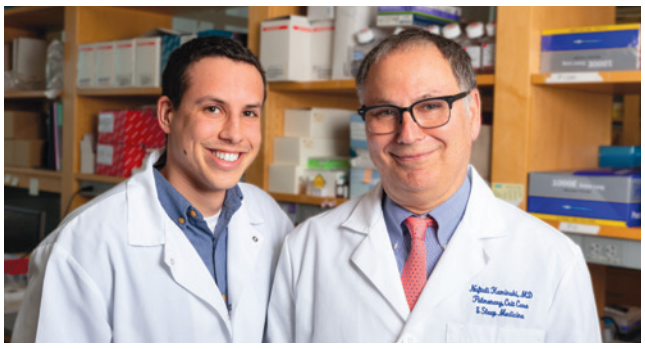
// Lung *(page 1)* Fibrosis Foundation. As many as 40,000 die from the disease every year.

Kaminski and his lab team are poised to take a major new step in IPF research, fueled by a gift of nearly $1 million from the venture philanthropy group Three Lakes Partners. The organization, whose mission is to accelerate progress in IPF research, was established by benefactor Thomas Hurvis, who lost his wife to IPF in 2015.

Using single-cell transcriptomics, Kaminski and his team plan to sequence the RNA (ribonucleic acid) of every cell in more than 100 donor lungs affected by IPF and other lung diseases. Ivan O. Rosas, MD, a physician at Brigham and Women's Hospital in Boston and associate professor of pulmonary and critical care at Harvard Medical School, is providing the lungs for this research as part of an ongoing collaboration. RNA contains a transcript of the DNA sequence, and influences gene expression. Analysis of the entire transcriptome can reveal which genes are turned on at certain times and which are turned off.

With prior available resources, this painstaking research would have taken years. But with the infusion from Three Lakes, the timetable will be far shorter. "Within three or four months, we hope to have 'The IPF Cell Atlas,' which will identify how the cell populations of the lung change during fibrosis and scarring," says Kaminski.

Kaminski, whose team led the field in applying high throughput genome scale transcript profiling to identify biomarkers and new drug targets using bulk tissue, anticipates that whole transcriptome single cell sequencing, to be performed at his section's Center for Precision Pulmonary Medicine (P2MED), will dramatically alter the understanding and management of IPF. "We have biomarkers that are good enough to predict mortality in patients, but not good enough to tell which pathways we should intervene with in every patient."



HAROLD SHAPIRO

Naftali Kaminski (right) is accelerating his lab's research into idiopathic pulmonary fibrosis (IPF), a disease that devastates the lungs, thanks to a gift from Three Lakes Partners, a venture philanthropy group whose mission is to conquer IPF. In 2017, lab member Taylor Adams (left) presented encouraging data that focused attention on the progress Kaminski and his team are making.

The new research, Kaminski says, would identify in detail all the aberrant pathways in every cell in the fibrotic lung, and could potentially lead to development of therapies to correct these pathways. It also could allow identification of biomarkers which would indicate what pathways are activated in each patient, leading to development of the sort of targeted individualized therapies that comprise the emerging field of precision medicine.

The onus to identify and develop applications for the research findings will not lie solely with the group at Yale. Kaminski's team does not just aim to complete the sequencing as soon as possible; it also will share the results in short order. In a field that desperately needs to accelerate progress for patients' sake, Kaminski bucks the notion that scientists ought to guard their data. In fact, a postbaccalaureate researcher in Kaminski's lab, Taylor Adams, presented the team's first single-cell data in a poster at last year's Pulmonary Fibrosis Foundation Summit in Nashville. That presentation, Kaminski believes, first attracted Three Lakes' attention.

Kaminski embraced the philosophy of sharing lab data nearly two decades ago when he trained under Dean Sheppard, MD, at the University of California, San Francisco. "I was worried about sharing data too early at some point," Kaminski explains, "and [Sheppard] said, 'You should be lucky [enough] to have data that someone else wants to steal from you.'"

The open approach aligns well with Three Lakes' vision for the project, which is to open as many viable avenues toward new and effective treatments as possible, and to do so with the utmost speed.

"Good science has the tendency to lead to more questions," says Ken Bahk, PhD, managing director of Three Lakes Partners. "This study should lead to so many new paths to investigate and ideally to a much better understanding of IPF and a more accurate and highly probable path to new therapeutics."

Scenes from celebration of 100 Years of Women at Yale School of Medicine

1. (l–r): Michele H. Johnson, MD, professor of radiology and biomedical imaging and of neurosurgery, and Diane M. Barnes, MD '77. **2.** (l–r): Anne McBride Curtis, MD, professor of radiology and biomedical imaging, and Shirley M. McCarthy, MD, PhD, professor emerita of diagnostic radiology. **3.** (l–r): Margretta R. Seashore, MD, professor emerita of genetics, and Carolyn R. Mazure, PhD, director of Women's Health Research at Yale. **4.** Approximately 500 attendees filled Harkness Auditorium on June 1, 2018. **5.** (l–r): Elizabeth A. Jonas, MD, professor of internal medicine (endocrinology) and of neuroscience; Valentina Greco, PhD, Carolyn Walch Slayman Professor of Genetics; and Susan J. Baserga, MD, PhD, professor of molecular biophysics and biochemistry, of genetics, and of therapeutic radiology. **6.** Joan A. Steitz, PhD, Sterling Professor of Molecular Biophysics and Biochemistry. **7.** Laura R. Ment, MD, professor of pediatrics (neurology) and associate dean for admissions and financial aid.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Grants and contracts awarded to Yale School of Medicine

March 2017–June 2017

Federal

Andrei Alexandrov, NIH, *Shotgun Method for Massive Mutational Interrogation of the Entire Human Genome*, 1.9 years, $418,750 • **Ranjit Bindra**, NIH, *Exploiting Mutant IDH1/2-induced Homologous Recombination Defects in Cancer*, 5 years, $1,959,240 • **Hilary Blumberg**, NIH, *Aging and Emotion Regulation Brain Circuitry in Bipolar Disorder*, 4.7 years, $3,848,099 • **Stuart Campbell**, NSF, *CAREER: A Systems Approach to Discovering Mechanical Sensors in Heart Muscle Cells*, 5 years, $500,000 • **Michael Cappello**, NIH, *Emerging Benzimidazole Resistance in Human Hookworms*, 5 years, $2,080,875 • **Kathleen Carroll**, NIH, *Computer Training in CBT for Spanish-speaking Alcohol Users*, 5 years, $2,573,076 • **Richard Carson**, NIH, *PET Imaging of Synaptic Density in Alzheimer's Disease*, 4 years, $2,761,546 • **Nashid Chaudhury**, NIH, *Molecular and Functional Links Between Two Distinct Inhibitory Receptors*, 2 years, $77,332 **Katarzyna Chawarska**, NIH, *Attentional, Temperamental, and Physiological Process Underlying Anxiety in Preschoolers with ASD*, 4.9 years, $3,904,335 • **Sidi Chen**, DoD, *Discovering Checkpoint Blockade Resistance Genes in Metastatic Lung Cancer*, 2 years, $586,250 • **Joseph Contessa**, DoD, *Small Molecule Inhibition of the Oligosaccharyltransferase for the Treatment of Breast Cancer*, 3 years, $628,125 • **Lynn Cooley**, NIH, *Oocyte Development in* Drosophila, 3.9 years, $2,643,119 • **Sabrina Diano**, NIH, *Role of Peroxisome Proliferation in Leptin Resistance*, 4 years, $1,843,735 • **Vishwa Dixit**, NIH, *Impact of Ketone Metabolites on Inflammasome Deactivation in Gout*, 4.9 years, 1,842,500 • **Deepak D'Souza**, NIH, *CB1R Availability in Synthetic Psychoactive Cannabinoid Users*, 2 years, $460,625 **Ronald Duman**, NIH, *Role of GABA Interneurons in the Rapid Antidepressant Actions of NMDA Receptor Blockade*, 5 years, $2,442,022 • **Brinda Emu**, NIH, (*PQ1*) *Lipid Metabolism, Inflammation, and T cell Dysfunction in HIV-associated Cancer*, 5 years, $3,155,302 • **Irina Esterlis**, NIH, *Role of Neuroinflammation in the Pathophysiology of Bipolar Depression*, 2 years, $460,625; NIH, *Glutamate Neurotransmission in Bipolar Depression and Mania*, 2 years, $460,625 • **Katherine Farley-Barnes**, NIH, PAX9, *Ribosome Biogenesis, and Congenital Disease*, 3 years, $83,416 • **Kathryn Ferguson**, NIH, *Regulation of Tie2 Activation by Homo- and Hetero-oligomerization*, 5 years, $1,915,780 • **John Forrest**, NIH, *Short Term Research Training: Students in Health Professional Schools*, 5 years, $1,177,679; NIH, *NIAAA Short-Term Training: Students in Health Professional Schools*, 5 years, $297,820 • **Antonio Giraldez**, NIH, *Molecular Mechanisms of the Maternal to Zygotic Transition*, 5 years, $3,905,334 • **Katherine Hastings**, NIH, *Mechanisms of Response and Resistance to Immune Checkpoint Inhibitors in Lung Adenocarcinoma*, 3 years, $172,926 • **Robert Heimer**, NIH, *Addressing Disparities in HIV Testing and Care among Displaced MSM*, 1.8 years, $447,242 • **Robert Hill**, NIH, *Uncovering Mechanisms of Myelin Formation and Regeneration in the Live Brain*, 2 years, $181,332 • **Mark Hochstrasser**, NIH, *Functions and Mechanisms of Deubiquitinating Enzymes*, 4 years, $1,433,579 • **Fahmeed Hyder**, NIH, *Energetics of Neuronal Populations by fMRI*, 4.8 years, $2,178,659; NIH, *Extracellular pH Mapping as Therapeutic Readout of Drug Delivery in Glioblastoma*, 3.8 years, $2,413,891 • **Akiko Iwasaki**, NIH, *B Cell Based Protection Against Recurrent Herpes*, 5 years, $2,093,750 • **Ryan Jensen**, NIH, *Elucidating Cancer Risk in BRCA2 and RAD51 Variants*, 5 years, $1,915,780 • **Kaveh Khoshnood**, NIH, *Masters Level Bioethics Program at Central South University in Changsha, China*, 5 years, $1,243,999 • **Harriet Kluger**, NIH, *Renalase Inhibition for Treatment of Unresectable Melanoma*, 5 years, $2,429,929 • **Hedy Kober**, NIH, *Meta-Analysis and Machine Learning: Toward Neuromarkers of Craving and Relapse*, 2.9 years, $1,327,980 • **Angela Lee**, NIH, *Sex Differences in Noradrenaline and Stress-Induced Reinstatement of Nicotine CPP*, 2 years, $57,060 • **Mark Lemmon**, NIH, *Understanding Signaling by Non-Canonical Receptor Tyrosine Kinases*, 5 years, $4,008,580 • **Haiqun Lin**, NIH, *Longitudinal Mediation Analysis to Identify Effective Intervention Components in Clustered Trial of RAISE-ETP* (*Recovery After an Initial Schizophrenia Episode-Early Treatment Program*), 2 years, $167,500 • **John MacMicking**, NIH, *A Novel CDN Sensor-Adaptor System for Host Defense Against Infection*, 5 years, $2,093,750 **Robert Malison**, NIH, *Imaging Synaptic Density in the Cocaine-Addicted Brain In Vivo using 11C UCB J PET*, 2 years, $418,750 • **Andres Martin**, NIH, *Research Education for Future Physician-Scientists in Child Psychiatry*, 5 years, $1,031,075 • **Thomas Melia**, NIH, *Regulation of Autophagosome Membrane Dynamics by the Atg8 Family of Proteins*, 3.8 years, $1,945,808 **Kathryn Miller-Jensen**, NIH, *Systems Analysis of Cell-to-Cell Variability and Paracrine Signaling Motifs Regulating TLR Activation*, 3.9 years, $1,181,674 • **Rosa Munoz Xicola**, NIH, *New DNA Repair Alterations in Hereditary Cancer Development*, 3 years, $521,964 • **Sukanya Narasimhan**, NIH, *Importance of Immunogenic Salivary Glycans in Eliciting Resistance to Ticks*, 2 years, $468,750 • **Michael Nathanson**, NIH, *A Swept-Field Confocal Microscope for Live Cell Imaging*, 1 year, $569,609 • **Laura Niklason**, NIH, *Engineered Tracheal Replacements*, 4 years, $2,454,258 • **John Pachankis**, NIH, *Development and Preliminary Trial of a Brief, Portable Health Intervention for Rural Sexual Minority Emerging Adults*, 2 years, $448,427 • **Rachel Perry**, NIH, *Regulation of Tumor Growth and Metabolism by Hyperinsulinemia*, 2 years, $297,004 • **Cristiana Pineda**, NIH, *Live-imaging the Interface Between Homeostasis and Cancer*, 2 years, $34,820 **Carla Rothlin**, NIH, *An Innate Immune Checkpoint in Cancer Immunotherapy*, 5 years, $2,288,150 • **Gary Rudnick**, NIH, *Conformational Change in NSS Transporters*, 3.9 years, $2,085,107 • **Molly Ryan**, NIH, *Understanding the Consequences of Oncogenic Mutations on FGFR Signaling*, 3 years, $131,196 • **Mehran Sadeghi**, NIH, *Novel Regulators of Calcific Aortic Valve Disease*, 4 years, $2,759,423 • **Tara Sanft**, NIH, *A Randomized Trial of Lifestyle Guidelines on Breast Cancer Biomarkers and Treatment Adherence*, 5 years, $3,280,907 • **Joseph Santos-Sacchi**, NIH, *Structural Correlates of Prestin Activity*, 5 years, $3,342,290; NIH, *Membrane Properties of the OHC System*, 5 years, $3,248,737 • **Brian Scassellati**, NSF, *WORKSHOP: The Pioneers Workshop at the 2017 ACM/IEEE International Conference on Human-Robot Interaction*, 1 years, $40,950 • **David Schatz**, NIH, *The Role of AID/APOBEC3 Proteins in Genome Instability in Multiple Myeloma*, 5 years, $2,033,080; NIH, *Targeting of Somatic Hypermutation in the Genome*, 4.9 years, $2,093,750 • **Gerald Shadel**, NIH, *Mitochondrial DNA Stress Activation of Interferon Signaling and Lupus Pathology*, 4.9 years, $2,169,040; NIH, *Inducible Mouse Models of Mitochondrial ROS Signaling and Environmental Stress*, 9 months, $237,749 • **Wendy Silverman**, NIH, *Fibroblast Growth Factor 2's Role in Fear and Approach Motivation in Anxious and Depressed Children and their Mothers*, 2 years, $460,625 • **Brian Smith**, NIH, *Immunohematology/Transfusion Medicine Research Training*, 5 years, $2,331,810 • **Dieter Soll**, NIH, *Studies of Transfer RNA*, 5 years, $5,220,121 • **Douglas Storace**, NIH, *Defining the Functions of Olfactory Bulb Processing Via Comparison of Input and Output*, 3 years, $502,500 • **Yajaira Suarez**, NIH, *HL-Regulation of Angiogenesis in the Obese Adipose Tissue by Secreted microRNAs*, 3.7 years, $2,105,358 • **Patrick Sung**, NIH, *Mechanistic Dissection of the Falconi Anemia Pathway of DNA Damage Response and Repair*, 5 years, $1,986,687 • **Joann Sweasy**, NIH, *Assessing the Role of the DNA Repair Landscape in Immune Checkpoint Therapy*, 2 years, $400,744 • **George Tellides**, NIH, *Characterization of TGFB-Dependent Mechanoresponses by Aortic Smooth Muscle Cells*, 4 years, $2,362,153 • **Vasilis Vasiliou**, NIH, *Novel Role of Corneal Crystallins as Modulators of Cell Growth and Transparency*, 3 years, $1,796,658 • **Stuart Weinzimer**, NIH, *On-body Ecosystem for Automated Insulin Delivery in Type 1 Diabetes*, 3 years, $2,976,398 • **John Wysolmerski**, NIH, *FGF23 Contributes to the Pathophysiology of Humoral Hypercalcemia of Malignancy*, 1.9 years, $405,350

Non-federal

Serap Aksoy, Fudan University Shanghai Medical College (NIH), *Influence of Gut Microbiota on Vector Competence*, 1 year, $41,875 **Sarah Amalraj**, Howard Hughes Medical Institute, *Myelin Regulatory Factor* (*MYRF*) *Plays an Unexpected Role in Left-Right Patterning and Cardiac Development: A Patient Based Discovery*, 1 year, $38,000 • **George Anderson**, VA Boston Healthcare System, *Plasma Analysis Agreement*, 5 years, $102,660 • **Raman Bahal**, Connecticut Innovations, *Site Specific Genome Editing of Hematopoietic Stem Cells for Sickle Cell Disease Gene Therapy*, 2 months, $100,000 **Stacy Castner**, **Graham Williams**, Unity Biotechnology, *Research Agreement with Unity Biotechnology*, 1 year, $397,645 • **Evan Chen**, Radiological Society of North America, *Identifying Enhancement-based Staging Markers on Baseline MR Imaging in Patients with Colorectal Cancer Liver Metastases Undergoing Locoregional Tumor Therapy*, 3 months, $3,000 **Leslie Curry**, Patrick and Catherine Weldon Donaghue Medical Research Foundation, *Translating Leadership Saves Lives for Greater Impact*, 1 year, $55,000 • **Amy Davidoff**, Commonwealth Fund, *Lack of Integration Between Medical and Prescription Drug Benefits Within Medicare: Implications For Quality, Value, and Beneficiary Access*, 10 months, $49,431 • **Caterina Di Pietro**, Cystic Fibrosis Foundation (CFF), *Ezrin and CFTR Crosstalk During Macrophage Activation*, 2 years, $128,550 • **Edward Doherty**, Arthritis Foundation, *MIF/CD74 Signaling as a New Candidate Target for Immunotherapy of Rheumatoid Arthritis*, 2 years, $373,804 • **Robert Dubrow**, Icahn School of Medicine at Mount Sinai (ISMMS) (NIH), *Optimizing Lung Cancer Treatment in HIV Infected Persons*, 1 year, $31,115 **Tarek Fahmy**, Toralgen, *Toralgen Research Agreement*, 1 year, $296,346 • **Rebecca Fine**, Howard Hughes Medical Institute, *Translocation*

ROBERT LISAK (7)

// 100 Years *(page 1)* of Gastrointestinal Sciences; professor of internal medicine, and professor of molecular & integrative physiology at the University of Michigan Medical School, noted that many women begin careers in academic medicine, but few reach the upper echelons of the tenure-track hierarchy. For women of color, the situation is bleaker; African American women represent only 2 percent of medical school faculty in the United States. Merchant, like many of the symposium's speakers, credits her success to multiple mentors who supported her along the way.

Naomi Rogers, PhD, professor in the history of medicine and of history, noted that Elizabeth Blackwell, the first woman to receive a medical degree in the U.S., was admitted in 1847 to New York's Geneva Medical College as a joke. The first three women Yale School of Medicine admitted a century ago—when studying medicine was still considered "unladylike"—included Louise Farnam, already a PhD in physiological chemistry, who would graduate with honors, win the Campbell Gold Prize for the highest rank in examinations, and be her class's commencement speaker.

While opportunities are not equal yet, women who have been witness to the last several decades say they see progress. "I never believed I would see women in leadership positions in science and academics and medicine," says Joan A. Steitz, PhD, Sterling Professor of Molecular Biophysics and Biochemistry, who earned her PhD from Harvard University in 1967. "That has all changed." In the session on current issues facing women, Marie E. Robert, MD, professor of pathology and former SWIM chair, noted that while there will always be work to do, many of the positive steps taken by the medical school in recent years, such as ensuring that women comprise 30 percent of governance committees and 50 percent of senior search committees at YSM, addressing gender-based salary inequities, and the recruitment of a deputy dean for diversity and inclusion, have been in partnership with SWIM.

The symposium venue included a series of banners highlighting women in all areas of medicine and science during the past century. Bia and Jonas also have worked to increase faculty engagement through activities such as a recent Internal Medicine Grand Rounds that was devoted to the history of women in the department. Heartened by the enthusiastic response to the 100 Years of Women at YSM celebration, they look forward now to seeing the momentum continue.

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of Gut Flora and its Role in Lupus Autoimmunity, 1 year, $38,000 • **Whitney Fu**, American Medical Association Foundation, *The Association Between Protein Citrullination and Complement Activation in Transplanted Allografts Undergoing Rejection, and the Utility of Anti-Cyclic Citrullinated Peptide Antibodies as a Diagnostic Biomarker for Graft Rejection*, 1 year, $2,454 • **Jonathan Gaillard**, Howard Hughes Medical Institute, *The Genetic Causes of Vein of Galen Malformation*, 1 year, $38,000 • **Sara Gallini**, Human Frontier Science Program Organization, *Understanding the Principles of Tissue Repair that Accelerate Tumor Initiation*, 3 years, $160,980 • **David Glahn**, Mind Research Network (NIH), *Mining the Genomewide Scan: Genetic Profiles of Structural Loss in Schizophrenia*, 5 years, $122,275 • **Steven Gore**, University of Miami (NIH), *Epigenetic Biomarkers of Response to Azacytidine in Myelodysplastic Syndromes*, 11 months, $41,625 • **Bonnie Gould Rothberg**, University of New Mexico (NIH), *Integration of Clinical and Molecular Biomarkers for Melanoma Survival*, 1 year, $26,335 • **David Hafler**, Benaroya Research Institute (NIH), *Regulatory Epigenetic Profile of Tregs in Multiple Sclerosis*, 10 months, $125,625; Shoreline Biome (NIH), *High Resolution Microbiome Profiling System*, 1 year, $34,961 • **Stephanie Halene**, **Manoj Pillai**, Connecticut Innovations, *Biology and Therapeutic Targeting of Splicing Factor Mutant MDS*, 3 years, $675,000 • **Annie Harper**, Center for Retirement Research at Boston College (SSA), *Financial Management Support for SSA Retired and Disabled Beneficiaries; Beyond Representative Payees*, 1 year, $45,000 **Christos Hatzis**, University of Texas M.D. Anderson Cancer Center (NIH), *Integrating Biospecimen Science into the Development of RNA-Based Clinical Assays for Patients with Metastatic Breast Cancer*, 1 year, $106,832 **Kathryn Hawk**, New York University School of Medicine (NIH), *NIDA Clinical Trials Network: Greater New York Node* (*XR-BUP ED Project*), 1 year, $303,094 • **Roy Herbst**, Brown University (DoD), *Chi3l1 Regulation of Checkpoint Regulating, Costimulatory and Coinhibitory Molecules in Primary and Metastatic Lung Cancer*, 1 year, $83,749 • **Kevan Herold**, University of South Florida (NIH), *NIDDK Type 1 Diabetes TrialNet Data Coordinating Center at USF*, 1 year, $20,323 **Erica Herzog**, Foundation for Sarcoidosis Research, *Development of an Ex Vivo Mimetic of the Sarcoidosis Lung Microenvironment*, 2 years, $150,000 • **Robert Hill**, Donors Cure Foundation, *Myelin Plasticity in Alzheimer's Disease and TREM2 Mutants*, 1 year, $50,000 • **Lawrence Hirsch**, Eisai, *Fifth Annual Comprehensive Epilepsy Research Retreat*, 1 month, $5,000; Upsher-Smith Laboratories, *Fifth Annual Yale Comprehensive Epilepsy Research Retreat*, 1 month, $5,000; Zimmer Biomet, *Fifth Annual Yale Comprehensive Epilepsy Retreat*, 1 month, $5,000 • **Mark Horowitz**, Orentreich Foundation for the Advancement of Science, *The Role of the Transsulfuration Pathway in Mediating the Effects of Methionine Restriction*, 1 year, $43,616 • **David Hudnall**, HHV-6 Foundation, *The Role of Human Herpesvirus 6 in Salivary Gland Cancer*, 1 year, $27,500 • **Natalia Ivanova**, Connecticut Innovations, *BCOR-PRC1 Repressive Complex as the Key Regulator of Pluripotency in Human Embryonic Stem Cells*, 4 years, $675,500 • **Akiko Iwasaki**, Brigham and Women's Hospital, *Defining the Role of Endogenous Retroviruses in Lupus Skin Disease*, 1 year, $50,250 • **Christopher Jackson**, Howard Hughes Medical Institute, *Development of Nanoparticle-encapsulated Chemo/Radio-Sensitizers for Intrathecal Delivery*, 1 year, $38,000 • **Jason Karimy**, Neurosurgery Research & Education Foundation, *Molecular Mechanisms of CSF Hypersecretion in a Model of Intraventricular Hemorrhage*, 3 months, $2,500 • **Steven Kleinstein**, Icahn School of Medicine at Mount Sinai (NIH), *Development of HIPC Data Standards*, 1 year, $108,875; Icahn School of Medicine at Mount Sinai (NIH), *Dengue Human Immunology Project Consortium* (*DHIPC*), 1 year, $100,500 • **Albert Ko**, University of Liverpool, *Optimal Control Strategies for Rodent-Borne Zoonoses in Brazilian Slum Settlements*, 2 years, $163,547 • **Kyle Kovacs**, ASCRS Foundation: American Society of Cataract and Refractive Surgery, *Choroidal Vascular Findings on Wide-Field Indocyanine Green Angiography Associated with Ocular and Systemic Disease*, 1 year, $5,000 • **Gary Kupfer**, Icahn School of Medicine at Mount Sinai (ISMMS) (DHHS), *Hemophilia Treatment Centers* (*SPRANS*), 1 year, $18,827 • **Soo Hyun Kwon**, American Academy for Cerebral Palsy and Developmental Medicine, *Hypoxemia and White Matter Development in the Motor Outcomes of Extremely Preterm Infants*, 1 year, $25,000 **Haifan Lin**, Connecticut Innovations, *Continued Support and Technology Development for Shared Core Facilities at the Yale StemCell Center*, 1 year, $500,000 • **Anthony Lisi**, Palmer College of Chiropractic, *Inter-Institutional Network for Chiropractic Research*, 5 years, $1,950,000 • **Wu Liu**, American Association of Physicists in Medicine, *Dosimetric Verification of a Focused Kv X-Ray System*, 4 months, $5,000 **Patricia LoRusso**, Astrazeneca UK Limited, *Master Research Agreement-Administrative Component*, 1 year, $250,000 • **Jun Lu**, Connecticut Innovations, *Functional Mapping of Non-Coding Genomic Elements*, 2 years, $200,000 **Patrick Lusk**, Dystonia Medical Research Foundation, *Determining the Role of Torsin in Nuclear Pore Complex Assembly*, 2 years, $130,000 **Nikhil Malvankar**, Charles H. Hood Foundation, *Targeting Bacterial Infections by Imaging Electrical Interactions Between Host Surface and a Pathogen*, 2 years, $150,000; Hartwell Foundation, *Targeting Bacterial Infections by Imaging Electrical Interactions Between Host Surface and Pathogens*, 3 years, $100,000 • **Wajahat Mehal**, Lifemax Biotechnology, *Characterization of the Interaction Between Digoxin and PKM2*, 1 year, $174,842 • **Ruth Montgomery**, University of Wisconsin-Madison (NIH), *Functional Immune Profiling in Asthma Treatment*, 5 months, $127,699; Icahn School of Medicine at Mount Sinai (NIH), *Dengue Human Immunology Project Consortium* (*DHIPC*): *Continued and Expanded Computational Analysis and Integration of Flow and Mass Cytometry Data Across HIPC Centers*, 1 year, $27,664; Icahn School of Medicine at Mount Sinai (NIH), *Dengue Human Immunology Project Consortium* (*DHIPC*): *Development and Optimization of Lyophilized Reagents to Facilitate and Improve Data Quality in Cytof Studies*, 1 year, $17,044 • **Gil Mor**, Wayne State University (NIH), *Subcontract with Wayne State University to Characterize the Contribution of the Placenta to the Immune Response to Infection During Pregnancy*, 1 year, $207,758 **Sarah Mougalian,** The William O. Seery Foundation, *Improving Adherence to Endocrine Therapy in Breast Cancer Using Mobile Technology*, 2 years, $90,000 • **Rosa Munoz Xicola**, Prevent Cancer Foundation, *New DNA Repair Alterations in Hereditary Cancer Development*, 2 years, $100,000 • **Linda Niccolai**, Drexel University (NIH), *Social Determinants of HIV/AIDS: The Intersecting Impacts of Mass Incarceration, Housing Policy and Housing Instability*, 6 months, $196,407 • **Laura Niklason**, Foundation for Anesthesia Education & Research, *Medical Student Anesthesia Research Fellowship 2017*, 7 months, $5,200 • **Jessica Nouws**, Robert Leet and Clara Guthrie Patterson Trust, *Insulin Resistance of Adolescent Obesity: Role of Inflammation and Fat Storage Capacity*, 2 years, $90,000 • **In-Hyun Park**, Connecticut Innovations, *Elucidating the Impact of Naïve Conditions on X Chromosome of Human Female Pluripotent Stem Cells*, 4 years, $675,500 **Marina Picciotto**, Brain & Behavior Research Foundation (formerly NARSAD), *Role of Intrinsic Hippocampal Cholinergic Neurons in Behaviors Related to Anxiety and Depression*, 1 year, $100,000 • **David Pitt**, National Multiple Sclerosis Society, *NFkB-related MS Risk Variants Drive Excessive Activation of Astrocytes in Multiple Sclerosis*, 2 years, $311,752 • **Lajos Pusztai**, Oregon Health Sciences University (NIH), *SWOG Network Group Operations Center of the NCTN*, 1 year, $63,886 • **Aaron Ring**, Gilead Sciences, *Generation and Analysis of Anti-B Klotho Nanobodies*, 1 year, $249,750 • **Marc Rosen**, New York University School of Medicine (Robin Hood Foundation), *Integrating Financial Management Counseling and Smoking Cessation*, 1 year, $8,410 **Kurt Schalper**, Surface Oncology, *Expression and Biological Role of Candidate Myeloid Cell Immunotherapy Targets in Human Tumors Using Quantitative Methods*, 1 year, $298,980 **Timothy Schmutte**, University of Pennsylvania (NIH), *Emergency Department Recognition of Mental Disorders and Short-Term Outcome of Deliberate Self-Harm in Older Adults*, 10 months, $144,202 • **Eugene Shapiro**, Columbia University (NIH), *VZV in the Enteric Nervous System: Pathogenesis and Consequences*, 4 years, $19,960 **Megan Smith**, Annie E. Casey Foundation, *Support Evaluation for Research Innovations in Building Adult Capabilities and Assessing Two-Generation Impact* (*MOM'S Partnership–AECF 2017-2018*), 1.4 years, $332,574 • **Mario Strazzabosco**, Connecticut Innovations, *Generation of CFTR-defective Biliary Cells from Human Induced Pluripotent-Stem Cells* (*iPSC*) *to Study the Role of Innate Immunity in Cystic Fibrosis Liver Disease*, 2 years, $100,000 • **Joann Sweasy**, University of Vermont (NIH), *Structure and Function of DNA Repair Enzymes and Cancer*, 1 year, $15,128; University of Vermont (NIH), *Structure and Function of DNA Repair Enzymes* (*03*), 1 year, $34,038; University of Vermont (NIH), *Structure and Function of DNA Repair Enzymes and Cancer* (*CB*), 1 year, $15,128 • **Reshef Tal**, Celmatix, *Study of Genetic and Phenotypic Risk Factors Underlying Female Infertility*, 1 year, $117,495 • **Takuya Toyonaga**, Society of Nuclear Medicine and Molecular Imaging, *2016-2018 SNMMI Wagner-Torizuka Fellowship*, 2 years, $48,000 • **Guangchuan Wang**, Cancer Research Institute, *Genetic Dissection of PD-1 Pathway Immune Checkpoint Blockade in Liver Cancer*, 3 years, $175,500 • **Stephen Waxman**, **Yang Yang**, Connecticut Innovations, *Using iPSCs to Understand Diseases Mechanism of Navl.7 Mutation Related Small Fiber Neuropathy*, 2 years, $200,000 • **Carol Weitzman**, Department of Children & Families, *Fetal Alcohol Spectrum Disorders FASD and Training on the Use of the Tool*, 3 months, $17,500 • **Nicholas Wilcox**, Howard Hughes Medical Institute, *Distinct Hypoxia-induced Translational Profiles of Embryonic- and Adult-Derived Macrophages; Implications in Cardiac Injury and Repair Responses to Ischemia*, 1 year, $38,000 • **John Wysolmerski**, Augusta University (Formerly Georgia Regents University) (NIH), *DiaComp Summer Student Funding Programs*, 4 months, $8,526 • **Yong Xiong**, Veterans Medical Research Foundation (NIH), *Enhancement of Infectivity by HIV-1 Nef via Antagonism of SERINC Proteins*, 5 years, $209,375 **Daniel Zegarra Ruiz**, Lupus Foundation of America, *Dietary Regulation of Type I Interferon in Lupus Pathogenesis*, 3 months, $4,000

Four from medical school elected to National Academy of Sciences

American Academy of Arts and Sciences also chooses two from School of Medicine

In recognition of their outstanding research achievements, four School of Medicine faculty members have been elected to the National Academy of Sciences (NAS). Akiko Iwasaki, PhD; Haifan Lin, PhD; David G. Schatz, PhD; and Günter Paul Wagner, PhD, were selected for one of the world's highest honors that can be bestowed on a scientist.

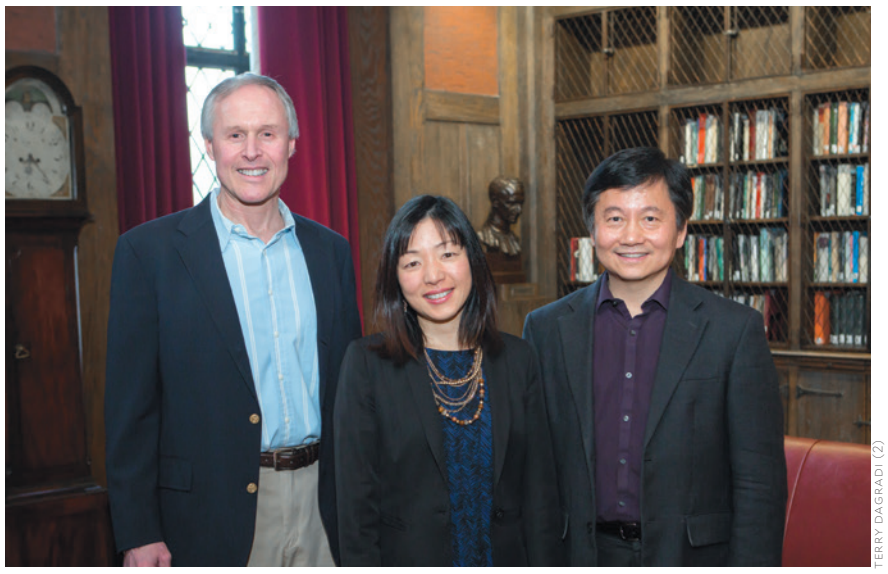
"This is a banner year for the School of Medicine," says Robert J. Alpern, MD, dean and Ensign Professor of Medicine. "Election to the National Academy of Sciences is based on the quality of research and I think it speaks volumes about the caliber and impact of Yale science that four of our faculty members were elected this year."

Iwasaki is Waldemar Von Zedtwitz Professor of Immunobiology and Molecular, Cellular and Developmental Biology and a Howard Hughes Medical Institute (HHMI) investigator. Her research focuses on the mechanisms of immune defense against viruses at mucosal surfaces. Her laboratory has made seminal contributions to the understanding of how innate recognition of viral infections leads to the adaptive immune response, and how adaptive immunity mediates protection against subsequent viral challenges. Her work spans diseases caused by such viruses as herpes, influenza, rhinovirus, human papillomavirus, and Zika.

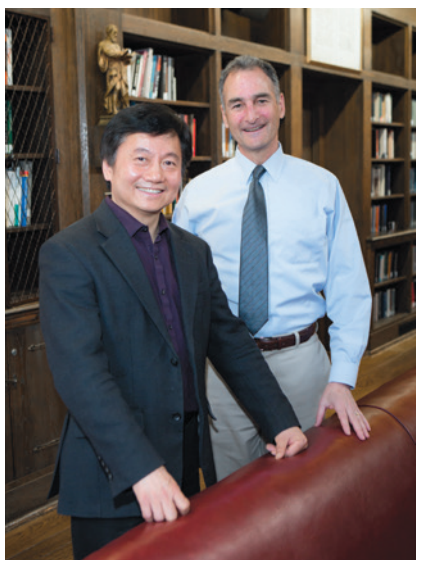
Lin is Eugene Higgins Professor of Cell Biology, professor of genetics and of obstetrics, gynecology, and reproductive sciences, and founding director of the Yale Stem Cell Center. He has made key contributions to the demonstration of stem cell asymmetric division and the proof of the stem cell niche theory. He discovered the Argonaute/Piwi gene family and its essential function in stem cell self-renewal and germline development. He is also a discoverer of a novel class of non-coding small RNAs known as piRNAs, which was hailed by *Science* as one of the top breakthroughs in 2006. More recently, he demonstrated the crucial roles of the Piwi-piRNA pathway in epigenetic programming and in post-transcriptional regulation of mRNA and long non-coding RNAs.

Schatz is chair and Waldemar Von Zedtwitz Professor of Immunobiology, professor of molecular biophysics and biochemistry, and an HHMI investigator alumnus. He has made fundamental contributions to the understanding of the mechanisms that assemble and diversify antigen receptor genes that encode antibodies and T cell receptors. He is best known for the discovery of the recombination activating genes *RAG1* and *RAG2*, subsequent biochemical insights into *RAG* function and evolutionary origins, and the discovery of two distinct levels of regulation of somatic hypermutation.

Wagner is Alison Richard Professor and acting chair of ecology and evolutionary biology at Yale University, with a secondary appointment in the medical school's Department of Obstetrics, Gynecology & Reproductive Sciences. Along with David Bercovici, PhD, and Igor B. Frenkel, PhD, from Yale University, the School of Medicine researchers are among 84 new members and 21 foreign associates. They join 64 other Yale faculty members—29 of whom are from the School of Medicine—who have been elected to the NAS.



TERRY DAGRADI (2)



Above (l–r): David Schatz, Akiko Iwasaki, and Haifan Lin (and Günter Wagner, not pictured), are School of Medicine researchers elected to the National Academy of Sciences, one of the highest honors that a scientist can receive.

Left: Lin also was elected in March to the American Academy of Arts and Sciences, together with Gerald Shulman.

In addition, Lin was elected in April to the American Academy of Arts and Sciences, which celebrates excellence in a wide range of disciplines. Joining him from the School of Medicine faculty is Gerald I. Shulman, MD, PhD, George R. Cowgill Professor of Medicine (Endocrinology), professor of cellular and molecular medicine, co-director of the Yale Diabetes Research Center, and HHMI investigator. Shulman pioneered the use of magnetic resonance spectroscopy to examine intracellular glucose and fat metabolism in humans for the first time. The approach has led to groundbreaking basic and clinical investigative studies on insulin resistance and a deeper understanding of type 2 diabetes.

Also entering the academy from Yale's faculty is John J. Collins, PhD, the Holmes Professor of Old Testament Criticism and Interpretation.

Other new inductees to the academy include former president Barack Obama and actor Tom Hanks.

Awards & Honors

Craig M. Crews, PhD, Lewis B. Culliman Professor of Molecular, Cellular, and Developmental Biology, and professor of chemistry, receives the Khorana Prize from the Royal Society of Chemistry, in recognition of pioneering contributions to the field of controlled proteostasis.

John Elefteriades, MD, William W.L. Glenn Professor of Surgery (Cardiac Surgery), has received an honorary PhD from the University of Liege, Belgium, recognizing "innumerable scientific publications of the highest caliber … on the genetics of aneurysms and the pathophysiologic mechanisms that favor their rupture."

Stephanie S. O'Malley, PhD, professor of psychiatry, has received the Research Society on Alcoholism's 2018 Distinguished Researcher Award, which honors a senior researcher who has made outstanding scientific contributions to the alcohol field. The society says O'Malley's contributions to the field "have been highly significant and innovative."

David H. Stitelman, MD, assistant professor of surgery (pediatrics) and of obstetrics, gynecology, and reproductive sciences, has received the Hartwell Foundation's Individual Biomedical Research Award, in support of his research into "Fetal Cure for Spina Bifida."

Stephanie C. Eisenbarth, MD, PhD, associate professor of laboratory medicine, of immunobiology, and of medicine (immunology), has received the National Blood Foundation's Award for Innovative Research, for work that has been instrumental in helping to determine why some patients become alloimmunized after transfusion.

Paul D. Kirwin, MD, associate professor of psychiatry, receives the Jack Weinberg Memorial Award in Geriatric Psychiatry from the American Psychiatric Association, given for special leadership and outstanding work in clinical practice, training, or research into geriatric psychiatry.

Sangini S. Sheth, MD, MPH, assistant professor of obstetrics, gynecology, and reproductive sciences, has received the American College of Obstetricians and Gynecologists' Immunization Champion Award, for demonstrating exceptional progress in increasing immunization rates among pregnant women in her patient population.

Robert M. Weiss, MD, Donald Guthrie Professor of Urology, has received the John W. Duckett, MD, Pediatric Urology Research Excellence Award from the Urology Care Foundation, for "significant contributions to drug delivery for benign and malignant diseases of the bladder as well as addressing bladder dysfunction through increased understanding of age-dependent factors in ureteral-vesical function."