Medicine@Yale

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Gains in melanoma research inspire generous gifts

Thirty years ago, a person with metastatic melanoma had a 5 to 10 percent chance of long-term survival. Today, estimates of five-year survival range from 40 to 50 percent. This substantial progress is due in large part to recent advances in immunotherapy, which activates the body's own defenses to attack tumors.

In certain instances, activation may involve disabling the body's own roadblocks against immune system activity, which are called checkpoints. These natural "brakes" are an essential defense against autoimmune diseases such as type 1 diabetes and rheumatoid arthritis, but checkpoints also can thwart the destruction of harmful tumors. Clinical researchers at Yale Cancer Center are leaders in efforts to develop corrective therapies.

JUDY SIROTA ROSENTHAL

Donors Roslyn and Jerome Meyer (center and right) with Cancer Center Director Charles Fuchs.

At times, results have been dramatic. Immune checkpoint inhibitors have freed the immune system to shrink tumors drastically and rapidly. The challenge // **Immunotherapy** *(page 7)*

Jon Sokoloff lost his mother to melanoma 15 years ago. Since then, he and his wife Sheryl have sought to do everything they can to support research into more effective treatments. The couple began funding research through the Melanoma Research Alliance (MRA) 10 years ago. In that time, they have seen stunning improvements in the outlook for people with this type of cancer.

"Eighteen years ago, when my mother got this diagnosis, it was total despair. There was nothing you could do," says Sokoloff. "It has been rewarding to watch the dramatic improvement in the availability of therapies that can combat the disease."

LEONARD GREEN & PARTNERS, L.P.

Jon Sokoloff is gratified by advances in melanoma research, and has funded promising new work.

Sokoloff has seen firsthand how well these new therapies can work. His cousin, whose advanced melanoma metastasized to his brain and lungs, is now cancer free after participating in a clinical trial with the immunotherapy drug ipilimumab (Yervoy®). // **MRA** *(page 7)*

New endowed chair to focus on ovarian cancer

Search is underway to fill professorship funded by alumna and her husband

The partnership between Mary Lake Polan, M.D. '75, PH.D. '70, M.P.H., and Frank Bennack is unique, more than simply a marriage. Both have a strong commitment to giving back, and they share a vision of philanthropy as a route to improving life for others.

With an interest in women's health, this past winter they created the Mary Lake Polan, M.D., PH.D., M.P.H. Professorship with a $3 million gift. There will be a nationwide search to fill the chair, which is the medical school's first endowed professorship specifically dedicated to the Department of Obstetrics, Gynecology & Reproductive Sciences.

Polan has had a distinguished career, first at Yale and then at Stanford University School of Medicine, where she was chair of obstetrics and gynecology for 15 years. She credits Yale for allowing her to take an untraditional approach to learning. "It was a golden time to be educated at Yale," she says. "They let you follow your interests and just wanted you to be successful."

After earning her PH.D. in molecular biochemistry and biophysics, Polan continued at Yale as a postdoctoral fellow under Joseph G. Gall, PH.D., who famously mentored an unusually large number of women scientists (then referred to as Gall's Gals). "After collaborating with other women scientists in Kline Biology Tower, I decided to go back to medical school," Polan recalls. "I liked the clinical side of science, which is medicine—talking to people, caring for them."

She became the first woman to complete a residency in obstetrics and gynecology at Yale. Following fellowships in gynecologic oncology and reproductive endocrinology, she joined the faculty, along the way pursuing a burgeoning interest in medicine in the developing world. After her service as department chair at Stanford, which ran from 1990 to 2005, Polan returned to the east coast, and is again on the Yale School of Medicine faculty as clinical professor of obstetrics, gynecology & reproductive sciences.

Bennack's career has been equally stellar. Now executive vice chair of the Hearst Corporation, he served two stints as Hearst's CEO. On the philanthropic side, he is chair of the Board of Trustees of New York-Presbyterian Hospital, chair of the Paley Center for Media, and chair emeritus of Lincoln Center for the Performing Arts.

COURTESY MARY LAKE POLAN AND FRANK BENNACK

Mary Lake Polan and Frank Bennack have endowed a professorship whose focus will be research on—and finding new treatments for—ovarian cancer.

The couple came together through a mix of business and serendipity. "For many years we // **Ovarian** *(page 6)*

Blavatnik fund to speed discoveries to patients

Len Blavatnik

Inspired by the long tradition of innovation at Yale University, particularly in the life sciences, The Blavatnik Family Foundation has donated $10 million to Yale University to promote and to accelerate the development, application, and commercialization of breakthrough research in the life sciences. The gift will help shorten the timeline between exciting discoveries in the sciences and their ultimate benefit to patients, a frequently frustrating aspect of the scientific process.

"Yale exemplifies the remarkable pace of growth and discovery in the life sciences," said American industrialist and philanthropist Len Blavatnik, founder and chair of Access Industries and head of the Blavatnik Family Foundation. "The Blavatnik Fund for Innovation will help Yale quicken the discovery-to-market pipeline and to nurture future leaders in scientific entrepreneurism." // **Fund** *(page 5)*

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TERRY DAGRADI

Among women who chair departments at the School of Medicine, Roberta L. Hines has served the longest—since 1994. The Department of Anesthesiology has expanded greatly in size and scope during that time, and women in the discipline have increased their prominence.

Excelling where men once reigned

Longtime chair expands her department's breadth and inspires more women to lead

Roberta L. Hines, M.D., chair and Nicholas M. Greene Professor of Anesthesiology, wants people to know that anesthesiologists do far more than sit behind the operating-room curtain. Rather, anesthesia is a multidisciplinary and often longitudinal discipline.

"The OR is always going to be our home, but we continue to expand our expertise outside this traditional clinical venue," she says. "Our current focus is directed toward identifying ways to positively impact patient outcome across the entire clinical spectrum."

Since taking over as chair of the Department of Anesthesiology in 1994, Hines has overseen a dramatic expansion in its clinical reach, pushing the specialty to realize more of its potential. Under her guidance, the department has set up a pre-screening clinic for surgical patients (it helps them get healthier for surgery); expanded its research to include tissue engineering and the study of postoperative cognitive impairment; and partnered with Smilow Cancer Center to provide specialized cancer-pain services.

The department also has grown in size and prominence. It cares for 55,000 children and adults each year, more than double what it did before Hines' leadership. Most of its 120 faculty have advanced fellowship training. Spanning four medical campuses, it trains 76 residents, 12 clinical fellows, and three physician-scientists annually. Its graduates include eight department chairs, something Hines is especially proud of. They, in turn, are impressed with the evolution of the place where they trained. "Many of the residents who have come back after having left five or 10 years ago are in awe of the change in the department," Hines says.

Hines says her proudest personal accomplishments are her 25 years' service as an examiner for the American Board of Anesthesiology; editing the major textbook *Anesthesia and Coexisting Disease*; and serving as president of the Association of University Anesthesiologists and the Association of Academic Anesthesiology Chairs.

In the latter organization, Hines is a rarity. Of 131 such chairs nationwide, she is one of just nine women—though she expects to see that change.

"We are seeing a growing number of women entering anesthesia," she says. "Two of my vice-chairs are female, many of my division and associate chiefs are female, and that really [speaks to] the fact that we're now training more women [for leadership]. Having more diverse chairs will be a positive thing at every level."

To that end, Hines makes mentorship a priority. "The lack of female mentors has been and will continue to be the biggest impediment to having women in leadership in medicine," she says.

Hines grew up in the rural hamlet of Canaan, New Hampshire—the daughter of a nurse and a construction worker—and recalls being surrounded by supportive adults. She became the first in her family to attend college and one of just six from her 67-person high school class, graduating from the University of New Hampshire and Dartmouth Medical School. She maintains active ties to the region by organizing elder care, working to reduce rural hunger and poverty, and administering scholarships for area students.

"I wouldn't be where I am today were it not for that very small regional high school, and I want to make sure that the students coming behind me have the same opportunities I did," Hines says.

Hines began a surgical residency at Yale New Haven Hospital before deciding to train in cardiac anesthesiology and critical care instead. Soon after joining the Yale faculty in 1984, she saw to it that a cardiothoracic intensive care unit opened at the hospital, making Yale's one of the first anesthesiology departments in the country to assume responsibility for post-cardiac surgery patient care.

That focus on what happens before and after surgery, not just during, will shape anesthesia's future, Hines believes. "There are many things that we need to focus on to ensure that our patients are getting the best possible care across their entire spectrum," she says. "That's where I would like to continue to drive the department and our specialty."

Library provides new tool to speed and improve systematic reviews

With increasing demand from faculty who want to produce systematic reviews in their fields of expertise, the Cushing/Whitney Medical Library has licensed a software program designed to make the process of evaluating as many as several thousand articles far less onerous.

The software package, called Covidence, became available in September. It is one of several such products that have emerged in the field, and Yale's is among just a handful of libraries that have licensed it university-wide, according to Holly Grossetta Nardini, M.L.S., associate director of the library.

"Systematic reviews are a hot topic in literature right now," says Grossetta Nardini, who notes that a systematic review that follows the National Academy of Medicine's strict guidelines is inevitably an intensive year-long process. The academy's standards include having two members of the research team, working independently of each other, screen and select—one by one—relevant

// Library *(page 8)*

Yale-Mayo center formed to advance regulatory science

Joseph Ross

The U.S. Food and Drug Administration (FDA) has awarded Yale and Mayo Clinic a grant of up to $6.7 million over two years to establish a Center of Excellence in Regulatory Science and Innovation.

The award will utilize the strengths of both institutions to address challenges presented by transformations in medical product development. Its goal is to take advantage of routinely collected real-world data sources, existing clinical trial data, and genomic and biobank data in order to inform regulatory decision making; build FDA capacity and capability to deploy advanced analytic methods; and disseminate the knowledge generated.

This information will be used to ensure patient-centered regulatory decision making; create better-informed regulators, manufacturers, clinicians and patients; and support shared decision making.

"This cooperative grant creates a unique opportunity for the faculty and trainees at Yale and Mayo Clinic to use their combined research expertise to examine massive amounts of data and engage with the FDA in meaningful, data-driven change, supporting efforts to protect the public's health, and improve health care for patients," says Joseph S. Ross, M.D., M.H.S., associate professor of medicine (general medicine) and of public health (health policy), who is principal investigator of the award.

Ross says Yale's role in the initiative reflects the achievements and support of the Schools of Medicine, Public Health, Management, and Law, as well as the Center for Outcomes Research and Evaluation at Yale New Haven Health.

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Enzyme to stop lung cancer is targeted

ISTOCKPHOTO.COM

A Yale-led research team has found that a fundamental cellular process can be interrupted to disable certain cancerous cells.

During the process of glycosylation, an enzyme called oligosaccharyltransferase (OST) helps transfer chains of saccharides to specific proteins to help those proteins fold correctly. Scientists assumed tinkering with the glycosylation pathway would automatically harm all cells.

Joseph N. Contessa, M.D., PH.D., associate professor of therapeutic radiology and of pharmacology, and colleagues isolated an inhibitor called NGI-1 that disrupted glycosylation by targeting the OST enzyme. They found it stopped cell division in lung cancer cells with epidermal growth factor (EGFR) and fibroblast growth factor (FGFR) receptor mutations. Noncancerous cells exposed to the NGI-1 inhibitor were unaffected.

The study was published Oct. 3 in *Nature Chemical Biology*. "The EGF and FGF receptors have a lot of sugars on them," Contessa says, "so disrupting glycosylation on a cell heavily dependent on those receptors is a very targeted approach."

Reminding retinal cells to regenerate

Retinal cells called Müller glial (MG) cells exist in humans and zebrafish, but function differently in the two species.

In zebrafish, these cells act like retinal stem cells and routinely replace damaged retinal neuronal cell types, including ganglion and photoreceptor cells, which are lost in glaucoma and macular degeneration, respectively.

In mammals, MG cells take on stem cell-like properties only if severe physical injury to the retina occurs. Even then, just a small number of cells are replenished. Reactivating human MG cells to behave as stem cells holds potential as a treatment for blindness-causing diseases.

Researchers led by Bo Chen, PH.D., associate professor of ophthalmology and visual science, and of neuroscience, found they could initiate stem cell behavior in mice MG cells by activating the Wnt/Lin28 signaling pathway without causing damage to the retina. As described in *Cell Reports*, published Sept. 27, they transferred the genes β-catenin or *LIN28* into adult mouse retinas, causing MG cells to behave like stem cells. About 5 percent of MG cells turned into retinal neuronal cells, but that was just a first step, says Chen. "Now we need to guide the cell cycle-reactivated MG cells to differentiate into ganglion or photoreceptor cells," Chen says.

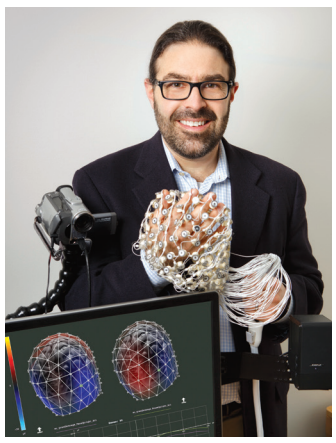
Striving for objective autism measures

A multisite study based at the Child Study Center seeks to develop biomarkers to better diagnose and treat the often baffling disorder

Their training is rigorous—and they use great skill in diagnosing and treating their patients—but without objective, quantifiable measures to characterize autism, clinicians who work with children who show symptoms of the disorder are at a disadvantage. Despite the "shrewd clinical eye" they bring to their practice, as James C. McPartland, PH.D., associate professor of child psychiatry and psychology in the Child Study Center (CSC), describes it, they still largely rely "on the same tools that were used when autism was first written about in 1943." Says McPartland, "We think we could do better, that we can measure the specific processes in the brain that are being impacted in autism."

McPartland is principal investigator, and the School of Medicine is the lead institution, in a five-site research study called the Autism Biomarkers Consortium for Clinical Trials (ABC-CT). The goal of the four-year effort is to meticulously monitor 200 children with autism and 75 typically developing children over a six-month period, and use the findings to establish a reliable set of biomarkers that can determine the most appropriate treatments and measure any resulting improvements from treatment.

Investigators will analyze readings from electroencephalograms (EEGs) and also from devices that precisely measure eye movements—including factors such as changes in pupil size—when children are shown social information. EEG data are recorded from caps containing 128 electrodes that children wear on their heads. According to McPartland, "We are examining the brain's activity at rest and also the brain's response to things we think are socially important, like human faces and point light displays of people moving."



They are doing so with unprecedented precision. From site to site, eye tracking equipment is identical, "right down to the manufacturer of the splitter cables," says Adam J. Naples, PH.D., associate research scientist in the CSC. "If you go through the literature," Naples explains, "you can read different papers and see different equipment. These things can change the data quality and they matter."

Naples traveled to Boston Children's Hospital; Duke University; the University of California, Los Angeles; and the University of Washington, setting up equipment and training the staff at each location. "We have totally identical equipment, totally identical protocols, down to what you can say to a child who is not looking at the screen," Naples says. "We have custom-built light meters. We can track the ambient light throughout the experiment. The level of standardization is unbelievable."

McPartland says multiple sites are necessary for two reasons. "One is that it will be really hard to get this many children in one place at one time. Two, part of the goal of the research is to create this infrastructure so that the government and industry can use us as a tool for future clinical trials. Those kinds of trials necessitate multiple sites, because if I want to try a drug for a certain kind of autism, there may not be enough patients to do it in New Haven, but if I have a network of five sites across the country, we can get the required sample reasonably."

Pharmaceutical companies are active participants in the National Institutes of Health (NIH)-led consortium that is funding and overseeing the project, because drug development is at a dead end without good biomarkers. "When a pharmaceutical company wants to see if its drug is working," McPartland explains, "it is not adequate to bring that child in and have me play with them and say whether I'm seeing something subjective. It's necessary to know that a particular neural circuit is being engaged and be able to quantify how it is changing."

Biomarkers may also be invaluable in cases where patient evaluation is especially difficult. "Sometimes we have kids who are challenging to clinically conceptualize," says Julie M. Wolf, PH.D., assistant clinical professor in the CSC, who is one of the clinicians evaluating Yale Medicine patients enrolled in the study. "Every now and then you get those kids where you're really on the fence. They have some traits of autism and other features that are not as consistent with the diagnosis, and you're not sure how best to help the child. So, something more quantitative could be really helpful in those instances."

Beyond the scientific and clinical ground it intends to break, ABC-CT is also an example of how the research infrastructure at the Yale Center for Clinical Investigation (YCCI) has advanced in ways that let medical school investigators do work that otherwise might be impossible. When McPartland learned of NIH interest in forming such a multisite consortium, he sought out Tesheia H. Johnson, M.B.A., M.H.S., deputy director and chief operating officer of YCCI and associate director for clinical research for the School of Medicine, who walked him through the ways YCCI could support this research.

HAROLD SHAPIRO (2)

James C. McPartland (left), displays an electroencephalogram cap used to collect detailed brain readings from children participating in the Autism Biomarkers Consortium for Clinical Trials (ABC-CT), a multisite study for which he is primary investigator. ABC-CT's goal is to develop reliable biomarkers for determining appropriate clinical treatments and measuring patient improvement. Members (above) of his research team are drawn from the Child Study Center and the Yale Center for Clinical Investigation.

As Johnson recalls, "I said, 'Well, we can cover biostats, informatics, the statistical coordinating center. Who's going to do your monitoring?'" YCCI was just forming its Multicenter Research Support Unit, which opened during the summer of 2016 as a standing resource for investigators who otherwise would need to assemble operational and administrative teams from scratch.

The unit worked with McPartland in writing the grant proposal, assured NIH of the resources it possessed in support of a scientist planning to direct an exceedingly complex study, and contributed personnel to the integrated ABC-CT team that McPartland now leads. Says Johnson, "The whole concept [for investigators] is to take your science and just plug it into a mechanism that's all ready to go with professionals who know how to do the work."

McPartland adds, "I think that YCCI has really specific expertise in areas that many investigators don't know how to do well. Tesheia and her team were critical, and continue to be critical."

Even before all the data come in, McPartland says children his team is assessing are already receiving some benefit. All participating children receive a detailed evaluation of their individual cognitive abilities, which results in a report that goes to their parents and teachers. "So, by virtue of being involved in our research, families and teachers are getting a better understanding of these children and how to help them."

Even better, concludes McPartland, will be a day he hopes is not far away, when biomarkers his team develops begin to help patients directly. "It's probably a field changer," he says. "People with autism are complex, and we need nuanced tools."

TERRY DAGRADI

October 20 At the annual Yale Child Study Center (CSC) **Associates Meeting**, donors mingled with CSC professors. From left, **Esther B. Fein**, former journalist and CSC donor; **Eileen M. O'Connor**, J.D., vice president of Yale's Office of Public Affairs & Communications; **Abha R. Gupta**, M.D., PH.D., assistant professor of pediatrics; **Tish Durkin**, CSC donor and Yale College Class of 1988 alumna; **Ellen J. Hoffman**, M.D., PH.D., assistant professor in the CSC; **Andres S. Martin**, M.D., M.P.H., Riva Ariella Ritvo Professor in the Child Study Center and professor of psychiatry.

MICHAEL MARSLAND

October 28 Yale gratefully hosted directors of the **Gustavus and Louise Pfeiffer Research Foundation**, shown here with inaugural Pfeiffer Fellow, M.D./PH.D. candidate **Wendy Xiao**, and the director of the M.D./PH.D. program **Barbara I. Kazmierczak**, M.D., PH.D., associate professor of medicine (infectious disease) and of microbial pathogenesis. The directors also met with Dean Alpern and other senior leaders of the medical school. From left to right: directors **Lise P. Chapman**, **Matthew Mayro Keeney,** and **Kimberly Herold Alvarez**; Xiao, Kazmierczak; directors **Matthew Gering Herold, Patricia Reid Herold,** and **Sarah S.P. McCarthy**.

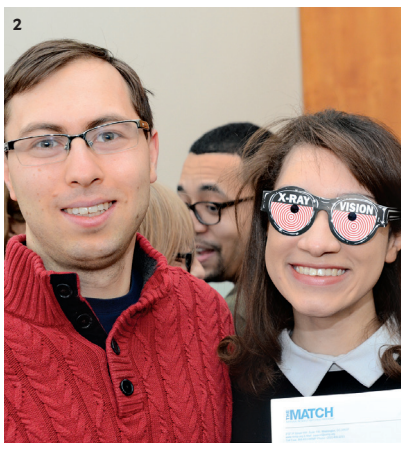
MATTHEW D'ALTO

February 4 At the **17th Annual Connecticut STEM Fair** at Darien High School, **Stephanie C. Eisenbarth**, M.D., PH.D., assistant professor of laboratory medicine, of immunobiology, and of medicine (immunology), gave the keynote speech, in which she described her career pathway as a physician-scientist.

November 17 At the annual **Hunger & Homelessness Auction**, Yale professional health students raised money for and heard stories from homeless people. **1.** Second-year medical student **Arash Fereydooni** (holding paddle) and **Andrea Roberts**, also Class of 2019, participate in a bid. **2.** From left: **Rebecca McCurdy**, **Yukari Suzuki**, **Neela Vaswani**, **Danielle Lockwood**, and **Taylor Dempsey**, all physician associate students in the Class of 2018. The event raised $28,400.

JOHN CURTIS (2)

JOHN CURTIS (2)



March 17 At noon Eastern time on **Match Day**, medical students across the country learned where they will complete their residency after graduation. The excitement was palpable inside Harkness Ballroom. **1.** From left, **Tsion Aberra**, **Pierre Martin**, **Gerneiva Parkinson**, **Emmanuel Ohuabunwa**, **Sean Mbachu**, **Adesuwa Ighodaro** and **Abiola Deborah Femi-Abodunde**, all Class of 2017 medical students. **2. Kimberly Murdaugh**, also a fourth-year medical student, with her husband, **Alexander Isakov**, said the special glasses did not let her see through the envelope before 12 o'clock after all.

Spine Center patient and her husband are now enthusiastic donors

A $1 million gift from the Howard and Maryam Newman Family Foundation to Yale School of Medicine will benefit the Yale Spine Center and the Department of Neurosurgery, and support the center's neurological robotic surgery initiative under the direction of Khalid M. Abbed, M.D., associate professor of neurosurgery and chief of the spine section in the Department of Neurosurgery.

Howard Newman, B.A., M.A. '69, is chair and CEO of Pine Brook Road Partners, a private equity firm, and his wife Maryam Razavi Newman, M.D., is a psychoanalyst. They were inspired to support Abbed's work at the Spine Center after Maryam Newman suffered a fall and required a complex, two-day surgery to correct the effects of her injury.

"We were very impressed not only by his skills, but also his personality, his willingness to spend time with us, to answer our questions, and the caring and warmth he projected," she says.

"Khalid's a star," says Howard Newman. With belief in his abilities and vision, the Newmans decided to support Abbed's efforts to expand and enhance the Yale Spine Center's robotics initiative, to be called the Howard and Maryam Newman Neurosurgical Robotic and Operative Navigation Program.

"Because of the Newmans' generous gift, we will be able to develop the most advanced and minimally invasive surgical techniques and technologies that will benefit patients in the future," says Abbed. "This new program will also enable us to teach

COURTESY H. AND M.R. NEWMAN

Maryam Razavi Newman and her husband Howard Newman are grateful Yale Spine Center donors.

students, residents, fellows, and other surgeons from around the world in the field of neurosurgical robotics and navigation."

"It will be good for Yale, and good for the community," says Howard Newman. "We are delighted to play a part in helping Khalid expand the medical school's expertise in this area."

The Newmans are long-standing donors to Yale University. The Howard and Maryam Newman Scholarship Fund supports one student in each of Yale College's residential colleges, each of whom comes to Yale from a non-traditional background, such as being the first in her/his family to go to college or being a first generation American. They also have endowed a chair in philosophy.

Howard Newman has served on the University Council and the Board of the Yale Climate and Energy Institute, and as chair of the Yale Alumni Fund.

"We believe in Yale's mission and priorities," he says. "Yale has a commitment to openness and diversity, as well as to scholarship and inquiry, which we appreciate. We want to make the Yale experience available to as many people as possible."

ADVANCES
Health & Science News

Molecule's link to seizures explained

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Hyperactive signaling of the protein complex mTORC1 has long been linked to a group of brain disorders that includes tuberous sclerosis complex and hemimegalencephaly, characterized by childhood seizures. Now, Yale researchers led by Angélique Bordey, PH.D., professor of neurosurgery and of cellular and molecular physiology, have revealed new details on how overactive mTORC1 actually changes brain development.

The scientists observed the placement of brain cells as mouse embryos developed and studied the effects of changing mTORC1. As expected, hyperactive signaling of the protein complex led to malformations in one area of the brain. Since mTORC1 affects many different cellular processes, they then altered different associated processes one at a time, testing whether each was responsible for the malformations.

Changing levels of one group of downstream proteins, 4E-BPs, was enough to disrupt the brain formation in a way similar to mTORC1. Moreover, restoring normal signaling of 4E-BPs prevented the effects of overactive mTORC1, the researchers reported Sept. 19 in *Proceedings of the National Academy of Sciences*, pointing toward a potential drug target to treat or even prevent the seizure disorders.

Pointing toward new brain tumor strategy

An existing, FDA-approved ovarian cancer drug may also treat brain cancers and leukemias that have mutations in the genes *IDH1* and *IDH2*.

In a new study, led by Ranjit S. Bindra, M.D., PH.D., assistant professor of therapeutic radiology and of pathology, and Peter M. Glazer, M.D., PH.D., chair and Robert E. Hunter Professor of Therapeutic Radiology and professor of genetics, the researchers wanted to know why IDH mutations make tumors more susceptible to radiation therapy and chemotherapy.

In the process of studying isolated cancer cells with the mutations, the team discovered that the cells are also sensitive to a class of drugs called PARP inhibitors.

Treating the cells with olaparib, a PARP inhibitor that was approved for use in hereditary ovarian cancer in 2016, killed 50 times more tumor cells than usual. And the drug slowed the growth of tumors on mice by eightfold, the researchers reported Feb. 1 in *Science Translational Medicine*.

The finding suggests that PARP inhibitors such as olaparib may be effective in treating a range of tumor types with IDH mutations and that blocking mutant versions of IDH—a current approach which would not be compatible with olaparib—may not be the ideal treatment strategy.

Discovery Fund spurs cancer innovation

The fund is an opportunity for donors to Yale Cancer Center to have gifts dedicated to research with potentially high reward

The wait for advances in cancer research to translate into clinical treatment can be an ordeal for patients and their loved ones, whose sense of passing time is heightened by the presence of the disease.

This feeling of urgency led to the launch in 2016 of the Yale Cancer Center Discovery Fund, whose donors provide individual $500,000 gifts to support research teams at the School of Medicine that propose high-risk, high-reward projects.

"Getting research achievements to patients takes time and a substantial amount of money," says Daniel C. DiMaio, M.D., PH.D., Waldemar Von Zedtwitz Professor of Genetics and professor of molecular biophysics and biochemistry, and of therapeutic radiology, and deputy director of Yale Cancer Center. "The main goal of the Discovery Fund is to bring Yale's outstanding science closer to clinical use."

The Discovery Fund comes at a time when public funding for cancer research is increasingly limited and less predictable. That means research with relatively less assurance of success can be passed over for proposals that appear to be safer bets. The Discovery Fund takes risks that more traditional funding sources might avoid.

"If every grant works, we're not taking big enough risks," says DiMaio. "We pick the grants that we think are likely to work, but certainly not ones that are guaranteed to work." For its inaugural competition, the fund received 31 letters of intent, from which 10 teams were invited to submit full applications. Ultimately, three multidisciplinary teams received grants, which are now in their second year.

"Everyone has been touched by cancer and our family is no exception," says Lisa Chênevert-Krause, whose family, which includes her parents Louis and Debra Chênevert and her sister Sophie Chênevert-Schilke, has made a gift to the Discovery Fund. The Chêneverts still feel the loss of Lisa and Sophie's great-grandmother, whose death from breast cancer at a young age left her children motherless for most of their lives. "One of the key goals of our family foundation is to help further advancements in cancer research so that people can take advantage of them."

It was clear to the entire family, she adds, that Yale was the obvious place for their contribution to go. "We have been supporting Yale for some time now. The staff and treatment options are best in class. It's the best care you can get, both in terms of the operations and the research that's bringing forward the next level of treatment options. It was a no-brainer that we would partner with Yale on this."

The Discovery Fund allows donors to follow the progress of individual research projects, a particularly appealing feature for those who may have been affected by cancer themselves.

"Our family has been ravaged by cancer," says Stephanie Stiefel Williams, who has pledged a gift to the next round of grantees with her husband Luke.

Williams decided to give after her brother Charlie Stiefel contributed to the inaugural fund. The Stiefels lost their parents, their uncles, and an 18-year-old brother to cancer. The remaining brothers have each beaten cancer. Williams underwent a preventive double mastectomy and oophorectomy last year after learning she carries the BRCA2 gene mutation. "I have a very personal grudge against cancer," she says. "Donating to cancer research seemed like the best way to fight against it."

COURTESY OF STIEFEL FAMILY

COURTESY OF CHÊNEVERT FAMILY

Debra and Louis Chênevert (above), along with their daughters, are donors to the Yale Cancer Center Discovery Fund. Charlie and Daneen Stiefel (left) also have donated, inspiring his sister to give as well.

Charlie Stiefel agrees. "If I had been diagnosed with advanced metastatic cancer two decades earlier than I was, I would have had virtually no chance of survival," says Stiefel, who donated with his wife Daneen. "Thanks to continuing advances—the direct result of cancer research—I have been cancer-free for nearly 10 years. In order to defeat this horrible disease, much more research is needed."

Additional Discovery Fund donors include Robert (Bobby) Balogh, Yale College '74, and his wife Cara Balogh; and cancer philanthropist Roslyn Goldstein.

// Fund *(page 1)* This new fund will be overseen by the Office of Cooperative Research (OCR) under Managing Director Jon Soderstrom, PH.D., the office most responsible for connecting Yale investigators with industry. Erika R. Smith, M.B.A., previously deputy director of the Yale Entrepreneurial Institute, is director of the fund. The Blavatnik Fund for Innovation will give investigators access to expertise and resources in key areas—such as prototype development or early-stage clinical trials—to help them demonstrate their cases to potential investors.

More than 60 investigators representing science disciplines across the university applied for the initial round of grants and related resources. In February, OCR identified 17 finalists, of whom 14 are affiliated with the medical school. Yale President Peter Salovey, PH.D., will announce the winning proposals on May 10 during the closing ceremony of the Yale Innovation Summit, a day-long event for Yale innovators and investors.

"I am deeply grateful to the Blavatnik Family Foundation, and especially to Len Blavatnik, not only for this exceptional support, but also for our shared commitment to entrepreneurship as a way to serve some of society's greatest unmet needs," says Salovey. "The fund will foster the next generation of leadership in innovation and help to translate Yale discoveries into real-world applications that can improve people's lives."

The multi-year grant also establishes the Blavatnik Fellows Program, offering a select group of young professionals access to Yale researchers as well as inventors, venture capitalists, and business leaders. The fellows will aid the researchers with the technical and business skills needed to prepare discoveries for the marketplace as they prepare themselves to develop into the next generation of scientific entrepreneurs.

Soderstrom says the gift will provide a boost for research at Yale School of Medicine. "The Blavatnik fund will provide strategic and dedicated resources to Yale faculty members who are developing commercially relevant research," Soderstrom says. "With this essential support, we will be able to transform new discoveries into marketable tools, treatments, drugs, and devices that have the potential to impact people's lives tremendously."

In an interview with *Medicine@Yale* weeks before her death in December, Carolyn W. Slayman, PH.D., deputy dean for academic and scientific affairs, Sterling Professor of Genetics, and professor of cellular and molecular physiology, said there is no shortage of discoveries by School of Medicine scientists that are candidates for commercial success. But the marketplace may overlook some of them, she said, if investment funds are lacking.

"There is a fine line," said Slayman, "between discoveries that instantly excite the pharmaceutical industry and others to which companies hesitate to commit. A bit more access to investment, such as the Blavatnik Fund now offers, can propel worthy discoveries from one side of that line to the other." Slayman said the fund's existence also gives investigators added incentive to do breakthrough work.

The Blavatnik Fund will be structured as a sustainable program, with a portion of revenues earned reinvested to support the next generation of projects.

Grants and contracts awarded to Yale School of Medicine

April 2016–June 2016

Federal

Vikki Abrahams, NIH, *Mechanisms Regulating Fetal Membrane and Neutrophil Responses to Polymicrobial Infection*, 4.9 years, $2,832,954 **Nii Addy**, NIH, *Ventral Tegmental Area Cholinergic Mechanisms Mediating Susceptibility to Stress*, 3.9 years, $1,667,169 • **Frederick Altice**, NIH, *Modeling HCV/HIV Transmission and Treatment as Prevention in U.S. Networks of People Who Inject Drugs*, 2 years, $480,366 • **Alan Anticevic**, NIH, *Characterizing Schizophrenia Progression via Multi-Modal Neuroimaging and Computation*, 4.8 years, $2,048,620 • **Jeffrey Bender**, NIH, *Modulation Neuroinflammation Through Interference of Cooperative microRNA-RNA-Binding Protein Interactions*, 2 years, $460,479 • **Julien Berro**, NIH, *Molecular Mechanisms of Force Production and Force Sensing During Clathrin-Mediated Endocytosis*, 5 years, $1,589,942 • **Angelique Bordey**, DoD, *Epilepsy Causes and Treatment in TSC*, 3 years, $697,777 • **Marcus Bosenberg**, NIH, *Congenic Mouse Models of Melanoma for the Characterization of Tumor Immune Responses*, 3 years, $1,654,425 • **James Boyer**, NIH, *The International Primary Sclerosing Chonagitis Study Group Meeting*, 1 year, $23,000 • **Susan Busch**, NIH, *Young Adults, Health Care Use and Psychosis*, 2.9 years, $1,289,504 • **Richard Carson**, NIH, *SV2A PET Imaging in Healthy Subjects and Epilepsy Patients*, 5 years, $2,765,725 • **Albert Chan**, NIH, *Optimizing HIV Reverse Transcriptase Inhibitors Through Structural, Kinetic and Cellular Approaches*, 3 years, $168,414 • **Bo Chen**, NIH, *Regeneration of Rod Photoreceptors from Muller Glial Cells in Adult Mouse Retina*, 4 years, $1,606,950 • **Jen-hwa Chu**, NIH, *Causal Inference of Disease-Relevant Regulatory Networks*, 3 years, $740,950 • **Joseph Craft**, NIH, *Immune Responses in Lupus*, 5 years, $2,134,625 **Peter Cresswell**, NIH, *Quality Control of MHC Class I Restricted Antigen Processing*, 5 years, $2,467,336 • **Alan Dardik**, NIH, *Enhancing Venous Adaptation to the Arterial Environment*, 4 years, $1,875,934 • **Ralph DiLeone**, NIH, *New Approaches for Studying Active Neural Ensembles in the Nucleus Accumbens*, 2 years, $404,250 • **John Elsworth**, NIH, *Developmental Factors for Reducing Dopamine Loss in Primate Models of PD and Aging*, 4.8 years, $2,374,895; NIH, *Biochemical and Synaptic Mechanisms in Prefrontal Cortex and Vulnerability for Cognitive Deficits*, 4.8 years, $3,169,704 • **John Forrest**, NIH, *NIA Short Term Research Training: Students in Health Professional Schools*, 5 years, $372,275 • **Xiao-Bing Gao**, NIH, *Metabolic Status and Cocaine-Induced Responses in Hypocretin Neurons*, 2 years, $460,501 **Thomas Gill**, NIH, *Research Training in Geriatric Clinical Epidemiology*, 5 years, $1,608,018 **Peter Glazer**, NIH, *Yale Cancer Biology Training Grant*, 4.9 years, $1,158,540 • **Andrew Goodman**, NIH, *Causes and Consequences of Interpersonal Microbial Variation*, 5 years, $1,642,726 • **Valentina Greco**, NIH, *Normal Stem Cells and Their Transition to Disease in the Skin*, 4.9 years, $2,207,205 • **Charles Greer**, NIH, *The Glomerular Connectome*, 2 years, $460,501 **Eduardo Groisman**, NIH, *Regulation of* Salmonella *Virulence by the PhoP Protein*, 4.9 years, $2,495,699 • **Erica Herzog**, NIH, *Neuroimmune Molecules in Scleroderma Lung Fibrosis*, 4 years, $1,689,207 • **Mark Horowitz**, NIH, *The Sixth International Conference on Osteoimmunology: Interactions of the Immune and Skeletal Systems*, 1 year, $15,000 • **Karl Insogna**, NIH, *The Role of Sphingosine Kinases in Bone Anabolism*, 4 years, $1,473,817 • **Leonard Kaczmarek**, NIH, *Expression of Ion Channels in the Auditory System*, 5 years, $1,779,157 • **Insoo Kang**, NIH, *Studying Lupus Th17 Cell Characteristics and their Modulations by IL-27*, 2 years, $460,501 **Dionna Kasper**, NIH, *Investigating the Role for Mir-223 in Hematopoietic Stem Cell Emergence*, 3 years, $174,090 • **Samuel Katz**, NIH, *Cell Death Regulation by Pro-Apoptotic BOK in Cardiomyocytes*, 5 years, $2,317,426 • **Barbara Kazmierczak**, NIH, *A Novel Regulator of Clumping and Dispersal Mechanisms in* P. aeruginosa, 1.9 years, $460,521 • **Brian Kiluk**, NIH, *Efficacy and Mechanisms of CBT4CBT for Alcohol Use Disorders*, 5 years, $2,682,902 • **Yuval Kluger**, NIH, *Efficient Spectral Approaches for Finding Underlying Structures in Big Data*, 2.9 years, $1,229,999 • **Hedy Kober**, NIH, *Regulation of Craving Under Stress: Novel Model and Neural Mechanisms*, 1 year, $299,829 • **Grace Kong**, NIH, *Vape Tricks on Social Media: Implications for Electronic Cigarette Regulation for Youth*, 2 years, $224,046 • **Katherine Launer-Felty**, NIH, *In Vitro and In Vivo Characterization of the Cyclic-di-GMP Riboswitch*, 2 years, $110,412 **Daeyeol Lee**, NIH, *Rapid Actions of Ketamine in the Prefrontal Cortex*, 4.8 years, $3,286,756 **Mark Lemmon**, NIH, *Understanding Wnt Signaling Through Ror and Ryk Family Receptor Tyrosine Kinases*, 1 year, $594,745 • **Ralf Leonhardt**, NIH, *Mechanism of Amyloid Formation During Melanosome Biogenesis*, 1.9 years, $405,166 **Karel Liem**, NIH, *Tubulin Beta 4a in Central Nervous System Development and Disease*, 5 years, $2,321,064 • **Brett Lindenbach**, NIH, *Molecular Determinants of Hepatitis C Virus Assembly*, 5 years, $2,093,126 • **Malaiyalam Mariappan**, NIH, *The Mechanism of Ire1-Mediated mRNA Cleavage During Endoplasmic Reticulum Stress*, 5 years, $1,653,900 • **Edward Miller**, NIH, *The Role and Regulation of the LKB1-AMPK Axis in Diabetic Cardiomyopathy*, 1 year, $89,413 • **Angus Nairn**, NIH, *Cell-Type Specific Psychostimulant Effects on the Neuronal Translatome*, 2 years, $367,500 • **Noah Palm**, NIH, *Illuminating Immunomodulatory Gut Microbes in Human Health and Disease*, 1.9 years, $270,000 **Abhijit Patel**, NIH, *Circulating DNA as a Marker of Treatment Efficacy and Failure in Lung Cancer*, 5 years, $1,915,209 • **Zorana Pringle**, National Endowment for the Arts/National Foundation on the Arts & Humanities, *To Support the Study of the Relationship Between Arts Participation and Psychological Resilience and Well-Being*, 1.6 years, $25,000 • **Yibing Qyang**, DoD, *Engineering of Pulsatile Conduits from Human Pluripotent Stem Cell-derived Cardiomyocytes*, 1.5 years, $332,999 • **Rachana Radhamani Chandran**, NIH, *Myofibroblasts in Pulmonary Fibrosis: Origin, Clones and KLF4*, 3 years, $168,414 • **Lynne Regan**, NIH, *Convergent Graduate Training in Engineering, Physics and Biology*, 5 years, $940,480 • **Karin Reinisch**, NIH, *Lipid Transporters and Lipid Homeostasis at Membrane Contact Sites*, 4 years, $1,512,114 **Matthew Rodeheffer**, NIH, *Cellular and Molecular Mechanisms of White Adipose Tissue Regulation in Development and Disease*, 1 year, $209,062 • **Naomi Rogers**, **Tess Lanzarotta**, NSF, *A Study in Arctic Alaska of Relations between Cold War Bio-medicine, Indigenous Politics, and Circumpolar Health*, 1 year, $12,808 **Douglas Rothman**, NIH, *Validation of GABA MRS as a Biomarker of Inhibition*, 3.9 years, $1,745,743 **James Rothman**, NIH, *Regulation of Vesicle Traffic*, 5 years, $4,336,927 • **Christian Schlieker**, NIH, *Structure-Function Analysis of Torsin ATPases in the Context of the Membrane*, 4.1 years, $1,312,968 • **William Sessa**, NIH, *NgBR as a Regulator of Endothelial Function*, 3.9 years, $2,009,742 • **Albert Sinusas**, NIH, *Ultra-High Performance microSPECT/CT System*, 1 year, $600,000 • **Serena Spudich**, **Brinda Emu**, NIH, *CSF & Blood Exosomal microRNAs, Immune Responses, and HAND in ART Suppressed HIV*, 1.9 years, $457,726 • **Stephen Strittmatter**, NIH, *Mechanisms of A-Beta Oligomer Induced Synapse Dysfunction in Alzheimer's Disease*, 5 years, $3,080,748 • **Denis Sukhodolsky**, NIH, *Neural Mechanisms of CBT for Anxiety in Children with Autism Spectrum Disorder*, 4.8 years, $2,838,889 • **Patrick Sung**, NIH, *DNA Repair Genes and Proteins of the RAD52 Group*, 5 years, $1,884,188 • **Joann Sweasy**, NIH, *The Role of a PARP1 Genetic Variant in Development of Lupus*, 2 years, $472,601 • **Narendra Wajapeyee**, NIH, *Nucleoporin NUP205-Driven Novel Pathway in Melanoma Tumor Growth and Metastasis*, 5 years, $1,915,590 • **Nicole Weiss**, NIH, *PTSD, Negative and Positive Emotion Dysfunction, and Substance Use in IPV Victims*, 5 years, $829,575 • **Jiansong Xu**, NIH, *Functional Networks Related to Cocaine Dependence and its Treatment and Relapse*, 2.9 years, $753,500 **Reza Yaesoubi**, NIH, *Improving the Control of Multidrug-Resistant Tuberculosis Through Targeted Screening and Use of Novel Anti-Tuberculosis Drugs*, 4 years, $517,724 • **Henry Yaggi**, NIH, *Mentoring in Sleep Research and Sleep Interventions in Heart Disease, and Stroke*, 5 years, $335,827 • **Jiangbing Zhou**, NIH, *Systemic Gene Therapy for Glioblastoma*, 5 years, $1,821,095

Non-federal

Jodie Ambrosino, American Psychological Association, *Smoking Practices and Perceptions of Health Risks in Tobacco Use Among Adolescents and Young Adults with Type 1 Diabetes*, 4 months, $500 • **Marcus Bosenberg**, Melanoma Research Alliance, *Metabolic Regulation of the Tumor Immune Response by the Microenvironment*, 3 years, $900,000 • **Sidi Chen**, Melanoma Research Alliance, *Genome Scale Identification of Genes Regulating Melanoma Metastasis*, 3 years, $225,000 • **Elizabeth Claus**, National Brain Tumor Society, *The International Low Grade Glioma Registry*, 2 years, $250,000 **Michael Crair**, Johns Hopkins University (NIH), *Spontaneous Activity in the Developing Auditory System*, 1 year, $193,264 • **Jeptha Curtis**, Johns Hopkins University (NIH), *MAESTRO-PAF: Major Adverse Events and Stroke in Paroxysmal Atrial Fibrillation*, 3.8 years, $9,990 • **Gail D'Onofrio**, **Lori Post**, State of Conn. Dept. of Public Health (DHHS), *CT DPH Prescription Drug Overdose Prevention for States #2016-0168*, 1.3 years, $305,479 • **Marie Egan**, **Emanuela Bruscia**, Cystic Fibrosis Foundation (CFF), *Increased Pannexin 1 Alters CF Macrophage Function*, 2 years, $216,000 • **Lynn Fiellin**, Schell Games (NIH), *Are You Positive That You're Negative? Encouraging HIV Testing and Counseling in Adolescents Using a Videogame Intervention*, 1 year, $123,776 • **Gerald Friedland**, Columbia University (NIH), *Promoting Engagement in the Drug Resistant TB/HIV Care Continuum in South Africa*, 5 years, $46,084 • **Joel Gelernter**, Washington University in St. Louis (NIH), *7/7 Psychiatric Genomics Consortium: Finding Actionable Variation*, 4.8 years, $184,653 • **David Glahn**, University of Texas Rio Grande Valley (NIH), *Neurodevelopment: Genes, Environment, and Their Interactions*, 1 year, $95,259 • **David Hersh**, Council on Medical Student Education in Pediatrics, *Evaluation of a Novel Approach to Teach Pediatric Ethics to Medical, Nursing, and Physician Assistant Students*, 2.1 years, $5,000 • **Erica Herzog**, Sanofi US, *Evaluation of IL-13Ra2 in Idiopathic Pulmonary Fibrosis (IPF), Chronic Obstructive Pulmonary Disease (COPD) and Interstitial Lung Disease in Systemic Sclerosis (SSc_ILD)*, 2 years, $186,135 • **Melody Hu**, Howard Hughes Medical Institute, *Cellular-Resolution Calcium Imaging to Characterize Changes in Excitatory-Inhibitory Balance During Reward-Directed Activity in a Rodent Model of Depressive Behaviors*, 1 year, $41,000 • **Amy Justice**, Vanderbilt University Medical Center (NIH), *Immune Function and the Risk of CVD Among HIV Infected and Uninfected Veterans*, 1.2 years, $42,179; Vanderbilt University Medical Center (NIH), *Cardiac Pathology and Risk Prediction for Sudden Cardiac Death in Patients with HIV*, 8 months, $43,493 • **Insoo Kang**, Alliance for Lupus Research, *Yale Lupus Clinical Investigators Network (LUCIN)*, 1 year, $80,000 • **Jennifer Kapo**, Milbank Foundation for Rehabilitation, *Yale Palliative Care Program*, 1 year, $1,000,000 **Samuel Katz**, Alliance for Cancer Gene Therapy, *Refining CART Immunotherapy for Solid Tumors by Multifactor Reprogramming*, 3 years, $250,000 • **Barbara Kazmierczak**, Cystic Fibrosis Foundation (CFF), *Immunomodulation by Patient-Derived Microbiota in Germ-Free CF Mice*, 2 years, $108,000 • **Kaveh Khoshnood**, Bhutan Foundation, *Training the Royal Institute of Health Sciences Faculty and Students in Capacity and Curriculum Development for New Public Health Programs in Bhutan*, 1.1 years, $33,126 • **Brigid Killelea**, Icahn School of Medicine at Mount Sinai (ISMMS) (NIH), *Insulin Resistance and Breast Cancer Prognosis in Black & White Women*, 6 months, $50,105 • **Harlan Krumholz**, **Joseph Ross**, SI-BONE, *Yale Open Data Access Project and SI-BONE Collaboration*, 1 year, $61,887 • **Tambudzai Kudze**, Howard Hughes Medical Institute, *Eph-B4-Regulated Arteriovenous Fistulae Maturation is Mediated by Akt-1*, 1 year, $41,000 **John Leventhal**, Cornell University (NIH), *Geographic Variation in Child Maltreatment and Foster Care Placement*, 2 years, $6,575 • **Wu Liu**, American Association of Physicists in Medicine, *Dosimetric Measurement of a Focused kV X-ray System for Commissioning*, 1 year, $5,000 • **Jun Lu**, Health Research (NIH), *Quantitative Modeling of microRNA: Target Interactions in Cell Fate Transition*, 1 year, $248,307 • **Robert McDougal**, SUNY Downstate Medical Center (NIH), *Extension of NEURON Simulator for Simulation of Reaction-Diffusion in Neurons*, 4.8 years, $279,798 • **Julio Montejo**, Howard Hughes Medical Institute, *Molecular Mechanisms of Recurrent Somatic SMARCB1 Missense Mutations in Meningioma Tumorigenesis*, 1 year, $41,000 • **Peter Morgan**, The Nicholson Foundation, *Analysis of Integration of Behavioral Healthcare into Primary Care*, 7 months, $18,246 **Kevin O'Connor**, National Multiple Sclerosis Society, *Defining How a Novel B Cell Population Contributes to MS Pathology*, 1 year, $43,752 **Mary O'Sullivan**, Lupus Foundation of America, *Contribution of Distinct Effector T Cells in Promoting SLE Autoantibodies*, 3 months, $4,000 **John Pachankis**, SUNY Stony Brook (NIH), *Temperamental Emotionality in Preschoolers and Risk for Depression*, 1 year, $23,808 • **Georgios Pantouris**, Robert Leet and Clara Guthrie Patterson Trust, *Targeting Hematological Cancers Using a Small Molecule Inhibitor with a Novel Mechanism of Action*, 2 years, $110,000 • **David Pitt**, Joan and Sanford I. Weill Medical College of Cornell University (NIH), *Multiple Sclerosis Lesion Magnetic Susceptibility Activity*, 1 year, $145,824 • **Jordan Pober**, The Research Institute at Nationwide Children's Hospital (NIH), *Development of an Improved Vascular Graft for Use in Congenital Heart Surgery*, 1 year, $39,965 **Neena Qasba**, Society of Family Planning, *A Pilot Study to Develop and Evaluate a Group Prenatal Contraception Counseling Model to Improve Postpartum Contraceptive Care*, 1.2 years, $99,805 • **James Reed**, Howard Hughes Medical Institute, *Mechanisms of Intracellular Receptor for Advanced Glycation Endproduct Signaling in Jurkat and Type 1 Diabetes Mellitus T Lymphocytes*, 1 year, $41,000 • **David Rimm**, Institut De Recherche Pierre Fabre, *OGF1R and Immumo-Onocolgy in Cancer*, 1 year, $199,200 • **Harvey Risch**, Johns Hopkins University (NIH), *Validation and Fine-Scale Mapping of Pancreatic Cancer Susceptibility Loci*, 1 year, $37,631 • **Wade Schulz**, Academy of Clinical Laboratory Physicians and Scientists, *Identification of Molecular Clonality and its Prognostic Impact in Acute Myeloid Leukemia*, 1 year, $10,000 • **Lorenzo Sewanan**, University of Hartford, *NASA CT Space Grant College Consortium Graduate Research Fellowship*, 7 months, $8,000 • **Pamela Valentino**, University of Tennessee (DHHS), *Ursodeoxycholic Acid Therapy in Pediatric Sclerosing Cholangitis: A Pilot Withdrawal/Reinstitution Trial*, 5 months, $9,275 • **Jessica Walrath**, Connecticut College of Emergency Physicians, *Resident-Driven Academic Detailing to Improve the Value of Emergency Care*, 6 months, $1,000 • **Stuart Weinzimer**, Harvard University (NIH), *Pediatric Artificial Pancreas for Enhanced Diabetes Management in Young Children*, 1.3 years, $649,816 **Tatiana Winkelman**, Autism Science Foundation, *Effects of Sleep Issues on Resting Brain Activity in Children with Autism Spectrum Disorder*, 1 year, $3,000 • **John Wysolmerski**, Augusta University (Formerly Georgia Regents University) (NIH), *DiaComp Summer Student Funding Programs*, 3 months, $8,163 • **Jiangbing Zhou**, American Brain Tumor Association, *A Nanotechnology Platform for Systemic Delivery of Chemotherapy to Malignant Gliomas*, 1 year, $50,000

// Ovarian *(page 1)* served on the board of Wyeth Pharmaceuticals," says Bennack. "Mary Lake was divorced and I was widowed. Fate played a hand and here we are." They married in 2005 and now engage in philanthropy together. One joint venture helps women in Eritrea who are in dire need of corrective gynecological surgery following childbirth. After Polan established a program to provide medical care, the couple raised funds to construct a residence to house the women before and after their surgery.

The professorship that Polan and Bennack have now endowed is inspired by the urgency they feel about combating ovarian cancer, one of the most difficult cancers to treat. "As a gynecologic oncology fellow I trained with Peter E. Schwartz, M.D. [John Slade Ely Professor of Obstetrics, Gynecology & Reproductive Sciences]. He is an outstanding physician," says Polan. "This was the most important clinical experience of my life, so cancer is where we hope to make a difference."

"Survival rates for ovarian cancer are dismal and treatments have not progressed significantly in decades," says Hugh S. Taylor, M.D., chair and Anita O'Keeffe Young Professor of Obstetrics, Gynecology & Reproductive Sciences; and professor of molecular, cellular and developmental biology. "Our primary focus is on finding innovative ways to treat it. This gift enables us to recruit an outstanding physician-scientist who will help us take our clinical care and research to the next level. We want to find that breakthrough that will beat this disease."

A warm, loving remembrance

On March 11, which would have been her 80th birthday, the School of Medicine held a memorial at Battell Chapel for Carolyn Walch Slayman, PH.D., deputy dean for academic and scientific affairs, Sterling Professor of Genetics, and professor of cellular and molecular physiology, who had died on Dec. 27.


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1. "Carolyn was a very patient person, and she was a perfectionist. And she only knew one way to do something, and that was slowly and perfectly." *—Dean Robert J. Alpern, M.D.* **2.** The Yale School of Medicine Symphony Orchestra, an all-volunteer ensemble featuring members of the Yale medical community, played a medley of Bach, Correlli, and Mozart. **3.** Clifford L. Slayman, PH.D., professor of cellular and molecular physiology—surrounded by colleagues and friends—delights in a story about his wife of 57 years. **4.** "Every time I left Carolyn's office, I not only left with the initial problem that I had taken to her solved, but also I left having regained part of my humanity." *—Daniel A. Colón-Ramos, PH.D.* **5.** "She talked little about her position as one of the very few women among her peers, but her leadership … was a powerful example of success to me as a young female assistant professor." *—Lynn Cooley, PH.D.* **6.** "In virtually every meeting with her I learned something about leadership, about how to treat people with respect, how to have difficult conversations, when to say yes, and how to say no gently but firmly." *—Steven M. Girvin, PH.D.* **7.** "Somehow, busy as she was, Carolyn conveyed a timeless, effortless presence that each of us simply trusted would be there always." *—Linda C. Mayes, M.D.* **8.** "She was always guiding me—helping me find my thoughts, and my way. There were so many special things about Carolyn: her calming presence, her passion for helping others, and her stories." *—Tesheia H. Johnson, M.B.A., M.H.S.*


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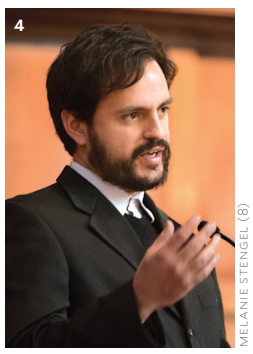
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MELANIE STENGEL (8)

// Immunotherapy *(page 1)* now is to explain why these treatments work in some patients and some cancers, but not others, notes Mario Sznol, M.D., professor of medicine (medical oncology). "For many years, we learned mostly through trial and error," Sznol says. "Today, despite our growing knowledge of tumor cells and the immune system, we are unable to accurately predict the efficacy of cancer treatments and to tailor them to individual patients."

Roslyn M. Meyer, PH.D. '77, and her husband, Jerome H. Meyer, M.D. '72, recently committed $2 million to Yale Cancer Center to support advanced scientific research over a span of five years. The goal is to yield discoveries that can be translated quickly into effective melanoma treatments.

"As a survivor of metastatic melanoma, I appreciate the incredible work of scientists and clinicians who are finding new ways to battle cancer," Roslyn Meyer says. "We hope that funding for Yale researchers can make a difference for the next generation of patients."

A portion of the gift will establish the Roslyn and Jerome Meyer Awards for Research in Melanoma and Immuno-oncology. Overseen by Sznol, the Meyer Awards will support innovative projects by faculty members aimed at expanding our understanding of the immune response against melanoma, the basic biology of the disease, its link to host immune responses, and methods to improve immune and targeted therapies, including drug delivery.

Each grant will provide a researcher with roughly $75,000 over two years—enough to set the stage for larger scientific investigations. "The Meyer Awards allow our researchers to test new ideas," says Sznol. "They can subsequently leverage these new data to seek further funds from the National Institutes of Health to take their projects to the next level."

The balance of the Meyers' gift will support research by Harriet M. Kluger, M.D., professor of medicine (medical oncology), in the area of brain metastases. When tumor cells spread to the brain, they share traits with cells in the other parts of the body but do not necessarily have the same response to therapies. The blood-brain barrier might prevent some drugs from reaching the brain, and as Kluger points out, the microenvironment in the brain differs from the rest of the body. Kluger and her colleagues hope to make inroads toward treating melanomas that have spread to the brain.

Charles S. Fuchs, M.D., M.P.H., Richard Sackler and Jonathan Sackler Professor of Medicine (Medical Oncology) and director of Yale Cancer Center, says, "Roslyn and Jerome Meyer have thought strategically about how to fund research leading to the next big breakthrough in cancer treatment. In a time of reduced federal funding, this type of support for early-stage research is more important than ever. Their gift has the potential to save lives."

// MRA *(page 1)* "We are just at the beginning of the wonderful drugs out there to be developed," Sokoloff says.

The Sokoloffs and MRA have made a new three-year, $900,000 award to a School of Medicine research team so it can further investigate the microenvironment in which melanoma tumors live. The team includes Marcus W. Bosenberg, M.D., PH.D., associate professor of dermatology and of pathology, Susan M. Kaech, PH.D., Waldemar Von Zedtwitz Professor of Immunobiology; Richard G. Kibbey, M.D., PH.D., associate professor of medicine (endocrinology) and of cellular and molecular physiology; and Sidi Chen, PH.D., assistant professor of genetics and systems biology. The team has the broad range of expertise needed to undertake the goals of the research, including the discovery of factors related to tumor growth that render T cells in the immune system too weak to fight the tumors.

"We believe our idea presents an entirely different perspective on how immunosuppression may be generated within tumors," Bosenberg says.

In an earlier study also funded by the Sokoloffs and MRA, published March 2016 in *Cell Reports*, Bosenberg and colleagues identified an enzyme that plays a crucial role in melanoma growth. They reported that DNMT3B —a DNA methyltransferase enzyme— regulates melanoma formation. When the investigators reduced the enzyme in mice, melanoma development was delayed due to the enzyme's effect on the protein Rictor, which controls tumor growth. Inhibitors of DNMT3B are currently being developed as a future cancer therapy by a Yale team led by Bosenberg.

Sokoloff says he is optimistic that recent advances in melanoma research will also lead to progress elsewhere. "Several of the early immunotherapy drugs that were approved for melanoma are now being shown to have applications in other cancers, such as lung and brain cancer," he says. "It is really the beginning of the immunotherapy tidal wave, which is one of the great hopes for combating cancer."

Scientists from medical school become AAAS fellows

The school's two newest inductees are a cell biologist and a neuroscientist

Two School of Medicine faculty members have become fellows of the American Association for the Advancement of Science (AAAS).

Charles A. Greer, PH.D., professor of neurosurgery and of neuroscience; and Martin A. Schwartz, PH.D., the Robert W. Berliner Professor of Medicine (Cardiology) and professor of biomedical engineering and of cell biology, are among 391 new members of AAAS who were officially installed in February.

Charles Greer

Martin Schwartz

AAAS named Greer to its section on neuroscience, recognizing his work on development and function of the mammalian olfactory system, which is a model for understanding brain wiring and neural processing. Greer earned his PH.D. at the University of Colorado at Boulder in 1978. After postdoctoral work at Yale, he joined the medical school faculty in 1983 and became a full professor in 1997.

Schwartz, now a fellow in the AAAS section on biological sciences, was recognized for his contributions to cell biology, particularly to understanding integrin signaling and mechanotransduction in vascular biology and medicine. Schwartz earned his PH.D. at Stanford University in 1979. After serving on the faculties of Harvard Medical School, the Scripps Research Institute, and the University of Virginia, he joined Yale's faculty in 2011.

AAAS, which publishes the journal *Science*, was founded in 1848 and is the world's largest multidisciplinary scientific society.

Connecticut's science and engineering academy inducts six faculty

Six members of the School of Medicine faculty are newly elected members of the Connecticut Academy of Science and Engineering (CASE). They are among 11 new members from Yale, and 24 chosen overall.

Alison Galvani

Jonathon Howard

Ann Kurth

Frederick Sigworth

Hugh Taylor

Sandra Wolin

The academy elected Alison P. Galvani, PH.D., the Burnett and Stender Families Professor of Epidemiology, professor of ecology and evolutionary biology, and director of the Center for Infectious Disease Modeling and Analysis at the School of Public Health, in recognition of her work developing mathematical models of disease transmission that use information from epidemiology, ecology, clinical medicine, economics, and psychology.

Jonathon Howard, PH.D., Eugene Higgins Professor of Molecular Biophysics and Biochemistry and professor of physics, is cited for seminal contributions in understanding the molecular properties of motor proteins, especially in deciphering how these evolutionarily conserved proteins operate as molecular machines to drive motion and regulate the growth and shrinkage of microtubules critical for biological processes such as mitosis and cellular motion.

Ann E. Kurth, PH.D., M.P.H., C.N.M., professor of epidemiology of microbial diseases and Linda Koch Lorimer Professor of Nursing; and dean, School of Nursing; was chosen for her work as an internationally recognized epidemiologist and clinically trained nurse-midwife. CASE honors Kurth for her major contributions to HIV/sexual and reproductive health prevention, screening and care, and to global health system strengthening in the U.S. and internationally.

Frederick J. Sigworth, PH.D., professor of cellular and molecular physiology and of biomedical engineering and of molecular biophysics and biochemistry, was cited for research that unravels the workings of ion channel proteins, the "molecular machines" that switch on and off the electrical currents carried by ions across biological membrane proteins. He developed methods for recording and analyzing the single-molecule events underlying the switching of currents, and now studies the structure of ion-channel proteins by electron cryomicroscopy.

CASE cites Hugh S. Taylor, M.D., chair and Anita O'Keeffe Young Professor of Obstetrics, Gynecology & Reproductive Sciences, as a world-renowned expert in reproductive sciences, with a focus on implantation, endometriosis, and menopause. His work has led to, among other insights, a better understanding of endometriosis, including the genetic cause and the role of stem cells in the disease.

Sandra L. Wolin, M.D., PH.D., emeritus faculty of cell biology and currently chief of the RNA Biology Laboratory at the National Cancer Institute, is cited for pioneering studies of how cells recognize and degrade unneeded, damaged, and harmful RNA molecules which could otherwise interfere with normal cellular function. Using a variety of organisms and approaches, Wolin has elucidated the functions of cellular machines that bind and destroy misfolded RNAs, including discovering a novel surveillance pathway.

The state's General Assembly chartered the Connecticut Academy of Science and Engineering in 1976.

// Library *(page 2)* studies supplied to them by a librarian or similarly trained search specialist.

Grossetta Nardini says the library's new tool, which even can be used on a mobile phone, makes the process more manageable. "Instead of screening in Excel or Endnote, which is a citation management program, I would say the new system is speeding up the ability to churn through results."

"It will present each article's title and abstract, and offer a choice of 'yes, no, maybe.' And if two people say no, then it's out, where if two people say yes, or yes/maybe, it passes forward to full-text review." Grossetta Nardini adds that the enhanced level of organization the tool provides can also lead to results that are sounder scientifically than many reviews have been in the past.

"It helps guide you through proper methodology," she says. "It forces you to follow proper steps."

"Covidence is a phenomenal resource to do a rigorous analysis of the literature and to extract eligible studies for a systematic review or meta-analysis. Two reviewers going through the abstracts make it a great learning experience for a resident or fellows to review the literature on the topic in sync with a more experienced physician," says Ajay Malhotra, M.B.B.S., M.D., associate professor of radiology and biomedical imaging, who has done a number of systematic reviews while at Yale, both prior to the new system and—more recently—using it.

Researchers from throughout the university can obtain access to the system through their librarian.

Awards & Honors

Roy S. Herbst, M.D., PH.D., Ensign Professor of Medicine (Medical Oncology), Associate Director of Translational Research at Yale Cancer Center and professor of pharmacology, has received the Paul A. Bunn Jr. Scientific Award from the International Association for the Study of Lung Cancer given for lifetime achievement in the research and treatment of lung cancer.

Marcella Nunez-Smith, M.D., M.H.S., associate professor of medicine (general medicine) and of epidemiology (chronic diseases), has received the Herbert W. Nickens Award from the Society of General Internal Medicine.

Marina Picciotto, PH.D., Charles B.G. Murphy Professor of Psychiatry and professor in the Child Study Center, of neuroscience, and of pharmacology, has been named president of the Society for Research on Nicotine & Tobacco.

Clarence T. Sasaki, M.D., Charles W. Ohse Professor of Surgery (Otolaryngology) has received the Giotakis-Psyrri Award from the Hellenic Society of Head and Neck Cancer for his lifelong and distinguished contributions to oncology research and education.

John E. Schowalter, M.D., professor emeritus in the Child Study Center, has received the American Academy of Child and Adolescent Psychiatry's Catchers in the Rye Award to an Individual.

William V. Tamborlane, M.D., professor of pediatrics (endocrinology), is the recipient of the 2017 Outstanding Achievement in Clinical Diabetes Research Award from the American Diabetes Association.