Blavatnik gift will fund research into the biology of survival

Medzhitov will investigate how organisms adapt to the most severe of environments

At first glance, a hibernating ground squirrel and a person with the flu appear to have little in common. But both are protected by physiological systems that have evolved to help them survive challenging conditions. Evolutionary principles tell us that all living systems—including humans, animals, and plants—allocate their precious resources to promote three major goals: growth, reproduction, and survival.

Each of these efforts, driven by fundamental biological processes, is essential for life and the preservation of species. But not all of them are well understood.

“We know a lot about growth and reproduction,” said Ruslan Medzhitov, PhD, Sterling Professor of Immunobiology and a Howard Hughes Medical Institute Investigator. “In contrast, we know little about the biology of survival.” To fill this gap, Medzhitov and his research team are working to uncover the mechanisms underlying survival strategies—also known as maintenance programs—an endeavor that will both advance fundamental biology and provide new therapeutic targets to prevent and treat disease.

Recognizing the potential to improve human health on a grand scale, the Blavatnik Family Foundation has donated $5 million to Medzhitov’s research into the biology of survival. The contribution continues an important chapter in philanthropy for medical research at Yale. In 2013, the Blavatnik Family Foundation, led by American industrialist and philanthropist Len Blavatnik, granted Medzhitov and Richard Flavell, PhD, Sterling Professor of Immunobiology, $10 million to further develop a groundbreaking theory linking inflammation and chronic disease. Three years later, the foundation gave $10 million to establish the Blavatnik Fund for Innovation at Yale, which provides support to expedite the development, application, and commercialization of life science breakthroughs taking place on campus.

A scholarship begets more scholarships

Donors want today’s and tomorrow’s students to receive what meant so much to them

Stephen C. Schimpff, MD ’67, speaks with appreciation when he talks about his years at Yale School of Medicine. “I started medical school two weeks after my wife Carol and I got married,” says Steve, a quasi-retired internist, professor of medicine and public policy, and former CEO of the University of Maryland Medical Center—and author of six books, including Longevity Decoded: The 7 Keys to Healthy Aging.

Now married to Carol for 55-plus years, Stephen says that med school was challenging but also that it shaped who he later became. “There is something unique about the Yale system of medical education. Instead of memorizing everything, we were taught to truly think about what we were learning, to always want to learn more.” While Steve was in school and residency training, Carol worked with the late Alvan Feinstein, MD, Sterling Professor of Medicine and Epidemiology, who became a mentor to both of them. The couple draw a direct line from their experiences in New Haven to what they were able to achieve in their careers. “Yale set us up for success,” says Steve. “Now, after long careers, raising a family, and living a thrifty lifestyle, we decided to share with Yale.” The lives of Carol and Stephen Schimpff received a boost when a scholarship let Carol go to college. They want to similarly help Yale medical students. They have given back, generously, in the form of the Carol R. and Stephen C. Schimpff Scholarship Fund for medical students, which will enable more students from all socioeconomic backgrounds both to attend the

New orthopaedics chair is named, will arrive in September

Lisa Lattanza, MD, has been appointed as chair of the Department of Orthopaedics & Rehabilitation at Yale School of Medicine and chief of Orthopaedics at Yale New Haven Hospital, beginning September 2019. She is currently professor of orthopaedic surgery and vice chair for orthopaedic surgery at the University of California, San Francisco (UCSF). She also serves as chief of the Division of Hand, Elbow and Upper Extremity Surgery and program director for the Hand and Upper Extremity Fellowship at UCSF.

Lattanza obtained her medical degree at the Medical College of Ohio (now the University of Toledo College of Medicine and Life Sciences). She did her internship at the Harbor-UCLA Medical

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A powerful relationship between the School of Medicine and the Paralyzed Veterans of America Spurs spinal and pain research.

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Revealing secrets of the microbiome

Goodman finds that gut organisms are responsible for more than digestion

In ecology, the branch of biology that investigates how organisms relate with each other and their environment, the points of interaction seem infinite. Those points riveted Andrew Goodman, MD, C.N.H. Long Professor of Microbial Pathogenesis, as he grew up near Portland, Oregon, and continued to absorb him throughout his undergraduate studies in ecology and evolutionary biology at Princeton University.

Toward the end of his time in New Jersey, intricate ecosystems of a different sort—communities of bacteria—caught Goodman’s attention. “I realized that microbial communities can be viewed as ecological systems that allow us to test our ideas in a way that is very hard to do in other environments,” Goodman says.

As academic interests instantly took a sharp turn. He shifted from a broad study of ecology that included tracking tigers in their natural habitat, to a focus on molecular biology. He began studying bacterial genetics for his graduate work at Harvard Medical School. “I’ve been fascinated with this interaction of ecology and mechanisms—the genes, pathways, and molecules—for 20 years,” Goodman says.

During his postdoctoral studies at Washington University School of Medicine in St. Louis, Goodman decided to focus on the bacterial communities that live in humans. He worked to bring techniques that were initially developed for studying disease-causing bacteria to the then-new field of human microbiome, and developed new approaches of his own. “The discovery that commensal bacteria are equipped with numerous specialized adaptations to live in the gut changed the way I thought about the microbiome,” he says. In 2010, when Yale offered Goodman an opportunity to join the newly formed Microbial Sciences Institute on Yale’s West Campus, he did not hesitate. Goodman saw the “West Campus idea”—to bring together researchers from different departments that would normally be separated into different buildings or campuses—as especially advantageous for addressing the challenge of understanding microbial diversity. In this environment, Goodman and colleagues collaborate with ecologists, chemists, and geneticists. In Goodman’s view, “What Yale has built at West Campus is truly unique in this regard. We get the chance to see more different approaches to thinking about microbes than you would at any other university in the country due to the proximity of different specialists.”

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Goodman says, “we decided need should not graduate students who would be most likely to succeed,” he says. “We don’t know whether microbes have a few enzymes that target many drugs, or if it’s more one-to-one,” he says. But knowing those answers could lead to exciting new therapies. “I think it’s safe to predict that we will be temporarily and reversibly changing people’s microbiomes before we’re changing their genomes.”

New faculty leaders named at Yale Center for Clinical Investigation

With the retirement of Robert S. Sherwin, MD, C.N.H. Long Professor Emeritus of Medicine (Endocrinology) and long-time associate dean for clinical and translational research, the Yale Center for Clinical Investigation (YCCI), of which Sherwin was founding director, has announced new leadership.

Brian Smith, MD, deputy dean for scientific affairs (clinical departments), professor and chair of laboratory medicine, and professor of biomedical engineering, is co-director for YCCI and co-principal investigator of the Yale Clinical and Translational Science Award program, along with John Krystal, MD, Robert L. McNell Jr. Professor of Translational Research, professor and chair of psychiatry, and professor of neuroscience and psychology. Eric J. Velazquez, MD, Robert W. Berliner Professor of Medicine (Cardiology) becomes YCCI’s deputy director of clinical trials innovation.

Medical school lowers student unit loan substantially

Yale School of Medicine announced in February that it is reducing the unit loan—the amount that medical students who receive need-based scholarships are expected to borrow—from $23,000 to $15,000 per year for all students attending in the 2019-2020 academic year and thereafter. Together with the unit loan reduction that went into effect for the just-ended academic year—from $30,000 to $23,000—it is a reduction of 50% in two years.

“Reducing our students’ debt burden has been one of our highest priorities,” said Robert J. Alpern, MD, dean and Ensign Professor of Medicine.

According to the Association of American Medical Colleges, 71% of medical students had educational debt in 2018, with a national average debt of $197,000 per student for all medical schools. With an average debt of $116,000 for the class of 2018, Yale already was below the norm. Starting with the Class of 2023, students with demonstrated need should not graduate with more than $60,000 in debt.

“Students who would never have considered applying to Yale School of Medicine can now be assured that Yale can be affordable for those of modest means,” says Laura Mant, MD, professor of pediatrics and neurology and associate dean for admissions and financial aid. Ment led a committee formed in 2017 that examined ways to provide financial relief to medical school students.
Advances in postmortem brain activity

There is a longstanding reluctance among minority populations to participate in clinical trials and studies to evaluate therapies for treating disease. From the now-infamous Tuskegee syphilis studies where infected African American men were deliberately left untreated, to the sterilization of many women in Puerto Rico without their informed consent, people of color have learned through bitter experience that their interests and those of the health care they receive may not coincide. “There was a kind of apprehension and kind of fear on the part of our community,” says Rev. Leroy Olinga Perry, DMin, pastor of St. Stephens AME Zion Church in Branford, Conn.

And in near New Haven, a wariness of working with researchers from Yale was a natural consequence, as it has long been in many minority communities located near American research universities. Yale has joined forces with the federal Food and Drug Administration (FDA) to ameliorate that, through a Memorandum of Understanding (MOU) they signed in 2018 to encourage minority participation in clinical trials.

Among the nation’s medical schools, Yale is especially well positioned to participate, because since 2011 it has worked to engage the local community through its Cultural Ambassadors program. The Ambassadors are leaders from Connecticut’s African Methodist Episcopal (AME) Zion Church, including Perry—and from Junta for Progressive Action, which advocates for Latinx/Latina people and provides social services. They have formed an alliance with Yale to convince their constituencies that the trials benefit both those who participate and the wider community. Perry calls it “a link that had been missing between the community and the scientific community.”

According to the FDA, “experience has shown that there can be important differences in how people of diverse groups respond to medical products … so it is important for patients in those populations who are more likely to be treated for a condition to be included in a trial.” African Americans are known to have disproportionately high rates of diabetes and heart disease, for instance, but unless they participate in trials affecting those conditions, their differing needs may be overlooked by the FDA approves new treatments. “We need to have enough diversity in clinical trials of drugs and devices to ensure that treatments are effective in all populations,” says Teslea H. Johnson, MBA, MHS, deputy director and chief operating officer of the Yale Center for Clinical Investigation (YCCI), which receives substantial support from a National Institutes of Health (NIH) grant.

They also advised Ordway on how to approach families in terms that would resonate with their lives, such as speaking of sleep deprivation as affecting children’s behavior and school performance rather than more distant concerns such as health risks later in life. “When I think about the success of my program, one of the first things that I think about is that meeting where they talked to me about how I frame this with families.” In turn, when some community members resisted cooperating with her, Ambassadors became her advocates. “Because they had already met with me and vetted my study, they were able to then speak to the quality, and the safety.”

Yale and the Food and Drug Administration join forces to further increase minority trial participation and produce more useful results

Recruiting for inclusive clinical trials

Yale scientists took the brains of pigs slaughtered at a meatpacking plant and, four hours after death, perfused them with a preservative solution that included hemoglobin, nutrients, oxygen, and cytoprotective components—which restored some cellular activities. The results, published on April 17 in Nature, suggest that postmortem brain decline may not be as rapid and irreversible as scientists previously thought.

Researchers led by Nenad Sestan, MD, PhD, Harvey and Kata Cushing Professor of Neuroscience, and professor of comparative medicine, genetics, and psychiatry, connected each pig brain to a mechanical circulatory system called BrainEx, which pumped the solution through the brain. While other brains circulated with a control solution deteriorated during the six-hour perfusion, those perfused with the preservative mixture maintained intact brain structures, functioning blood vessels, and metabolic activity. Hippocampal neurons fired spontaneously and in response to stimulation. The investigators did not observe any brain-wide electrical activities associated with consciousness. “As a result, the research would have been stopped.”

The possibility of restoring cellular activities in a postmortem brain may lead to research that could shed new light on brain disorders, such as stroke.
November 30 After a documentary film screening of Far From The Tree, based on the namesake book by author Andrew Solomon YC ’85, John Krystal, MD, Robert L. McNeil, Jr. Professor of Translational Research, chair and professor of psychiatry, and professor of neuroscience, led a panel discussion about families’ deep compassion and acceptance while raising children whom society might describe as “abnormal.” From left, filmmaker and director Rachel Dretzin; Krystal; James McPartland, PhD, associate professor in the Yale Child Study Center and of psychology; Solomon; and Christy Olczeski, PhD, assistant professor of psychiatry.

January 25 A retirement party honoring Robert Sherwin, MD, C.N. Long Professor Emeritus of Medicine (Endocrinology) and longtime associate dean for clinical and translational research, for 44 years of service to the School of Medicine, was held at the New Haven Lawn Club. During his career, Sherwin provided invaluable guidance to generations of clinician scientists and was founding director of the Yale Center for Clinical Investigation (YCCI).

From left, Sara Sapire, Sherwin’s daughter; Sherwin; his wife, Leslie Sherwin; his son, Benjamin Sherwin; and daughter Jenny Blumberg. From left, Sherwin; one of his mentees, Ania Jastreboff, MD, PhD, assistant professor of medicine (endocrinology) and of pediatrics (endocrinology); William Tamborlane, MD, professor of pediatrics (endocrinology); and Paul Barash, MD, professor emeritus of anesthesiology. 3. Sherwin, John Krystal, MD, Robert L. McNeil, Jr. Professor of Translational Research, chair and professor of psychiatry, professor of neuroscience, and co-director of YCCI; and Rajita Sinha, PhD, Foundations Fund Professor of Psychiatry and professor in the Yale Child Study Center, and co-director of education at YCCI.

December 6 The 26th annual Hunger & Homelessness Auction held at Harkness Hall raised money to support organizations in the New Haven area that work to help people in need. 1. William Stewart, PhD (left), associate professor of surgery (gross anatomy); and Jack Tang, Class of 2022, admire a bow tie, one of the biddable prizes, which brought in $2,078 toward fundraising. 2. John “Jack” Hughes, MD, professor of medicine (general medicine) served as auctioneer for the evening.

March 30 In the Fourth-Year Show, a theatrical performance that resurrected the 70-year tradition of what had been the Second-Year Show, medical students mimicked, impersonated, and mocked other students, faculty, and administrators. 1. From left, Tess O’Meara as David Stittelman, MD, Andrea Roberts representing Kirsten Wilkins, MD, FW ’06, and Anusha Singh as Augustine Fortin VI, MD, MPH. 2. The show, called “The Final Master Course,” was produced by, and starred, members of the Class of 2019.

April 5 Medical faculty, students, fellows, and residents attended the annual M.D.R.E. (Minority Organization for Retention and Expansion) Retreat, hosted by Darin Latimore, MD, (far right) deputy dean and chief diversity officer and associate professor of internal medicine (general medicine), at the New Haven Lawn Club.

OUT & ABOUT
Ongoing support from paralyzed veterans

Foundation’s generosity bolsters two areas of research

Gene discoveries on neurological disease

In a new mouse study, researchers at Yale uncovered the impact of a gene mutation that has been associated with autism, schizophrenia, bipolar disorder, and epilepsy. Studies have previously shown that mutations in the gene, TRIO, are found in a significant number of people with these neurodevelopmental disorders. Now, a team led by Anthony Kolasek, PhD, professor of molecular biophysics and biochemistry and of neuroscience, genetically engineered mice to lack one of their two copies of TRIO.

The animals, they found, had higher levels of anxiety, impaired social behaviors, and decreased coordination than normal mice. Moreover, the mice had smaller brains and their brain cells did not have the same branching patterns or connections with each other. The researchers went on to discover a set of proteins that are found at lower levels when TRIO is missing. Using drugs to increase levels of these proteins helped when TRIO is missing. Using drugs to increase levels of these proteins helped when TRIO is missing.

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Similar drugs might treat neurodevelopmental diseases in humans with TRIO mutations, the researchers suggest. The results were published on March 5 in Cell Reports.

Gene pairs are tied to cancer spread

Cancer is most deadly when it metastasizes, or spreads. While metastasis might result from malfunctions of single genes, interactions among multiple genes may also be the cause, complicating metastasis genetics. As reported April 8 in Nature Methods, Sidi Chen, PhD, assistant professor of genetics, has developed an approach designed to sort out which gene pairs most drive cancer’s spread.

Using the gene-editing technique CRISPR, Chen and colleagues knocked out 325 pairs of genes individually suspected of promoting metastasis from lung cancer cells. Next, with a subcutaneous injection, they transferred the cancer cells, which carried genetic barcodes indicating which genes had been knocked out, into immuno-deficient mice. Six weeks later, the researchers removed both the primary tumors from under the skin and those that had metastasized to the lungs.

Through the barcodes, they determined which gene-knockout combinations were more prevalent in the lung tumors than in primary tumors and, therefore, which gene pairs had likely promoted metastasis. In addition to helping scientists understand cancer genetics, this approach could help researchers probe gene interactions in other contexts, the authors write.
Lattanza has received numerous awards for both her clinical and outreach efforts. She received UCSF's Compassionate Physician Award in 2013 and Exceptional Physician Award in 2015. She also received the 2013-2014 Community Service Award for Community Service in 2014, and has been ranked by her peers as a Bay Area Top Physician for multiple years. In addition to her other leadership roles, she served as president of the American Academy of Orthopaedic Surgeons in 2017 and is active in the American Academy of Orthopaedic Surgeons, the American Society for Surgery of the Hand, and the American Orthopaedic Association.
As a psychiatrist, David R. Kessler, MD '55, understands the mix of anxiety and fear that can consume individuals who identify as LGBTQ during their struggle to come out about their sexual orientation.

Kessler is not only trained in such knowledge. He experienced it. From the intense anxiety attacks he suffered as a closeted gay medical student in the 1950s to the fears of persecution he and other closeted gay doctors shared in the 1970s, Kessler lived through a turbulent time for LGBTQ people in American history.

Now retired and living on the West Coast, Kessler publicly affirmed his sexuality in 1978. He helped launch the country’s first formal gay doctors’ organization, the Bay Area Physicians for Human Rights. Kessler later served as president of the National Gay Caucus of Members of the American Psychiatric Association, which became the American Association of Gay and Lesbian Psychiatrists.

He now wants to help additional LGBTQ individuals who may be struggling to come out or who are dealing with stigma, oppression, and other issues that have an impact on their mental health.

“Coming out was a fantastic experience for me and that’s why I’m so interested in helping others,” Kessler says, “because I realized from my own experience what a meaningful, life-changing event it is.”

Kessler recently made a gift of $200,000 to support the work of Yale School of Public Health (YSPH) Associate Professor John Pachankis, PhD, and his Estem Research Group, which is dedicated to addressing the depression, anxiety, and substance use problems that disproportionately affect the LGBTQ community and can erode healthy relationships and behaviors. A clinical psychologist, Pachankis is internationally known for his development of novel psychosocial interventions to improve LGBTQ individuals’ mental health.

“I’m very supportive of his work not only in this country but internationally, which is really unbeliev- able,” says Kessler. “People around the world are dealing with issues related to coming out and John is studying how it affects them in a sci- entific and rigorous manner, which is very impressive.”

Kessler also is directing $5 mil- lion from his estate to YSPH, part of which is intended for the creation of a David R. Kessler Endowed Professorship. The professorship and accom- panying resource fund will support teaching and research associated with improving LGBTQ mental health.

A stigma against many of the so- ciety, people who identify as LGBTQ are subject to continuous assaults on their self-esteem and sense of belong- ing in their families, schools, and workplaces,” says Sten H. Vermund, MD, PhD, dean and M.R. Laufer Professor of Public Health, and profes- sor of pediatrics. “I cannot think of a higher impact pro- gram in which Dr. Kessler could invest than Dr. Pachankis’ Estem Program.”

Pachankis’ re- search is dedicated to delivering effective LGBTQ-affirmative mental health treat- ments to populations both in the United States and around the world—such as those in rural Appalachia, China, and Eastern Europe.

Some of the programs Pachankis has initiated since arriving at Yale in 2013 involve improved training for mental health providers, delivering mental health treatment via the inter- net and mobile applications, and find- ing ways to sustain such treatments in areas where LGBTQ stigma is present and strong.

“David’s journey inspires all of us to be as courageous and creative as his generation has been in living proudly and meaningfully in the face of societal and emotional barriers,” says Pachan- kis. “For a lot of LGBTQ people, that journey includes supporting the next generation of LGBTQ individuals.”

Kessler says he was interested in creating something at Yale for years, but it took two tries to get it done. The first time he approached the university in the early 1990s, the people he met with were not sure where the funds should be directed or how they might be used, and Kessler chose instead to create the David R. Kessler Lectures in Lesbian and Gay Stud- ies at his other alma mater, the City University of New York. A longtime supporter of Yale School of Medicine, Kessler decided to make the estate gift to the School of Public Health after speaking with Vermund and YSPH Deputy Dean and Chief Diversity Officer Darin Latim- more, MD, who introduced him to Pachankis last year.

“Now Yale is ready, willing, and able with a research program in full swing that is very close to my heart,” Kessler says. “I am delighted to be able to come back and do it even bigger and better.”

David Kessler (left) has pledged a gift of more than $5 million to support LGBTQ-related work by John Pachankis (right) to reduce stigma and improve the health of LGBTQ people, and endow a professorship to enhance teaching, research, and training for mental health providers.