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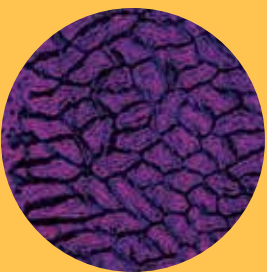
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SPRING

FEATURED STORY

STRENGTHENING SUPPORT OF AUTISM RESEARCH

Lisa Yang gives boost to
Harvard Tan-Yang Center,
where discoveries abound

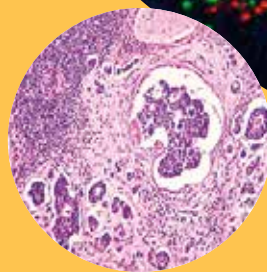
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CATALYZING WORK TOWARD CURING BRAIN DISEASES

Moorheads enthusiastically
back new ideas in neuroscience

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STRIVING TO STOP ONSET OF BRCA-RELATED CANCERS

Gray Foundation bolsters
Brugge Lab's research

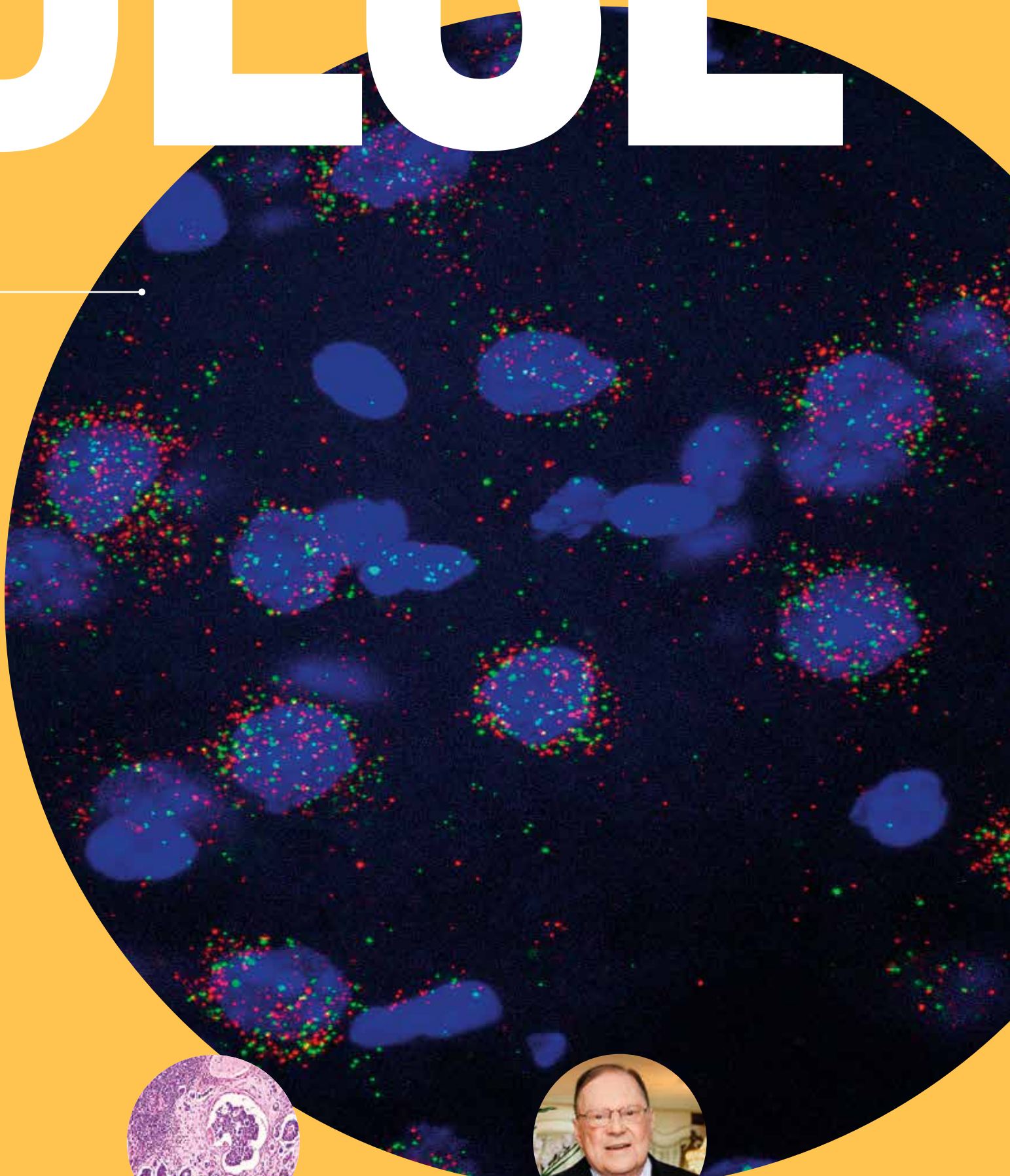
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HONORING FOUNDER'S PHILANTHROPIC LEGACY

Pearce Foundation broadens backing
of autoimmune disease project

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ACCELERATING AUTISM RESEARCH

Scientists make significant progress at Harvard
Tan-Yang Center thanks to sustained support

→ Lisa Yang's unwavering commitment to improving the well-being of others is the common thread that runs through her wide-ranging philanthropic interests. She is particularly invested in improving the lives of people with disabilities and learning differences, having raised two children with autism spectrum disorder (ASD).

In 2019, she and Hock Tan, MBA '79, gave \$20 million to launch the Hock E. Tan and K. Lisa Yang Center for Autism Research at Harvard University, which focuses on the biological basis of neurodevelopment as it relates to ASD. Yang (pictured at right) then made a \$4 million gift to establish the Y. Eva Tan Postdoctoral Fellowship at the center in honor of her daughter. Recently, she gave an additional \$10 million to bolster the center's work.

FLUORESCENCE IN SITU HYBRIDIZATION (FISH) IMAGE OF ACTIVITY-DEPENDENT MOLECULES OF INTEREST IN MOUSE CORTICAL TISSUE
IMAGE: GREENBERG LAB

"We are thrilled to have Lisa's continued support," says the center's leader, Michael Greenberg, PhD, the Nathan Marsh Pusey Professor of Neurobiology in the Blavatnik Institute at Harvard Medical School. "We have already made several important discoveries, and we plan to build from those by sharpening our focus."

HMS Dean George Q. Daley, AB '82, MD '91, PhD, says he deeply values Yang's involvement with the School, which includes her service on both the Board of Fellows and the Discovery Council. He expressed thanks for what he described as her "tremendous" gift to fund the Harvard Tan-Yang Center's next phase of scientific investigation and discovery. "I am so grateful for Lisa's investment in our neurobiology researchers and the collaborations with MIT that her visionary generosity has catalyzed," Daley says.

The Harvard center is home to two project teams: the Autism Genetics and Brain Development group, led by Greenberg, and the Sensory Experiences and Social Behavior group. Greenberg and his team have advanced several interconnected questions about the neurobiology of brain development in ASD. They have a longstanding interest in how sensory experiences influence neuronal activity and the development of neural circuits. For the past five years, they have investigated the role of genetic variation in shaping differences in brain development.

"We've made significant progress in our understanding of how mutations in ASD genes can cause changes in the expression of activity-dependent genes, and how those changes can alter neural circuit development and plasticity," Greenberg says.

The Sensory Experiences and Social Behavior group, meanwhile, is focused on ASD patients' hypersensitivity to sensory stimulation—notably, sensitivity to touch. Group members seek to understand the circuits and pathways in the

somatosensory system in mouse models of ASD to better understand the fundamental mechanisms of social touch and, ultimately, social behavior.

"We're also working to identify biomarkers for touch over-reactivity in patients, as well as new approaches to lessen the burden of touch over-reactivity, with the goal of enhancing the quality of life for those suffering from debilitating forms of sensory over-reactivity," says group member David Ginty, PhD, the Edward R. and Anne G. Lefler Professor and chair of the Department of Neurobiology.

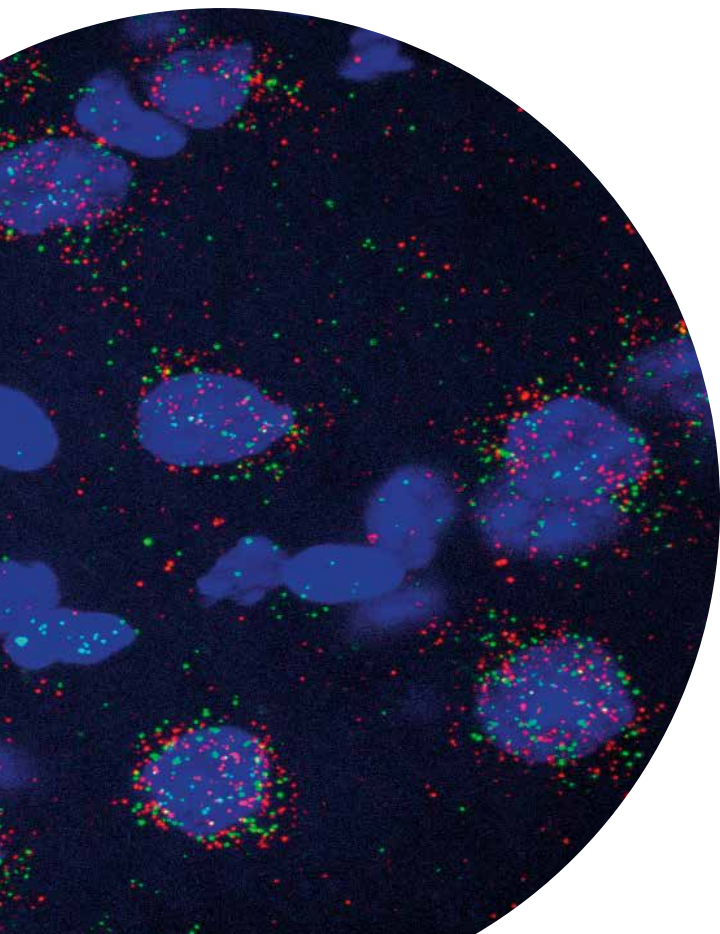
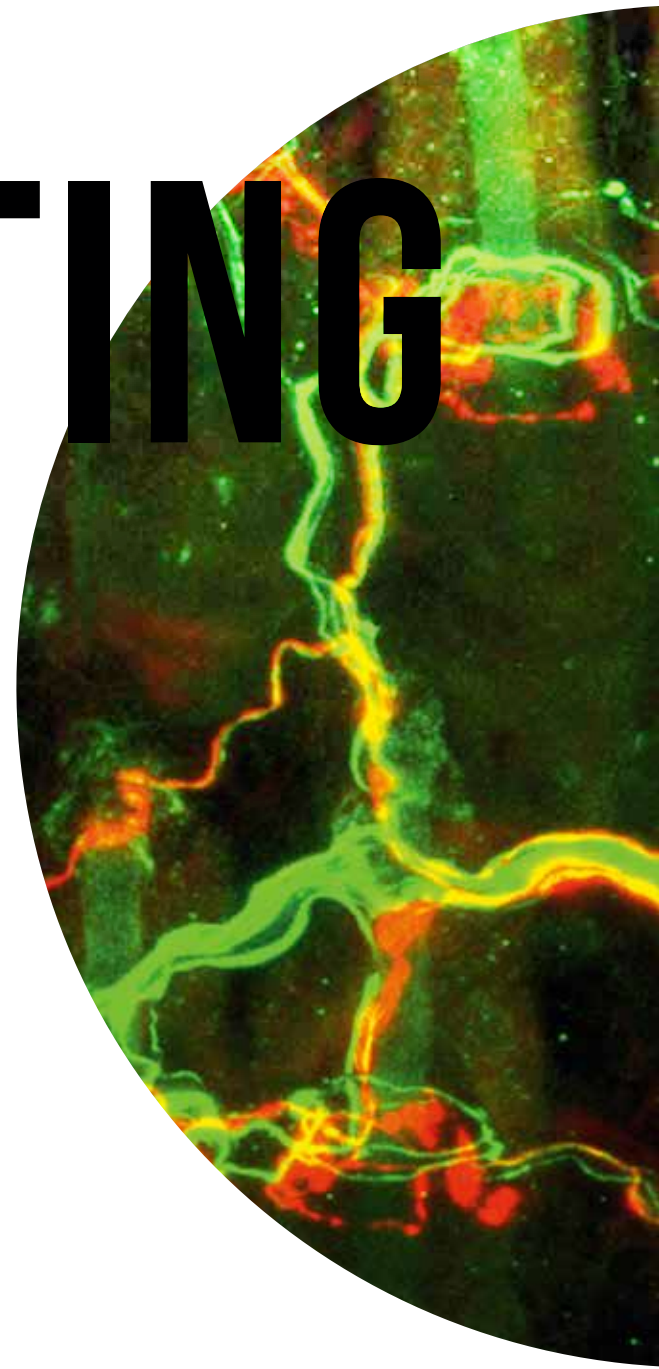


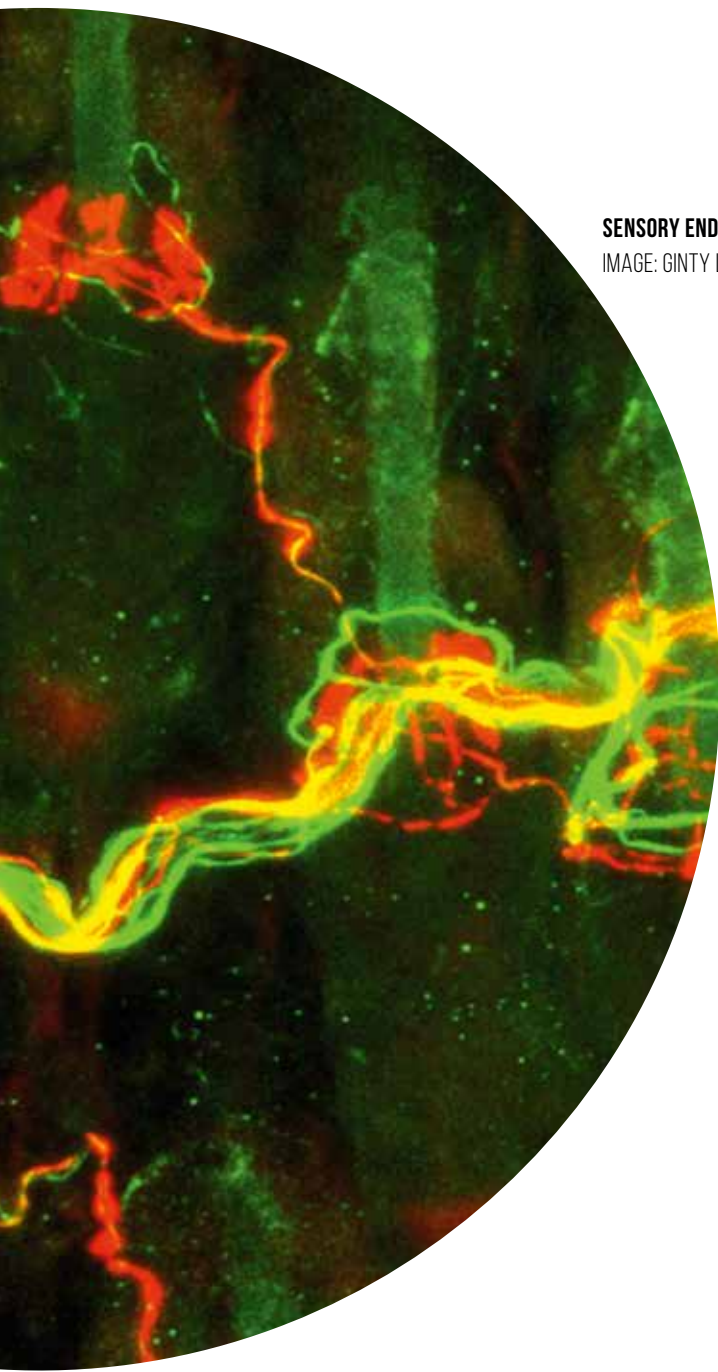
Both project teams collaborate with peer researchers at the Hock E. Tan and K. Lisa Yang Center for Autism Research at MIT.

"The (Harvard) center has greatly impacted our ability to interact with our MIT colleagues," says Ginty. "We consider the MIT center our 'sister center' with complementary strengths."

Yang's recent gift will support the center's research and the aforementioned fellowship program, which Greenberg says will expand. The program aims to train the next generation of scientists in hopes that the scientific community being built in the center will exist in perpetuity.

"Over the last five years, we have awarded seven outstanding postdoctoral fellows whose research





SENSORY ENDINGS IN THE SKIN
IMAGE: GINTY LAB

focuses on mechanisms of autism spectrum disorder, and we are delighted to use this new gift to elevate and grow this community of young scientists,” Greenberg says.

Yang is exceedingly proud to have supported dozens of fellows through her support of HMS and MIT. “I love to give young people the chance to succeed and make an impact,” she says. “These are the people who will shape and lead the future.”

“OVER THE LAST FIVE YEARS, WE HAVE AWARDED SEVEN OUTSTANDING POSTDOCTORAL FELLOWS WHOSE RESEARCH FOCUSES ON MECHANISMS OF AUTISM SPECTRUM DISORDER, AND WE ARE DELIGHTED TO USE THIS NEW GIFT TO ELEVATE AND GROW THIS COMMUNITY OF YOUNG SCIENTISTS.”

MICHAEL GREENBERG

Greenberg and Ginty agree that Tan and Yang’s vision for a unified center of excellence at Harvard dedicated to understanding the neurobiology of ASD has inspired a wave of progress in their collective work.

“We have come together to forge collaborations that would not have existed without their vision, and we have made immense progress in areas of neurobiology that will have a lasting impact in the field of autism spectrum disorder and lead to a better understanding of the ASD experience,” says Ginty.

HARVARD TAN-YANG CENTER RESEARCH HIGHLIGHTS



THE CHEN LAB

Chinfei Chen, MD '91, PhD '91
Professor of neurobiology, HMS

The Chen Lab has found that the synaptic glomerulus in the thalamus plays a crucial role in refining sensory information through experience. The lab identified ASD-related mutations affecting the synaptic glomerulus’s function, leading to altered integration and transmission of sensory information. **This research is essential for understanding how impaired information integration in the thalamus contributes to sensory processing symptoms in autism.**



THE DATTA LAB

Sandeep Robert “Bob” Datta, MD '04, PhD '04
Professor of neurobiology, HMS

The Datta Lab pioneered the use of machine learning to develop tools for quantitatively evaluating mouse behavior. These tools identify subtle repeated behavioral syllables, enabling researchers to correlate neural activity with real-time free behavior. **These tools significantly enhance scientists’ ability to analyze mouse behavior and have the potential to revolutionize the study of genetic and circuit regulation in social behaviors within autism models.**



THE GINTY LAB

David Ginty, PhD
Edward R. and Anne G. Lefler Professor and chair of the Department of Neurobiology, HMS

The Ginty Lab highlights the spinal cord’s role in transmitting touch signals to the brain, using ASD mouse models to detail atypical tactile reactions and explore the integration of tactile processing in the spinal cord and brainstem. The lab discovered a direct pathway from skin sensory neurons to the brainstem for high-frequency vibration communication and an indirect pathway to the dorsal horn for encoding pressure intensity. **This work is essential for understanding tactile reactivity in individuals with autism.**



THE GREENBERG LAB

Michael Greenberg, PhD
Nathan Marsh Pusey Professor of Neurobiology, HMS

The Greenberg Lab has discovered transcription factor complexes that regulate the development and refinement of neural circuitry and are often mutated in ASD. Activity-dependent gene transcription is integral to this process. The lab has identified a novel protein complex that assembles in activated neurons to coordinate inducible gene transcription and dynamically reorganize active neural circuitry. **Investigating these factors offers vital insights into autism’s fundamental molecular mechanisms.**

BEQUEST ENABLES RESEARCH RELEVANT TO UNDERSTANDING HEART DEFECTS

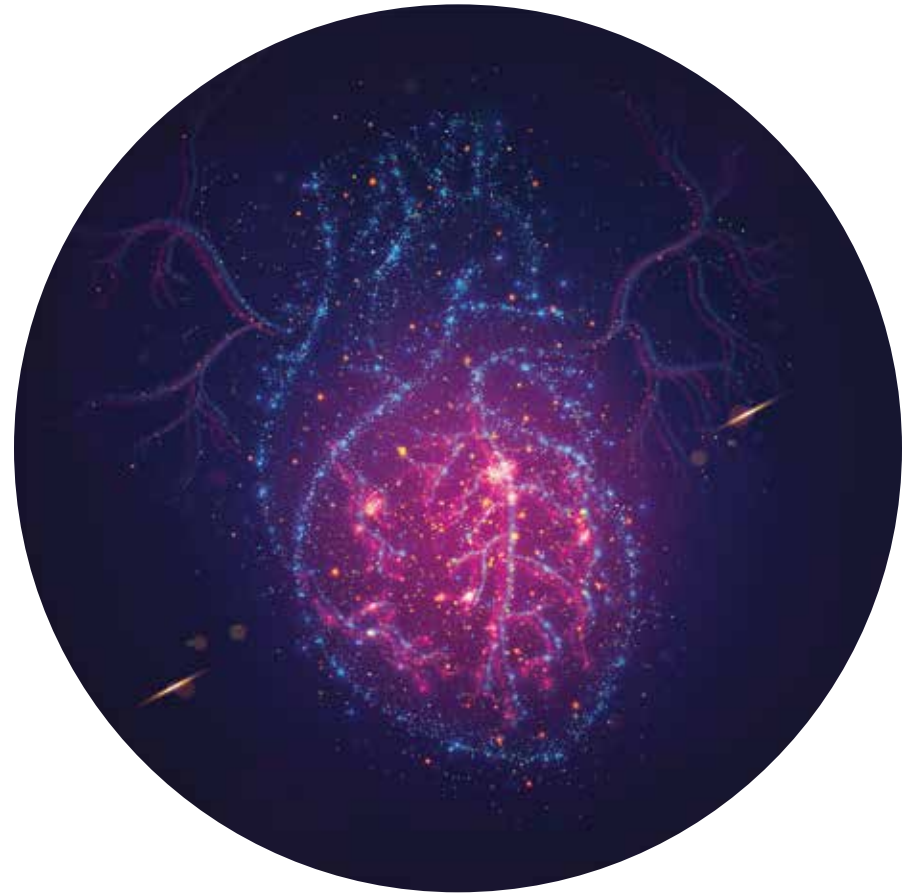
- ➔ Congenital heart defects are the most prevalent form of birth defects in the U.S., affecting about 40,000 births per year, according to the Centers for Disease Control and Prevention. Yet, abnormalities in establishing the left-right orientation of the heart—a major cause of congenital heart defects—remain poorly understood.

The Tabin Lab at Harvard Medical School is trying to change that.

“THE BEQUEST FROM ANN F. HOWARD WILL ALLOW US TO ADDRESS THIS EXTREMELY IMPORTANT PROBLEM.”

CLIFF TABIN

“While we know the genes that first mark the cells on the left as different from those on the right in the very early embryo, there is a gap in our knowledge regarding how this genetic information is maintained until the much later time that the heart and other asymmetric organs actually form,” says Cliff Tabin, PhD, the George Jacob and Jacqueline Hazel Leader Professor and chair of the Department of Genetics in the Blavatnik Institute at HMS.



A recent \$352,000 bequest from the Ann F. Howard Trust will help Tabin’s lab close this knowledge gap. Howard had established the trust with her husband, Vincent, who predeceased her. She designated her gift for heart research at HMS.

“The bequest from Ann F. Howard will allow us to address this extremely important problem, supporting fundamental studies of direct relevance to congenital heart disease that would have been very difficult to fund by traditional federal grants,” says Tabin.

SYMPOSIUM HONORS 2023 WARREN ALPERT PRIZE WINNER

- ➔ Harvard Medical School hosted a scientific symposium Oct. 11 in honor of David J. Lipman, MD (pictured), winner of the 2023 Warren Alpert Foundation Prize. Lipman was recognized for his visionary work in the conception, design, and implementation of computational tools, databases, and infrastructure that transformed how biological information is analyzed and accessed freely and rapidly worldwide.

Currently a senior science adviser for bioinformatics and genomics for the Food and Drug Administration, Lipman earned the award for work he did in the 1980s and 1990s before and after becoming the founding director of the National Center for Biotechnology Information, a position he held until 2017.

“The foundational work of David Lipman in the field of computational biology and the tools that he envisioned and created have an impact that is

nearly impossible to measure on the fields of biology, medicine, and beyond,” said David M. Hirsch, MBA ’67, director and chairman of the board of The Warren Alpert Foundation.

The Warren Alpert Foundation bestows this \$500,000 annual prize, which is administered by HMS, in recognition of work that has improved the understanding, prevention, and treatment of disease.

“The scientists involved in the nomination and selection process have a deep understanding of the field and have themselves made some of the most important biomedical discoveries,” said Lipman. “So, this honor holds a special significance to me.”



▶ VISIT [WARRENALPERT.ORG](https://warrenalpert.org) TO LEARN MORE ABOUT THE WARREN ALPERT PRIZE AND ITS RECIPIENTS.

SEEDING NEUROSCIENCE BREAKTHROUGHS

➔ In 2014, Rodman W. Moorhead III, AB '66, MBA '68, and his wife, Alice, gave \$1 million to Harvard Medical School to create a collaborative grants fund for the Harvard Brain Science Initiative (HBI), which had launched that year to promote interactions among neuroscientists across the University and HMS's affiliated hospitals. The Moorheads wanted to breathe life into small, innovative projects focused on uncovering the biological bases of brain diseases. A few years later, impressed by the HBI's work, the couple gave an additional \$250,000 to their fund.

Fast forward to today, and the Moorheads, who say they have been deeply gratified to learn about the impact of their philanthropy on brain research at Harvard, have established the Alice and Rodman W. Moorhead III Neurobiology Seed Grants Fund at HMS with a new \$1 million gift.

"These scientists are doing such remarkable work—things we couldn't have imagined possible a short while ago—and we are excited to see what new discoveries these grants can seed," says Rod Moorhead, a member of the HMS Board of Fellows and the HMS Discovery Council.

The Moorheads' interest in understanding the human brain is rooted in their family members' experiences with attention-deficit/hyperactivity disorder, language-learning issues, and Parkinson's disease. The couple seek to catalyze innovative research projects that will treat and ultimately cure diseases and disorders of the brain.

Founded in 1966, the HMS Department of Neurobiology consists of nearly 30 research laboratories that study neuroscience at the molecular, cellular, circuit, and systems levels, fueled by curiosity and a commitment to addressing disorders of the nervous system.

The seed grants are selected from a large number of applications through a competitive process, which is overseen by David Ginty, PhD, the Edward R. and Anne G. Lefler Professor and chair of the Department of Neurobiology at HMS. He says the Moorheads' unwavering enthusiasm to back new ideas in the field of neuroscience is "deeply palpable and highly appreciated."

"The Moorheads' recent gift provides a much-needed opportunity to support high-risk, high-reward research in its early stages, especially for faculty who have seeds of ideas but need assistance to pursue and cultivate those ideas into bona fide research programs," Ginty says.

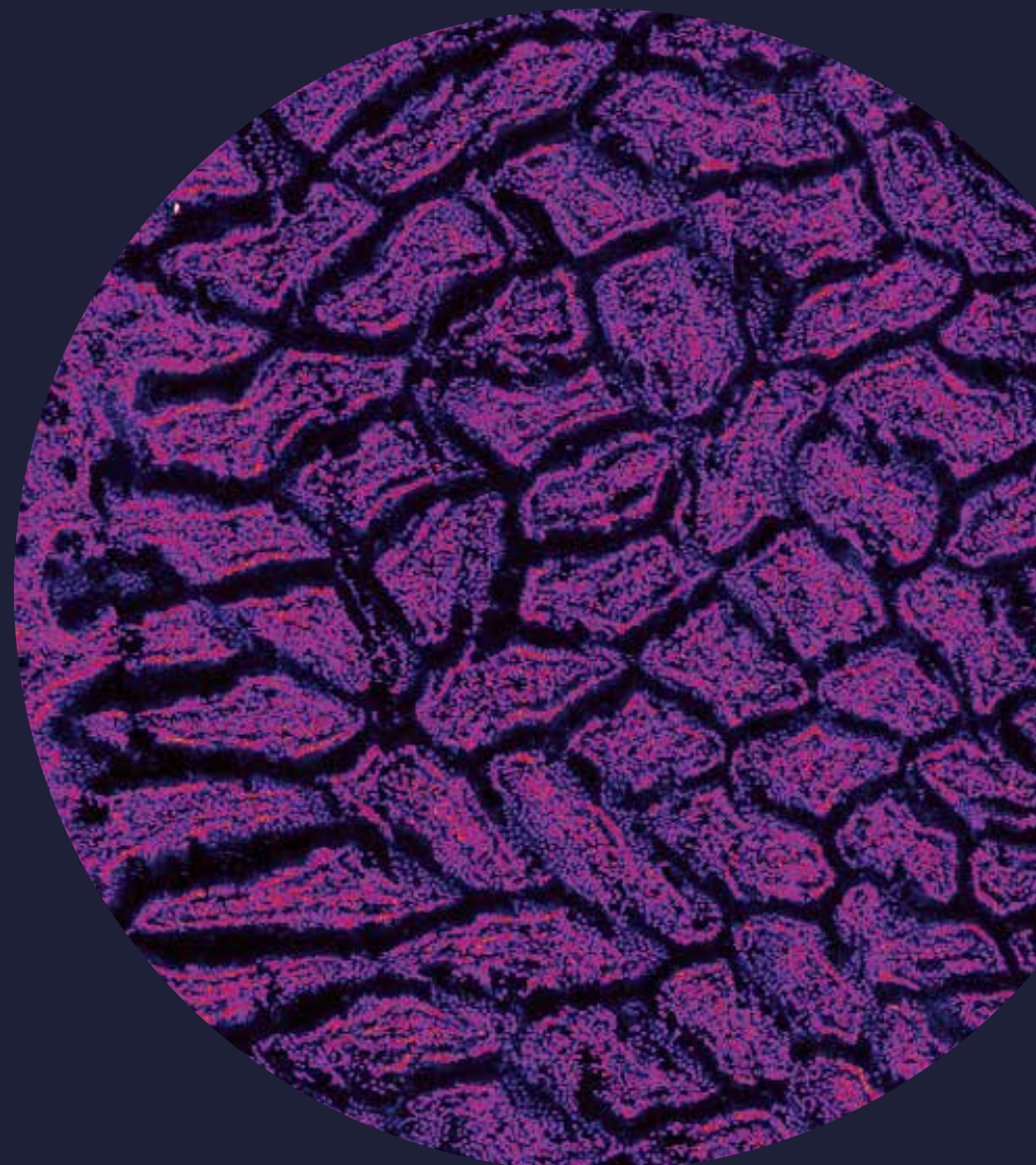
**REACTIVE OXYGEN SPECIES
ACCUMULATION IN THE SMALL
INTESTINE OF A MOUSE AFTER
FIVE DAYS OF SLEEP DEPRIVATION**
IMAGE: ROGULJA LAB

**"THE MOORHEADS' RECENT GIFT PROVIDES
A MUCH-NEEDED OPPORTUNITY TO SUPPORT
HIGH-RISK, HIGH-REWARD RESEARCH IN ITS
EARLY STAGES."**

DAVID GINTY

Dragana Rogulja, PhD, an associate professor of neurobiology in the Blavatnik Institute at HMS, is the first recipient of funding from the Moorheads' new fund. She is investigating how gut dysfunction resulting from sleep loss leads to the development and progression of different types of maladies.

"With a majority of adults not getting the proper amount of sleep each night, this project and its findings may have strong implications for how we address sleep disturbances in our society and promote the importance of prioritizing good sleep," Rogulja says.



A MAJOR NEW DATABASE FOR BREAST CANCER RESEARCH

➔ The Gray Foundation, which has committed \$190 million in total to researching the treatment and prevention of BRCA-related cancers, recently pledged \$3 million to support a new effort to catalog breast tissue co-led by Joan Brugge, PhD, the Louise Foote Pfeiffer Professor of Cell Biology in the Blavatnik Institute at Harvard Medical School. This Breast Pre-Cancer Atlas will profile epithelial, stromal, and immune cells in breast tissue from women who carry pathogenic variants of the BRCA1 or BRCA2 gene, comparing them to a control group.

“THE BREAST PRE-CANCER ATLAS ... PROMISES TO IDENTIFY THE EARLIEST PRECURSORS OF CANCER, WHICH WILL BE IMPORTANT FOR DEVELOPING INTERVENTIONS TO PREVENT CANCER DEVELOPMENT IN BRCA1 AND BRCA2 MUTATION CARRIERS.”

JOAN BRUGGE

Brugge’s team of internationally recognized basic and clinical scientists is carrying out single-cell and bulk-tissue analyses of tissue from 100 women: 30 with pathogenic BRCA1 variants, 30 with pathogenic BRCA2 variants, and 40 with wild-type BRCA1 and BRCA2 genes. Age, menstruation, pregnancy, menopause, weight differences, birth control medication, hormone replacement therapy, alcohol, and many other factors cause hormonal changes in women, explains Brugge. “It’s important to collect large numbers of samples so that we can rule out confounding factors as being responsible for differences in tissues that are actually due to mutations in BRCA1 or BRCA2 and identify aberrant cells that represent precursor lesions of cancer.”

Once complete, the atlas will be shared with the broader scientific community, bolstering research into how genetic variation and other variables affect breast tissue. Exposing the vulnerabilities of cancer precursors will hopefully lead to new strategies for their detection and elimination and transform the ability to predict and prevent breast cancer in BRCA mutation carriers.

The team is building on important new findings obtained from its previous Gray Foundation-supported work. It will integrate data from several platforms to identify associations among genomic, epigenetic, and transcriptional differences in the various cell types. This integration will offer insights that would not have been revealed by any one approach alone. As the project proceeds, computational scientists will join the team to assist with the higher-level integration of data from all of the different platforms.

“This type of atlas generation involves complex orchestration that is not typically involved in academic research,” says Brugge. “Working with

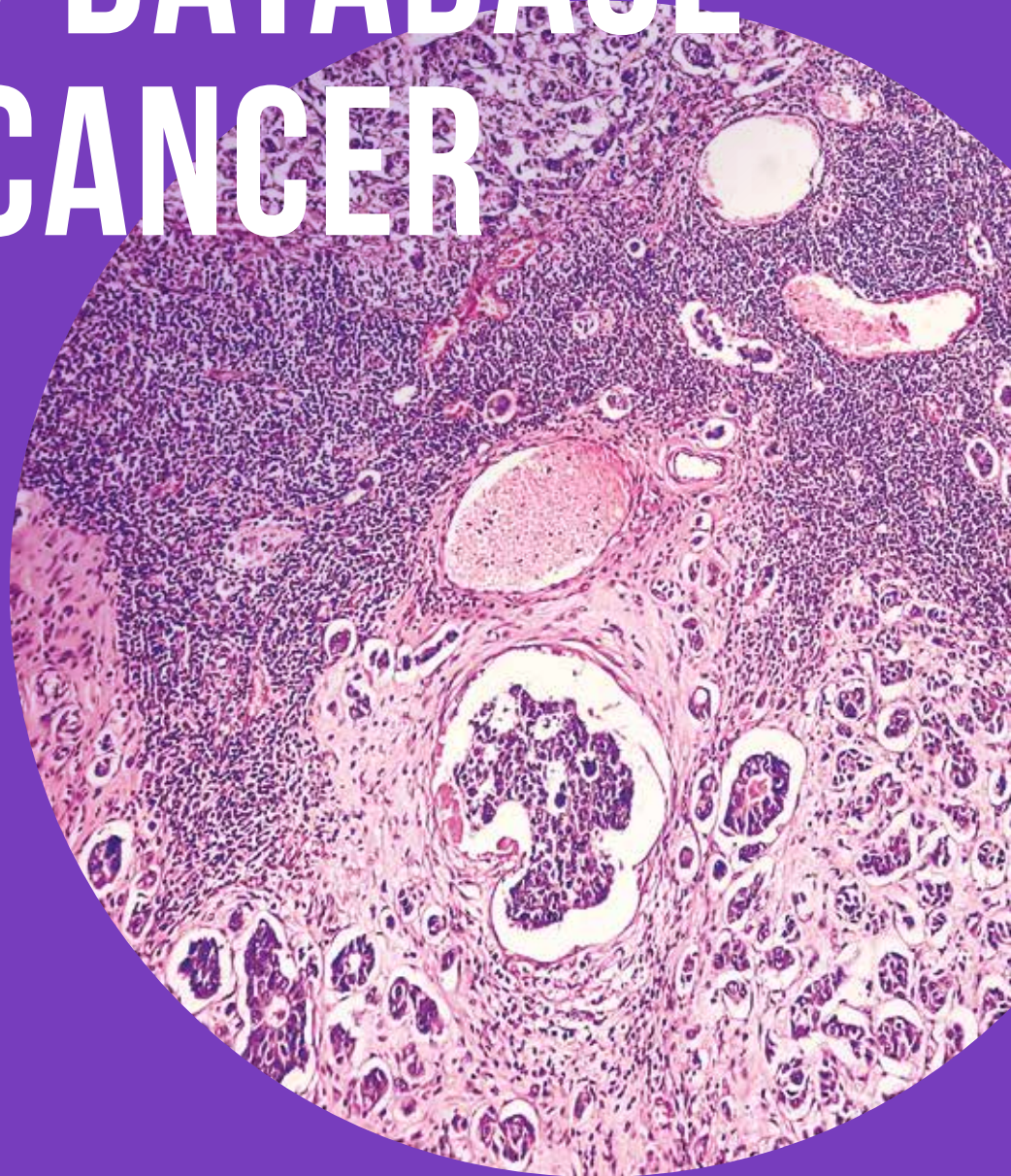
members of the teams from the University of Pennsylvania, Massachusetts General Hospital, and the Dana-Farber Cancer Institute, we developed and standardized the protocols that make it feasible to collect, process, and transport the samples to sites where the analyses are carried out.”

While the logistical work continues, Brugge is excited about the direction of the project and its potential for rapid translation to clinical impact. “Previous Gray Foundation funding to our team led to important new insights about cells that may represent the first precursors of tumor cells, and a manuscript we have submitted for publication that I think will be newsworthy,” she says. “I expect that the Breast Pre-Cancer Atlas will be no less significant, as it promises to identify the earliest precursors of cancer, which will be important for developing interventions to prevent cancer development in BRCA1 and BRCA2 mutation carriers.”

Approximately one American woman in eight will be diagnosed with breast cancer in her lifetime. This risk is greatly elevated for those with certain genetic mutations. By age 70, approximately 55–65% of women with a BRCA1 mutation and approximately 45% of women with a BRCA2 mutation will develop breast cancer.

SOURCE: NATIONAL BREAST CANCER FOUNDATION

THIS PHOTOMICROGRAPH OF A BREAST CORE BIOPSY SHOWS INVASIVE DUCTAL CARCINOMA (IDC), GRADE 2, WITH LYMPHOVASCULAR INVASION PRESENT. ACCORDING TO THE AMERICAN CANCER SOCIETY, IDC MAKES UP ABOUT 70–80% OF ALL BREAST CANCERS.



ADDRESSING PATIENTS' SPIRITUAL NEEDS

EZEKIEL
HERSEY
COUNCIL

➔ Harvard Medical School's legacy donors gathered virtually Feb. 28 for the Ezekiel Hersey Council Annual Recognition Event, which featured a keynote address exploring spirituality's role in medicine.

Council Chair Jordan J. Cohen, MD '60, delivered opening remarks, after which HMS Dean George Q. Daley, AB '82, MD '91, PhD, expressed his gratitude to those in attendance. "To all of you here supporting Harvard Medical School, whether it's through philanthropy or volunteerism, you have my sincere thanks," said Daley.

He then introduced featured speaker Tracy Balboni (pictured), MD '02, MPH '06, a professor of radiation oncology at HMS and co-director of the Initiative on Health, Spirituality, and Religion at Harvard University. Balboni spoke about the importance of care that embraces all aspects of human health and illness in a way that brings hope and meaning.



"The evidence that is available supports a multifaceted role of spirituality within health and within illness, and it really points to the need to integrate spirituality as a component of patient-centered health care," she said. "Of course, much further research is needed, but it's worthy research to be done."

EZEKIEL HERSEY COUNCIL

The Ezekiel Hersey Council recognizes those who have created a life income gift, named HMS as a beneficiary of a retirement account or existing donor-advised fund, or included HMS in their will or trust. **Learn more at hms.harvard.edu/EHC.**

EZEKIEL
HERSEY
COUNCIL

EHC SPOTLIGHT: CAROLYN C. COMPTON, MD '77 (CLASS OF 1974), PHD '77



COMPTON SERVED ON THE CLASS OF 1974 REUNION COMMITTEE AND CELEBRATED HER 50TH REUNION IN EARLY JUNE.

"Supporting the next generation of physician-scientists at HMS is now a key piece of my legacy. My own experience as a student at HMS, coupled with my lifetime career, informed my bequest gift. I hope to help pave the way for students who come after me, and who also hope to make transformative change in medicine."

COLLABORATIONS DRIVE NEUROSCIENCE RESEARCH

➔ Several scientists in the Blavatnik Institute at Harvard Medical School are using recent grants from the Simons Foundation to propel forward the frontiers of autism and neuroscience research.

Steven A. McCarroll, PhD, the Dorothy and Milton Flier Professor of Biomedical Science and Genetics, is seeking to identify aging-associated changes in gene expression in the human brain as part of a larger collaboration spanning eight research groups and focused on two well-defined aims: to pinpoint, across a diverse array of organisms, changes in gene expression within individual cells that occur during aging, and to identify targets for interventions aimed at affecting brain function, from the cellular level to cognition.

Sandeep Robert “Bob” Datta, MD '04, PhD '04, a professor of neurobiology, and Bernardo Sabatini, BS '91, MD '99, PhD '99, the Alice and Rodman W. Moorhead III Professor of Neurobiology, are working in collaboration with two other labs toward discovering how the neural circuits that support learning, attention, and decision-making evolve with age and how these changes contribute to age-related shifts in behavior. They hypothesize that many age-related differences in behavior and learning capacity arise not from neurodegeneration but from active remodeling of neural circuits. To test this hypothesis, they are tracking age-related changes in mice from gene expression to complex behavior.

The projects described above are part of the Simons Collaboration on Plasticity and the Aging Brain (SCPAB). This program aims to understand the changes in the brain that unfold throughout

“OUR RESEARCH WILL CHART THE MOLECULAR AND NEURONAL UNDERPINNINGS OF GUT-BRAIN COMMUNICATION IN NEUROTYPICAL INDIVIDUALS AND IN THOSE WITH AUTISM, MAKING PROGRESS TOWARD DEVELOPING DIAGNOSTIC AND THERAPEUTIC STRATEGIES TARGETING THE GUT-BRAIN AXIS.”

MARITO HAYASHI

normal aging and contribute to poorer memory and other age-related cognitive decline. SCPAB and other Simons Foundation collaborations bring together groups of scientists to address topics of fundamental scientific importance in which a significant new development has created a novel area for exploration in an established field.

Another such program is the Simons Collaboration on the Global Brain (SCGB), which aims to better understand the role of internal brain processes in the arc from sensation to action, thereby discovering the nature, role, and mechanisms of the neural activity that produces cognition. Working with two other labs, Datta and Sabatini are continuing an SCGB project in which they will use new technology to automatically track a mouse's movements and body position as it forages around its cage and performs tasks. At the same time, they will monitor the activity of a brain region called the striatum, which is involved in rewards, movements, and cognition.

Marito Hayashi, PhD, is using a SFARI Bridge to Independence Award to pursue his postdoctoral research on gut-brain communication and sensory processing in autism. (SFARI stands for Simons Foundation Autism Research Initiative.) The Bridge to Independence Award enables early-career scientists from diverse backgrounds to pursue autism research and facilitates their transition into independent faculty positions at research institutions.

“When completed, our research will chart the molecular and neuronal underpinnings of gut-brain communication in neurotypical individuals and in those with autism, making progress toward developing diagnostic and therapeutic strategies targeting the gut-brain axis,” says Hayashi, a postdoctoral fellow in the lab of cell biology professor Stephen Liberles, AB '94, AM '96, PhD '00.

THIS CROSS SECTION OF INTESTINAL TISSUE SHOWS INTESTINAL SENSORY CELLS (YELLOW) THAT DETECT NUTRIENTS AND TOXINS AND RELEASE HORMONES LIKE SEROTONIN AND GLP 1; NEURONAL FIBERS (CYAN); BLOOD VESSELS (MAGENTA); AND A COUNTERSTAIN OF INTESTINAL TISSUE (BLUE).

IMAGE: MARITO HAYASHI



FACES OF HMS

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01 The HMS Center for Primary Care launched the Junior HealthTech Fellowship program in 2021 to foster diversity among students entering STEM fields. The program teaches participants—11th-grade students at Brooke High School, a Boston public charter school—to solve health care problems using a framework known as biodesign that was developed at Stanford University. The students (pictured are members of the 2022–23 cohort) spend seven months learning under the guidance of HMS HealthTech Fellows—health care professionals with a background in health care, engineering, and business who are also training in biodesign.

02 On Jan. 18 at HMS, the Center for Primary Care (CPC) sponsored a forum titled “Leadership and Health Care Transformation in Medically Underserved Communities,” featuring keynote speaker Bill Anoatubby (left), governor of the Chickasaw Nation, who discussed how his leadership shaped the health care transformation of the Chickasaw Nation. The event included a panel discussion moderated by David Duong, MD '15 (right), director of the Program in Global Primary Care and Social Change, which is part of the CPC.

03 American Medical Association President Jesse M. Ehrenfeld, MD, MPH (second from right), delivered the Class of 1958 Commemorative Lecture on March 15 at the Tosteson Medical Education Center. Flanking him, from left, are Jules Dienstag, MD, the Carl W. Walter Professor of Medicine at HMS; Fidencio Saldaña, MD '01, MPH '05, dean for students at HMS;

and Howard A. Corwin, AB '54, MD '58. Corwin and his classmates established the annual lecture in honor of their 50th Reunion as a gift to the graduating class to reinforce the idealism, humanism, and nobility of medicine.

04 Steven E. Hyman, MD '80, a core institute member of the Broad Institute of MIT and Harvard and director of the Broad's Stanley Center for Psychiatric Research, presents the 101st George W. Gay Lecture in Medical Ethics on Nov. 2 in the Tosteson Medical Education Center. His keynote speech was titled “The Ethical Conundrum of Medicalizing Self-Control: An Examination of Addiction, Obesity, and ADHD.” The HMS Center for Bioethics, led by Rebecca Weintraub Brendel, MD, JD, hosts the annual lecture, which was established in 1917 by a gift from George Washington Gay, MD 1868.

05 Peter Lee, PhD, corporate vice president of research and incubations at Microsoft and co-author of “The AI Revolution in Medicine: GPT-4 and Beyond,” delivers the Kantoff-Sang Dean's Lecture on Dec. 18 in the Tosteson Medical Education Center. Curated by HMS Dean George Q. Daley, AB '82, MD '91, PhD, this annual lecture features prominent guest speakers discussing their fields of expertise. Mark S. Hughes, AB '82, MD '86, and Delia N. Sang, AB '71, MD, established the endowed lectureship in honor of Philip Kantoff, MD, and in memory of Delia's father, Heng-Kang Sang, AM '46, PhD '47, who was a patient of Kantoff's.

06 Eden Sayed, a Gordon Doctoral Fellow who is pursuing a dual PhD in neurobiology and philosophy at Harvard University, and Saloni Sharma, PhD, a Gordon Postdoctoral Fellow conducting research in the Department of Neurobiology in the Blavatnik Institute at HMS, presented their research findings Jan. 26 at the ninth annual research day for the Ellen R. and Melvin J. Gordon Center for the Cure and Treatment of Paralysis at Spaulding Rehabilitation Hospital and Harvard Medical School.

07 Laura L. Adams (center), a senior adviser at the National Academy of Medicine, explored the hope, hype, promise, and peril of artificial intelligence in health care during her keynote speech at the Gilbert S. Omenn Lecture on Nov. 1. Hosted by the HMS Department of Biomedical Informatics (DBMI), the annual lecture is made possible through the generosity of Gilbert S. Omenn, MD '65, PhD (right), who was central to the formation of the department. At left is Isaac Kohane, MD, PhD, the Marion V. Nelson Professor and chair of DBMI.

08 More than 600 people—MD students, loved ones, and HMS faculty and staff—gathered on the HMS campus March 15 for Match Day, when graduating MD students find out where they will do their clinical training, launching their careers as physicians. For details about where the students matched, read the full story at tinyurl.com/HMSmatchday24.

PEARCE FOUNDATION PROPELS MYASTHENIA GRAVIS PROJECT

➔ In 2017, M. Lee Pearce, MD (pictured), a longtime Harvard Medical School benefactor and member of the HMS Board of Fellows, committed \$500,000 to HMS to create a research fund that he hoped would ultimately help those suffering from myasthenia gravis (MG), a chronic autoimmune neuromuscular disease characterized by weakness in the skeletal muscles.

Pearce's gift supported the research and development of nanoparticle-based therapies for MG under the direction of Arlene Sharpe, AB '75, AM '76, PhD '81, MD '82, Kolokotronis

University Professor and chair of the Department of Immunology in the Blavatnik Institute at HMS, and Francisco Javier Quintana, PhD, a professor of neurology at Brigham and Women's Hospital.

Sadly, Pearce would die in October 2017, but The Dr. M. Lee Pearce Foundation, entrusted with carrying on its founder's philanthropic legacy, was encouraged by the success of this collaborative project and recently gave \$300,000 to establish the Dr. M. Lee Pearce Foundation Fund for Myasthenia Gravis Research at HMS.

"The myasthenia gravis research proposal is a great match for the Pearce Foundation's goal of improving patient care and quality of life," says Michael A. Carpenter, president and chairman of the board of the Pearce Foundation.

Sharpe and Quintana will continue collaborating toward developing a platform for personalized approaches to treat MG and other autoimmune diseases. "We are incredibly grateful for this gift," says Sharpe. "Our goal is to use this platform to suppress pathogenic antibody responses in patients with MG."

Their approach involves designing groundbreaking messenger RNA (mRNA) vaccines that target the aryl hydrocarbon receptor. The ultimate objective is to induce immune system tolerance to specific antigens, thereby alleviating autoimmune reactions associated with conditions like MG.

The Dr. M. Lee Pearce Foundation has upheld Pearce's philanthropic values since his death, focusing on patient-centric care and on closing the gap between health span and life span. Its philanthropic dedication to HMS has helped to alleviate suffering for patients globally and thus is a meaningful testament to Dr. Pearce's legacy.



A 3D ILLUSTRATION OF
AN MRNA MOLECULE

MASTER'S ALUMNI IMPART WISDOM TO STUDENTS



➔ More than 150 Harvard Medical School master's students, alumni, faculty, and staff gathered in person at the Inn at Longwood Medical or joined online from around the world April 5 for the 10th annual HMS Master's Program Symposium, which featured research presentations and a virtual poster session.

Dean for Graduate Education Rosalind Segal, AB '79, MD, PhD, told attendees in her welcome remarks that presenters from all nine HMS master's degree programs would touch on "exciting areas in the medical and natural sciences as they share the progress they've made on the most pressing issues in their fields."

In a first, HMS master's program alumni held a panel session to share their post-graduation experiences and insights with current students. Alumni panelists spoke about memorable moments at HMS, how the skills they learned in their degree programs apply to their careers, and how they get through difficult days.

"One thing I appreciate about these programs is their targeted skills acquisition," said panelist Mark Murakami, MD, MMSc '16, who earned his master's in biomedical informatics and is now an HMS assistant professor of medicine at Dana-Farber Cancer Institute.

Harvard University has approved two new master's programs at HMS—one in therapeutics and one in clinical research—that will have their first cohorts of students starting in fall 2025.

A hematologist-oncologist, Murakami said he did not have any informatics skills when he entered, but during his first year in the program he and a classmate published a paper that had practical use and led to dozens of interactions with other investigators. That kind of practical learning, combined with the networking provided through the programs, creates transformative change, he said.

AT THE HMS MASTER'S PROGRAM SYMPOSIUM IN APRIL, SUSANA ORREGO VILLEGAS AND CONSTANTINE PSIMOPOULOS (BOTTOM PHOTO) WERE AMONG THE ALUMNI PANELISTS WHO SHARED INSIGHTS WITH MASTER'S STUDENTS, INCLUDING (TOP PHOTO, FROM LEFT) IBRAHIM GASSAMA, BRIGHT MAILOSI, CLAUDIA BEJARANO ZAMBRANO, AND HANSEL MUNDACA HURTADO.

"It's really great to have the alumni back," said Evan Walsh, career adviser for HMS graduate education. "What resonated with me most was that they all expressed resilience, connection, and community as three things that came out of their experience at HMS."

SNAPSHOTS EVENT EXPLORES THE STUDENT EXPERIENCE AT HMS

➔ Yoseph Boku, AB '21, MD Class of 2025, said that when he entered Harvard Medical School immediately after graduating from Harvard College, he was still in "the pre-medical mindset" of being constantly stressed and worried about grades.

"But I was rather surprised that it ended up being a lot more collaborative (at HMS)," he said. "There was less of a focus on grades and more of a focus on learning—and learning with each other. That was really helpful for me (and) allowed me to explore other interests."

Boku shared this observation Dec. 6 during Snapshots: A Portrait of Today's Students. This virtual event offered attendees an opportunity to gain insights into the current student experience and learn more about the School's innovations in teaching and learning.

Dean for Medical Education Bernard S. Chang, AB '93, MD, MMSc '05 (far left), moderated the discussion by the student panel, which featured (left to right) MD-PhD candidate Logan Beyer; Yoseph Boku; Lois Owolabi, MD Class of 2025; and Tonatiuh Liévano Beltrán, SB '14, MD '24.



ALBRIGHT SYMPOSIUM FOCUSES ON INNOVATIVE APPROACHES TO SURGICAL CARE

➔ HMS Dean George Q. Daley, AB '82, MD '91, PhD, told attendees of the 2024 virtual Hollis L. Albright, MD '31 Symposium that curtailing rates of maternal morbidity and mortality on a global scale is a public health imperative.



“Although pregnancy and childbirth are among the most elemental of biological functions, they come with serious risks, and that’s where Bethany’s and Adeline’s efforts are so vital,” said Daley, referencing the March 26 event’s featured speakers, Bethany Hedt-Gauthier, SM '05, PhD '08 (top), an associate professor of global health and social medicine at HMS, and Adeline Boatin, AB '04, MPH '09, MD (bottom), an HMS assistant professor of obstetrics, gynecology, and reproductive biology at Massachusetts General Hospital.



Hedt-Gauthier and Boatin, who are co-directors of research for the HMS Program in Global Surgery and Social Change, presented two case studies showing how digital technology—for example, a wireless monitor worn for 24 hours after an emergency cesarean section that alerts clinicians to abnormal vital sign readings—can overcome some of the resource and system challenges affecting surgical health care in low- and middle-income countries. Both cases were centered around C-sections, which are the most common surgical procedure performed among women worldwide.

“Across these two studies, we’ve demonstrated that digitally supported community health workers can feasibly follow women at their home, and that this type of care is acceptable both to the community health workers and to the women who are receiving care,” Hedt-Gauthier said.

Tarika Srinivasan, MD Class of 2025, was recognized during the symposium as the recipient of the 2024 Albright Scholar Award for her demonstrated excellence in the surgical sciences. After graduation, Srinivasan, who is also working toward a Master of Medical Sciences degree in global health delivery, plans to pursue surgical training in otolaryngology.

Former Albright Scholar Award recipient Coleen S. Sabatini, MD '04, MPH '04, now a professor and vice chair of orthopedic surgery at the University of California San Francisco, also spoke during the symposium. She reflected on the impact of her Harvard Medical School education and expressed how grateful she was to receive the Albright Award in 2003.

Tenley E. Albright, MD '61, delivered the symposium’s opening remarks. She and her brother, Nile L. Albright, AB '61, MD, established the endowed symposium at HMS in memory of their father, who devoted his life to surgery, patient care, and student mentorship.

POUSSAINT LECTURER TALKS TRIBAL HEALTH CARE

➔ “Make no mistake, this promise is broken,” keynote speaker Yvette Roubideaux, AB '85, MD '89, MPH '97, told attendees of the 20th annual Alvin F. Poussaint, MD Visiting Lecture, which was held March 28 on the Harvard Medical School campus.

She was referring to the federal government’s promise to provide certain services and benefits to American Indian and Alaska Native tribal nations, including health care. “This responsibility is in exchange for the lands that were lost for my people and the ways of life that were lost,” said Roubideaux, who is American Indian.

She stressed that American Indians and Alaska Natives still overall suffer many significant health, social, and economic disparities. “There is still so much for the government to do to live up to that promise.”

Roubideaux is a member of the Rosebud Sioux Tribe and is descended from the Standing Rock Sioux Tribe. An adjunct professor in the Department of Health Systems, Management and Policy at the Colorado School of Public Health, she previously served as director of the Policy Research Center at the National Congress of American Indians, where she conducted and translated policy research and data to improve outcomes for American Indian and Alaska Native tribal nations. She is also the former director of the Indian Health Service, an agency within the U.S. Department of Health and Human Services.

The lectureship fund was established in 2004 with a gift from HMS alumni to honor Poussaint, who delivered the inaugural lecture in 2005. He retired in 2019 after a half-century of service to the School, most recently as director of the Office of Recruitment and Multicultural Affairs.



YVETTE ROUBIDEAUX (RIGHT)
WITH HMS DEAN FOR DIVERSITY
AND COMMUNITY PARTNERSHIP
JOAN Y. REEDE

IN BRIEF

The following grants totaling \$250,000 or more were awarded to members of the Harvard Medical School community in support of their work to alleviate suffering and improve health and well-being for all.



The **Chan Zuckerberg Initiative** has awarded Marinka Zitnik, PhD, an assistant professor of biomedical informatics in the Blavatnik Institute at HMS, \$930,000 to

develop foundation artificial intelligence models to support research on new therapies for diseases with significant unmet needs. Zitnik's lab is tackling three projects with this funding: "All-Disease Drug Repurposing Benchmark: Creating a Virtuous Circle of Discovery and AI Innovation," "Augmenting Cell Census to Support Single-Cell Research on New Therapies," and "Single-Cell AI Engine for Rare Disease Diagnosis and Treatment."

Over the past several years, the **Leon Lowenstein**

Foundation has invested in building the capacity of mobile health care, which plays a crucial role in reducing racial and ethnic health disparities. Mobile clinics not only deliver health care to marginalized populations (e.g., immigrants, people experiencing homelessness, and rural residents) but also connect patients with essential resources. The foundation recently extended its support for the Mobile Health Map, a collaborative research network that works with researchers and front-line mobile clinic staff to evaluate and improve the work of mobile clinics. Mollie M. Williams, DrPH, MPH, executive director of The Family Van and the Mobile Health Map—both programs of HMS—will use a two-year grant in the amount of \$850,000 to demonstrate and effectively communicate the health and economic benefits of high-quality mobile health care in underserved urban and rural communities.



The **Glenn Foundation for Medical Research** has given an additional \$800,000 to the Paul F. Glenn Center for Biology of Aging Research at HMS, increasing its total support for the center to \$54 million since the center's launch in 2018. The leaders of the center's four labs study the basic biology of aging in hopes of developing interventions to extend the healthy years of a person's life.



Two scientists in the Blavatnik Institute at HMS have received Odyssey Awards from the **Richard and Susan Smith Family Foundation**. These awards fund high-risk, high-reward pilot projects to drive innovation and creativity. Alan Brown, PhD (left), an associate

professor of biological chemistry and molecular pharmacology, and Ruaidhrí Jackson, PhD (below, left), an assistant professor of immunology, will each get \$400,000 over two years. Brown will study whether liquid-like biomolecular condensates have a structured core. Biomolecular condensates are reportedly involved in almost all biological processes but are shrouded in mystery



and remain controversial due to a lack of direct visualization using high-resolution methods. Jackson aims to illuminate the functionality of a novel class of mRNAs in innate immunity and uncover the general principles and molecular mechanisms underpinning interchromosomal RNA chimerism in mammals. This work could uncover an unknown mechanism of gene regulation with potentially far-reaching implications for transcriptome/proteome annotation and gene functionality in all human diseases.

Jonathan Abraham, AB '05, PhD '10, MD '12, an associate professor of microbiology in the Blavatnik Institute at HMS, is using a \$700,000 grant from the **G. Harold & Leila Y.**



Mathers Charitable Foundation to test whether the ability of eastern equine encephalitis virus and western equine encephalitis virus to attach to three particular cellular receptors explains the ability to cause severe brain infections. This work could inspire the development of drugs that block alphavirus interactions with receptors and thus help meet an urgent need for antivirals against these emerging pathogens in humans.



The **Nancy Lurie Marks Family Foundation** has awarded a renewal grant to Bernardo Sabatini, BS '91, MD '99, PhD '99, the Alice and Rodman W. Moorhead III Professor of Neurobiology in the Blavatnik Institute at HMS, to continue a collaborative autism research project with Massachusetts Eye and Ear researchers Daniel Polley, PhD, and Anne Takesian, PhD, both of whom also received renewal grants. The three labs are examining the neural circuits by which normal sensory experiences lead to abnormal motor action—think of the hypersensitivity and repetitive motor actions of individuals with autism.

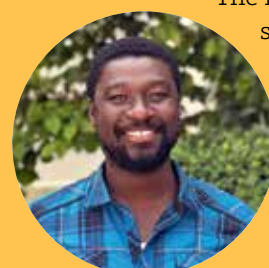


The **Charles A. King Trust** has awarded more than \$400,000 to two research fellows in the Blavatnik Institute at HMS. Sven Lange, PhD (left), who is based in the Department of Biological Chemistry

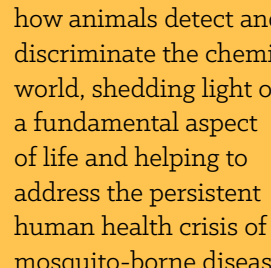
and Molecular Pharmacology, will use a grant of \$201,800 to uncover the fundamental principles of how receptors are moved out of cilia. Disruption of this removal process can lead to serious diseases, including blindness or cognitive impairments. Rudolf Pisa, PhD (right), who's based in the Department of Cell Biology, is using his award of \$201,800 to investigate how the machinery responsible for misfolded protein degradation recognizes and handles its substrates. This work will provide insights into an important cellular process and could aid in the design of new therapeutic approaches for degradation of disease-causing proteins.



James Osei-Owusu, PhD, a research fellow in biological chemistry and molecular pharmacology in the Blavatnik Institute at HMS, has been selected as a Hanna Gray Fellow by the **Howard Hughes Medical Institute**. Osei-Owusu will receive \$400,000 over four years to support his efforts to elucidate the molecular mechanism of relaxin family peptide receptor 1 (RXFP1) signaling by determining the inactive-state structure of RXFP1.



The insight from these structural studies will facilitate the rational design of RXFP1-targeted therapeutics. RXFP1 has emerged as an important drug target for cardiovascular diseases and reproductive cancers.



Josefina del Mármol, PhD, an assistant professor of biological chemistry and molecular pharmacology in the Blavatnik Institute at HMS, is utilizing a \$300,000 grant from **Pew Charitable Trusts** to study the olfactory system of a mosquito species that transmits deadly diseases that infect millions of people every year and disproportionately impact the developing world. This work will substantially expand our understanding of how animals detect and discriminate the chemical world, shedding light on a fundamental aspect of life and helping to address the persistent human health crisis of mosquito-borne diseases.



PROFESSORSHIP CELEBRATIONS

The following newly established Harvard Medical School professorships were recently celebrated, recognizing the generosity of their respective benefactors and the accomplishments of their inaugural incumbents.



01

SELTZER PROFESSORSHIP IN RADIOLOGY

Steven E. Seltzer, MD (left), chair emeritus of the Department of Radiology at Brigham and Women's Hospital (BWH), and Marcelo F. Di Carli, MD, enjoy a celebration held Oct. 25 at Gordon Hall to mark Di Carli's appointment as the inaugural Steven E. Seltzer, MD, Professor of Radiology at BWH.



02

CHEAH PROFESSORSHIP OF GLOBAL HEALTH

Jeffrey Cheah, the founder and chairman of the Sunway Group, and Mercedes C. Becerra, AB '91, SM '93, SD '99, share a laugh Oct. 25 at Gordon Hall, where Becerra was honored for her appointment as the inaugural Jeffrey Cheah Professor of Global Health and Social Medicine at HMS.



03

KAUL PROFESSORSHIP OF BIOMEDICAL INNOVATION AND TRANSLATION

Samir Kaul, MBA '02 (right), a founding partner and managing director at Khosla Ventures, joins Mark Namchuk, PhD, on Oct. 30 at the Four Seasons Hotel Boston, where Namchuk was celebrated as the inaugural Puja and Samir Kaul Professor of Biomedical Innovation and Translation at HMS.



04

DONOVAN-CHIEN FAMILY PROFESSORSHIP

Megan Kate Donovan-Chien (center) and Kenneth Randall Chien, AB '73, MD, PhD, celebrate with Sabine Wilhelm, PhD, of Massachusetts General Hospital on April 24 at the Harvard Club of Boston, where Wilhelm was recognized as the inaugural Donovan-Chien Family Professor in the Field of Psychology at HMS.



05

LANCER PROFESSORSHIP OF DERMATOLOGY

Harold Lancer, MD (right), joins David E. Fisher, MD, PhD, in front of Gordon Hall on April 1, when Fisher was celebrated as the inaugural Lancer Professor of Dermatology at Massachusetts General Hospital.



06

FARMER PROFESSORSHIP AND CHAIR

Vikram Patel, MBBS, MSc, PhD, enjoys a celebration at Gordon Hall on April 16, when he was honored as the inaugural incumbent of the Paul Farmer Professorship and Chair of Global Health and Social Medicine at HMS.



07

MANNICK PROFESSORSHIP OF SURGERY

Michael Belkin, MD, delights in a gathering held in his honor Nov. 1 at the Harvard Club of Boston, where he was recognized as the inaugural John Anthony Mannick, MD Professor of Surgery at Brigham and Women's Hospital.



Q&A WITH JOAN BRUGGE

We sat down with Joan Brugge, PhD, the Louise Foote Pfeiffer Professor of Cell Biology in the Blavatnik Institute at Harvard Medical School and co-director of the Ludwig Center at HMS, to discuss some of her lab’s cancer research.

01
Your lab investigates the mechanisms of cancer initiation, progression, and drug resistance. What goals do you set for this research?

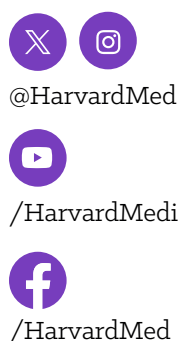
As you can imagine, we set goals based on different time scales. Each project has a set of near-term, intermediate, and long-term goals. The lofty ambitions motivating me and my lab in the long term are centered around a cancer initiation project and a drug resistance project. For the former, we aim to identify cells that serve as the earliest precursors of breast cancer and identify strategies to track these cells in BRCA1/2 mutation carriers and to eliminate them before they progress to cancer. For the latter, we aim to identify therapeutic strategies to kill ovarian cancer tumor cells that initially survive chemotherapy in order to prevent their relapse.

02
You've been a cell biology professor at HMS for more than 25 years—10 of those as chair of the department. In that time frame, which technological advances have had the greatest impact on your lab's cancer research?

Far and away, the most significant technological advances have been in RNA and DNA sequencing of single cells. These advances have transformed our research programs in ways that we would not have imagined 10 years ago and have led to new insights that change the way we think about cancer initiation and resistance.

03
Looking ahead to the next 25 years, which areas of cancer research inspire and excite you? What are your lab's future priorities?

If only I could be alive in 25 years to take advantage of the advances in cancer research that will be available then! I think that information being derived now from spatial and molecular profiling of tumors will significantly enhance the ability of machine learning to predict treatment outcomes of cancer therapeutics. Hand in hand will be advances in the development of drugs that inhibit a broader range of cancer targets and of combinations that more effectively treat cancers.



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COLLABORATIONS PROPEL
NEUROSCIENCE RESEARCH

08

CELEBRATING THE HEART AND IMPACT OF THE HMS COMMUNITY

PULSE

SPRING 24

NOBEL WINNER DOUDNA DELIVERS DUNHAM LECTURES

Jennifer A. Doudna, PhD '89, the Li Ka Shing Chancellor's Chair in Biomedical and Health Sciences at the University of California, Berkeley, discussed genome editing as the featured speaker at the Edward K. Dunham Lectureship, which brought huge crowds to the Joseph B. Martin Conference Center at HMS on April 10 and 11. This prestigious lectureship was established in 1923 by Mary Dows Dunham in honor of her late husband, Edward Kellogg Dunham, MD 1886, to strengthen the bonds of fellowship and understanding among students, investigators, and faculty within the medical and basic sciences for the purpose of advancing medical science in the broadest sense. Doudna shared the 2020 Nobel Prize in Chemistry with Emmanuelle Charpentier for their discovery of one of gene technology's sharpest tools: the CRISPR/Cas9 genetic scissors.

