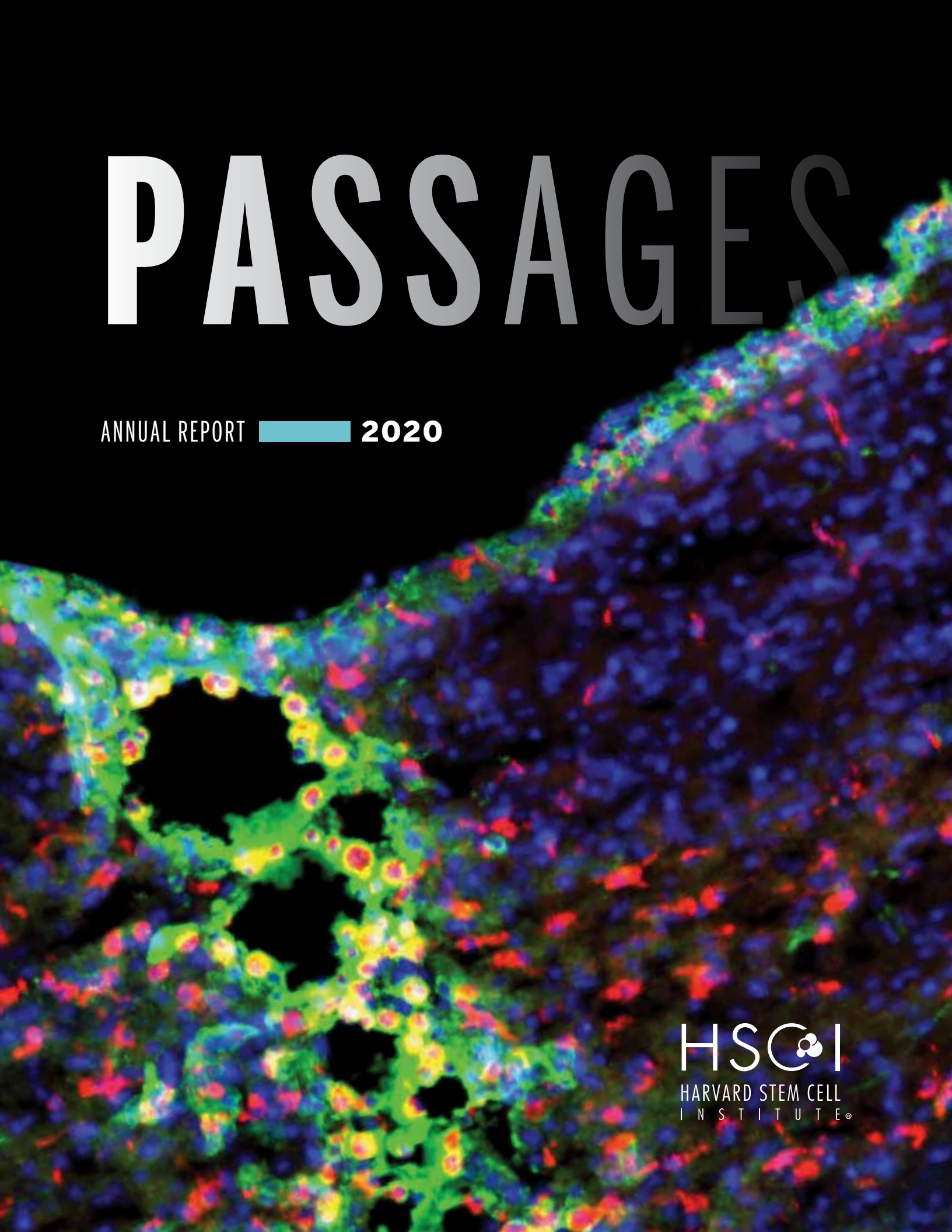
PASSAGES

ANNUAL REPORT 2020



HSCI
HARVARD STEM CELL INSTITUTE®

MESSAGE FROM

DOUGLAS MELTON, PH.D.

At the Harvard Stem Cell Institute, time and timing are a key aspect of both our science and our approach for bringing discoveries to patients. Stem cells are crucial to the early stages of the body's developmental processes, with the potential to become many different types of cells. As a result, they can teach us how to turn back the clock and regenerate tissues that are damaged by disease. But these passages through time are just the beginning: transforming the promise of stem cells into cures for patients requires bold, innovative thinking, so we support our researchers' promising ideas at the earliest stages when they would not otherwise be funded by more traditional sources.

In 2020, the power of our approach became clear when the novel coronavirus pandemic demanded urgent solutions. Over a decade ago, HSCI funded an early project investigating how to deliver mRNA into cells, with the goal of reprogramming them into an earlier stem cell state. That discovery ultimately led to the creation of the biotechnology company Moderna, which adapted the approach for therapeutics and was able to develop a coronavirus vaccine in record time. With the support of our donors, HSCI will continue to make such early investments to enable the next generation of transformative therapies.

We are proud that during the pandemic, HSCI scientists quickly adapted their research and applied their expertise to tackle the coronavirus. Our researchers originally developed lung organoids — miniature 3D cell cultures — to study diseases such as cancer, but

DAVID SCADDEN, M.D.

THE DIRECTORS

are now using them to model coronavirus infection and rapidly screen potential drugs. HSCI researchers have also been part of an effort to catalog every cell type in the lung, and were able to mine the preexisting data to find exactly which cells are targeted by the virus.

Beyond these important contributions, HSCI researchers continued the momentum we have built over our 16 years and made advances in many areas. For instance, we now have better tools than ever before to study how the body develops. When HSCI was first founded, one of our earliest projects involved reprogramming a patient's skin cells to an earlier developmental state, then converting those stem cells into the type of neuron affected by amyotrophic lateral sclerosis (ALS). That reprogramming technology has now come of age, and is used in different cell therapies in the clinic and as the basis for drug discovery.

BROCK REEVE, M.PHIL., M.B.A.

But even as we refine these therapies, HSCI researchers are studying development in ever more detail to fuel the next wave of medicines. For example, recent advances in DNA sequencing technology enable us to track how the physical structure of each chromosome in an individual cell changes over time.

Over the years, HSCI scientists have also changed the way we think about disease, by discovering more connections between diseases that were previously considered separate. As the world population ages, we are seeing higher rates of diseases such as cancer and neurodegenerative conditions. HSCI researchers are identifying common links that underlie these diseases of aging, such as a weaker immune system that causes more inflammation, in order to better treat them.

Along with the research showcased in this report, these are just a few highlights of what HSCI accomplished in 2020 and where our passages will take us in the years to come. Our work would not be possible without the support of our donors, and we hope you will join us as we continue to harness the power of stem cells to improve patients' lives.

Sincerely,

Douglas Melton, Ph.D.
Founding Co-Director

David Scadden, M.D.
Founding Co-Director

Brock Reeve, M.Phil., M.B.A.
Executive Director

THE POWER OF THE HSCI NETWORK

The Harvard Stem Cell Institute brings together researchers across Harvard's schools, centers, and hospitals to harness the power of stem cells to cure human disease. Our scientists pursue innovative ideas at their earliest stages, collaborate across disciplines to find solutions, and ultimately translate their discoveries from the lab into the clinic.

EARLY-STAGE RESEARCH

Seed Grants

We support early-stage research that is typically not funded by traditional sources, which has high risk but also high potential for return.

Junior Faculty Programs

Our early-career faculty members work on highly collaborative projects that tackle major challenges.

Barry Family HSCI Innovation Award

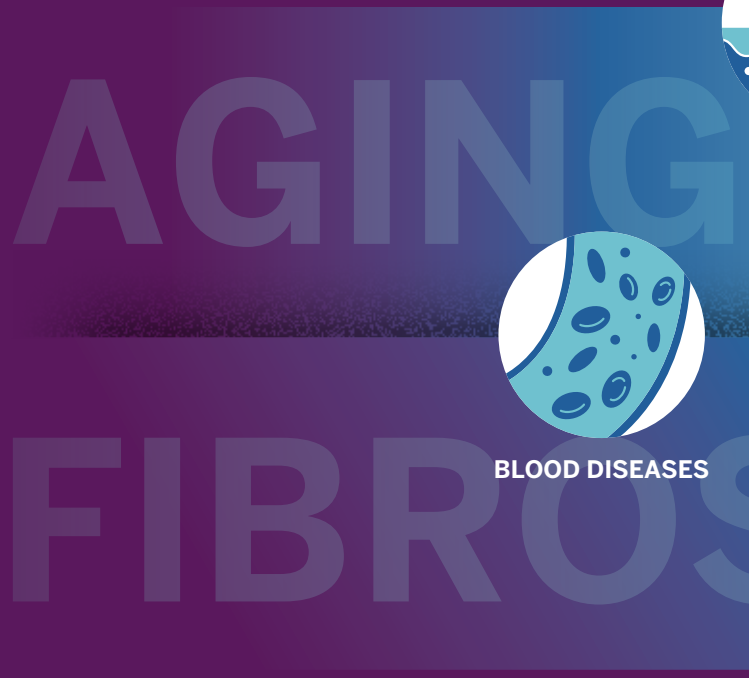
Early-career investigators pursue innovative ideas with the potential to transform the field of stem cell research.

The HSCI Internship Program

We train the next generation of stem cell scientists by giving first-hand research experience to undergraduate students from around the world.

RESEARCH FOCUS

Our scientists channel resources toward some of the most prevalent, devastating diseases for which stem cell research holds promise. They also make advances in research areas that transcend individual disorders and have broad applications across human disease.



CORE FACILITIES

To accelerate stem cell research, our core facilities provide centralized resources and services to HSCI scientists, covering technologies such as induced pluripotent stem cells, bioinformatics, and flow cytometry.

KIDNEY DISEASES

MUSCULOSKELETAL DISEASES

NERVOUS SYSTEM DISEASES

DIABETES

SKIN DISEASES

CARDIOVASCULAR DISEASES

CANCER

TRANSLATION

40+
STARTUP COMPANIES

Commercialization

Our faculty have formed over 40 startup companies to move their discoveries from the lab to market.

Clinical Trials

Our researchers at Harvard teaching hospitals lead clinical trials to find safe and effective treatments for patients.

Industry Collaborations

Our scientists work with biopharmaceutical companies to discover new targets and pathways, and to introduce new approaches that accelerate drug discovery.

14
HARVARD SCHOOLS & RESEARCH HOSPITALS

all within a

4-mile
RADIUS

380+
FACULTY MEMBERS

TARGETING RESISTANT CANCER

Blood cancers like leukemia can be effectively treated with chemotherapy, but relapse usually occurs, due to resistant cancer cells that evade the original drug regimen.

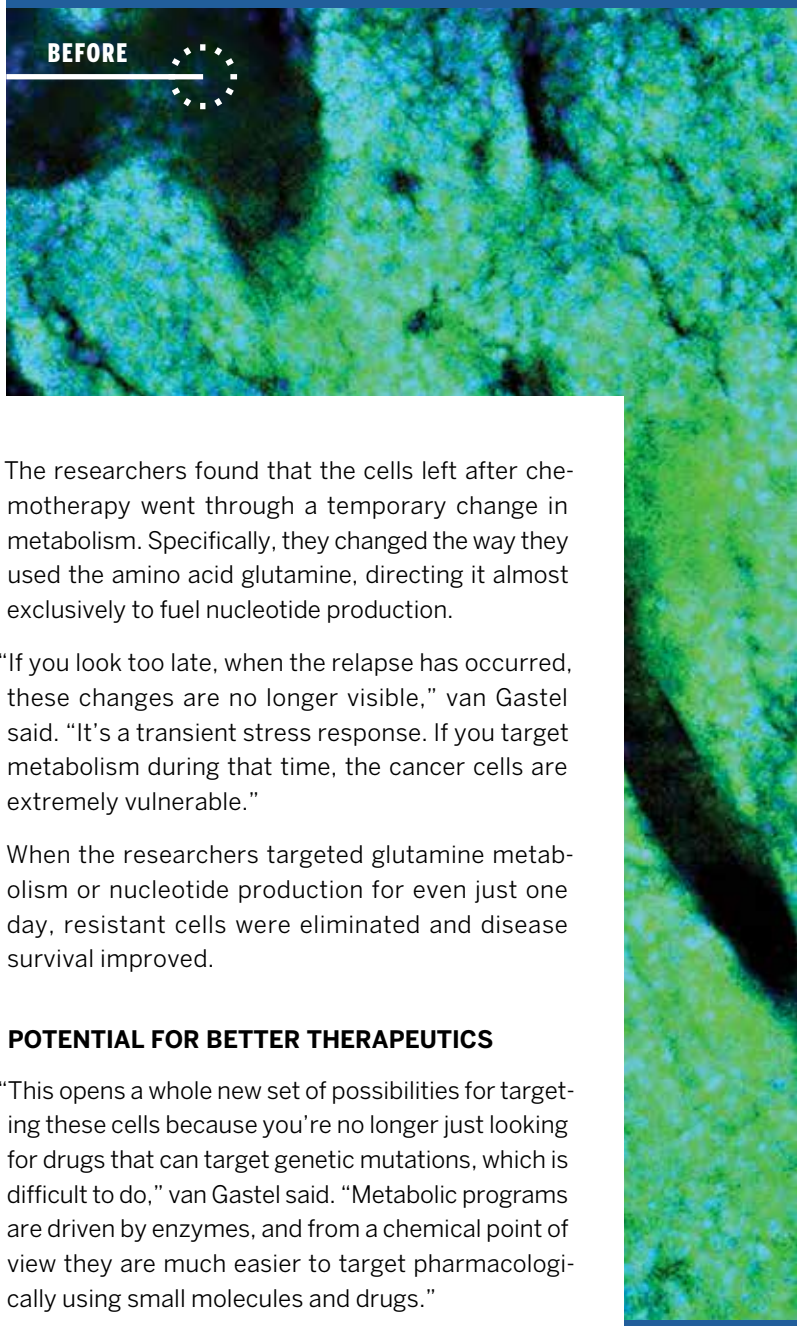
Researchers led by Harvard Stem Cell Institute Co-Director David Scadden, M.D., identified a unique characteristic of resistant cancer cells: a temporary change in metabolism, or how they use nutrients. The findings pave the way for using drugs to target the metabolic pathway at a specific timepoint and eliminate resistant cells.

"In the cancer field, we usually think about resistance as a concept linked to permanent genetic changes. Our findings show that there are other mechanisms contributing to why some cells survive chemotherapy and others do not—the nutrients they have in their microenvironment and how they use them might matter just as much as the genetic background," said Scadden.

TAKING ADVANTAGE OF A TEMPORARY CHANGE

Resistant cancer cells are rare, so they are difficult to detect after chemotherapy. To identify the cells and track their progression over time, the researchers used a mouse model of acute myeloid leukemia and labeled the cells with a bioluminescent protein and a fluorescent protein. The researchers honed in on the cells at two specific timepoints.

"We studied the cells when the cancer relapsed, which is normally the point that resistance is studied, because it is clinically obvious," said first author of the study Nick van Gastel, Ph.D. "But we also isolated the cells at the point of maximal chemotherapy response, which is basically the moment that you have the fewest cells left. Those are the cells that endured the chemotherapy stress and can now cause relapse."



The researchers found that the cells left after chemotherapy went through a temporary change in metabolism. Specifically, they changed the way they used the amino acid glutamine, directing it almost exclusively to fuel nucleotide production.

"If you look too late, when the relapse has occurred, these changes are no longer visible," van Gastel said. "It's a transient stress response. If you target metabolism during that time, the cancer cells are extremely vulnerable."

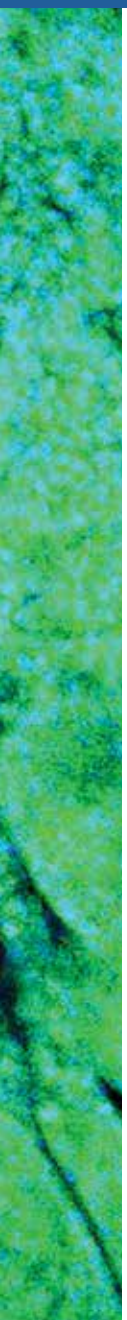
When the researchers targeted glutamine metabolism or nucleotide production for even just one day, resistant cells were eliminated and disease survival improved.

POTENTIAL FOR BETTER THERAPEUTICS

"This opens a whole new set of possibilities for targeting these cells because you're no longer just looking for drugs that can target genetic mutations, which is difficult to do," van Gastel said. "Metabolic programs are driven by enzymes, and from a chemical point of view they are much easier to target pharmacologically using small molecules and drugs."

AT THE **RIGHT TIME**

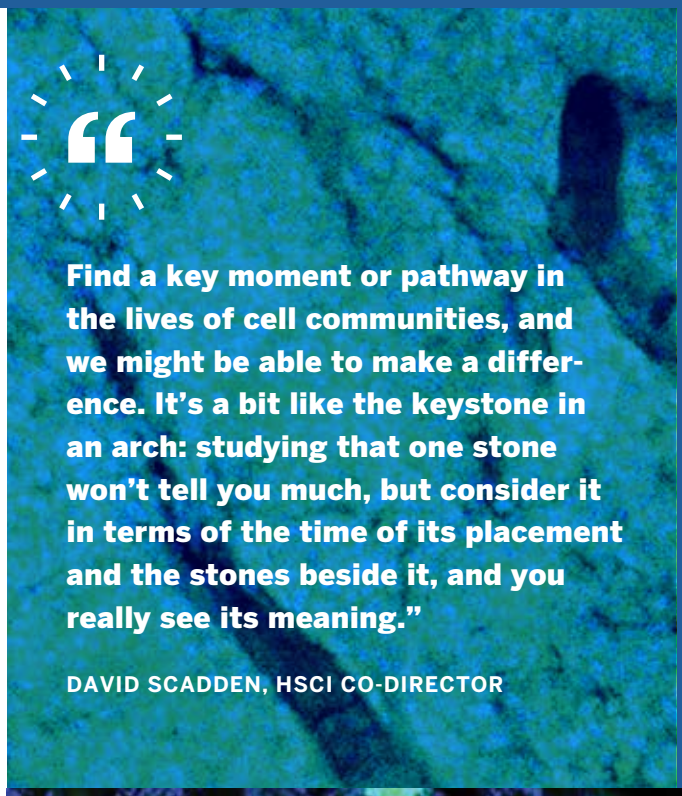
HSCI RESEARCHERS TARGET CHEMOTHERAPY-RESISTANT LEUKEMIA BY USING METABOLISM



Currently, several companies are developing potential drugs that inhibit this metabolic pathway, although not necessarily intended for cancer treatment. The researchers hope that an inhibitor can be repurposed and combined with chemotherapy to improve patient outcomes.

"If you give the inhibitor to patients who have undergone chemotherapy, you might not need to give them this new drug for a very long period. You can really target that exact moment of metabolic change, which might avoid some of the toxicity issues associated with longer term treatments," van Gastel said.

Beyond leukemia, the researchers' approach could have broader applications. Scadden said: "In other types of cancer and diseases, the cells' environment contributes to and often drives the outcome. Viewing these problems in the context of dynamic ecosystems can often lead to new approaches, but it does require moving away from the reductionist view of single genes or single cells. Find a key moment or pathway in the lives of cell communities, and we might be able to make a difference. It's a bit like the keystone in an arch: studying that one stone won't tell you much, but consider it in terms of the time of its placement and the stones beside it, and you really see its meaning."



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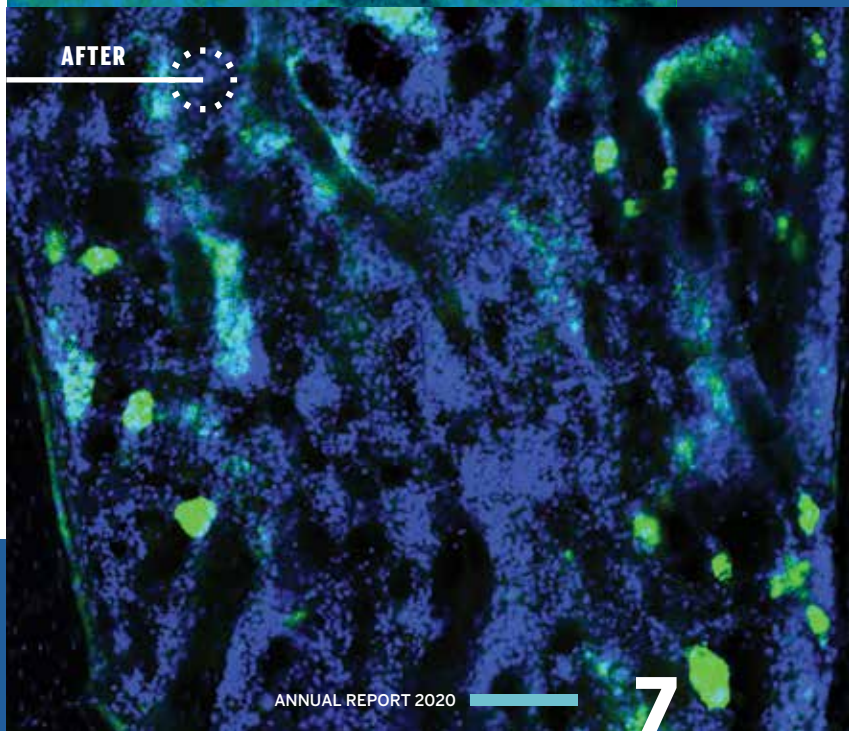
DAVID SCADDEN, HSCI CO-DIRECTOR

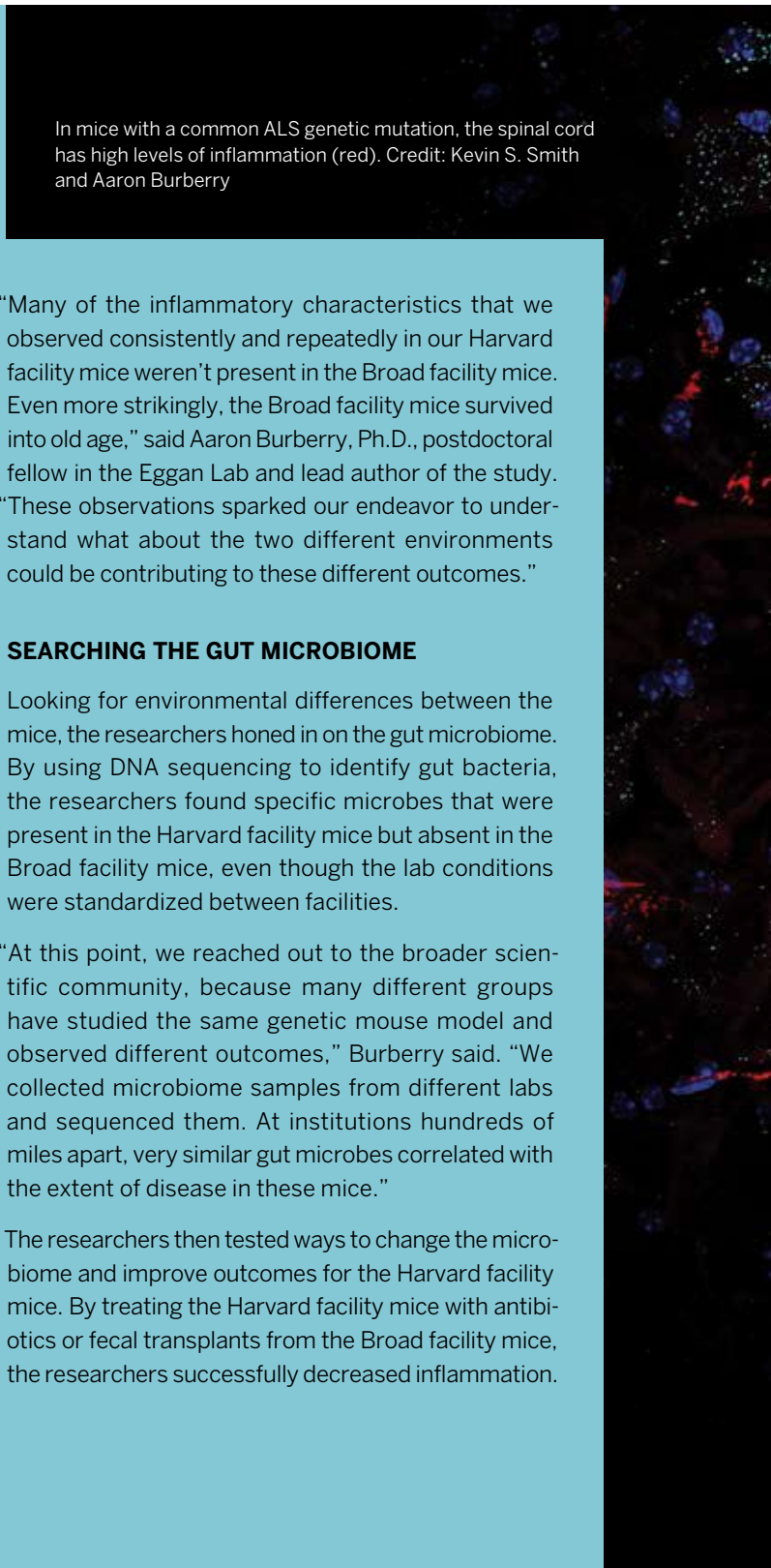


The bone marrow containing acute myeloid leukemia cells (green). After chemotherapy treatment, the resistant cells that remain must be targeted at the right moment.

INVESTIGATING THE GUT-BRAIN

By studying two disease models at the same time, Harvard Stem Cell Institute scientists discovered a new gut-brain connection in amyotrophic lateral sclerosis (ALS), a neurodegenerative disease associated with aging. Led by HSCI Principal Faculty member Kevin Eggan, Ph.D., the researchers found that in mice with a common ALS genetic mutation, changing the gut microbiome using antibiotics or fecal transplants could prevent or improve disease symptoms. Their findings provide a potential explanation for why only some individuals carrying the mutation develop ALS, and point to a possible therapeutic approach based on the microbiome.

"Our study focused on the most commonly mutated gene in patients with ALS. We made the remarkable discovery that the same mouse model — with identical genetics — had substantially different health outcomes at our different lab facilities," Eggan said. "We traced the different outcomes to distinct gut microbial communities in these mice, and now have an intriguing hypothesis for why some individuals carrying this mutation develop ALS while others do not."



In mice with a common ALS genetic mutation, the spinal cord has high levels of inflammation (red). Credit: Kevin S. Smith and Aaron Burberry

DIFFERENT FACILITIES, DIFFERENT OUTCOMES

The researchers initially studied the ALS genetic mutation by developing a mouse model at their Harvard lab facility. The mice had an overactive immune response, including inflammation in the nervous system and the rest of the body, which led to a shortened lifespan.

In order to run more detailed experiments, the researchers also developed the mouse model in their lab facility at the Broad Institute, where Eggan is the director of stem cell biology at the Stanley Center for Psychiatric Research. Unexpectedly, although the mice had the same genetic mutation, their health outcomes were dramatically different.

"Many of the inflammatory characteristics that we observed consistently and repeatedly in our Harvard facility mice weren't present in the Broad facility mice. Even more strikingly, the Broad facility mice survived into old age," said Aaron Burberry, Ph.D., postdoctoral fellow in the Eggan Lab and lead author of the study. "These observations sparked our endeavor to understand what about the two different environments could be contributing to these different outcomes."

SEARCHING THE GUT MICROBIOME

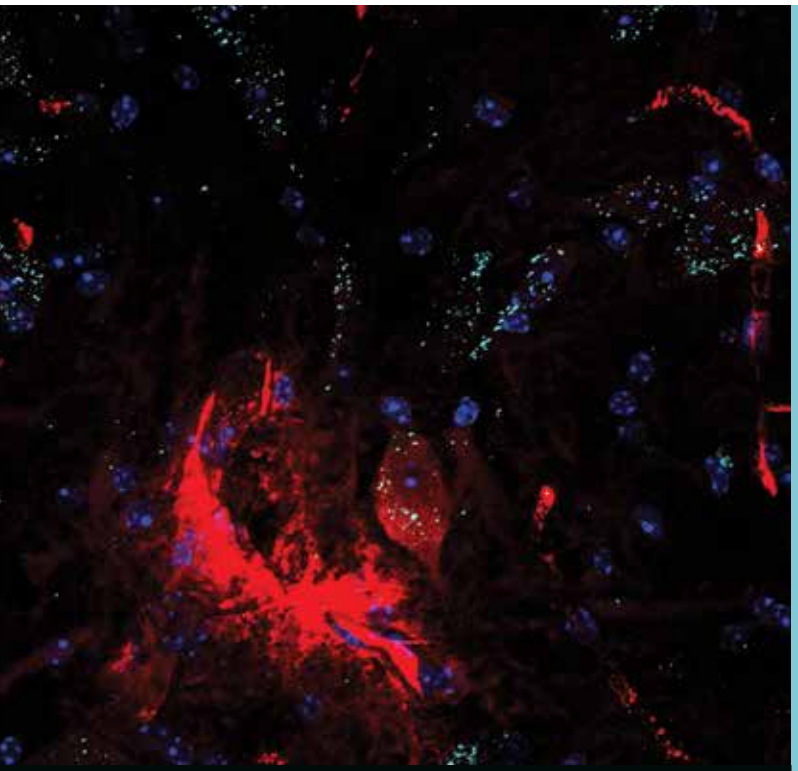
Looking for environmental differences between the mice, the researchers honed in on the gut microbiome. By using DNA sequencing to identify gut bacteria, the researchers found specific microbes that were present in the Harvard facility mice but absent in the Broad facility mice, even though the lab conditions were standardized between facilities.

"At this point, we reached out to the broader scientific community, because many different groups have studied the same genetic mouse model and observed different outcomes," Burberry said. "We collected microbiome samples from different labs and sequenced them. At institutions hundreds of miles apart, very similar gut microbes correlated with the extent of disease in these mice."

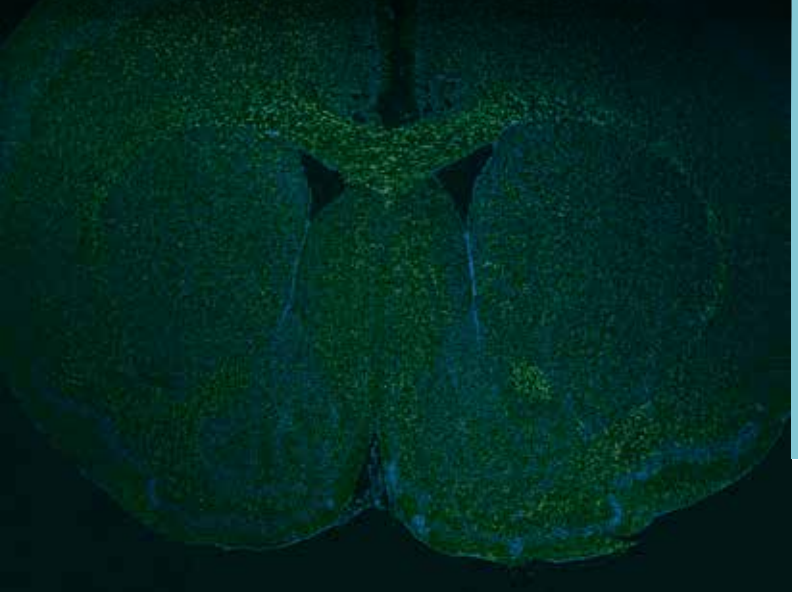
The researchers then tested ways to change the microbiome and improve outcomes for the Harvard facility mice. By treating the Harvard facility mice with antibiotics or fecal transplants from the Broad facility mice, the researchers successfully decreased inflammation.

CONNECTION

HSCI RESEARCHERS STUDY HOW THE GUT MICROBIOME AFFECTS ALS AND THE AGING BRAIN



Cross-section of a mouse brain, with green representing one of the top genes whose expression changes with aging. Credit: Rubin Lab, Harvard University



EXPANDING THE GUT-BRAIN CONNECTION

By examining the connection between genetic and environmental factors in ALS, the researchers identified an important gut-brain connection. The gut microbiome may influence the severity of disease — whether individuals with the genetic mutation develop ALS, the related condition frontotemporal dementia, or no symptoms at all — and could be a potential target for therapy.

"Our study provides new insights into the mechanisms underlying ALS, including how the most common ALS genetic mutation contributes to neural inflammation," Eggan said. "The gut-brain axis has been implicated in a range of neurological conditions, including Parkinson's disease and Alzheimer's disease. Our results add weight to the importance of this connection."

Based on these findings, the researchers will further investigate which specific bacteria in the microbiome are involved, and whether they can be found in patients with ALS. Eggan is also teaming up with HSCI Executive Committee member Lee Rubin, Ph.D., who studies the brain during the healthy aging process.

Rubin has developed tools to track exactly how the brain changes during aging, by looking at whether new neurons and blood vessels are generated, as well as which genes are expressed by each cell type. By applying these approaches in mice with different microbiomes, researchers will be able to understand the gut's influence on the brain and the nervous system; how it changes over time, especially in conditions of inflammation which increase with age; and how it can be managed through controlling the microbiome.

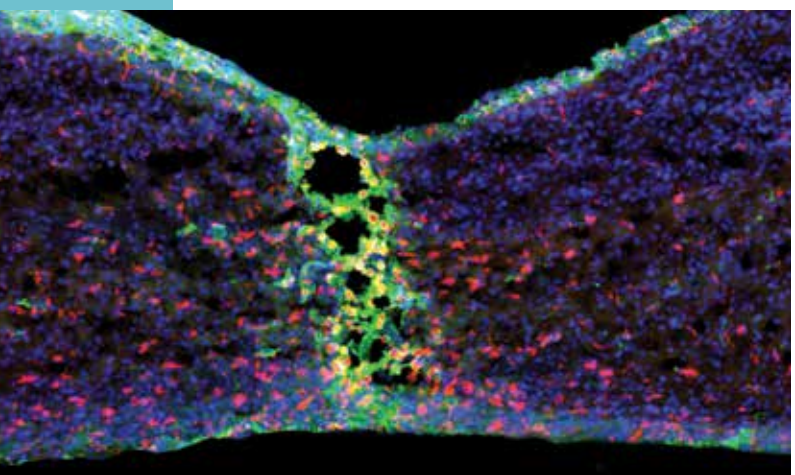
TURNING BACK THE CLOCK

Neurons can regenerate while the body develops, but rapidly lose that capability after birth. To tackle conditions where neurons are damaged, such as spinal cord injury and vision loss, Harvard Stem Cell Institute Principal Faculty member Zhigang He, Ph.D., B.M., is turning back the clock and helping neurons to regain their youthful regenerative state.

HEALING SPINAL CORD INJURIES WITHOUT SCARS

In adult mammals, axons — the long projections of neurons that transmit signals — do not regrow after spinal cord injury. Moreover, many types of harmful cells accumulate around the injury site, further interfering with the axons' ability to reconnect. To find a solution, HSCI researchers studied spinal cord injury and repair responses in two-day-old mice.

"Unexpectedly, we found that the injury in these young pups lead to scar-free healing that permitted the growth of axons through the site of the lesion," said He.



A spinal cord injury is repaired in the newborn mouse with the help of a specialized cell type, the microglia. Credit: He Lab

The researchers identified that microglial cells, a type of immune cell found in the brain and spinal cord, play an essential protective role in scar-free wound repair. First, they help re-form bridges between the severed axon ends. Second, microglia from newborn mice — but not adult mice — produce molecules that interfere with the action of certain harmful proteins.

"These protein inhibitors are involved in quickly tamping down the inflammatory response after spinal cord injury," said He. "The microglia essentially orchestrated swift removal of harmful cell debris after injury and stopped inflammation."

The researchers next tested whether axons could be regenerated in adult mice with spinal cord injuries. They found that transplanting microglia from newborn mice into adult mice with spinal cord lesions significantly improved healing and axon growth. They also saw similar results when transplanting adult microglia that were pre-treated with the helpful protein inhibitors.

The researchers are now testing several types of protein inhibitors to see which may be most effective in boosting the scar-free healing potential of microglial cells. Their discovery may also help advance treatments for neurodegenerative conditions such as Alzheimer's disease, ALS, and Parkinson's disease.

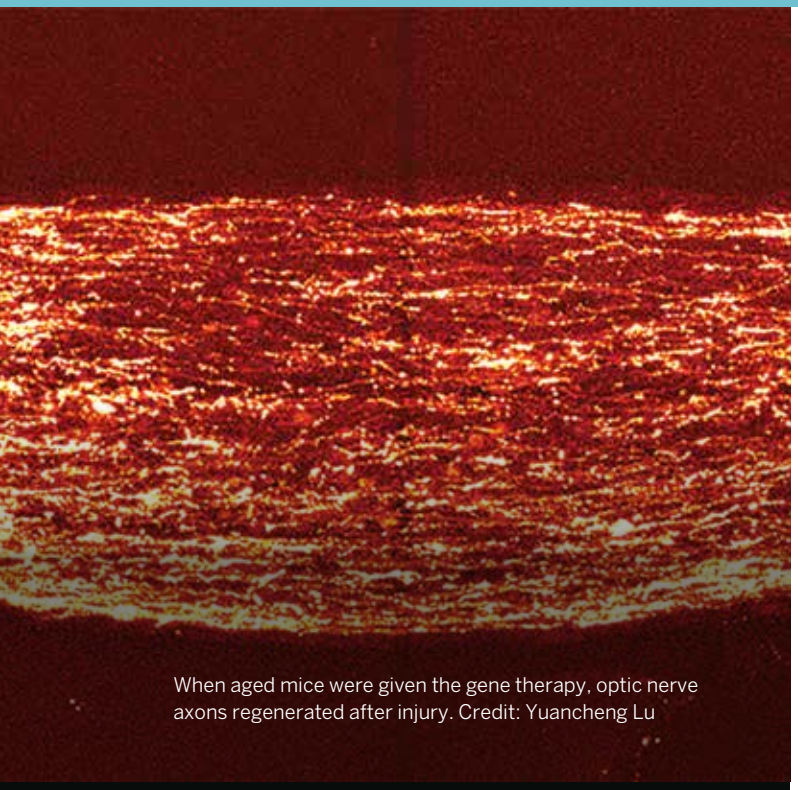
"One of the key players in these diseases is microglia," said He. "Perhaps we can find a gene that might convert those chronically active microglia to treat neurodegeneration."

REVERSING AGING IN THE EYE

Vision loss occurs when the optic nerve is damaged, either due to injury or the aging process. HSCI researchers were part of a team that developed a gene therapy to reprogram neurons to an earlier age and restore vision.

TO REGENERATE **NERVES**

TREATING SPINAL CORD INJURY AND VISION LOSS BY RESTORING CELLS' REGENERATIVE ABILITY



When aged mice were given the gene therapy, optic nerve axons regenerated after injury. Credit: Yuancheng Lu

Mouse retina after gene therapy. Credit: Yuancheng Lu

In addition to He, the project's leaders were David Sinclair of Harvard Medical School, HSCI Affiliate Faculty member Bruce Ksander, and Meredith Gregory-Ksander of the Schepens Eye Research Institute.

The researchers' approach focused on the epigenome, the collection of chemical modifications to DNA that control which genes are turned on and off. The pattern of epigenomic markers changes as cells age, so the researchers designed a therapy to deliver three genes that restore the youthful pattern from embryonic development.

The researchers first tested the gene therapy in adult mice with optic nerve injury, and the treatment led to improved cell survival and nerve regrowth. Next, the team tested the therapy in a mouse model of glaucoma, a condition that is associated with aging and a leading cause of blindness. The treatment led to increased neuron electrical activity and a notable increase in visual acuity, as measured by the animals' ability to see moving vertical lines on a screen. Remarkably, this improvement happened after the glaucoma-induced vision loss had already occurred.

The treatment worked similarly well in elderly, 12-month-old mice with diminishing vision due to normal aging. Following treatment of the elderly mice, the gene expression patterns and electrical signals of the optic nerve cells were similar to young mice, and vision was restored.

"Regaining visual function after the injury occurred has rarely been demonstrated by scientists," Ksander said. "This new approach, which successfully reverses multiple causes of vision loss in mice without the need for a retinal transplant, represents a new treatment modality in regenerative medicine."

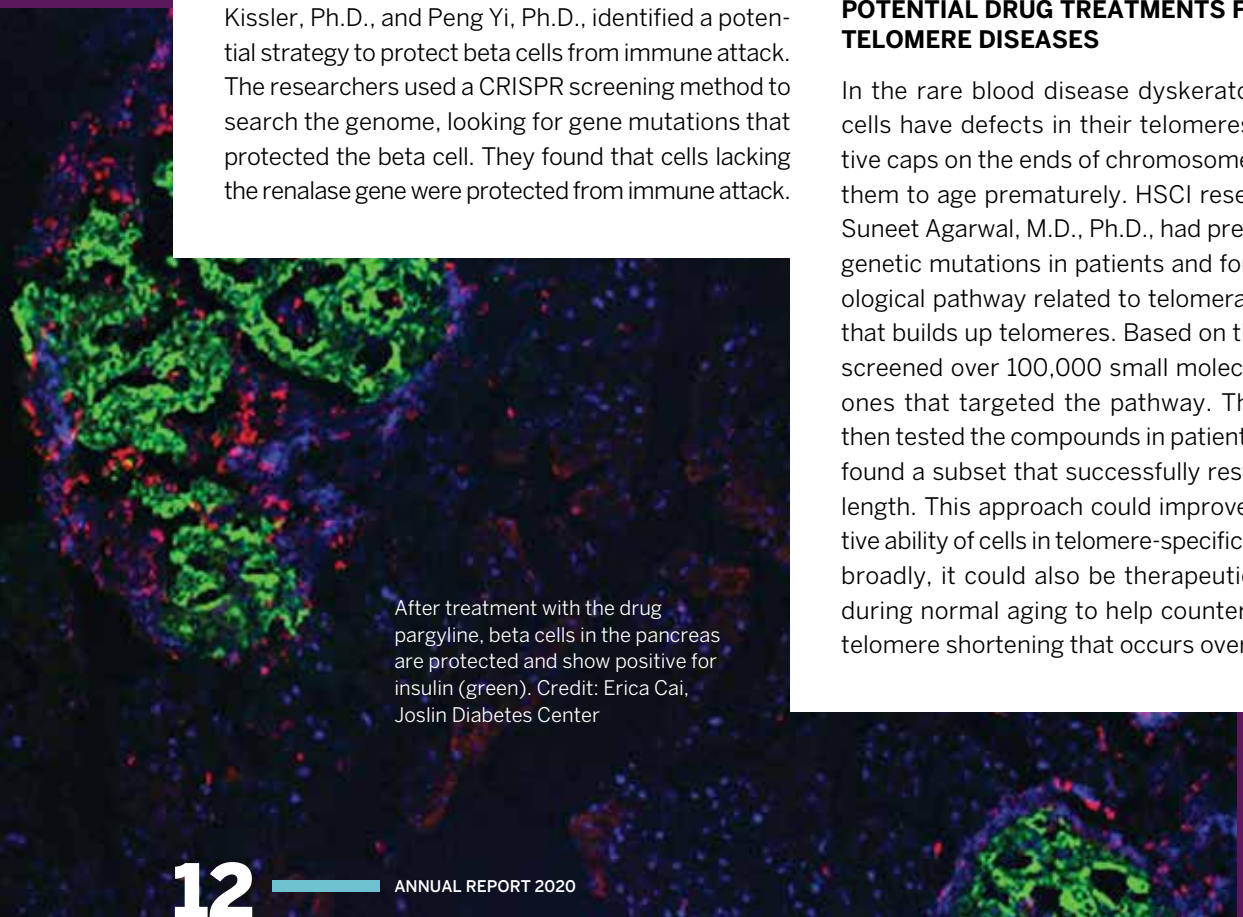
RESEARCH

Harvard Stem Cell Institute researchers work across disease areas and disciplines to improve patients' lives, from investigating fundamental biological mechanisms to developing advanced therapies. In 2020, HSCI researchers published over 260 studies — here, we highlight just a few examples.

ADVANCES IN TYPE 1 DIABETES

Type 1 diabetes is an autoimmune disease, where immune cells attack the insulin-producing beta cells of the pancreas. To better understand the root causes of this process, HSCI researchers led by Douglas Melton, Ph.D., developed a way to model human disease in a lab dish. They used induced pluripotent stem cells from patients to make beta cells, then introduced immune cells from the same individuals to observe an autoimmune reaction. The method can be used to study the cells' interactions in further detail, and to test beta cell transplants for possible reactions.

In a separate study conducted in mice, Stephan Kissler, Ph.D., and Peng Yi, Ph.D., identified a potential strategy to protect beta cells from immune attack. The researchers used a CRISPR screening method to search the genome, looking for gene mutations that protected the beta cell. They found that cells lacking the renalase gene were protected from immune attack. Further, the FDA-approved drug pargyline was able to inhibit renalase and increase beta cell survival. The results may lead to the development of new drugs that could help protect transplanted beta cells, or even slow the original onset of the disease.



After treatment with the drug pargyline, beta cells in the pancreas are protected and show positive for insulin (green). Credit: Erica Cai, Joslin Diabetes Center

GENE THERAPY FOR BARTH SYNDROME

HSCI researchers led by William Pu, M.D., successfully tested a gene therapy in mice for Barth syndrome, a rare disease that can cause life-threatening heart failure. The researchers previously studied a stem cell model of Barth syndrome and found that the gene *TAZ* is responsible for heart dysfunction. Based on that work, the researchers developed a mouse model that lacked *TAZ* to study the disease's whole-body effects. The animals' hearts had more scarring, thinner walls, and lower pumping capacity. When the researchers used gene therapy to replace *TAZ* in the mice, the symptoms were reversed, demonstrating the potential for using the approach to treat patients.

POTENTIAL DRUG TREATMENTS FOR TELOMERE DISEASES

In the rare blood disease dyskeratosis congenita, cells have defects in their telomeres — the protective caps on the ends of chromosomes — that cause them to age prematurely. HSCI researchers led by Suneet Agarwal, M.D., Ph.D., had previously studied genetic mutations in patients and found a faulty biological pathway related to telomerase, the protein that builds up telomeres. Based on that result, they screened over 100,000 small molecules to identify ones that targeted the pathway. The researchers then tested the compounds in patient stem cells and found a subset that successfully restored telomere length. This approach could improve the regenerative ability of cells in telomere-specific diseases. More broadly, it could also be therapeutically beneficial during normal aging to help counteract the typical telomere shortening that occurs over time.

HIGHLIGHTS

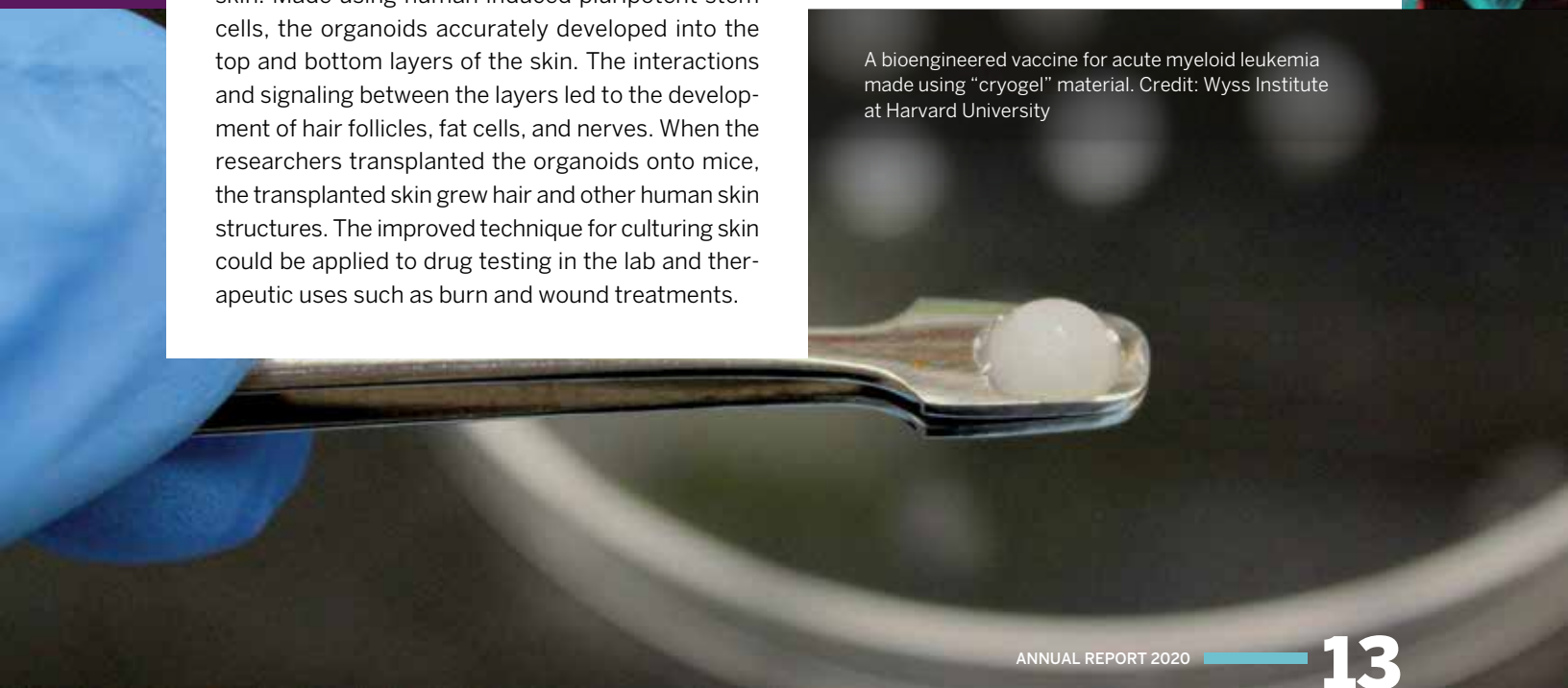
Improved skin organoid with hair follicles and nerves. Credit: Jiyoon Lee, Boston Children's Hospital

IMPROVING SKIN ORGANOIDS

Scientists have been recreating human skin in the lab for decades, but all of these models have lacked many of the component cells and structures of normal skin, including hair. HSCI researchers led by Karl Koehler, Ph.D., developed improved skin organoids, or miniature 3D cell cultures, that better model the skin. Made using human induced pluripotent stem cells, the organoids accurately developed into the top and bottom layers of the skin. The interactions and signaling between the layers led to the development of hair follicles, fat cells, and nerves. When the researchers transplanted the organoids onto mice, the transplanted skin grew hair and other human skin structures. The improved technique for culturing skin could be applied to drug testing in the lab and therapeutic uses such as burn and wound treatments.

A SOLID VACCINE FOR LIQUID TUMORS

Acute myeloid leukemia is a blood cancer that can be treated with chemotherapy, but has a high rate of relapse. For a longer-lasting therapeutic approach, David Scadden, M.D., and David Mooney, Ph.D., collaborated on an injectable biomaterial-based vaccine. They created a "cryogel" scaffold that contained different molecules to attract and activate immune cells, and to teach the immune system to recognize and attack cancer cells. When tested in mice, the vaccine successfully led to lasting recovery and immunity, demonstrating the potential of this bioengineering approach.



A bioengineered vaccine for acute myeloid leukemia made using "cryogel" material. Credit: Wyss Institute at Harvard University

HSCI

In 2020, the Harvard Stem Cell Institute's commitment to keeping our community safe during the COVID-19 pandemic meant that we had to reimagine how we work together. Our scientists rose to the challenge and continued to forge connections in a virtual setting, ensuring that HSCI's collaborative work could go on and especially supporting the early-career researchers who will make the next generation of advances.

2020 ANNUAL RETREAT

At the HSCI annual retreat, 250 researchers gathered online for a day of scientific presentations and knowledge exchange.

The program highlighted research across a diverse range of disease areas. HSCI Principal Faculty member Stuart Orkin, along with Erica Esrick, kicked off the program by sharing what it took to transform a basic discovery from the lab into a gene therapy for sickle cell anemia that is currently being tested in a clinical trial. In sickle cell disease, a mutated hemoglobin gene results in blood cells that are misshapen and cannot carry oxygen. But the fetal form of hemoglobin is not affected by the mutation, and in 2008 Orkin — along with now HSCI Principal Faculty member Vijay Sankaran — discovered a genetic switch that increases its production. Now, after years of further lab work and preclinical testing, Esrick and HSCI Principal Faculty member David A. Williams are leading a promising clinical trial at the Dana-Farber/Boston Children's Cancer and Blood Disorders Center to bring this gene therapy to patients.

Students and trainees in the HSCI network had the opportunity to present their research and attend professional development sessions, which focused on how to get an academic job and how to find the right scientific question to pursue. The research community voted on the top trainee presentation, which was awarded to Ryoko Hamaguchi from the Christine Lian and George Murphy Labs, for her talk on using bioengineering techniques to investigate skin stem cell biology.

The formal program culminated in the announcement of the inaugural Barry Family HSCI Innovation Award for Early Investigators. The honor was awarded to Jessica Whited, assistant professor in Harvard's Department of Stem Cell and Regenerative Biology, in recognition of her innovative work in nerve regeneration which has the potential to open a new field of stem cell research.

DISEASE PROGRAM SEMINARS

HSCI's disease programs bring together scientists across Harvard-affiliated institutions who share interests in how stem cell science applies to their disease of focus. Additionally, the programs enable joint projects across diseases. In order to spark new ideas and collaborations, we launched a series of virtual seminars in the fall of 2020 to share advances and highlight work done by trainees and junior faculty.

Diabetes Program

Stephan Kissler • **Joslin Diabetes Center**
"Immune regulation"

Nayara Leite • **Harvard University**
"Induced pluripotent stem cells for type 1 diabetes in vitro modeling and immune protection of β cells"

Blood Program

Satish Nandakumar & Lara Wahlster • **Boston Children's Hospital**
"How inherited variation can alter hematopoiesis and the blood cancer risk"

Musculoskeletal Program

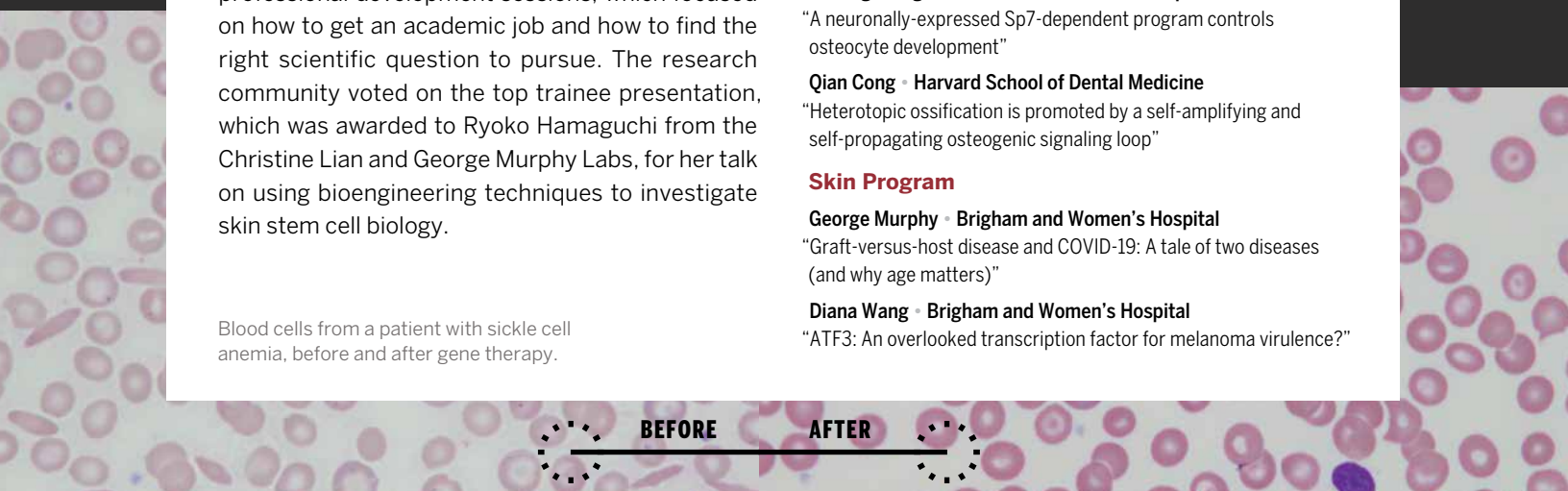
Jialiang Wang • **Massachusetts General Hospital**
"A neuronally-expressed Sp7-dependent program controls osteocyte development"

Qian Cong • **Harvard School of Dental Medicine**
"Heterotopic ossification is promoted by a self-amplifying and self-propagating osteogenic signaling loop"

Skin Program

George Murphy • **Brigham and Women's Hospital**
"Graft-versus-host disease and COVID-19: A tale of two diseases (and why age matters)"

Diana Wang • **Brigham and Women's Hospital**
"ATF3: An overlooked transcription factor for melanoma virulence?"



Blood cells from a patient with sickle cell anemia, before and after gene therapy.

CONNECTIONS

HSCI INTERNSHIP PROGRAM

For 15 years, the HSCI Internship Program (HIP) has connected undergraduate students from around the globe to our world-class stem cell labs, where they gain first-hand research experience. Although the program was paused in 2020 and will be again in 2021 due to the ongoing pandemic, HSCI remains committed to supporting the next generation of leaders in stem cell science. Here are just a few highlights from our past interns about their HIP experience and how it helped them get to where they are now.

Anna Dulencin

THEN: 2006 INTERN FROM RUTGERS UNIVERSITY, NEW JERSEY

NOW: PROGRAM COORDINATOR, EAGLETON INSTITUTE OF POLITICS

At a time when stem cell research was at the forefront of a contested political debate, my experience as an intern inspired me to pursue opportunities at the intersection of science, politics, and public policy."

Alana Van Dervort

THEN: 2011 INTERN FROM FLORIDA INTERNATIONAL UNIVERSITY

NOW: PH.D. STUDENT, HARVARD UNIVERSITY

The program was more than an inflection point in my career — the science changed my mind and the people changed my life."

Can Aztekin

THEN: 2013 INTERN FROM SABANCI UNIVERSITY, TURKEY

NOW: EPFL LIFE SCIENCES INDEPENDENT RESEARCH SCHOLAR, SWITZERLAND

HIP set the bar for the research and work ethic required to conduct world-class science, by introducing me to a superb research environment, as well as with its courses and very interactive social program."

Richard Giadone

THEN: 2014 INTERN FROM UNIVERSITY OF MASSACHUSETTS LOWELL

NOW: POSTDOCTORAL FELLOW, HARVARD UNIVERSITY

As the first person in my family to attend college, HIP opened my eyes to just what a career in academic research is."

Jorge Diego Martin Rufino

THEN: 2017 INTERN FROM UNIVERSITY OF SALAMANCA, SPAIN

NOW: PH.D. STUDENT, HARVARD UNIVERSITY

The tremendously enriching experience at the HSCI decisively influenced me to start a Ph.D. at Harvard after finishing my medical degree in Spain, and to pursue a career as a physician scientist."

LEADERSHIP

The Harvard Stem Cell Institute is led by faculty directors Douglas Melton and David Scadden, and executive director Brock Reeve. Together with the Executive Committee, HSCI leadership brings together deep expertise in science and business from across Harvard and its teaching hospitals. Their combined intellectual venture capital guides HSCI's strategy in harnessing the power of stem cell science to improve patients' lives.

FACULTY DIRECTORS

Douglas A. Melton, Ph.D.

Xander University Professor of Stem Cell and Regenerative Biology, Harvard University

Investigator, Howard Hughes Medical Institute

David T. Scadden, M.D.

Gerald and Darlene Jordan Professor of Medicine, Harvard University

Professor of Stem Cell and Regenerative Biology, Harvard University

Director, Center for Regenerative Medicine, Massachusetts General Hospital

EXECUTIVE DIRECTOR

Brock Reeve, M.Phil, M.B.A.

EXECUTIVE COMMITTEE

Leonard Zon, M.D., Chair

Professor of Stem Cell and Regenerative Biology, Harvard University

Grousbeck Professor of Pediatrics, Harvard Medical School

Director, Stem Cell Program, Boston Children's Hospital

Investigator, Howard Hughes Medical Institute

Joseph V. Bonventre, M.D., Ph.D.

Chief, Division of Renal Medicine, Brigham and Women's Hospital

Chief, Division of Engineering in Medicine, Brigham and Women's Hospital

Samuel A. Levine Professor, Harvard Medical School

Susan Dymecki, M.D., Ph.D.

Professor of Genetics, Harvard Medical School

Albert Edge, Ph.D.

Director, Tillotson Cell Biology Unit and Principal Investigator, Eaton-Peabody Laboratories, Massachusetts Eye and Ear

Professor of Otolaryngology—Head and Neck Surgery, Harvard Medical School

Jenna Galloway, Ph.D.

Assistant Professor, Center for Regenerative Medicine and Department of Orthopedic Surgery, Massachusetts General Hospital

HSCI Musculoskeletal Program Leader

Carla F. Kim, Ph.D.

Professor of Genetics and Professor of Pediatrics, Harvard Medical School

Principal Investigator, Stem Cell Program, Boston Children's Hospital

Jeffrey Macklis, M.D., D.Sc.Tech.

Max and Anne Wien Professor of Life Sciences, Harvard University

Professor of Stem Cell and Regenerative Biology, Harvard University

Professor of Neurology, Harvard Medical School

Faculty Member, Harvard University Center for Brain Science

Jerome Ritz, M.D.

Executive Director, Connell and O'Reilly Families Cell Manipulation Core Facility, Dana-Farber Cancer Institute

Professor of Medicine, Harvard Medical School

Vicki Rosen, Ph.D.

Professor of Developmental Biology and Chair of the Department of Developmental Biology, Harvard School of Dental Medicine

HSCI Musculoskeletal Program Leader

Lee Rubin, Ph.D.

Professor of Stem Cell and Regenerative Biology, Harvard University

HSCI Nervous System Diseases Program Leader

Amy Wagers, Ph.D.

Forst Family Professor of Stem Cell and Regenerative Biology, Harvard University

Co-chair, Harvard Department of Stem Cell and Regenerative Biology

Senior Investigator, Joslin Diabetes Center

AWARDS

In 2020, HSCI faculty were recognized widely as leaders in the fields of stem cell biology and regenerative medicine. Here we highlight just a few representative examples.

HARRINGTON DISCOVERY INSTITUTE

Stuart Orkin, M.D., received the 2020 Harrington Prize for Innovation in Medicine. His breakthrough discoveries about red blood cells offer new treatments for patients with sickle cell disease and beta-thalassemia.

LEO FOUNDATION

Ya-Chieh Hsu, Ph.D., received the 2020 LEO Foundation Award, which recognizes extraordinary contributions to dermatology research that advance our understanding of skin diseases and pave the way for new and improved treatments.

NATIONAL INSTITUTES OF HEALTH

David Scadden, M.D., is part of a multi-institutional team that was awarded a $14.6 million grant from the National Institutes of Health. The team is developing a potential cure for HIV using gene and cell therapy approaches, including Scadden's pioneering technology for safer and more effective blood stem cell transplants.

PARKINSON'S DISEASE AWARDS

Vikram Khurana, M.D., Ph.D., received awards from three organizations to advance his innovative research on Parkinson's disease: the Michael J. Fox Foundation for Parkinson's Research, as part of the Ken Griffin Alpha-synuclein Imaging Competition; Aligning Science Across Parkinson's; and the National Institutes of Health.

NEW YORK STEM CELL FOUNDATION

José Ordovas-Montañes, Ph.D., was named a NYSCF–Robertson Investigator. His cutting-edge research focuses on how epithelial stem cells in barrier tissues—such as the airway, intestine, and skin—can "remember" inflammation.

NEW FACULTY MEMBERS

In 2020, HSCI welcomed six new Principal Faculty members from schools and hospitals across our network.

Fei Chen, Ph.D.
Assistant Professor of Stem Cell and Regenerative Biology, Harvard University
Core Institute Member, Broad Institute of MIT and Harvard

Ryan Flynn, M.D., Ph.D.
Assistant Professor of Stem Cell and Regenerative Biology, Harvard University
Principal Investigator, Stem Cell Program, Boston Children's Hospital

Ruth Franklin, Ph.D.
Assistant Professor of Stem Cell and Regenerative Biology, Harvard University

Leslie Kean, M.D., Ph.D.
Director, Stem Cell Transplant Center, Dana-Farber/Boston Children's Cancer and Blood Disorders Center
Robert A. Stranahan Professor of Pediatrics, Harvard Medical School

Kara McKinley, Ph.D.
Assistant Professor of Stem Cell and Regenerative Biology, Harvard University

Marc Wein, M.D., Ph.D.
Endocrine Unit, Massachusetts General Hospital
Assistant Professor of Medicine, Harvard Medical School

CHAN ZUCKERBERG INITIATIVE

Four HSCI faculty members were awarded grants from the Chan Zuckerberg Initiative to expand the Human Cell Atlas, a global effort to map every cell in the human body: Allon Klein, Ph.D., for blood stem cells; Jonathan Seidman, Ph.D., and Christine Seidman, M.D., for the heart; and Jayaraj Rajagopal, M.D. for the lung.

AMERICAN LUNG ASSOCIATION

Carla Kim, Ph.D., received the Lung Cancer Discovery Award from the American Lung Association. Her innovative research uses lung organoids—3D cultures derived from stem cells—to model the earliest stages of lung cancer and help identify new therapeutic targets.

CATALYZING DISCOVERY

HOW HSCI DONORS ARE MAKING A DIFFERENCE

In 2020, the Harvard Stem Cell Institute launched the Barry Family HSCI Innovation Award for Early Investigators. With the generous support of the Barry family, this annual award enables early-career HSCI scientists to pursue bold, innovative ideas that have the potential to transform stem cell science and make a difference in patients' lives.

"With this award, we are supporting our junior faculty whose new ideas can change the course of the field. We're placing early bets on big ideas with the potential to change a field," said HSCI Co-Director Douglas Melton, Ph.D. "If successful, these projects will attract more funding and speed the development of new treatments. Not every project will hit a home run, because of the nature of how science works, but the ones that do will have a lasting impact."

The first recipient of the award is Jessica Whited, Ph.D., assistant professor of stem cell and regenerative biology at Harvard. Her lab studies the axolotl, a salamander that can regenerate its limbs throughout life. The lab primarily focuses on the limb regeneration process, providing fundamental clues for future efforts aimed at human applications. But the award is supporting a project that is slightly off the beaten path and could reach the clinic sooner: repairing peripheral nerve injuries.

The project focuses on the brachial plexus, the network of nerves that controls movement and sensation in the arm. The nerves can be damaged in situations such as car accidents and gunshot wounds, or as Whited is modeling in the axolotl, during birth injury. Her goal is to identify molecules that help axolotls regenerate nerves and use them to improve the success of surgery in patients, where a functional nerve from a different part of the body is used to reconnect the brachial plexus.

Cross section of an axolotl spinal cord, with nerves shown in green. Credit: Burcu Erdogan, Whited Lab

"This award has been absolutely catalytic in taking the project to a completely different level," Whited said. "We can now do the discovery-based studies that are important in early-stage research."

With the award, Whited has established a collaboration with Dr. Andrea Bauer, an orthopedic surgeon at Boston Children's Hospital. For the first time, they can study patient samples and see which genes are expressed compared to the axolotl.

In the future, HSCI's network of scientists can help Whited develop her discoveries into therapeutics. "What's so great about doing this work at Harvard is meeting potential collaborators who have expertise in translational research," she said. "They can help us test potential molecules in other models and create bioengineered scaffolds for delivering the molecules, which will be instrumental in getting our work into the clinic and helping patients."

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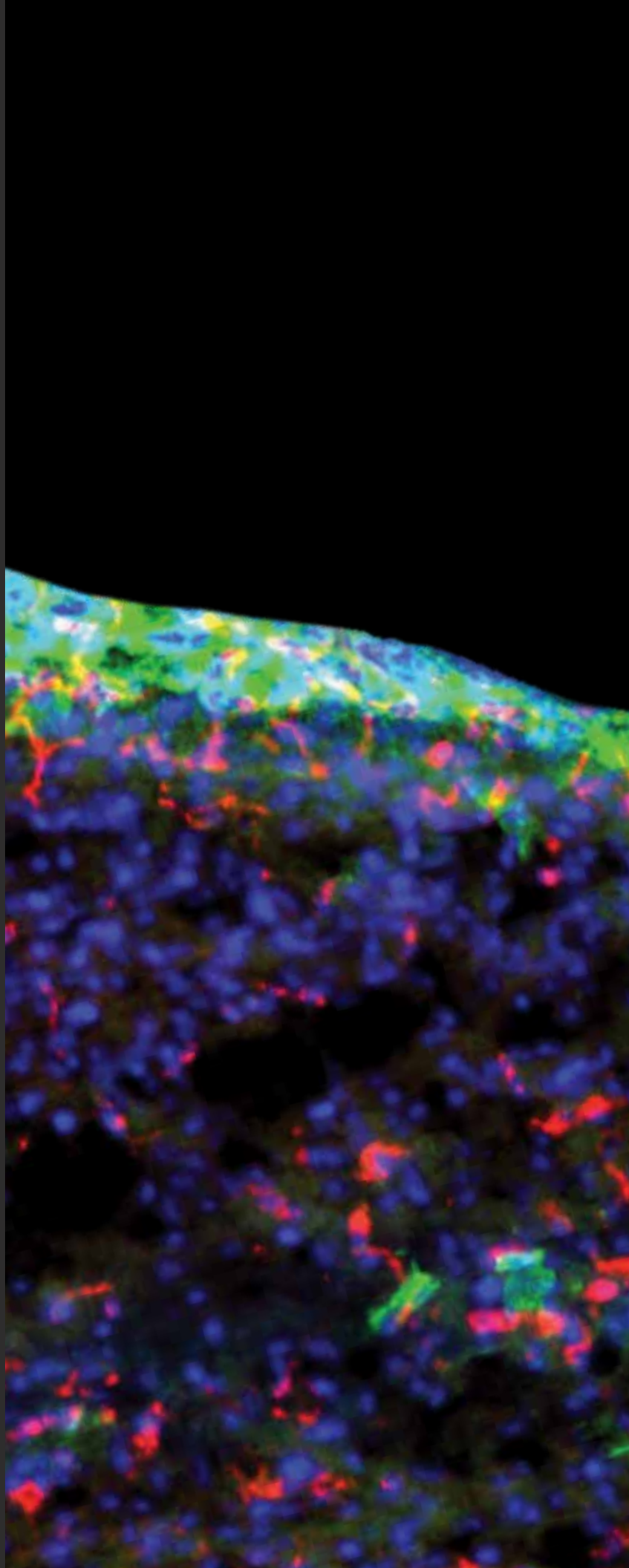
ON THE COVER
A spinal cord injury is repaired in a mouse. Image courtesy of the Zhigang He Lab.



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