Harvard Stem Cell Institute

ReNewal

Annual Report 2009

Contents

From the Scientific Directors	2
From the Executive Director	3
Leading	4
Collaborating	10
HSCI Milestones	14
Supporting	16
Educating	20
Selected Scientific Publications	24
Financials	26
Leadership	27
Donor Honor Roll	28
HSCI at a Glance	29

ReNewal

Renewal. What an apt theme for the Harvard Stem Cell Institute's annual report on the occasion of our fifth anniversary.

After all, renewal — specifically, the capacity for indefinite self-renewal — is one of the defining properties of stem cells, the remarkable cells from which all of the more than 200 cell types that constitute the human body arise.

This has also been a year of renewal, both for stem cell science and HSCI.

With the lifting of the federal ban on funding for some types of embryonic stem cell research, coupled with recent scientific breakthroughs that are propelling the field forward at a faster pace than perhaps anyone imagined a couple of years ago, the entire HSCI community feels a renewed sense of optimism about the promise and pace of stem cell research. Looking back at what we have accomplished in the first five years gives us much hope for what we can achieve in the next five.

We also feel a renewed sense of urgency. Patients and families whose lives are profoundly affected by diseases such as cancer, neurodegenerative diseases, diabetes, cardiovascular disease, and many others, are looking to HSCI and other stem cell scientists to find treatments and cures. Not today, but soon.

"Everything I know about...the work of Harvard Stem Cell Institute makes me feel that we really do live in historic times — something people will look back on years from now and see as a watershed in our understanding of human biology and in our capacity to seek treatments and cures for a myriad of diseases."

— Harvard University President Drew Faust, PhD

As HSCI enters its next phase — a phase that promises to be as exhilarating and transformative as its first — it does so with a renewed determination to harness the power of stem cells as tools of discovery and as therapies and, in so doing, to vanquish diseases that are responsible for so much human suffering.

From the Scientific Directors

Douglas A. Melton, PhD

David T. Scadden, MD

HAS IT REALLY BEEN FIVE YEARS?

On one hand, it's hard to get our minds around the fact that the Harvard Stem Cell Institute is now in its sixth year. When we look at what has been accomplished, and when we place that record of accomplishment against those of previous sea changes in biology, it's hard to believe that we haven't been at this for decades.

On the other hand, has it *already* been five years? It feels like only yesterday that the field of stem cell biology was emerging as something so many people had an interest in, yet so few of us were working together on. Was it really five years ago when we saw that there was a tremendous need to create new relationships in order to take advantage of a community that had, in addition to its obvious academic strength, the unique ability to bring therapies to patients?

So what has HSCI accomplished thus far, in spite of a virtual ban on federal funding of embryonic stem cell research? With the exception of Kyoto University's Shinya Yamanaka's initial breakthrough development of induced pluripotent stem (iPS) cells, many of the critical advances in the field have been achieved under the HSCI umbrella.

As you will read in the following pages, HSCI researchers have, among other accomplishments:

- created a unique scientific community in which collaboration is a given, rather than an exception
- created the majority of the embryonic stem cell lines being used today by researchers around the world
- created more than 20 disease-specific stem cell lines and cell types, allowing scientists to study disease development in laboratory dishes
- isolated the stem cells that participate in cardiac development
- successfully reprogrammed one type of fully formed adult pancreatic cell into another, *without* going through the stem cell stage
- improved the efficiency of blood stem cell transplantation
- initiated a therapeutic screening program that holds the promise of speeding the development of new treatments for a host of chronic diseases
- created a new paradigm for stem cell research, in which we use stem cells as *tools* to advance the understanding and treatment of disease, rather than as ends in themselves
- launched the careers of many younger scientists, from undergraduates to new instructors
- created Harvard's first interdisciplinary, inter-school department, and with it a new undergraduate concentration in Human Developmental and Regenerative Biology

And what do we hope all this leads to in the coming period of renewal? What do we hope to be able to write in the directors' letter in the Harvard Stem Cell Institute annual report for 2013?

By the end of our first decade we hope to be able to tell you that the breakthroughs at HSCI, coupled with the growth of our therapeutic screening program, have led to the development of new drugs for the treatment of one or more diseases. We hope to be able to tell you that our research has made possible improvements in cell replacement therapy for blood diseases and diabetes. We hope to be able to tell you that we have an improved understanding of Parkinson's disease, ALS, and a number of other diseases.

Most important, we *know* that five years from now we will be able to tell you that the HSCI experiment allowed us to re-imagine how science is done, shifting from a single-investigator, independent laboratory-based paradigm to one in which collaborative goals and vision trump individual ego and career focus. And that, we *know*, will speed results and bring treatments and cures to patients who so desperately need them.

Finally, we would be remiss if we did not underscore the fact that our work over these past five years would not have been possible without the extraordinary generosity and foresight of so many individuals, foundations, corporations, and funding agencies. We are grateful for this support—this expression of confidence and belief in the work of the Harvard Stem Cell Institute—and the platform it has given us to build on over the next five years.

David T. Scadden, MD, and Douglas A. Melton, PhD
Co-Directors, Harvard Stem Cell Institute

From the Executive Director

CONSIDERING HOW MUCH HAS BEEN ACCOMPLISHED — BOTH ON THE organizational front and, as the Scientific Directors' letter describes, on the scientific front — it is difficult to believe that it was just five years ago that Harvard Stem Cell Institute was established. Few start-up organizations, especially ones of such size and complexity and with such a bold agenda, can claim so much progress in such a short period of time.

During our first five years — a period we refer to as phase one — we were able to provide proof of concept for HSCI. We showed that this unique collaboration involving all of Harvard's schools and more than 900 scientists across 11 Harvard-affiliated hospitals and research institutions works — and works well. We demonstrated that we can achieve important scientific results that attract significant support from private donors, foundations, and the commercial sector, which is essential to rapidly moving these results from laboratory benches to patients' bedsides. In five short years, HSCI has become the acknowledged international leader in stem cell research.

As we enter our next five-year period — phase two — we are doing so with a renewed sense of confidence in, and excitement about, what we can accomplish. We will continue to invest in our seed grants and support our junior faculty collaborations, which have been a resounding success in terms of early career development and scientific breakthroughs. We will continue to push collaborative brainstorming and decision-making in our program think tanks, which are key to identifying our research priorities and staying on course. And we will continue to re-invest in and expand our core facilities, particularly our Therapeutic Screening Center and the iPS Core, which are unique in the field.

Phase two is also when we will cease to be an exclusively virtual community and many faculty members will come together in a single location — a move that will foster and renew fruitful collaborations. Although the construction of the Allston Science Complex had to be put on hold because of challenging economic conditions, the University has an unwavering commitment to stem cell biology research and education. So, beginning this fall, two contiguous buildings in the heart of the Cambridge campus will undergo a major renovation. When this work is completed in 2011, these will be the new home of the administrative offices and core faculty of HSCI and Harvard's closely aligned Department of Stem Cell and Regenerative Biology.

In the coming years, HSCI will surely benefit from the availability of federal funding for some types of human embryonic stem cell research made possible by the recent easing of the Bush administration's restrictions. While we certainly welcome this change, it does not alter the fact that HSCI will continue to rely heavily on philanthropy and commercial-sector alliances to continue moving the field rapidly forward.

One reason is that, regrettably, not all types of embryonic stem cell research are eligible for federal funding. Another is that the focus and ongoing funding levels of the National Institutes of Health have not changed, at the same time that the competition for research dollars is especially fierce. Meanwhile, HSCI's funding from disease foundations, whose endowments have suffered during the economic downturn, has also decreased.

In this, our fourth, annual report we are proud to share with you many of the highlights of an incredibly exciting year. As we embark on a new year and our next new phase, we urge you to support us with a renewed sense of hope for the enormous promise of stem cell research.

Brock C. Reeve, MPhil, MBA
Executive Director, Harvard Stem Cell Institute

LEADING

BY ANY AND ALL MEASURES, IN JUST FIVE YEARS OF ITS existence, Harvard Stem Cell Institute has become the international leader in stem cell research. During this short time span, HSCI has:

- created a new paradigm for how biomedical research can be conducted — through collaboration and a shared commitment to finding treatments and cures for many intractable diseases that afflict millions
- created and distributed more human embryonic stem cell lines than any other institution, supplying more than 200 research programs worldwide
- achieved some of the most significant scientific breakthroughs in stem cell research
- established core facilities that are unique in an academic setting and are expediting the pace of bringing discoveries from bench to bedside
- supported the early careers of innovative young scientists who have already gone on to make significant contributions to the field

With 190 faculty members and 900-plus scientists working collaboratively across 11 world-class hospitals and research institutions in diverse but interrelated areas, from diabetes and cancer to stem cell aging, HSCI has been, and will continue to be, the leader in stem cell science.

With the knowledge gained in just the past five years of HSCI's existence, scientists now realize that stem cells have enormous potential not only for cell-based therapies, or regenerative medicine, but also as powerful tools to study diseases as they develop — which could reveal new targets for therapy — and to search for therapeutic agents that are both safe and effective.

PATIENT-DRIVEN RESEARCH

Consistent with its focus on ultimately "taking out" many prevalent diseases, HSCI research is organized into disease programs. Each program crosses the boundaries of institutions, departments, and laboratories, resulting in the cross-fertilization of ideas and sharing of resources that hasten the pace of discoveries and their translation to the clinic.

During its next phase, as HSCI continues to mature and expand, it is likely that new disease programs will emerge. Because many areas of stem cell science pertain to multiple diseases, HSCI also has several Scientific Programs that span our disease programs, as well as a Translational Research Program, which has the specialized expertise to help move HSCI's discoveries from bench to bedside quickly and efficiently.

HSCI Disease Programs

- Blood Diseases
- Cancer
- Cardiovascular Disease
- Diabetes
- Kidney Disease
- Nervous System Diseases

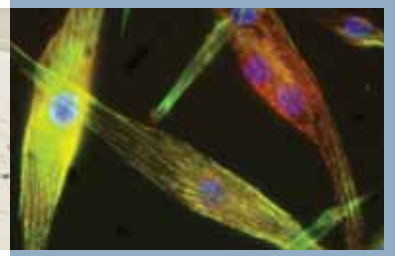
Other HSCI Scientific Programs

- Junior Faculty Program
- Cell Development
- Epigenetics of Stem Cell Function and Aging
- Stem Cell Regulation
- Translational Research

400+ Scientific Publications

One metric by which scientific progress is measured is publication in peer-reviewed scientific journals, where advances in stem cell research are shared with scientists worldwide. By this measure alone, HSCI is the unequivocal leader. In fact, HSCI has published more papers in high-impact journals than any other stem cell group, anywhere.

Between June 2008 and June 2009, for instance, more than 400 papers on a wide range of topics relating to stem cell research — on average, more than 33 a month — were authored by HSCI principal faculty members and published in influential journals such as *Nature, Cell Stem Cell, Science*, and others. This compares to "only" 280 papers published by HSCI principal faculty over the same period just two years ago.



2008-2009 RESEARCH BREAKTHROUGHS

The past year, in particular, has been impressive in terms of the strides made in stem cell research — many of which took place at HSCI. Indeed, in some areas — particularly the exploding field of cell reprogramming — the word "leaps" is more accurate, as these advances have fast-forwarded scientists' ability to turn back the cellular clock to learn what goes awry to cause a disease and to screen disease-specific cells for potential therapeutics.

Following, in chronological order, are brief summaries of some notable HSCI research breakthroughs during 2008-2009; details about these and other major findings are available on the HSCI website (www.hsci.harvard.edu).

ALS in a dish

From the skin cells of patients suffering from a specific disease — amyotrophic lateral sclerosis (Lou Gehrig's disease) — HSCI researchers use the new induced pluripotent stem (iPS) cell technology to produce motor neurons, the very cell type destroyed in this disease. By creating this "disease in a dish," scientists are now able to study what causes this fatal neurodegenerative disease. This technology can also be used to create other disease-specific cell lines with which to observe how a disease develops, identify targets for therapy, and screen for compounds that are both safe and effective. *Kevin Eggan, PhD, and colleagues*

Multiple disease-specific stem cell lines

Using the iPS cell technology, HSCI scientists produce 20 disease-specific human stem cell lines for diseases including Parkinson's disease, type I diabetes, Huntington's disease, Down syndrome, two forms of muscular dystrophy, and others, and make these available through HSCI's new iPS Core Facility to researchers worldwide. *George Daley, MD, PhD, and colleagues*

Direct reprogramming

For the first time, HSCI researchers convert one type of adult cell (a pancreatic exocrine cell) directly into another type of

High-Impact Science

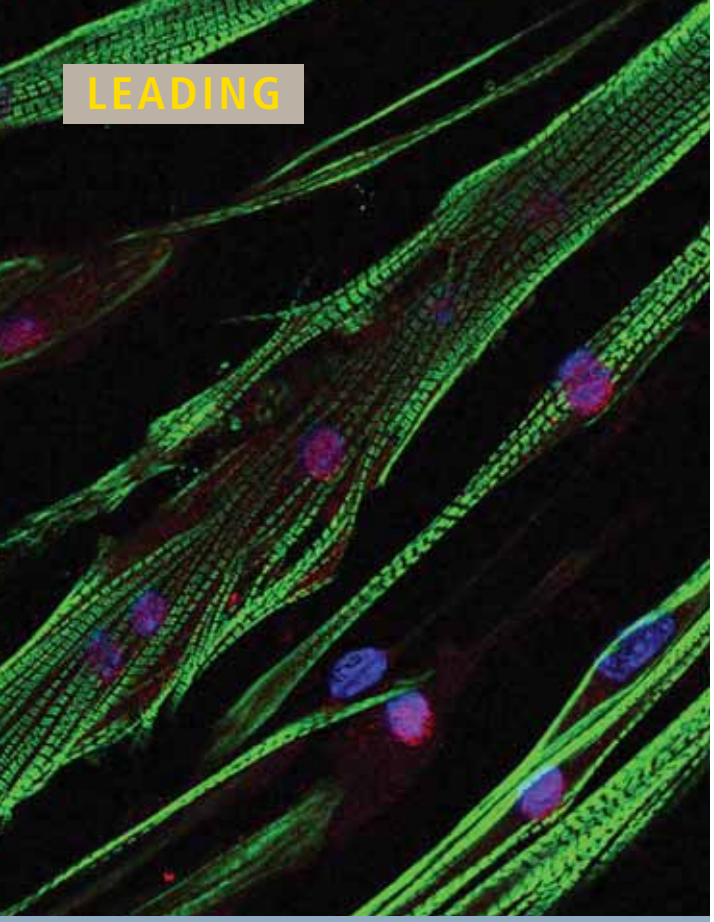
HSCI recently conducted its annual survey asking principal investigators whose projects it has funded about the impact this support had on various aspects of their work. Some of this year's results:

41%
were able to attract **additional, external funding**

85%
reported **new findings**

60%
reported **publications** in leading journals

10%
created new **intellectual property**



HSCI: The Acknowledged Leader Worldwide

HSCI comprises the greatest concentration of stem cell scientists in the world, and is the acknowledged leader in stem cell research nationally and internationally. An independent study of 3,300 institutions worldwide conducted two years ago showed that HSCI was number one in 11 out of 14 areas of stem cell research.

adult cell (an insulin-producing beta cell, which is missing in individuals with Type 1 diabetes), in mice. This is a simpler, more direct approach than the multi-step process required to turn an adult cell to an embryonic-like state (the iPS, or induced pluripotent stem cell, technology) and then direct it to become another type of adult cell. *Douglas Melton, PhD, Qiao Zhou, PhD, and colleagues*

Making iPS cells safer

Two groups of HSCI researchers find new, safer ways to produce induced pluripotent stem (iPS) cells, bringing them one step closer to the clinic. Production of these embryonic-like cells from adult cells formerly required the use of four genes, two of them cancer-causing, inserted into the cells' genome using retroviruses, which also have the potential to cause tumor growth. One group (*Konrad Hochedlinger, PhD, Gordon Weir, MD, and colleagues)* discovered that it is possible to create mouse iPS cells using adenoviruses, which do not incorporate into cells' DNA, to ferry the genes. Using a different approach, the second group (*Douglas Melton, PhD, Danwei Huangfu, PhD, and colleagues)* used a chemical known to be safe in humans to eliminate the need for two of the four genes — the cancer-causing genes. Work is underway to determine if chemicals and other approaches could be used to replace all four genes.

Using stem cells to improve muscle function in mice with muscular dystrophy

By transplanting muscle stem cells from healthy mice into mice with the most common form of muscular dystrophy (MD), HSCI researchers demonstrate for the first time that these cells could improve muscle function in the diseased mice, and also provide a reservoir of additional healthy stem cells that could be reactivated for future muscle repair. This breakthrough provides proof of concept that stem cell transplantation can treat a muscle degenerative disease such as MD. *Amy Wagers, PhD, and colleagues*

Identification of the mechanism that directs blood stem cells to their destination

HSCI researchers identify in mice the cellular mechanism that directs blood stem cells to their ultimate destination in the body. This finding could benefit patients undergoing bone marrow transplantation (a form of stem cell therapy), as well as other therapies using stem cells, which to be clinically useful must efficiently home in on their target. The group also reports already-approved drugs that stimulate this pathway and improve cells' homing ability. *David Scadden, MD, and colleagues*

A drug that increases blood stem cells in umbilical cord blood is evaluated in patients

Umbilical cord blood is a readily available source of hematopoietic (blood-producing) stem cells (HSCs) for patients who may not have another source. However, cord blood has too few HSCs for use in many adults. A drug identified by HSCI researchers that increases HSCs in cord blood is now being evaluated in cancer patients in a phase 1 clinical trial. If this and subsequent trials show that the drug, which was identified from studies using zebrafish, is safe and effective, many cancer patients could benefit. *Leonard Zon, MD, Trista North, PhD, Wolfram Goessling, MD, PhD, and colleagues*

From human embryonic stem cells, discovery of a master heart cell from which the three major tissue types of the heart develop

From human embryonic stem cells, HSCI researchers are the first to identify and isolate the earliest master human heart cell from which all three of the major cell types of the heart arise. This breakthrough, which builds on the 2007 HSCI discovery of a master heart cell in mice, has major implications for understanding and perhaps eventually preventing or treating congenital heart disease (CHD) and adult-onset heart disease, such as heart failure and heart attack, the leading cause of death in developed nations. Especially exciting is the group's discovery that some forms of CHD arise from these master cells — a finding that suggests new targets for therapeutic intervention for the leading birth defect in children worldwide. *Kenneth Chien, MD, PhD, and colleagues*

A beating heart and flowing blood are needed for the development of blood stem cells

In studies of zebrafish, mice, and mouse embryonic stem cells, two groups of HSCI researchers found that the biomechanical stresses created by a beating heart and flowing blood are necessary for the development of the blood system. In multiple experiments, they also showed that nitric oxide, which increases in the presence of flowing blood, is a key regulator of the process of blood stem cell production across vertebrate species. Understanding how the blood system develops may suggest new therapeutic strategies for patients with diseases of the blood, such as leukemia, immune deficiency, and sickle cell anemia. *Leonard Zon, MD, Trista North, PhD, Wolfram Goessling, MD, PhD, George Daley, MD, PhD, and colleagues*

TWO CORE FACILITIES HASTEN THE PACE OF RESEARCH

Ever mindful of its mission to accelerate the pace of stem cell research, HSCI has made significant investments in core facilities that are shared by the entire HSCI research community. HSCI's cores not only provide highly specialized expertise and costly technologies that no single laboratory or institution could afford on its own, but also serve as important hubs for scientific interaction and collaboration.

While all the cores are vital to stem cell research, two — the Therapeutic Screening Center, established in late 2006, and the iPS Core Facility, which was launched last summer — set HSCI apart from other stem cell research enterprises worldwide. Their unique capabilities, which more typically reside in the commercial sector, play a vital role in hastening discoveries arising from

HSCI Core Facilities at a Glance

iPS Core Facility:

stores iPS cells produced by HSCI scientists, generates new disease-specific iPS cell lines, and distributes iPS cell lines to HSCI and the scientific community

Therapeutic Screening Center:

provides expertise and technologies to identify factors that direct stem cell differentiation and proliferation, and to screen stem cells for understanding of disease mechanisms and therapeutic agents

Genome Modification Facility:

provides expertise and develops genetically modified mouse models for HSCI researchers

Flow Cytometry Core Facilities:

provide high-speed cell sorters, cell analyzers, data-analysis computers, and other instruments required by scientists across the HSCI community

HSCI's laboratories into the clinical setting for the benefit of patients. Indeed, the Therapeutic Screening Center's expertise in the drug-discovery process has attracted significant attention and support from pharmaceutical companies, disease foundations, and the federal government, alike. Funding sources include GlaxoSmithKline, Vertex Pharmaceuticals, Eli Lilly, the SMA Foundation, the ALS Association, the National Institutes of Health, and the Department of Defense, among others.

The Therapeutic Screening Center (TSC) uses state-of-the-art technologies, such as high-throughput cell-based screening, to search for compounds that might safely treat a given disease, or to identify factors that direct stem cells to differentiate and proliferate in order to create new assays that could, in turn, lead to new therapies. The TSC serves the entire HSCI research community and works in many disease areas, but has made especially noteworthy advances in devastating motor neuron diseases like spinal muscular atrophy and amyotrophic lateral sclerosis. In fact, the TSC has already identified molecules that increase the levels of SMN, the protein that is defective in patients with SMA, and is now testing these in mice.

Just last year HSCI established its iPS Core Facility in order to tap the full potential of exciting advances in induced pluripotent stem (iPS) cell technology, many of which were developed in HSCI laboratories. Overseen by a committee of HSCI's cell reprogramming experts, the iPS Core serves as a laboratory to generate disease-specific iPS cell lines, as a repository for HSCI iPS cell lines, and as a distribution center from which to share these valuable resources with HSCI scientists and the scientific community. The iPS Core has many strengths — most notably its ability to quickly incorporate advances in reprogramming technology as they are made by scientists, coupled with its close relationship with the Harvard-affiliated hospitals for access to patients with diseases of interest. Even though the iPS Core is still in its early stages, it has already distributed many cell lines to researchers in North America, Asia, and Europe.

HSCI INNOVATORS EARN HHMI APPOINTMENTS

HSCI fosters a culture in which innovation and creativity are encouraged and supported. Within this unique environment, many young scientists have found the ideal milieu in which to pursue novel ideas, however risky they might seem.

This spring, the prestigious Howard Hughes Medical Institute (HHMI) selected four HSCI faculty members as winners of its Early Career Science Competition, citing their demonstrated

Therapeutic Screening Center Achievements

In 2006, HSCI made a major investment in its Therapeutic Screening Center (TSC), betting that this core facility would "pay off" in terms of tangible results in perhaps five years.

In fewer than three years, the "bet" has already paid off — in significant scientific achievements across many disease areas, pivotal scientific papers, and additional funding from multiple sources, including the commercial sector. Following are a few of the TSC's many achievements, all of which involved collaborations with HSCI researchers.

Spinal muscular atrophy (SMA) – identified pathways that regulate the level of the protein (SMN) that is defective in SMA; identified the only class of molecules that increase SMN levels and prolong survival of motor neurons; tested several small molecules in mice that increase SMN

Amyotrophic lateral sclerosis – identified several motor neuron survival-promoting compounds that are currently being tested; established a screening based on the new understanding of the ALS disease process that arose from HSCI work

Parkinson's disease – created dopaminergic neuron progenitors; currently inducing these cells to differentiate into functional dopaminergic neurons for studying disease mechanisms and for screening

Huntington's disease – created medium spiny neuron (MSN) progenitor cells; currently inducing these cells to differentiate into functional MSNs that can be used for studying disease mechanisms and for screening

Diabetes – derived strategy to produce pancreatic progenitors from human embryonic stem cells

Reprogramming – identified molecules that replace the essential cell reprogramming factors

Neuropathy – generated pain neurons (nociceptors) from human embryonic stem cells; currently further characterizing these cells

ability to approach science with creativity and innovation.

Among the 50 young scientists nationwide chosen to have their work supported by HHMI were HSCI faculty members Bradley Bernstein, MD, PhD, Kevin Eggan, PhD, Konrad Hochedlinger, PhD, and Amy Wagers, PhD. A fifth Harvard researcher, Rachel Wilson, PhD, of Harvard Medical School, was also selected for the award. All four HSCI faculty are past recipients of HSCI seed grants, which fund innovative, early-stage research (*see page 16*).

Each of the new HHMI Early Career Scientists will receive a six-year appointment to HHMI, which includes full salary, benefits, and a total research budget of $1.5 million. HHMI will also cover other expenses, including research space and the purchase of critical equipment.

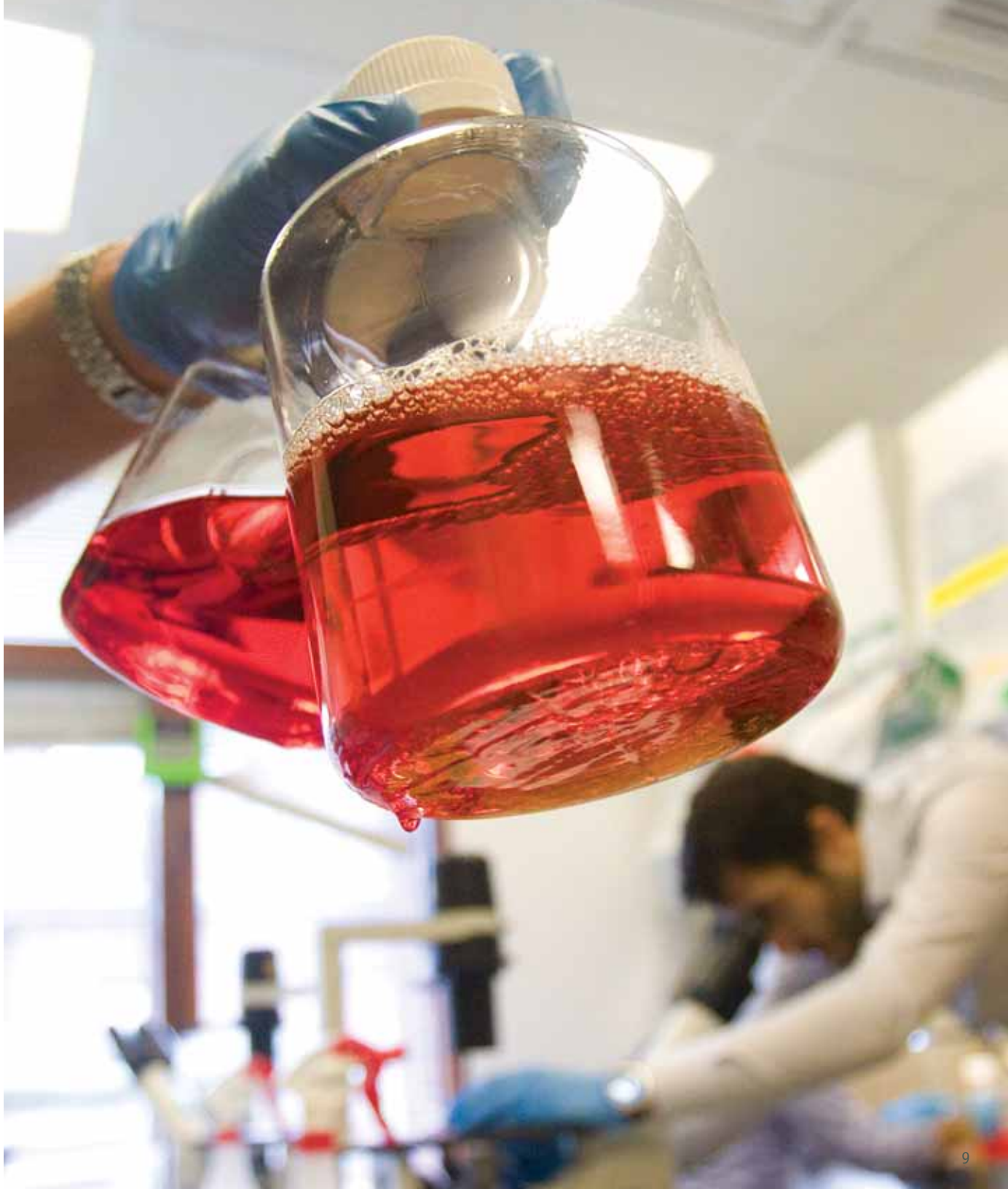
HSCI SCIENTIFIC LEADERSHIP WIDELY RECOGNIZED

HSCI's leadership in stem cell science is widely recognized, from the halls of Congress to national media outlets.

In 2009, for example, for the second time in three years, HSCI Co-Director Douglas Melton, PhD, was named by *Time* magazine as one of the 100 most influential people in the world. This year, Melton was nominated by U.S. Senator Orrin Hatch, of Utah; in 2007, Melton was nominated by actor Michael J. Fox, who has Parkinson's disease.

Last year, *Time* magazine also cited work done by HSCI faculty member Kevin Eggan, PhD, and his colleagues in creating the first motor neurons from patients with amyotrophic lateral sclerosis (Lou Gehrig's disease) as its top medical breakthrough in 2008.

When *Time* magazine published a February 2009 cover feature on the state of stem cell science, "How the Coming Revolution in Stem Cells Could Save Your Life," it focused largely on the achievements of Melton and other HSCI faculty.



COLLABORATING

COLLABORATION IS ESSENTIAL TO MAKING PROGRESS AGAINST diseases as complex as cancer, diabetes, cardiovascular disease, and neurological disorders — among the many diseases for which stem cell research could lead to treatments or cures.

But for meaningful collaboration to take place, scientists must be given the encouragement, resources, opportunities, and incentives to reach beyond the relative isolation of their laboratories, their institutions, their countries — even their own specialties and disciplines — to learn from, share with, and join forces with others in academia and industry who are focusing on the same big challenges. As a critical part of its mission, HSCI fosters collaboration, both internally and externally, in many ways.

THINK TANKS

Three years ago, a group of leading neuroscientists from the United States and abroad gathered in Cambridge for an intensive two-day meeting under the auspices of HSCI's Nervous System Diseases Program. The agenda was to share their current knowledge about Parkinson's disease, identify gaps in that knowledge, and define the most promising areas of research going forward.

Based on the success of this inaugural event, the Nervous System Diseases Program has hosted a think tank every year since. Among the many positive outcomes of these meetings has been the creation of new cross-institutional collaborations and research projects.

"HSCI has been very instrumental in my science in the way it has fostered interactions and brought scientists with diverse backgrounds together. It embodies what the environment should do in enhancing an individual scientist's work."

— Joseph V. Bonventre, MD, PhD, HSCI Kidney Program leader and Principal Faculty member, Brigham and Women's Hospital

For example, inspired by his attendance at the 2006 and 2007 Parkinson's disease think tanks, an HSCI Affiliated Faculty member proposed a project that was later funded by HSCI. This project, which could someday suggest therapeutic strategies in Parkinson's disease and other, related degenerative movement disorders, includes a collaboration with a leading Swedish neuroscientist who participated in the 2006 think tank.

Based on the success of this approach and using the Nervous System Diseases think tanks as a model, the other HSCI Disease Programs soon began hosting their own think tanks. In 2007, for example, the Cardiovascular Program convened its first think tank, which drew renowned cardiovascular and bio-engineering experts from around the globe to focus on identifying key areas of cardiovascular stem cell research.

This year, each of HSCI's six Disease Programs has hosted or plans to host a think tank. Organized by the program leaders and customized to the specific challenges facing each disease area, these events provide an invaluable forum for sharing findings, collaborating, and making decisions about future directions with the global stem cell research community. This summer, HSCI also co-hosted a one-day think tank with Harvard's new Wyss Institute for Biologically Inspired Engineering — to share scientific plans and explore potential avenues for collaborations that would leverage the expertise of each group.

HSCI/GSK ALLIANCE

This past year the pharmaceutical company GlaxoSmithKline (GSK) entered into a five-year, $25 million-plus collaborative agreement with HSCI. One of the first major investments of its kind by a leading pharmaceutical company, this partnership came about in recognition of HSCI's unmatched strengths in stem cell biology and leadership in areas such as iPS technology, which are bringing this research one step closer to the clinic. This unique alliance will integrate HSCI's world-class stem cell expertise with GSK's pharmaceutical capabilities to drive research in drug discovery that will hasten the development of treatments for a wide range of diseases.

Jointly defined and led, the HSCI-GSK collaboration is emblematic of how the academic and commercial sectors are working together differently than in the past. The overall program is led by a joint steering committee comprising scientists and staff from both organizations. It is focusing on research projects that were jointly defined by the lead scientists in six major disease areas — cancer, cardiovascular, diabetes, musculoskeletal, neurological, and obesity — and are taking place in five HSCI-affiliated hospitals. The GSK investment also funds an annual grant in the HSCI Seed Grant Program (*see page 16*).

One project, which involves HSCI researchers at two hospitals, is focusing on using novel therapeutic approaches to selectively target leukemia stem cells. Another, being led by researchers at Harvard and three hospitals, is searching for new agents to block pain. In the cardiovascular area, HSCI researchers at Massachusetts General Hospital and Harvard's School of Engineering and Applied Sciences are teaming up on a project to identify compounds to treat heart failure using an innovative platform they developed that models heart disease.

This year, HSCI is in active discussions with several other pharmaceutical companies, all of which recognize the value of collaborating with the leader in stem cell research. Based on the surging interest among corporations and disease foundations in collaborating with HSCI, it is anticipated that corporate- and foundation-sponsored research will continue to grow significantly over the next few years.

FOURTH ANNUAL RETREAT

Every June, hundreds of members of the diverse HSCI community take a day away from their laboratories and many other commitments to gather at the Harvard Business School for HSCI's Annual Retreat.

This day-long event provides an opportunity for the HSCI community to learn what is going on within HSCI's disease programs and core facilities; hear from HSCI leadership about the institute's progress, goals, and new initiatives; review scientific posters by young HSCI investigators; and, just as importantly,

"The opportunity to interact with the larger HSCI community on a regular basis during retreats, inter-lab meetings, and symposia has been invaluable."

— David Breault, MD, PhD, HSCI Affiliated Faculty, Children's Hospital Boston

International Collaborations

One measure of the phenomenal growth in stem cell research is attendance at the annual International Society of Stem Cell Research (ISSCR) meeting. This summer, more than 2,500 attended the ISSCR annual meeting in Barcelona, Spain — an increase of 25 percent from last year.

HSCI Fosters New Collaborations

HSCI recently conducted its annual survey asking principal investigators whose projects it has funded about the impact this support had on various aspects of their work. Nearly 66% of respondents reported new collaborations as a result of HSCI's support.

interact with fellow scientists, which may spark new ways of thinking about a challenge or lead to new collaborations.

Each year attendance has steadily grown, indicating the strong interest in and value of this annual gathering to the HSCI community. This year's retreat drew roughly 350 members from across the HSCI community, who can stay virtually connected throughout the year via HSCI's intranet service, "iStem."

INTER-LAB MEETINGS

Another significant way in which HSCI actively fosters a sense of community and collaboration is through its inter-lab meetings. Every other month throughout the academic year, HSCI inter-lab meetings draw about 100 members of the HSCI community to Harvard Medical School to hear junior and newly appointed faculty, postdoctoral fellows, and graduate students discuss their recent work. Moderated by senior HSCI faculty, inter-lab meetings present the work of three different labs on a common theme. Popular recent topics have included emerging technologies in stem cell research, organogenesis, and the biology of stem and progenitor cells.

SEMINAR SERIES

Through its twice monthly Seminar Series, HSCI hosts preeminent scientists from around the nation and the world to present their research on a broad range of stem cell-related topics to the HSCI community and engage in an active dialogue with their peers.

One recent seminar, presented by a renowned scientist from the Max Planck Institute in Germany, addressed multi-lineage regeneration in amphibians. Another, presented by the director of the Center of Regeneration Medicine at the University of California, San Francisco, focused on neural stem and progenitor cells in the developing human cortex.

In addition to giving a public lecture, the speakers spend the day with HSCI scientists in one-on-one and small group meetings. As a result, this well-attended series provides an opportunity for the HSCI community to stay abreast of cutting-edge stem cell research taking place nationally and globally, and to exchange ideas and develop collaborations with fellow stem cell scientists beyond Harvard.

ANNUAL STEM CELL SYMPOSIUM

Last fall, for the fifth consecutive year, HSCI hosted the Tony and Shelly Malkin Symposium, which brings together a distinguished international panel of scientists to address research advances in a specific area within the stem cell field.

The full-day event, which is typically attended by upwards of 350 people, provides another opportunity for members of the HSCI community to keep abreast of global developments, network with fellow scientists, and form new connections that might result in collaborations. Through its scientific poster session, this and other HSCI events also give young HSCI investigators the opportunity to present their findings and learn about one another's research.

Building on the recent, exciting developments in cell reprogramming, last year's symposium focused on "Regeneration and Repair" within tissues and organs. Previous symposia themes have centered on cancer stem cells, cell reprogramming and pluripotency, stem cell biology and therapy in organ systems, and stem cells and their micro-environment in development and disease.

"Stem Cell Research in Diabetes and Metabolism" is the topic of the Sixth Annual HSCI Stem Cell Symposium, which will be held in early November. HSCI's Co-Director Douglas Melton, PhD, will lead the panel of speakers.

STEM CELL SUMMIT

In keeping with HSCI's patient-focused mission, "Moving Stem Cell Research from Bench to Bedside" was the theme of HSCI's third Stem Cell Summit, which drew about 300 people to Harvard Medical School last fall.

The day-long event, which is geared primarily for non-scientists with an interest or stake in stem cell research, featured updates on HSCI's disease programs and core facilities, panel discussions that addressed government policies during an election year, and the outlook for commercialization from the perspective of venture capitalists and industry.

As part of our fifth anniversary, HSCI is taking a fresh approach this year. Instead of a full-day summit, this year HSCI will host a panel discussion entitled "Renewal: Stem Cells and the Next Five Years."

NATIONAL AND INTERNATIONAL COLLABORATIONS

As members of the world's preeminent stem cell research collaborative, HSCI faculty are frequently sought after by colleagues worldwide to speak at seminars and discuss joint projects. Over the past year, for instance, HSCI faculty members presented at both the 2008 and 2009 International Society of Stem Cell Research meetings. They also gave talks or participated in symposia at locations across the United States — from New York to California — as well as in Western Europe, Singapore, China, Australia, and Asia.

"I believe that HSCI events and annual retreats are very helpful in our general education, and in creating new collaborations and developing new research approaches to stem cell therapy."

— Kameran Lashkari, MD, 2007 HSCI Seed Grant recipient, Schepens Eye Research Institute

In turn, HSCI faculty actively reach out to scientists from around the world to come to Cambridge and Boston to give talks and participate in think tanks and other collaborative educational and research initiatives.

These frequent interactions ensure that, regardless of institutional or international boundaries, members of the global stem cell research community have ample opportunities to collaborate.

HSCI is increasingly being approached by organizations and governments seeking to establish themselves in a field that they view, appropriately, as the future of biomedical research. These new relationships could potentially be yet another important mechanism to collaborate and accelerate the pace of research.

Collaboration by the numbers

20
Number of HSCI member institutions

190
Number of Principal and Affiliated HSCI faculty

900+
Number of HSCI scientists

MILESTONES

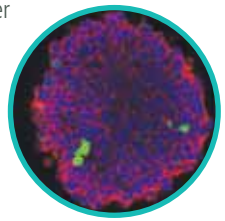
2004

HSCI™
HARVARD STEM CELL INSTITUTE

2004

Harvard announces the establishment of the Harvard Stem Cell Institute

- First symposium, "Stem Cells and Their Microenvironment in Development and Disease," is held
- Distribution of human embryonic stem cell lines to other research institutions initiated



2005

- Seed Grant Program launched to fund early-stage research

- Flow cytometry core facilities established
- Disease Programs identified
- Interlab and Seminar Series programs begin

- HSCI Internship Program launches
- Skin cells fused with embryonic stem cells to create "embryonic-like" cell lines

2006

- Standing agreements established among all HSCI institutions
- Disease Programs funded
- HSCI holds its first Stem Cell Summit
- First HSCI Retreat
- HSCI convenes its first think tank, focusing on nervous system diseases
- HSCI opens the Therapeutic Screening Center
- Faculty Bioethics Brown-Bag Discussion series initiated
- Non-Harvard students accepted into HSCI Internship Program
- HSCI researchers generate mouse embryonic stem cells by parthenogenesis

- Two teams of HSCI researchers independently discover a master cardiac cell in mice that gives rise to all major cell types of the heart
- HSCI initiates a clinical trial to improve stem cell transplantation for leukemia and lymphoma

2007

- Harvard authorizes the formation of the Department of Stem Cell and Regenerative Biology, the University's first cross-school department
- Public Forum series launched
- Genome Modification Facility opens
- *StemBook* designed

- First summer course for high school teachers
- First Junior Faculty Program symposium with the California Institute of Regenerative Medicine
- First HSCI Radcliffe Fellow
- HSCI researchers identify a drug that increases stem cells in the blood; planning for a clinical trial begins
- HSCI researchers create first ALS mouse stem cell line
- HSCI researchers create first iPS cell lines from volunteer research subjects

2008

- HSCI enters its first major corporate-sponsored research agreement, a $25 million alliance with GlaxoSmithKline
- HSCI researchers create the first patient-specific cells from iPS cells — motor neurons from ALS patients
- HSCI launches its iPS Core Facility
- *StemBook* goes live
- HSCI researchers create 20 disease-specific stem cell lines
- HSCI researchers directly reprogram one type of adult cell (exocrine cells) into another (insulin-producing beta cells)

- HSCI faculty help found Fate Therapeutics
- First federal funding for training awarded to HSCI

2009

- The first patient is treated in a Phase 1 clinical trial to evaluate a drug that expands blood stem cells in umbilical cord blood
- For the second time in three years, *Time* magazine names HSCI Co-Director Douglas Melton, PhD, one of the 100 most influential people in the world

- Disease Program think tanks expanded to all programs
- HSCI Seed Grant and Internship program applications reach record highs

- *StemBook* officially recognized as a scientific reference
- Four junior HSCI faculty receive HHMI Early Career Awards
- HSCI faculty help found iPierian

HSCI celebrates its fifth anniversary, and enters its second phase

2009

SUPPORTING

From 'Crazy Idea' to a Seed Grant Success Story

The impact of HSCI's Seed Grant Program is well illustrated by the experience of Kevin Eggan, PhD, an HSCI principal faculty member and assistant professor of Stem Cell and Regenerative Biology at Harvard.

In 2005, HSCI awarded a Seed Grant to Eggan for his project "Derivation of ALS disease-specific human embryonic stem cell lines."

As a result of HSCI funding and the research it enabled, Eggan obtained additional funding from Project ALS, the Spinal Muscular Atrophy Foundation, and the New York Stem Cell Foundation. His research led to several important findings, which were published in leading scientific journals. One of his many achievements — creating the first motor neurons from patients with ALS — was hailed by *Time* magazine as the top medical breakthrough in 2008.

"HSCI Seed Grant funding allowed me to take an idea that most thought was crazy at the time and turn it into a new, exciting, and proven methodology for studying mechanisms of neural degeneration, as well as a new platform for drug discovery," said Eggan.

This year, Eggan was one of four HSCI faculty (all of whom were HSCI Seed Grant recipients) selected as a winner of the Howard Hughes Medical Institute's Early Career Science Competition, which provides each recipient with a total $1.5 million research budget plus salary and research expenses for six years.

THROUGH ITS ONGOING SUPPORT OF PROMISING YOUNG scientists and clinician-scientists conducting stem cell research, HSCI enables innovative projects to take root and, in many cases, bear fruit. HSCI's support is particularly crucial during scientists' early careers.

SEED GRANT PROGRAM

Now in its fifth year, HSCI's Seed Grant Program has consistently demonstrated the criticality of supporting scientists who are conducting innovative high-risk, high-return projects. Indeed, a review of the last three years of seed grants concluded that 70 percent led to useful findings, a considerably higher percentage than is typical of early-stage projects.

The seed grants, which provide two years of funding for projects that align with HSCI's mission, provide important early funding for projects that, because they may lack sufficient data or are highly exploratory, are not typically eligible for grants from the federal government or other traditional funding sources.

Since the program's inception, 53 seed grants and more than $9 million dollars have been awarded primarily to junior faculty in the early stages of their independent careers, as well as senior faculty embarking on new, therefore often difficult to fund, areas of research.

"Receiving this funding has been transformative, and I expect that the observations and data gained through this support will form the foundation of my work for years to come."

— Benjamin Humphreys, MD, PhD, 2007
HSCI Seed Grant recipient

HSCI's return on its investment in this program is significant and measured in many ways — in key scientific advances, productive new collaborations among HSCI's junior faculty and with stem cell researchers globally, major papers, intellectual property, and subsequent funding from other sources, such as the National Institutes of Health and disease foundations, to carry on the work and realize its full potential. For example, one 2007 grant recipient reported that by the conclusion of his project he had been able to attract $2.60 in funding for every $1 that HSCI had invested.

In 2009, HSCI awarded eight seed grants totaling nearly $1.5 million ($180,000 for the two-year grant period for each recipient) to investigators selected from a large pool of applicants from across HSCI-affiliated institutions. This year's grants support stem cell research spanning a broad range of disease areas, such as cancer, liver disease, nervous system disorders, and obesity, as well as research in broadly applicable areas of stem cell biology, such as DNA repair, embryonic stem cell differentiation, and bone formation.

Consistent with HSCI's commitment to support and expand the community of clinician-scientists involved in stem cell research — and, in so doing, expedite the translation of stem cell science from bench to bedside — this year's Seed Grant recipients include three MD/PhDs.

2009 SEED GRANT RECIPIENTS

Wolfram Goessling, MD, PhD*
Brigham and Women's Hospital
Mark Damone Johnson, MD, PhD
Brigham and Women's Hospital
David Langenau, PhD
Massachusetts General Hospital
Trista North, PhD*
Beth Israel Deaconess Medical Center
Sharad Ramanathan, PhD
Faculty of Arts and Sciences, Harvard University
Derrick Rossi, PhD
Immune Disease Institute
Yu Hua Tseng, PhD
Joslin Diabetes Center
David Weinstock, MD
Dana-Farber Cancer Institute
Paul Yu, MD, PhD
Massachusetts General Hospital

❖ *Collaborators on a joint Seed Grant*

2008 SEED GRANT RECIPIENTS

Paola Arlotta, PhD
Massachusetts General Hospital
Sangeeta Bhatia, MD, PhD*
Brigham and Women's Hospital
Caroline Burns, PhD
Massachusetts General Hospital
Stephen Haggerty, PhD
Massachusetts General Hospital
Xue Li, PhD
Children's Hospital Boston
Judy Lieberman, PhD**
Immune Disease Institute
William Pu, MD
Children's Hospital Boston
Zhong Wang, PhD
Massachusetts General Hospital
Rebecca Wingert, PhD
Massachusetts General Hospital
Sean Wu, MD, PhD
Massachusetts General Hospital

** In 2007, the Millipore Foundation made a gift of $500,000 to the HSCI Seed Grant Program. Sangeeta Bhatia, MD, PhD, was named HSCI's first Millipore Foundation Seed Grant Fellow.*

*** In 2008, GlaxoSmithKline made a gift to support HSCI's Seed Grant Program. Dr. Lieberman is the first recipient of a GSK-funded Seed Grant.*

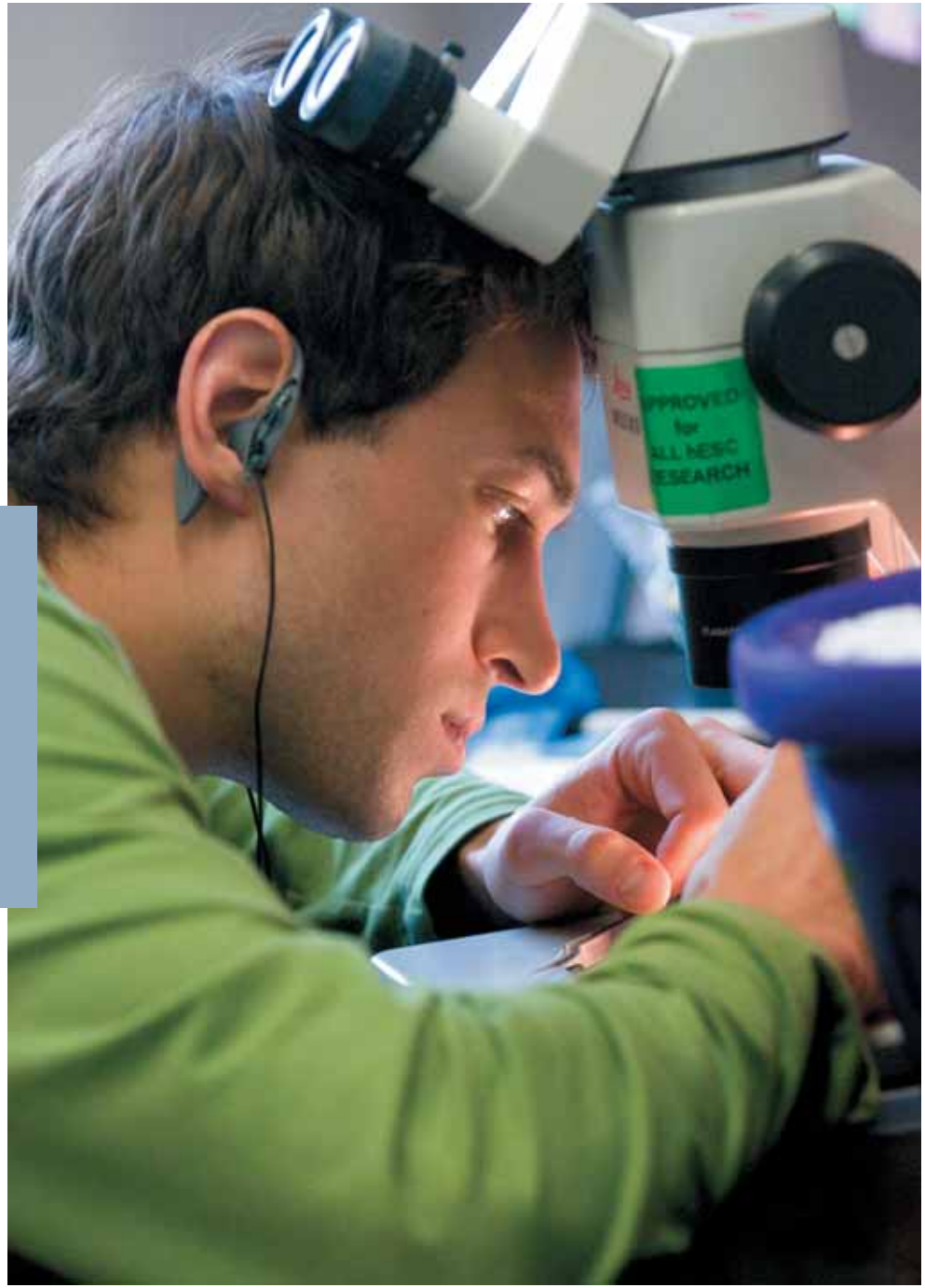
THE JUNIOR FACULTY PROGRAM

One compelling example of HSCI's commitment to nurturing and supporting the careers of brilliant young scientists — and how this, in turn, supports HSCI's mission — is the Junior Faculty Program.

Each year since 2007, HSCI has provided three years of funding to groups of young HSCI faculty members who, through their shared research interests, have on their own initiative reached across institutional boundaries to collaboratively focus on important questions in stem cell research.

The first — and the inspiration and model for the subsequent two Junior Faculty Projects — was the Cell Development Project, followed last year by the Stem Cell Regulation Project and, this year, the Epigenetics of Stem Cell Function and Aging Project.

The *Cell Development Project* originated when six young



Junior Faculty Program by the numbers

18
Number of principal investigators

7
Number of participating institutions

scientists from four different HSCI-affiliated institutions with a common interest in cell reprogramming decided that they could achieve far more by collaborating and sharing resources than by working separately in their individual labs. They joined together and, with ongoing support from HSCI, have in just a few short years achieved results that have been nothing short of stunning.

For example, members of the project have been at the forefront of the progress in cell reprogramming. In addition to the development and refinement of the methodology of reprogramming itself, their noteworthy achievements include the creation of motor neurons from patients suffering from ALS and the discovery that muscle stem cells improve muscle function in mice with the most common form of muscular dystrophy.

In collaboration with two other HSCI-affiliated labs, this group's pivotal work in cell reprogramming led to the establishment of HSCI's new iPS Core Facility (*see page 7*), a resource for scientists worldwide eager to use these disease-specific stem cells to study diseases and to screen for compounds with which to safely treat them.

Also as a result of their unique collaboration, members of the Cell Development Project have received major awards and public recognition, developed external collaborations worldwide, created intellectual property, and attracted additional funding. This summer, for instance, it was announced that three members were winners of the Early Career Science Competition sponsored by the Howard Hughes Medical Institute, which provides each with $1.5 million in research funding over six years (*see page 8*), and one was the recipient of the International Society of Stem Cell Research's Outstanding Young Investigator Award.

Like its predecessor, the *Stem Cell Regulation Project* comprises young scientists across several institutions who are working on a common goal: in this case to understand the molecular regulation of stem cell identity, maintenance, and differentiation in both normal development and disease. This work is essential to being able to fully realize the promise of using induced pluripotent stem (iPS) cells and adult tissue-specific stem cells to study

and potentially treat diseases. The group's projects currently focus on a number of diverse but interconnected areas. These include investigating the role of microRNAs in the regulation of stem cell fate, the pathways that regulate stem cells in normal and cancerous lungs, the factors that maintain hematopoietic (blood-producing) stem cells, and the mechanisms that direct the differentiation of neuronal subtypes in the brain.

As with the group that preceded it, members of this project are actively involved in many HSCI activities, share their expertise through monthly "chalk talks," and engage in intellectual exchanges with their peers nationally and globally. Last fall, for example, members of the program met in Los Angeles with junior faculty from the California Institute of Regenerative Medicine (CIRM). As they did two years ago, CIRM junior faculty will travel to Boston this fall.

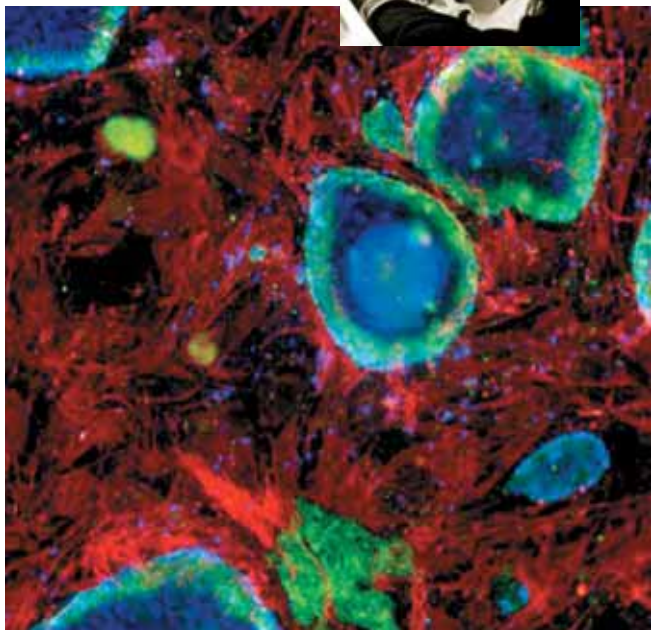
Funded by HSCI beginning in 2009, the *Epigenetics of Stem Cell Function and Aging Project* consists of junior faculty from five laboratories at four HSCI-affiliated institutions who are collectively focusing on gaining novel insights into the molecular mechanisms involved in stem cell aging, regenerative capacity, and pluripotency. This work has relevance to many diseases, particularly those that occur with greater frequency as people age: diseases like cancer and heart failure, as well as potentially debilitating conditions such as the loss of muscle mass. With the aging of the population in the United States and many other developed nations, this research becomes even more important to reducing age-related morbidities.

"I am thankful for the support and mentorship I've received from all my colleagues at HSCI; the open and interactive environment fostered by HSCI was a tremendous help to me in getting my lab started, and continues to enhance my research on a daily basis."

— **Amy Wagers, PhD, HSCI Cell Development Project and Executive Committee member**

"This has been a fantastic program that has helped me toward a physician-scientist career in which I can hopefully translate our basic science understanding of stem cells toward…cell-based therapies."

— **Ashutosh Jadhav, MD, PhD, 2005-2007 HSCI Medical Scientist Fellow, Massachusetts General Hospital**



SUPPORTING MEDICAL-SCIENTISTS

Because they straddle both worlds, clinicians who also conduct basic research are in a unique position to bridge the gap between the laboratory and the clinic, which is critical to rapidly bringing advances in stem cell research into the patient-care setting.

For this reason, and because federal funding for medical training has decreased, since 2005 HSCI has supported the training of MD/PhD students through its Medical Scientist Training Fellowship. Coordinated jointly with the Harvard-MIT Combined MD/PhD Program, the fellowship provides two years of tuition support and a stipend to qualified MD/PhD students whose thesis or long-term research goals involve stem cells.

Since its inception, the fellowship has been supported, in part, by the late Ruthe B. Cowl, a longtime generous HSCI donor. This year, the fellowship received a major boost as a result of a $1.5 million bequest from Mrs. Cowl to create an endowment for the program, plus a $2 million gift from the pharmaceutical company GlaxoSmithKline. These additional funds have enabled HSCI to continue and expand its support of the early careers of deserving clinician-scientists as they launch their labs at the postdoctoral and instructor stages of their careers.

The 2009 recipient of the HSCI Medical Scientist Training Fellowship is Srinivas Viswanathan, PhD, a *summa cum laude* graduate of Yale University and student at Harvard Medical School, who distinguished himself on many fronts while working as a graduate student in the laboratory of HSCI Faculty Executive Committee member George Daley, MD, PhD.

The previous fellowship recipients are Zuzana Tothova, MD, PhD (2007-2009), who is now in clinical training at Boston's Brigham and Women's Hospital, and Ashutosh Jadhav, MD, PhD (2005-2007), who is doing his clinical training at Massachusetts General Hospital.

EDUCATING

THROUGH A BROAD RANGE OF EXISTING AND NEW INITIATIVES, HSCI reaches out to educate and inspire current and aspiring scientists, teachers, policymakers, journalists, and the general public about stem cell science and its related ethical and policy issues.

ONLINE *STEMBOOK*

In a field as rapidly evolving as stem cell biology, disseminating information solely by conventional means — primarily textbooks and scientific journals — virtually ensures that information will be outdated even before the ink is dry.

To provide the global research community, including stem cell and non-specialist researchers, with the most up-to-date information on stem cell research, last fall HSCI launched *StemBook*, a freely available, open-access online textbook.

Overseen by an international editorial board of prominent stem cell scientists, *StemBook's* content includes original, peer-reviewed chapters written, by invitation, by top stem cell researchers from institutions throughout the world. *StemBook* was funded, in part, by an anonymous foundation.

Presented in a scientific journal format familiar to biomedical researchers, *StemBook's* interactive chapters contain videos and links to terms, sources, and cited journal articles. Authors update their chapters at least every other year to ensure that they remain current. Recently, *StemBook* chapters were selected to be indexed on MEDLINE, which is part of PubMed, a freely accessible, online database of biomedical journal citations and abstracts used by researchers worldwide.

StemBook began with 16 chapters; it now has 48 chapters online, and 80 have been commissioned. Within five months of its launch, the site had nearly 10,000 unique visitors, demonstrating its growing value as a reputable source of information to those seeking to stay abreast of a fast-moving field.

As word about *StemBook* continues to spread, it is anticipated that the number of chapters and users will continue to grow. And several disease foundations are borrowing the concept and the highly collaborative technical platform for *StemBook*, which was developed by HSCI in collaboration with Harvard's Initiative in Innovative Computing.

StemBook by the numbers

48
Chapters online

80
Chapters commissioned

10,000
Unique visitors within five months of launch

NEW UNDERGRADUATE MAJOR

Beginning this fall, Harvard undergraduates will have the opportunity to pursue a new concentration, or major, in Human Developmental and Regenerative Biology. One of the first such majors in the nation, the new concentration is among many new and planned initiatives of the Department of Stem Cell and Regenerative Biology (SCRB), Harvard's first inter-school department.

Established in 2007 and chaired by HSCI co-directors Douglas Melton, PhD, and David Scadden, MD, SCRB is a joint department of the Faculty of Arts and Sciences (FAS) and Harvard Medical School (HMS). In addition to educating undergraduates, SCRB is dedicated to the education of graduate, postdoctoral, and medical students throughout FAS, HMS, and its affiliated hospitals.

Taking advantage of SCRB's unique strengths, especially its cross-institutional faculty, the new concentration will focus on an interdisciplinary approach to understanding human development, disease, and aging while also while providing "hands-on" science education from the very first semester.

Specifically, students will learn how human beings develop from a fertilized egg, are maintained and repaired throughout adulthood, and how they age until the end of life. Courses in the new concentration, some of which — "From Egg to Embryo to Organ," for example — are already being offered, cover subjects such as stem cell biology, experimental and human genetics, neurodegenerative disease, and human developmental and experimental embryology.

It is anticipated that this new concentration will entice undergraduates to consider a career in human developmental and regenerative biology, while offering them a pathway to realizing that goal.

"The HSCI/CWRU course not only updated me on some of the most cutting-edge stem cell research; it also made me consider how my work in stem cell biology relates to so many important ethical and policy issues."

— Heather L. Heine, PhD, University of British Columbia, Canada, a bioethics course attendee

COURSE ON ETHICAL AND POLICY ISSUES

Since its inception HSCI has taken a leadership role in discussing the tough questions regarding the ethics of stem cell research — through undergraduate courses, ongoing bioethics discussions at HSCI-affiliated hospitals, public forums, and participation in policy-setting at the national level.

The justifiable excitement over recent strides in cell reprogramming has led some to mistakenly conclude that the ethical debate regarding the use of human embryonic stem cells (hESCs) is no longer relevant. Yet stem cell experts at HSCI and elsewhere strongly believe that research using hESCs, the "gold standard" of stem cells, must continue concurrently with research involving reprogrammed cells, especially since it is not yet known whether alternative types of cells are identical in all respects to hESCs.

Additionally, the new cell reprogramming technologies raise ethical and policy issues in their own right. And, as embryonic

stem cell research begins to move from bench to bedside — the first clinical trial of embryonic stem cell therapy was approved by the U.S. Food and Drug Administration earlier this year — the ethical and policy issues become even more complex.

Mindful of the need to address these issues, this summer HSCI collaborated with the Department of Bioethics at the Case Western Reserve University (CWRU) School of Medicine in Cleveland to offer an intensive course, "At the Cutting Edge of Stem Cell Science: Ethical and Policy Issues," on the Harvard University campus.

Led by multidisciplinary faculty from the schools of Harvard, CWRU School of Medicine, and Massachusetts Institute of Technology, the week-long program addressed the major issues in the science, ethics, and policies of stem cell research. Geared to a broad audience that included policymakers, patient advocates, and industry representatives, as well as clinicians and scientists, topics included donation and procurement of human materials for research, intellectual property, and genetic modification.

HSCI RADCLIFFE FELLOWSHIP PROGRAM

In collaboration with the Radcliffe Institute for Advanced Study at Harvard, HSCI funds a year-long fellowship for an individual whose work in the field is highly interdisciplinary. Fellows are chosen by the Radcliffe Institute for their superior scholarship, research, or artistic endeavors, as well as the potential of their projects to have a long-term impact.

This year, Linda Griffith, PhD, a professor of biological and mechanical engineering at Massachusetts Institute of Technology, was named the second HSCI Radcliffe Fellow for the academic year 2009-2010. Griffith's project is aimed at using novel approaches, including molecular engineering, nanofabrication, and microfabrication, to probe the complex feedback loops by which stem cells regulate their own behavior. She will then use this knowledge to explore the possible connections between when this self-regulation process goes awry and certain women's reproductive disorders, such as endometriosis.

The first HSCI Radcliffe Fellow was stem cell scientist Christine Mummery, PhD, now chair of the Department of

HSCI Internship Program by the numbers

100
Applicants in 2006

375
Applicants in 2009

"I'm doing a research project relating to muscle aging and regeneration in the laboratory of Andrew Brack [PhD] at Mass. General Hospital. I'm so impressed by the HSCI faculty and facilities — and it's wonderful to learn about stem cell biology and career options from experts in the field. This is an amazing opportunity, especially since I plan to pursue a career in stem cell research."

— Darren Ruane, a senior at Trinity College, Ireland, and a 2009 HSCI Internship Program intern

Anatomy and Embryology at the Leiden University Medical Center in the Netherlands. During her 2007 fellowship, Mummery collaborated with members of the HSCI Cardiovascular Disease Program and the Harvard School of Engineering and Applied Sciences to advance research aimed at finding novel strategies to repair damaged hearts with cardiac stem cells.

HSCI INTERNSHIP PROGRAM

Recently concluding its fifth successful year, the HSCI Internship Program (HIP) has exposed more than 175 undergraduates from Harvard and many other colleges to an unparalleled experience. Interns selected for the program spend a summer working in the laboratory under the supervision of an HSCI scientist. They also participate in a focused educational program that includes a weekly stem cell seminar series and a stem cell course led by an HSCI faculty member.

HIP students learn critical skills: how to design and perform scientific experiments, read and critique scientific literature, create a scientific poster, and present their research findings at the HIP Symposium at the end of the summer. The goal of the program is not only to encourage students to consider a career in stem cell research — indeed, many have done just that — but also to learn skills that are valuable in any career pursuit: how to think critically, analyze problems logically, and conduct inquiry-driven research.

This year, approximately 375 applicants applied for the 35 openings in the ten-week, paid internship. Of these, 18 were from Harvard College and, in keeping with HSCI's goal of reaching beyond its boundaries, the rest were non-Harvard students, including five international students. By comparison, in 2006, 100 students applied to the program, reflecting the growing interest in stem cell research at the undergraduate level.

BOSTON STEM CELL EDUCATION SYMPOSIUM

Many researchers' interest in a career in science was first piqued when they were in high school, often by a teacher who was excited by the latest advances in science. Recognizing the important role of high school teachers in educating and inspiring the next generation of stem cell scientists, for several summers HSCI offered a popular week-long Teacher Professional Development Course in stem cell science taught by HSCI faculty members.

Last fall, HSCI teamed up with the Broad Institute and the Whitehead Institute to co-sponsor a new educational offering for local high school teachers — The Boston Stem Cell Education Symposium. Fifty teachers participated in the free day-long symposium, which featured presentations on cutting-edge stem cell research by Harvard and Massachusetts Institute of Technology scientists, panel discussions with scientists and educators about the challenges of teaching stem cell science, laboratory tours, and discussion groups with fellow teachers about stem cell lesson plans.

FIRST FEDERAL FUNDS FOR TRAINING AWARDED

In 2008, HSCI was awarded its first federal funding for training — a $2 million National Institutes of Health Training Grant to support up to eight pre- and postdoctoral trainees in stem cell science. The HSCI Training Program is under the direction of HSCI Co-Director, David Scadden, MD.

Fellows, who are selected through a competitive application process, train in the lab of an HSCI Principal Faculty mentor and receive tuition, a stipend, and other training funds. In the program's first year, five trainees were appointed to labs in four HSCI-affiliated locations: Children's Hospital Boston, Harvard's Faculty of Arts and Sciences and its School of Engineering and Applied Sciences, and Harvard Medical School.

LEUKEMIA DOCUMENTARY

HSCI faculty are featured in a new 30-minute video documentary, "Finding a Cure for Leukemia: A Stem Cell Story," which was developed in association with HSCI and produced and directed by local young filmmakers Amy and E. W. Steptoe, of Steptoe Siblings Pictures.

The documentary follows the personal story of Sandra Crowe, who underwent bone marrow transplantation for leukemia at Dana-Farber Cancer Institute. Combining interviews with HSCI faculty and Crowe's care providers with lively graphics, the video describes the often-lifesaving role of bone-marrow transplantation (a stem cell treatment) for patients battling leukemia, and educates viewers about stem cells and their potential as both tools and therapies for a wide range of diseases. The documentary can be viewed on Cambridge Cable Television (CCTV) or the HSCI website (www.hsci.harvard.edu).

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FINANCIALS

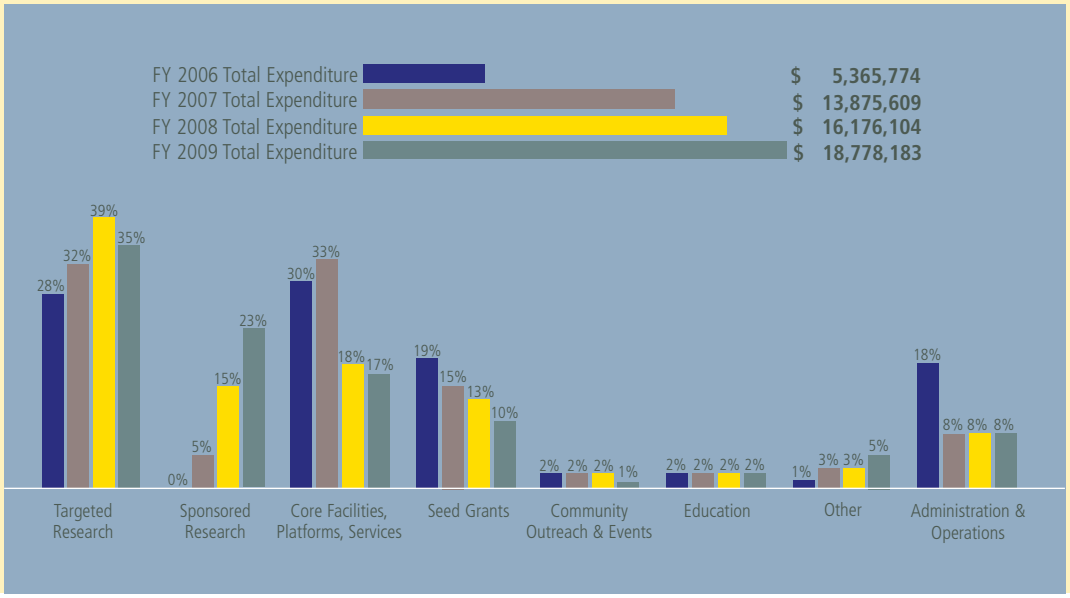
TOTAL EXPENDITURE FOR HARVARD STEM CELL INSTITUTE IN THE FISCAL YEAR ENDING June 30, 2009 reached $18.8 million, exceeding the level in fiscal year 2008 by $2.6 million. This was a 16% increase, but lower than the original budget as well as our mid-year forecast, as we reduced expenditures in line with the economic challenges of the year. We were able to increase spending in areas where we received new, directed funding.

Spending in overall research programs grew to $15.6 million, representing 83% of the total expenditure in FY 2009. Spending in sponsored projects reached $4.4 million in FY 2009 and exceeded that of the prior year by almost 60%. The increase was driven primarily by the sponsored project awards from Eli Lilly and GlaxoSmithKline (GSK). FY 2009 marked the start of a $25 million, five-year agreement with GSK for joint research in major disease areas including diabetes, muscle, aging, cardiovascular, and pain. While the GSK alliance project is managed by HSCI, the majority of the funding flows directly to HSCI's principal members through affiliated hospitals, and is not recognized by HSCI as operating income and expense. Additionally, several research projects with leading disease foundations in the Therapeutic Screening Center started or expanded.

Spending in targeted research grew a modest 6% from the prior year. The number of new seed grants awarded in FY 2009 was 10 and held at the same level as FY 2008. The reduction in total seed grant expenses from the FY 2008 level was due to the second-year payment of the 12 seed grants awarded in FY 2007. Spending in the core platforms grew by 11% largely as a result of the new iPS Core facility. A gift from GSK also enabled a new program supporting young physician scientists at different stages in their careers.

Spending in administration and operations in fiscal year 2009 increased by 12% but held steady compared to the prior year in relation to overall spending, reflecting success in managing expanding programs with growing administrative responsibilities.

FY 2009 was an extraordinarily challenging year for the Harvard University community as it saw losses in the value of endowment funds impact programs and workforce. As a young organization with direct support, HSCI has not been as adversely affected as some of the other parts of the university. The strong financial contributions made in the last year to advance research in stem cell science have allowed HSCI to continue investing in critical research, core facilities, community building, and education programs. This coming year, we will have the opportunity to further leverage that investment by competing for federal support as a result of new National Institutes of Health policies. As we start fiscal year 2010, we are optimistic that we can continue to raise the necessary funds to pursue our mission to fulfill the promise of stem cells.



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