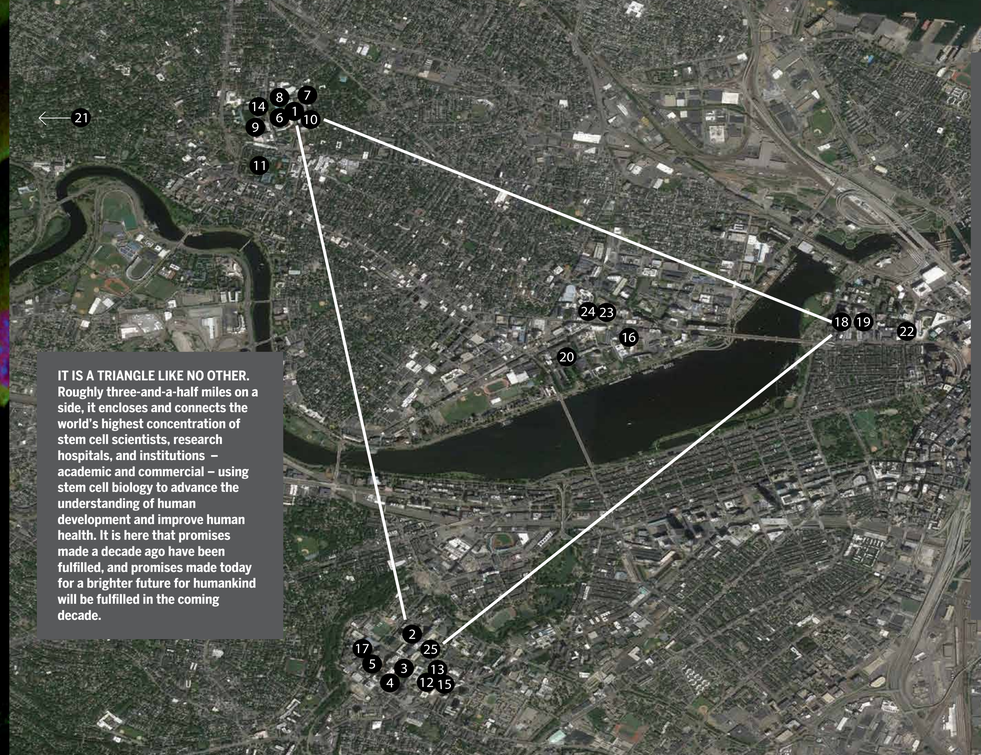
Harvard Stem Cell Institute

10

Years and Counting



IT IS A TRIANGLE LIKE NO OTHER. Roughly three-and-a-half miles on a side, it encloses and connects the world's highest concentration of stem cell scientists, research hospitals, and institutions – academic and commercial – using stem cell biology to advance the understanding of human development and improve human health. It is here that promises made a decade ago have been fulfilled, and promises made today for a brighter future for humankind will be fulfilled in the coming decade.

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2. Beth Israel Deaconess Medical Center
3. Boston Children's Hospital
4. Brigham and Women's Hospital
5. Dana-Farber Cancer Institute
6. Harvard Department of Chemistry and Chemical Biology
7. Harvard Department of Molecular and Cellular Biology
8. Harvard Department of Organismic and Evolutionary Biology
9. Harvard Department of Physics
10. Harvard Department of Stem Cell and Regenerative Biology
11. Harvard Faculty of Arts and Sciences
12. Harvard Medical School
13. Harvard School of Dental Medicine
14. Harvard School of Engineering and Applied Sciences
15. Harvard School of Public Health
16. Harvard-MIT Division of Health Sciences and Technology
17. Joslin Diabetes Center
18. Massachusetts Eye and Ear Infirmary
19. Massachusetts General Hospital
20. Massachusetts Institute of Technology
21. McLean Hospital
22. Schepens Eye Research Institute
23. The Broad Institute
24. Whitehead Institute for Biomedical Research
25. Wyss Institute of Biologically Inspired Engineering

Leadership Gifts

Our deepest gratitude goes to the donors listed below for their profound commitment to stem cell science at Harvard. We recognize these top supporters, whose cumulative gifts and pledges total $100,000 or more as of the fiscal year that ended June 30, 2014. Their enduring leadership helps Harvard sustain its excellence in stem cell science.

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Fiscal Year 2014 Support

We gratefully acknowledge all donors who made new gifts or pledges during the fiscal year that ended June 30, 2014. Each of these individuals and organizations provided crucial support to stem cell science at Harvard.

Anonymous (4)
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Memorial Gifts

Memorial gifts help the Harvard Stem Cell Institute sustain programs that are central to its mission. Thank you to those supporters who chose to remember a loved one through a memorial gift. Those who were memorialized with gifts to the Harvard Stem Cell Institute in the fiscal year that ended June 30, 2014, are listed below.

Margaret Aertsen
Irvin Brewer
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James Fisk, Sr.
G. Peabody Gardner, Jr.
Arlene Grossman
Ronald O. Hurston
Helen McKenna
Alfred Nutile
Madeline O'Keefe
Alison M. Urzan
Clayton Lee Willis

1,000 Scientists
One Goal:
Life-Changing Medicines

When this report was first conceived, we planned to write just a few words to add a personal note to a traditional Annual Report. But on reflection, we decided that rather than mark the end of the Harvard Stem Cell Institute's 10th anniversary year with a summary of the past year, we would instead use this opportunity to give you our personal thoughts about what's been accomplished in this foundational first decade, and what we are going to accomplish in the coming decade.

Ten years ago, human stem cell research was at the center of a political firestorm, and most of it was cut off from the government funding needed to fulfill its promise as the foundation of regenerative medicine.

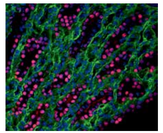
Against that background, Harvard made a bold bet, supporting us in establishing a new collaborative institute dedicated to reinventing the way scientific research is done and advancing discoveries in stem cell biology from laboratories all across the Harvard landscape—Harvard Yard, Harvard Medical School, the University's affiliated hospitals—to patients' bedsides.

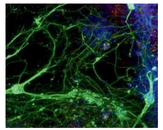
With your generous support, we created dozens of new stem cell lines and kick-started the new field by distributing those lines free to researchers around the globe. Simultaneously, we forged new links among Harvard and its research hospitals, starting with a few dozen scientists and physician researchers. Now, 10 years later, we can say without hesitation that we achieved our initial goals.

Today, HSCI is firmly established as the preeminent stem cell research program in the world with 115 primary investigators and more than 1,300 scientists, including undergraduates, graduate students, and post-doctoral fellows. Working across boundaries that typically segregate academic disciplines, departments, and schools, HSCI scientists have assumed leadership roles in every area of this new arena. With the establishment of the Department of Stem Cell and Regenerative Biology in the Faculty of Arts and Sciences and Harvard Medical School—the first interschool department in Harvard's history—stem cell biology is now taught to undergraduates, who in just a few years have made this department's concentration the most popular in the life sciences. And in several important projects, we are either in, or nearing, the clinical development phase, moving forward on the promise of stem cell science to develop treatments and cures for heretofore intractable conditions.

Bringing the results of discoveries in ALS, diabetes, and many other diseases to the clinic and to the market requires close partnerships with industry and investors. Sitting in the middle of the Greater Boston life sciences cluster, we are fortunate to have many corporate collaborators with whom we are conducting research and working on commercializing our discoveries.

At the same time, however, it would be disingenuous to say that when our first decade began we knew precisely where we would be today. As in other areas of scientific discovery, the advance of stem cell science has been an unpredictable progression, taking us in directions we couldn't have imagined in 2004. For example, the advent of reprogramming and gene-editing technologies came faster than expected. Fortunately, the nimble decision-making and financial structure of HSCI allowed us to capitalize on advances in both areas and lead the field. Similarly, the use of human cell-based models of disease was a risky area when we first invested heavily in cell-based therapeutic screening, but it is now a commonly accepted practice.





April 2004
Harvard Stem Cell Institute (HSCI) is co-founded by Doug Melton, PhD, and David Scadden, MD. HSCI begins with 7 Harvard schools, 7 teaching hospitals, 25 principal investigators, and nearly 100 scientists.

August 2005
Cowan, Melton, and Eggan labs fuse adult skin cells with embryonic stem cells to reset adult cells to an embryonic form.

November 2007
Hochedlinger Lab is one of three research groups to independently use four genes to transform adult cells into cells with embryonic-like properties.

April 2007
Harvard Department of Stem Cell and Regenerative Biology (HSCRB) is established, bringing together researchers from Faculty of Arts and Sciences and Harvard Medical School. It's the first academic department in Harvard's 371-year history based in more than one school.

Eggan Lab develops first mouse stem cell lines carrying human genes for ALS - Lou Gehrig's disease, making study of in vitro treatments possible.

Zon Lab identifies hormone in zebra fish that expands blood stem cell numbers– this will lead to a clinical trial about four years later.

January 2007
HSCI opens therapeutic screening center under Lee Rubin, PhD, to use cells as in vitro models for drug discovery.

But what makes HSCI unique?

• We are the world's single largest collaborative network of stem cell scientists—colleagues who are all within a short cab or subway ride of one another, allowing face-to-face interactions at a moment's notice, creating depth and breadth of expertise at scale.

• We have the power to leverage every area of science across Harvard, from the basic research in the University's labs, to the bioengineering work of the Wyss Institute, to the genetic powerhouse that is the Broad Institute, to the world-leading Harvard-affiliated hospitals.

• We are centered in the biotech, pharmaceutical, and venture capital community of Cambridge and Boston, the single largest life science community in the world.

December 2008
Eggan Lab derives spinal motor neurons from human embryonic stem cells and uses them to replicate ALS disease process in a lab dish.

October 2008
Melton Lab makes human iPS cells using chemicals in place of two cancer-causing genes.

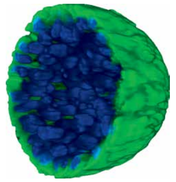
September 2008
HSCI launches Stembook, an updated online textbook of stem cell science for the research community.

August 2008
Daley, Cowan, and Hochedlinger labs create 20 disease-specific stem cell lines, providing valuable tools to study disease.

Melton Lab bypasses stem cells altogether and transforms a type of adult mouse pancreatic cell that does not produce insulin into one that does.

July 2008
Eggan Lab creates first patient-specific iPS cells, marking first time scientists ever produced a human stem cell line from adult patients with a genetic disease (ALS).

Wagers Lab treats muscular dystrophy in mice with muscle stem cell transplants.



June 2009
HSCI establishes iPS Core at Massachusetts General Hospital, providing cells for the entire Harvard stem cell community. The facility later moves to Harvard campus.

March 2009
Scadden Lab identifies mechanism directing blood stem cells to their destination in the body.

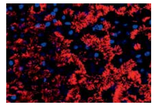
February 2009
Melton Lab's work in diabetes and HSCI are primary focus of cover story in TIME magazine.

• We have created, and continue to focus on creating, a culture of team science—a new way of doing science to enable a new science.

With our foundation solidly established, it is time to for us to build for the coming decade, concentrating our focus without abandoning the exploration of deep scientific questions that have brought us this far. In the coming years, we will place special emphasis on those areas in which we can have the most immediate clinical impact. These are:

• Diabetes and Metabolic Diseases, where we are now able to produce billions of fully functional, insulin-producing, human beta cells. We are working with researchers at several institutions on ways of shielding them from immune attack and expect initial human trials within the next few years. This advance holds the promise of completely reshaping the diabetes landscape.

• Neurodegenerative and Neurologically Related Diseases, an area in which we already have a possible treatment for ALS in an initial clinical trial in collaboration with Massachusetts General Hospital and Boston Children's Hospital. This work, and similarly promising advances in cell therapy for Parkinson's disease and drug therapy for Spinal Muscular Atrophy, is made possible by the HSCI developed "disease-in-a-dish" technology. Additionally, we are developing new approaches to the treatment of pain, spinal cord injury, multiple sclerosis, and a number of diseases of the eye and ear.



November 2010
Rinn Lab identifies new genetic elements involved in cellular reprogramming.

September 2010
Rossi Lab identifies safer way to make iPS cells using modified messenger RNA. This enables a new way to deliver therapeutics.

January 2010
Wagers Lab finds factors in blood of young mice that make blood stem cells in old mice start to act like those in young mice.

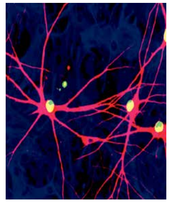
November 2011
Macklis Lab shows neuronal transplants can repair brain circuitry and normalize function in mice with brain disorders.

August 2011
Eggan Lab creates induced motor neurons, which can be used to study the development of ALS and spinal muscular atrophy.

April 2011
Lee Lab discovers certain stem cells in bone marrow are capable of stimulating certain cells in the heart to repair damaged tissue.

March 2011
Zon Lab finds a drug target for melanoma tumors.

• Aging, a research area in which a team of biologists, cardiologists, and neurologists have discovered a protein that can seemingly "turn back the clock" in older animals, improving cardiac function, muscle repair, and, most astonishing, some aspects of cognition. Additionally, we are focusing on improving the efficiency of stem cell transplants in cancer—in fact, we have brought discoveries initially made in fish and mice to a clinical trial in patients around the country, testing a way to make umbilical cord blood transplant safer for people with blood cancers—and possible treatments for kidney disease, both of which increase with age and have a major impact on the aging process. As one can imagine, our work on aging has implications in almost all areas of disease and injury.



December 2012
Biogen Idec selects Lee Rubin, PhD, to participate in multi-center consortium to identify treatments for ALS.

July 2012
Janssen Pharmaceuticals enters into Evotec-HSCI "CureBeta" partnership to develop and test diabetes drug targets.

April 2012
Rajagopal Lab grows lung surface tissue from stem cells, a major step toward finding a treatment for cystic fibrosis.

January 2012
Evotec and HSCI launch "CureNephron" initiative to find novel therapeutic targets for kidney disease.

October 2013
Zon Lab publishes initial results of Phase 1b human clinical trial testing a therapeutic licensed to Fate Therapeutics. The treatment enhances engraftment of stem cells of umbilical cord blood for adult transplantation.

May 2013
Wagers and Lee labs identify protein in mouse and human blood that may be the first effective treatment for age-related heart failure.

April 2013
Benjamin Humphreys, MD, PhD, and two lab members are the grand prize winner of the first Deans' Health and Life Sciences Challenge for their business plan, aimed to help fibrosis-related diseases.

Ott Lab transplants functional lab-grown kidneys into rats. When transplanted, these organs start filtering the rodents' blood and making urine.

Rubin Lab uses stem cell-based drug screening technology to identify compound more effective at protecting neurons killed in ALS.

March 2013
Tseng Lab discovers mechanism regulating production of energy-burning brown fat.

AstraZeneca invests $240M in Moderna Therapeutics, a startup company founded by Derrick Rossi, PhD, with an HSCI seed grant.

January 2013
Arlotta Lab discovers possibility of turning one type of differentiated neuron directly into another *in vivo*.

Edge Lab demonstrates that cells lost to noise trauma can be regenerated in mammalian ear.

• Drug Discovery, where the HSCI-pioneered "disease-in-a-dish" technology promises to be a paradigm shifter for the pharmaceutical industry because it makes possible the discovery and development of new therapies using the cells attacked by a particular disease. This approach will significantly reduce the time and risk of the drug development process. Further, combining stem cell technology, genomics, and gene-editing technology will finally usher in an age of personalized medicine.

Although we will emphasize these four areas, we will not neglect the basic science that has brought us this far, nor the other disease areas in which we are making progress. We will continue to leverage the strength of our large community through comparative projects across organ systems, such as cancer or fibrosis, to identify solutions that a more narrowly focused effort might miss.

But we are prepared to "double down" on those four areas. We firmly believe that, in partnership with industry, in collaboration with other researchers around the world, and with your continuing support, when we celebrate the end of our second decade, we will be doing so in a world in which a number of today's most difficult medical challenges are the stuff of medical history, rather than the problems of patients' daily lives.

Doug Melton and David Scadden
Founding Co-Directors

May 2014
In two complementary papers, Wagers and Rubin labs show protein found in both mice and humans reverses signs of aging in mouse brain and muscles.

April 2014
Eggan and Woolf labs find iPS cell-derived motor neurons from ALS patients point to a common problem among different forms of the disease. FDA-approved epilepsy drug addresses the problem in a dish, leading directly to a clinical trial, for which patients are now being recruited.

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