Harvard Stem Cell Institute

Annual Report 2013

HSCI 2013

From the Directors


Douglas A. Melton


David T. Scadden


Brock C. Reeve

For this year's annual report, our ninth, we have chosen to highlight the powerful concept of ROI – Return on Innovation and Return on Investment, which have been our focus since the Harvard Stem Cell Institute's very first day.

The entire purpose of creating an Institute made up of Harvard Stem Cell scientists, clinicians, students, technical staff, and support staff, from multiple disciplines, was, and remains, to turn novel scientific ideas into medical treatments for patients – the ultimate Return on Innovation. Similarly, the ideas we help launch with HSCI seed grants and disease program research provide unparalleled Return on Investment.

If ever there has been a year in our nine-year history that demonstrates ROI, this year has been it. Investments that helped us grow our basic understanding of biology and disease resulted in four big announcements:

- a new model for drug discovery using patient-derived stem cells in a dish;
- phase 1b clinical trial results for a drug that enhances engraftment of stem cells for therapy;
- the discovery of a new path to expanding populations of insulin-producing beta cells; and
- a way to reverse the typical decline in our cells' ability to regenerate and repair that comes with age.

Every one of this year's advances, breakthroughs, and firsts are just beginnings. They validate our vision, and the faith you have placed in it. They constitute the foundation on which we are building for the future and are laying the groundwork for what we will achieve in our upcoming second decade of reinventing science and discovery in this, the century of the cell.

Next spring, we will be marking the 10th anniversary of the creation of the HSCI and Harvard University's commitment to assume an international leadership role in the then nascent field of stem cell biology. Ten years is a long time in most areas of human endeavor; in science it is but a day. And the list of scientific accomplishments to emerge from HSCI laboratories in that first "day" is truly remarkable.

So we are able to say, with neither hyperbole nor hesitation, that, with your help, this coming decade will bring the fulfillment of a host of predictions and promises to fruition, changing the face of 21st-century medicine, of aging, and of the treatment of chronic and heretofore fatal diseases. We hope that you are as enthusiastic about these discoveries as we are, as each of them represents enormous Return on Innovation, and on Investment. And, we expect and believe that with your ongoing support there will be many more exciting breakthroughs to come.

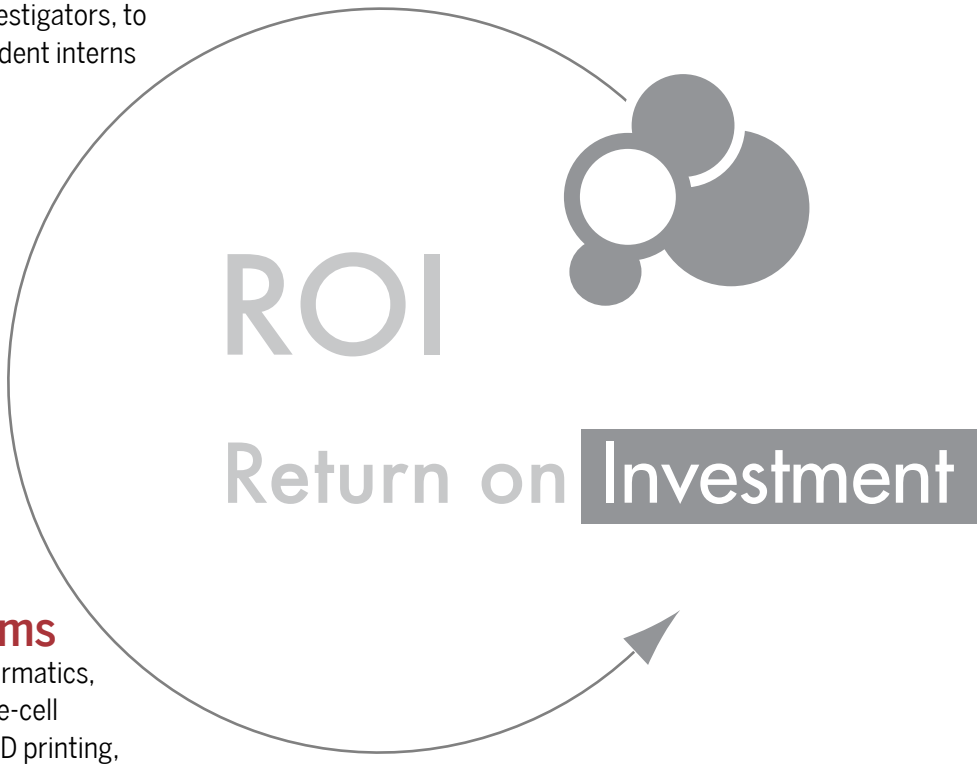
With thanks,

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

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

Going Forward

Areas of Investment for the Next Five Years



People
from undergraduates, to senior principal investigators, to student interns

Projects
from basic embryonic stem cell research to complex, multi-institution clinical trials

Platforms
from bioinformatics, to new single-cell analytics, 3-D printing, and biomaterials

Partnerships
with fellow academics, disease foundations, and leading biopharmaceutical companies

Our overarching goal for the next five years remains what it's been for the last nine: to use stem cell biology to improve human health. And the multiple, impressive discoveries made in those past nine years have brought us to the point where we can jump to the next level.

Since our founding, our work has identified specific stem cell populations within the body, taught us how to control cell fates, and created stem cell-derived cells to discover effective and safe drugs. The next wave of effort will continue this work and expand in complexity to create cells in three-dimensional constructs, fully re-create human diseases in animal models, and develop therapeutic applications.

We are able to accomplish these goals because we have created a unique collaborative and entrepreneurial research culture. We focus resources on young investigators, invest in innovation as the catalyst for a steady flow of breakthroughs in both scientific knowledge and research methods, and have a passion for using new scientific knowledge to bring therapies for chronic and fatal diseases to the clinic as quickly as possible. In response to our creation of this unique environment, Harvard and Boston have become a magnet for students and scientists at all career levels from around the globe.

Return on Investment

Clinical Trial Results

Chemical found in zebrafish promises to improve cord blood transplants in humans

This year marked another major demonstration of HSCI scientists' ability to take stem cell science from bench to bedside.

HSCI Executive Committee chair Leonard Zon, of Harvard Medical School and Boston Children's Hospital, working with HSCI colleague Corey Cutler, of Dana-Farber Cancer Institute, and collaborators at Massachusetts General Hospital, carried a discovery made in 2007 in zebrafish all the way through Phase 1b human clinical trials.

The chemical the researchers found enhances the engraftment of cord blood stem cells, thereby making the use of umbilical cord blood a possibility for reconstituting the immune systems of adults with blood cancers. The long-term goal is to make the treatment of those cancers far more effective. Fate Therapeutics, a San Diego-based biopharmaceutical company of which Zon is a co-founder, along with David Scadden, has in-licensed this technology and is bringing it to the next phase of clinical trials, showing a very real Return on Investment and Innovation.

New Diabetes Hormone

Breakthrough hormone, found in humans, stimulates growth of insulin-producing beta cells

One of 2013's true out-of-the-box discoveries came from the lab of HSCI Co-director Douglas Melton.

Thanks to the use of flexible funds, Melton was able to have a postdoctoral fellow named Peng Yi step back from the Melton lab's primary focus on finding a cure for insulin-dependent type 1 diabetes, to go off on what many laboratories and institutions might have considered a "wild-goose chase." And it turned out the wild geese led to the discovery of a previously unidentified hormone, found in both mice and humans, that causes insulin-producing beta cells in the pancreas to multiply at previously unknown rates.

German biotech company Evotec and global pharmaceutical giant Johnson & Johnson are partnering to develop small and large molecules to target this hormone, which Melton and Yi named betatrophin. Betatrophin may not only be a new approach to curing type 2 diabetes, one of the biggest global health challenges today, but also may prove useful for type 1 diabetics with residual beta cells.

Return on Innovation

Age Reversal Protein

Protein turns back the clock on the aging heart; a potential therapeutic for heart failure

HSCI Principal Faculty members Amy Wagers and Richard Lee, she a basic scientist and he a scientist and practicing cardiologist, published a paper this year that may radically redraw our picture of aging.

Following a trail pioneered by Wagers in her postdoctoral years, and based upon some of her work in skeletal muscle repair that showed a loss of the ability of muscle stem cells to repair and regenerate with age, the collaborators successfully showed that a protein in the blood of young mice can make the failing, enlarged hearts of old mice revert to a much healthier, better functioning, younger state.

The protein identified by Wagers, Lee, and colleagues in Harvard laboratories and Brigham and Women's Hospital is also present in humans, and the two HSCI researchers now are collaborating with other colleagues to understand how it affects other tissue systems.

Disease in a Dish

Drug discovery approach uses patient-derived stem cells to find therapeutics for genetic diseases

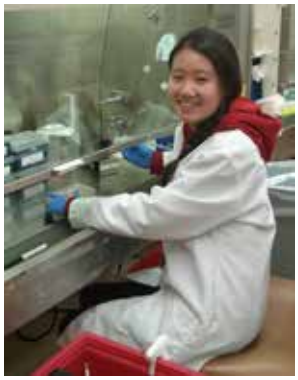
One of our most important findings came from HSCI Executive Committee member Lee Rubin and colleagues in which they demonstrated that their stem cell-based drug screening technology could change the economics of drug discovery.

Testing a library of drugs on human neurons developed from amyotrophic lateral sclerosis (ALS) patients, they found a compound that is more effective in protecting the neurons killed in ALS than two drugs that failed in clinical trials after large sums were invested in them.

Rubin's model is built on an earlier proof of concept developed by HSCI Principal Faculty member Kevin Eggan, who demonstrated that it was possible to move a neuron-based disease into a laboratory dish using stem cells carrying the genes of patients with that disease.

Tomorrow's Innovators

Return on Education: The HSCI Internship Program and Medical Training Fellowship Award



One of Bianca Ho's favorite memories of her 2013 HSCI Internship Program experience was a going-away present for a laboratory technician who was leaving to pursue his PhD. The gift was a pair of dirty socks that he kept in the lab, but thought he'd thrown out.

"It just showed me the kind of community you become," the McGill University junior said. "It's not just the work; when you're researching side by side with people, you become close friends."

Bianca spent her summer at HSCI developing a tool using single cell clones to study metastasis in breast cancer. Before she applied, she shared the common perception that stem cells are only valuabe for their regenerative abilities. She quickly learned that stem cells are also valuable tools for learning about basic cell biology and drug discovery.

This year, 44 students became a family as they spent 10 weeks in HSCI-affiliated labs and learned what it means to become a stem cell physician and/or scientist. For the first time, the program had corporate sponsorship, and welcomed representatives from Biogen Idec, EMD Millipore, GlaxoSmithKline, Novartis, and Sanofi Aventis, who spent an evening talking about their career paths.

The goal of developing future stem cell scientists is also met by HSCI's Medical Training Fellowship Award, made possible by a $1,500,000 bequest from Jack and Ruthe B. Cowl, specifically intended to support Harvard-MIT MD/PhD students pursuing stem cell science and its application. This year's fellow, James Harris, is pursuing his interest in neurological disorders in the lab of HSCI Principal Faculty member Paola Arlotta.

Finances in Brief

Fiscal Year 2013 Expenditures Continue Emphasis on Research Investment

During the period July 1, 2012 through June 30, 2013, the Harvard Stem Cell Institute's expenditures totaled $16.5M, approximately 85% of which was invested in directed research projects.

New major gifts for Alzheimer's disease and type 1 diabetes research supported our targed research efforts (38% of expenditures) which are channeled through HSCI's various disease-focused programs.

HSCI invested $2.9M in core facilities, which expedite research and foster scientific collaborations. This year, a new Flow Cytometry Core based at Harvard Medical School became part of the HSCI network.

The Seed Grant program (11% of expenditures) supported 10 new innovative projects in various research areas proposed by junior faculty.

Community building (1% of expenditures) included co-sponsorship of the International Society of Stem Cell Research Annual Meeting in Boston and an associated public forum highlighting HSCI scientists' work.

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