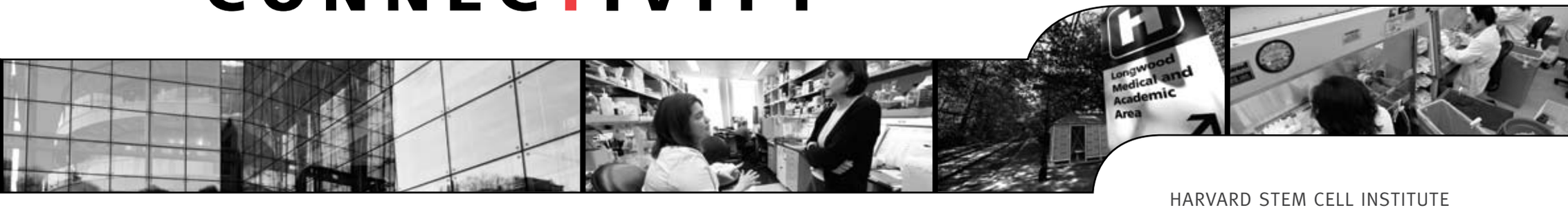
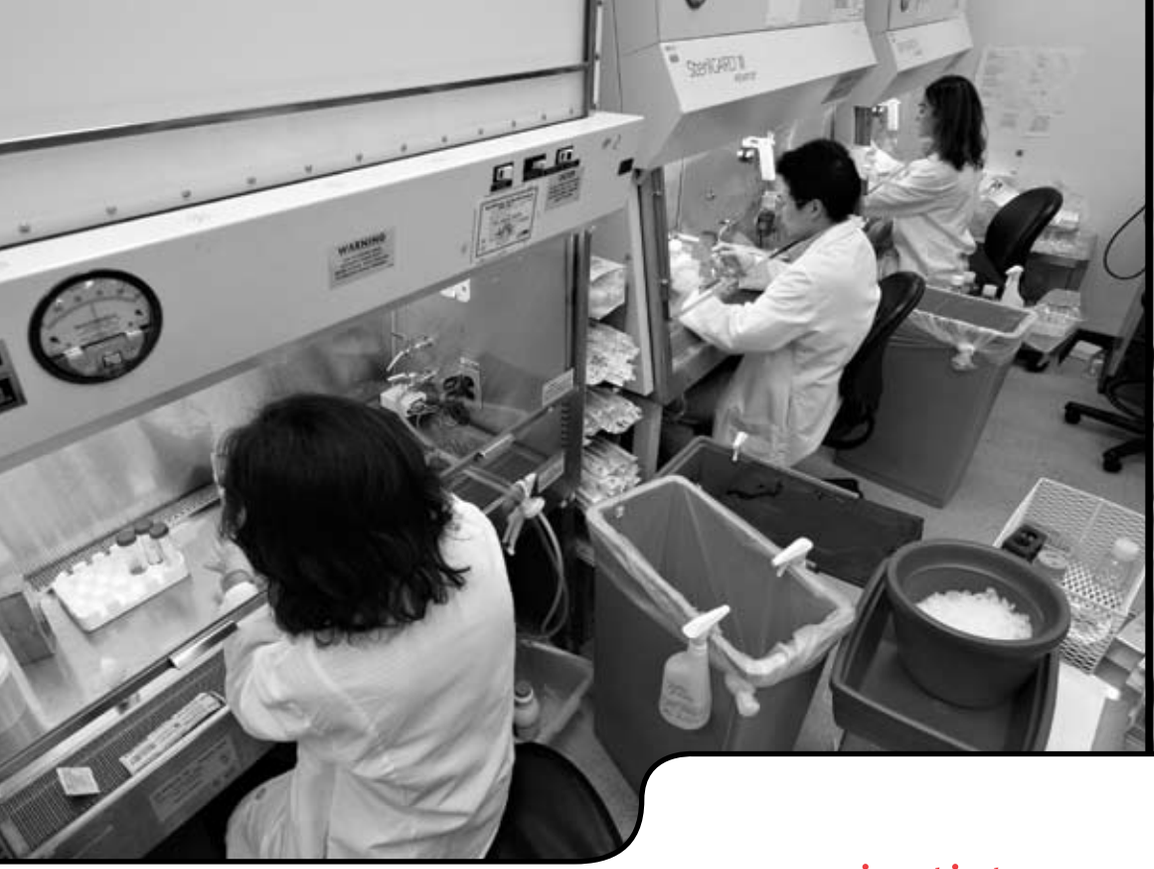
CONNECTIVITY



HARVARD STEM CELL INSTITUTE

ANNUAL REPORT 2006



750 scientists
119 laboratories
11 institutions
8 stops
one purpose

More than *750* scientists. In *119* different laboratories. At *11* of the world's leading research hospitals scattered across the Boston area.

Faculty from all the schools of one of the world's leading universities.

And there are two things uniting us into a cohesive whole called the **Harvard Stem Cell Institute.**

The first of these is a single-minded desire to answer one of the most basic and important challenges facing biologists today, and that is identifying and learning to control the properties that make human stem cells the self-replicating building blocks for every system in the body.

As the largest collaborative of its kind, the Harvard Stem Cell Institute is a truly unique scientific enterprise that is the magnetic North for a whole community of scientists whose ultimate goal is harnessing stem cell science to bring new treatments to the clinic, and new life to patients with a wide range of chronic illnesses and diseases.

HSCI: The largest collaborative of its kind.

While other institutions may focus on a particular disease, organ system, or technology, HSCI scientists, working independently together, sharing inspirations and results, are primarily focused on five major disease programs—blood, cardiovascular, cancer, diabetes, and nervous system diseases—and key underlying technologies. This cross-section of interests means that when, for example, a diabetes researcher reaches a fundamental understanding of stem cell differentiation, that finding is shared across the Institute, advancing the battle against other diseases we're working on.

And what else unites our teachers, scientists, students, laboratories, and institutions? The shared parentage of the greater Harvard University in its various locations as linked together by the shared infrastructure supporting the geography of Boston. Eight stops on the venerable "T," the first subway system in America and the commuter rail, serve to connect the scientists of the Harvard Stem Cell Institute who are now working on one of the fundamental new technologies of the 21st century. A common goal and a common affiliation—even a common transportation system—tie us together in our uncommon aspirations.

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From the Scientific Directors

In 2004, Harvard University announced the establishment of a unique institution called the Harvard Stem Cell Institute, a collaboration of 100 scientists, led by 25 principal investigators based at seven of the Harvard-affiliated teaching hospitals dedicated to advancing stem cell science from laboratory bench to patient bedside.

As we end our second fiscal year in mid-2006, the HSCI community is a powerhouse of discovery fueled by the intellect and dedication of 119 PIs, leading more than 750 scientists, at 11 of the affiliated hospitals in our continuing quest to fulfill the promise of stem cell biology as the basis for cures and treatments for a wide range of chronic medical conditions.

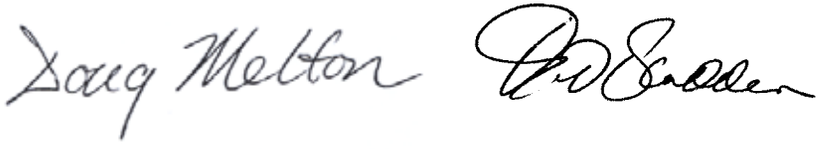
Though our growth has been exceptional, it has not been easy. We continue to work in a political environment in which politics sometimes trumps science, and the federal government at best fails to support, and at worst tries to block, work aimed at unlocking the secret of this family of self-replicating cells that produces every tissue type in the body. Hopefully the farsightedness we are seeing in state capitals from Hartford to Sacramento—and in the Legislature here in Massachusetts—will eventually make its way to Washington. But in the meantime it is up to us, with your continuing help, to find ways to forge ahead.

And forge ahead we have. In fact, as you'll read in this, our first formal Annual Report, this past year has been a momentous one:

Architectural planning has begun for HSCI's permanent home in a new 500,000-square-foot science complex whose construction will mark the beginning of the development of Harvard's 21st century Allston campus; we have hired a new Executive Director, Brock Reeve; our major disease programs are all established, organized, and up and running; we have established a novel therapeutic screening program under the leadership of Dr. Lee Rubin, who came to HSCI from the biotech industry; we are already into our second cycle of funding for seed grants to young investigators; we are regularly holding interlab meetings and other formal and informal gatherings that have proven critical to the cooperation and collaboration among researchers in speeding their discoveries; we continue to meet with our scientific counterparts from around the world; and, our educational programs and efforts in the area of ethics and public policy are well underway.

HSCI investigators are regularly publishing their findings in leading scientific journals, and making news with their discoveries, advancing us ever closer to the day when our understanding of stem cell science will pay off with new treatments that save and improve patients' lives.

But we cannot continue moving forward without your support, which has brought us as far as we've come. We hope that, after reading the rest of this report, you will be as committed to supporting the Harvard Stem Cell Institute as we who constitute HSCI are to advancing stem cell science.



Doug Melton, Ph.D., and David Scadden, M.D.
Scientific Co-Directors

From the Executive Director

My first official act upon joining HSCI early this spring was to explain to a meeting of the Institute's Executive Committee why I was excited to be here and had eagerly accepted this role. I outline for you now the reasons I gave them then, as they speak both to our goals and what I see as our unique position in the field:

• I was drawn by the chance to be involved with a new, cutting-edge biotechnology. Stem cells are clearly one of the few fundamental new technologies of our lifetime and the opportunities for progress are impressive. Having the chance to work with a large group of world-class researchers and clinicians in this area is very exciting and one that few people have. At the same time, the complexity of the biology means that many domains of knowledge, many experts from multiple fields, need to be brought together to achieve this progress.

• We are creating a new business model. The commercial life sciences industry has a well known research productivity and output problem. The network of institutions that HSCI represents gives us the ability to truly go from "bench to bedside" in many disease categories and with many technologies under one "umbrella." As a result, HSCI should be able to move more quickly and be more productive in a complex field than others.

• We need to wrestle with the complex, but fascinating, ethics and policy implications of the work. As we all know, stem cells are not just about the science. The social ramifications of the technology raise important fundamental questions that we need to tackle. Stem cells pose a multi-dimensional problem. With its deep resources in law, policy, philosophy, and government as well as medicine, what better place to take this on than Harvard?

• Like many of you, I am drawn to the work for deeply personal reasons. Unfortunately, we all have friends and family who have been affected by the diseases that we at HSCI ultimately hope to minimize if not cure. As a result, this work means that we all have a personal stake. For all of us, success is not only an exciting new paper in a peer-reviewed journal but improving the lives of many suffering people, including those near and dear to us.

In the course of this, our first Annual Report, you will hear more about each of these topics from various perspectives. As David and Doug outlined in their letter, you will see that we have accomplished a significant amount this year and have set the platform in place to accelerate our progress this year and beyond. I look forward to being able to report on even more exciting news at this time next year.

Thank you to all those who support us with your money, your time, your expertise, and your good wishes. I hope this report shows you what we have done with those and how we have tried to take advantage of all that you have offered us.

Sincerely yours,

Brock Reeve
Executive Director

Disease Programs

Blood

It is a given in biology and medicine that to understand a disease process, you have to first understand the normal development or function of the affected organ. It is for this reason that HSCI's Blood Diseases Program is currently focusing on understanding hematopoiesis, the formation and development of normal blood cells, with particular emphasis on the development and function of blood stem cells.

Blood stem cells were first identified about 40 years ago. Today, transplanted blood stem cells, found in bone marrow and cord blood, save the lives of tens of thousands of people with leukemias and other blood system diseases each year.

The blood stem cell is the best characterized of all stem cell types. Access to well-defined, isolatable populations of stem cells from developing and adult organisms from fish to man is unique to the blood system. Further, stem cells from both normal and malignant conditions in both mouse and man are readily identified and manipulated. Joining together laboratories with extensive expertise in the isolation, characterization, manipulation, and evaluation of blood stem cells is at the heart of this program. Together these labs will use shared data sets, and powerful genetic tools and coordinate intervention to define a comprehensive knowledge of stem cell self-renewal in the blood system. This knowledge resource will then be applied to other stem cell systems to assess whether the principles learned are shared and whether a common set of tools can then be applied to regeneration and malignancy across tissue types.

"Finding out about the self-renewal properties of hematopoietic stem cells will give us ways of expanding stem cell populations," explains Dr. Daniel Tenen, the Beth Israel Deaconess Medical Center-based leader of the Blood Diseases Program. "Second," he continues, "it will give us knowledge of the normal blood cell process, which will help us understand the abnormal."

Members of the Blood Diseases Program, who are spread across the Harvard system, "are using a number of different experimental approaches," says Tenen. "Some of the investigators will be focusing on zebrafish models; some will be focusing on embryonic stem cells, not hematopoietic cells at all; some of us will be looking at the differences between stem cells and progenitor cells, both in the normal state and in leukemia." The ability for Tenen to compare his laboratory's findings with those reached by a different approach will lead to insights and collaborations that may not have been sparked otherwise.

"Another thing that's important to note," he adds, "is that most of what we and the other people in the program are doing, we're able to do because of the existence of the Blood Diseases Program. Most of the things we're going after, we couldn't go after on our own because of a lack of resources, both individual and shared."

An example of such a resource that HSCI provides is the flow cytometry core facilities. "They're a key component of the blood program," Tenen says, and have "helped people not only working in blood, but in other areas as well. Having those available when you need them, not having to wait for time, is like going from the Neanderthal age to the 21st century."

Today, transplanted blood stem cells, found in bone marrow and cord blood, save the lives of tens of thousands of people with leukemias and other blood system diseases each year.

Cancer

"The kind of cross-institutional collaborations we're developing wouldn't be possible without HSCI."

—Gary Gilliland, M.D.

The current ways we treat cancer are much like "trying to kill a weed by cutting off all the leaves and branches—but leaving the root," says Gary Gilliland, M.D., Ph.D., who directs HSCI's Cancer Stem Cell Program.

"We're working on the premise that there is a very small subset of cells in every tumor that is responsible for the growth and propagation of the tumor. Tumors reappear because virtually none of the current therapies effectively target cancer stem cells," explains Gilliland.

HSCI's Cancer Stem Cell Program was established to respond to this need, bringing together basic scientists and clinicians from across the Harvard community, each contributing their expertise in the endeavor to understand the biology of cancer stem cells—how they differ from other tumor cells and normal cells—and to develop novel therapeutic approaches based on these insights.

In past year the Cancer Stem Cell Program has grown to include 40 investigators located across the University and seven Harvard-affiliated teaching hospitals and institutions, including Dana-Farber Cancer Institute, Brigham and Women's Hospital, Beth Israel Deaconess Medical Center, Massachusetts General Hospital, Joslin Diabetes Center, Children's Hospital Boston, and Harvard Medical School. Working across multiple types of cancer, the program has three main components: identification of cancer stem cells and their biological properties; understanding the microenvironment of tumor cells; and, developing drugs that target cancer stem cells for therapy.

In order for researchers to identify and characterize the cancer stem cells in tumors, they need tumor material to search. Part of the Cancer Stem Cell Program involves the collection of fresh tumor samples from solid tumors that include ovarian, lung, GI, and melanoma patients at Brigham and Women's Hospital and Massachusetts General Hospital. This is no small feat, as the process includes obtaining approvals from the Institutional Review Boards (IRBs), patient consents, advance notification of scheduled surgeries and close coordination between scientists and clinicians. It also shows that value of having both clinical and research capabilities at hand and aligned.

"The kind of cross-institutional collaborations we're developing wouldn't be possible without HSCI," says Gilliland.

Ultimately, the researchers hope to identify the self-replicating cells that drive tumor proliferation. The program can then study what Gilliland calls their "stem cell-ness" and the environment necessary for their growth, allowing the development of drugs that will specifically target the cancer stem cells.

Gilliland also expects that insights gained in the cancer program will benefit the other disease programs, such as the leukemia research activities in the Blood program. As with the close relationship between normal hematopoietic stem cells and leukemia stem cells, normal tissue cells may be very similar to the corresponding cancer stem cells. Normal stem cells in most adult tissue are not well characterized, and identifying cancer stem cells in solid tumors may help in identifying their normal counterparts. For example, a kidney cancer stem cell may be similar to normal kidney stem cells, which have yet to be identified. And while it may appear to be a far cry from figuring out how to turn off cancer stem cells to turning on other stem cells (to direct them to produce insulin-producing islet cells, for example), "there's a real synergy here between programs," Gilliland says. "If we can learn to turn the switches off that generate cancer stem cells, we should be able to turn them on to regenerate tissue, and vice versa."

Cardiovascular

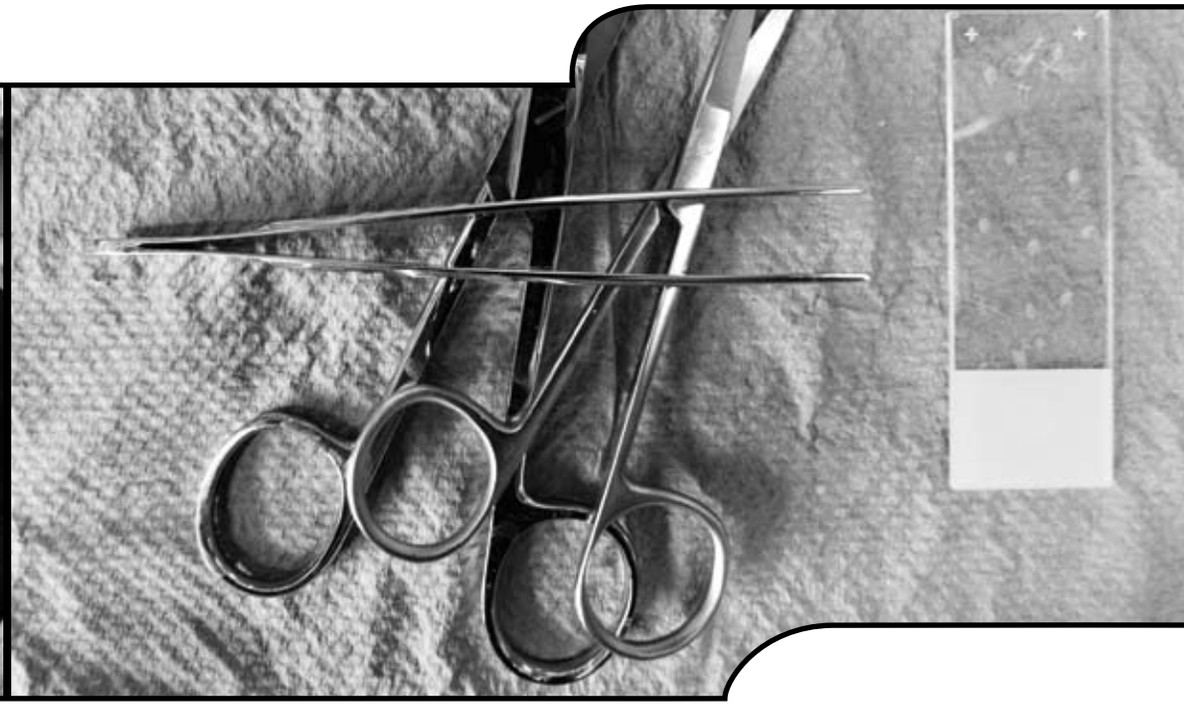
"It's going to be a long road to develop all the technology required to regenerate your entire heart from stem cell origins... What we're doing now is forming the foundation for that."

—Dr. Kenneth Chien

"I voted with my feet and came here for the program and infrastructure HSCI has set up—I didn't come here for the weather," said Dr. Kenneth Chien, head of HSCI's Cardiovascular Diseases Program. "In California they're talking about doing stem cell research; here we're doing it; we're on the frontiers of human stem cell technology," adds the now-Massachusetts General Hospital-based cardiologist, who left positions at UC San Diego and the Salk Institute.

"We've established a program where we can actually couple state of the art stem cell biology in multiple systems from mouse to humans, with cardiovascular disease and disease models," says Chien, whose lab last year discovered cardiac progenitor cells, cells that can develop into the three main cell types comprising the cardiovascular system. The program, comprised of about 130 scientists at MGH, Harvard's Faculty of Arts and Sciences, Children's Hospital Boston, and Dana-Farber Cancer Institute, has the unique opportunity for access to neonatal and adult human heart tissues and cells for studies with cardiac progenitor cells because so many HSCI researchers are based at clinical institutions.

"The program is now positioned to start isolating master cardiovascular stem cells from human embryonic stem cells," Chien explains, adding that at this point the program is more focused on using stem cells to screen potential drug treatments for cardiovascular diseases than on using stem cells to repair damaged tissue.



"It's going to be a long road to develop all the technology required to regenerate your entire heart from stem cell origins," Chien says, "I think it's going to happen, but it's going to be at least a decade away. What we're doing now is forming the foundation for that."

"But in the interim we can use embryonic stem cells as a disease model and for drug discovery," says Chien. "Near term is going to be the development of human-based models of human disease. The cardiovascular system has many inherent advantages—a lot of the diseases are due to defects in the cardiac cells themselves, so you can do the screening right on the cell system," he adds.

Ultimately, however, the program will, among other projects, be working to use stem cells to promote the growth of cardiac arteries for patients with cardiac artery disease. "We're not just talking about replacement vessels," says Ken Chien, "We're not just talking about vein grafts, but trying to use master heart stem cells to trigger the growth of your own coronary arteries."

Diabetes

The ultimate goal of the Harvard Stem Cell Institute's Diabetes Program is an audacious one: Develop a cure for a debilitating disease from which 20.8 million Americans and 194 million people world wide suffer.

But HSCI researchers believe that this goal is also realistic, because they know that the disease is caused by a shortage of a single cell type—the pancreatic beta cells that produce insulin. So diabetes is an ideal target for researchers looking to use some form of stem cell therapy to develop a cure.

If the team of scientists at Harvard's Faculty of Arts and Sciences, the Joslin Diabetes Center, Brigham and Women's Hospital, and the Harvard/MIT Broad Institute can find a way to replace, increase the number of, or protect beta cells, they should be able ultimately to cure diabetes.

"What we're trying to do is make more human beta cells that can be used for beta cell replacement therapy through a better understanding of both differentiation and proliferation," says Dr. Gordon Weir, the Joslin-based researcher who heads the HSCI Diabetes Program.

Some diabetics are now treated with beta cells harvested from cadaver pancreases, "which gives us a proof of principle," Weir says, "but the cells are in short supply—it takes four pancreases to get someone off insulin, and within two years most of them are back on insulin." So the program has to figure out how to produce enough cells, and how to keep them from being destroyed by the underlying disease process.

The Diabetes Program has been divided into two subgroups, one headed by HSCI Co-Director Doug Melton, based in the Faculty of Arts and Sciences, the other headed by Dr. Richard Maas, at Brigham and Women's Hospital. Melton's group is primarily focused on working with embryonic stem cells to find ways to direct those cells from which all tissues arise to become pancreatic beta cells. Additionally, Melton's lab is working to develop molecular markers that will make it possible to tell in what developmental direction an embryonic stem cell is headed. And Melton and HSCI's Kevin Eggan have been given all the necessary approvals to use Somatic Cell Nuclear Transfer to produce diabetes-specific stem cells, which can be used to achieve greater insight into the development of the disease process.

The other part of the program, lead by Richard Maas, is working to explore the capacity of beta cells to replicate, and will then seek ways to 'prod' that replication. Both programs are truly multi-institutional and involve investigators from Dana Farber and the Medical School, in addition to the Joslin, Brigham and Women's, FAS, and the Broad Institute. While individual researchers were working on these problems prior to the founding of HSCI, the existence of the Institute has "pushed us to work together," explains Gordon Weir. "Much of this wouldn't have happened without HSCI. I didn't even know about Dick Maas, and what he was doing," admits Weir, noting that Maas's lab is only a short walk from his.

Nervous System

Diseases of the nervous system are among the most complex, intractable, and poorly understood challenges facing patients, physicians, and scientists today. The injury, degeneration, and/or death of specific types of neurons underlie most of the nervous system diseases affecting a staggering 50 million Americans.

Led by Massachusetts General Hospital-based Dr. Jeffrey Macklis, the HSCI Nervous System Diseases Program has in two short years grown from an idea to a collaboration of 45 faculty members with their lab groups at institutions including the Harvard Faculty of Arts and Sciences, Harvard Medical School, McLean Hospital, MGH, Schepens Eye Research Institute, Mass Eye and Ear Infirmary, Dana-Farber Cancer Institute, Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, and Children's Hospital Boston.

As Macklis explains, the Nervous System Diseases Program is divided "into five working groups: motor systems disorders, which includes the broadest range of diseases—from ALS and developmental neuron diseases, to stroke, cerebral palsy, and Huntington's Disease; Parkinson's Disease, a very specific disease target that has already been the target of cellular therapies; retinal-based disorders, which includes various vision and blindness disorders; hearing-based disorders, which focuses primarily on the inner ear and hair cells, but also other sensory neurons in the hearing system; and finally, what we call glial disorders, which include multiple sclerosis and certain types of cerebral palsy. Each of those groups has its own leader and, in turn, the group leaders constitute a steering committee for the Nervous System Diseases Program as a whole."

In the motor systems area, one of the program's first efforts is "aimed at the biology and repair of corticospinal motor neurons, or 'upper motor neurons', the brain motor neurons that die in ALS (also known as Lou Gehrig's disease) and other related motor neuron disorders, and are injured in spinal cord injuries and contribute to the loss of motor function," says Macklis. This program is making progress on several fronts. For example, the Macklis lab has identified a broad program of gene regulation and genetic control of the brain motor neurons that are involved in ALS. "This is brand new biology," explains Macklis, "in that it is the first time that the program and control genes that govern the birth, development, and function of a specific type of neuron in the brain" have been identified.

On another front, the Nervous System Diseases Program hosted a two-day, international 'think tank' on Parkinson's Disease this spring, which helped define the program's research efforts, and it has already led to an international collaboration. Macklis notes: "By engaging the world's top leaders in the field, and by both presenting our most recent results and debating the pressing issues to accelerate progress to new therapies, we focused in on the critical areas where HSCI could uniquely move the entire field forward. We have now embarked on an exciting parallel effort to that already ongoing at HSCI for ALS and spinal cord injury. The 'think tank' will be an annual progress review meeting to achieve real milestones and chart new directions."

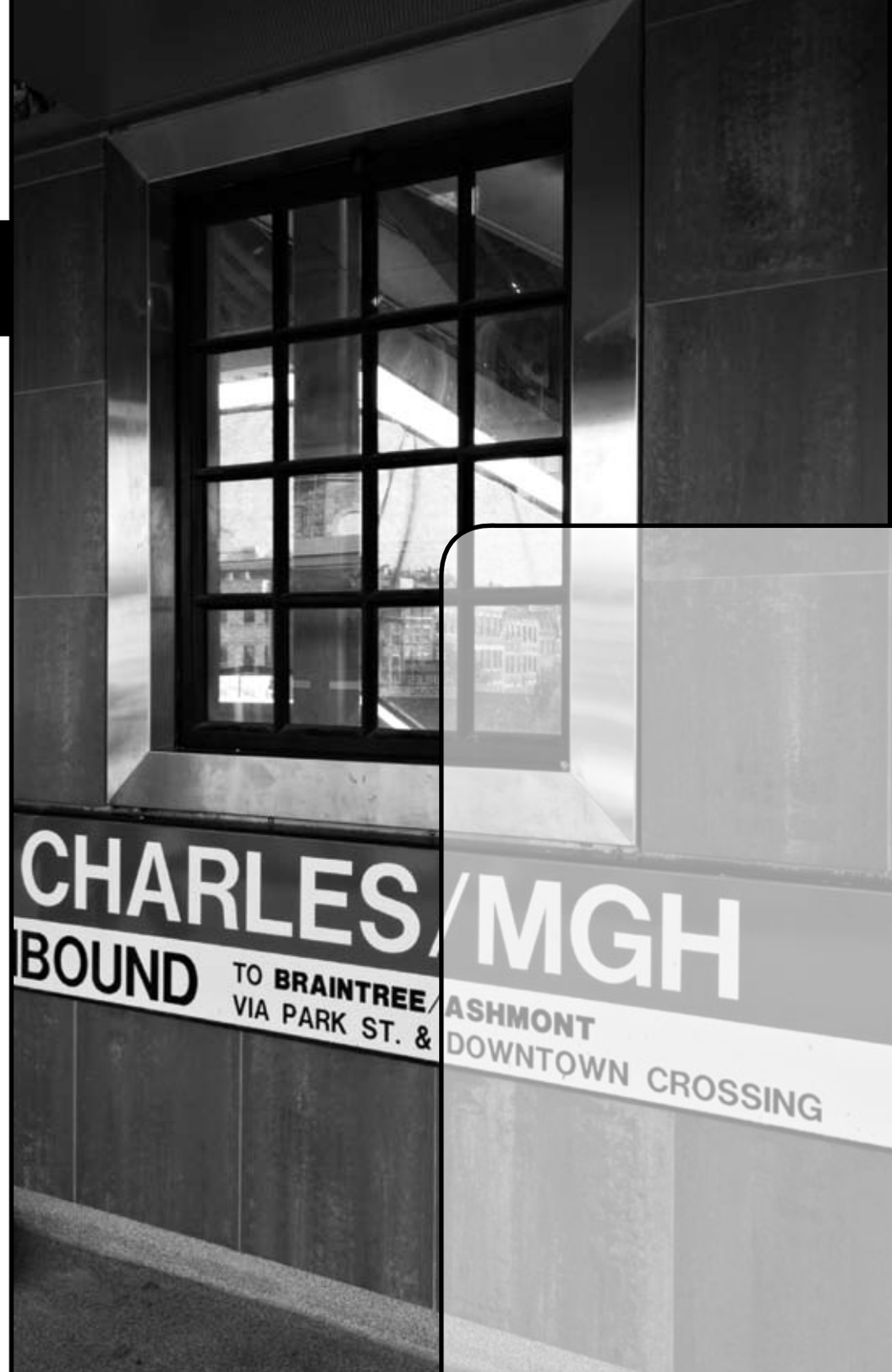
Other Scientific Programs

KIDNEY DISEASE:

An estimated 5% of adults 20 years of age and older have physiological evidence of chronic kidney disease. The Kidney Disease Program is researching how stem cells could one day replace renal function that is lost in response to a variety of acute and chronic kidney diseases. Using multiple animal models, the program is addressing key questions in kidney development, injury and repair, and immunomodulation, as well as designing extracorporeal devices for both therapeutic and toxicology purposes. The program is also studying how stem cells may play a central role in the pathogenesis of renal cell carcinoma.

TISSUE ENGINEERING AND ORGAN STRUCTURE:

The goal of the Tissue Engineering and Organ Structure Program is to determine the materials and cells best suited to tissue transplantation and engraftment. The availability of a renewable source of cells that have been developed from stem cells makes it possible to effectively explore the construction of synthetic tissues that provide proper physiological function. For example, the program's first project focuses on creating a vasculature with embryonic stem cell-derived endothelial cells on a specialty scaffold.



CELL DEVELOPMENT:

It is possible to coax embryonic stem cells into becoming differentiated cell types. However, the clinical use of these cells is restricted by the need to genetically match them with the patient in order to prevent immune rejection. The goal of the Cell Development Program, which brings together several faculty members from various institutions who are pursuing separate but related research in cellular reprogramming, is to explore alternative means of obtaining patient-specific stem cells.

TRANSLATIONAL RESEARCH PROGRAM:

Mesenchymal stem cells (MSCs) can be isolated from bone marrow, umbilical cord blood, amniotic fluid, and other tissue types and have the ability to differentiate into many different cell types. It is the HSCI Translational Research Program's goal to standardize and characterize these cells for use in phase I/II clinical trials for blood disease, and develop additional clinical applications of MSCs. In the future, the program's experience in working with MSCs will serve as a platform for HSCI's disease programs to develop various stem cell therapies.

IMAGING:

Imaging technologies play a central role in stem cell research because they allow the characterization and isolation of the cells, and provide a way for scientists to study how stem cells function in living organisms. Based at Massachusetts General Hospital, the Imaging Program uses state of the art technology for specifically visualizing stem cells in animal models, providing a critical resource and expertise that is valuable to all the disease programs.

REPRODUCTIVE SYSTEM:

The role of germ cells in cell development, as well as diseases associated with the reproductive organs, makes research of the human reproductive system central to HSCI's scientific mission. The program is pursuing research in two important areas: the derivation of oocytes from human embryonic stem cells and the progression of ovarian cancer.

SKELETAL DISEASE:

Led out of the Harvard School of Dental Medicine, the skeletal program has two main areas of scientific focus. The first is on bone repair with tissue-engineered bone using stem cells. This area has no significant clinical needs and builds on the Harvard hospitals' collective significant clinical expertise, particularly in oral and maxillofacial surgery and restorative dentistry. The second area focuses specifically on the engineering of dental tissues and the development of a biological replacement tooth. Again, there is a large, unmet clinical need and the project can reach the clinic in a step-wise manner over time starting with implants and culminating in a biological tooth.

Program in Ethics and Public Policy

Judging by what the media reports, there is little room for the true exchange of ideas or search for mutual understanding, in the current emotionally and politically charged atmosphere surrounding human stem cell research. Which is why those unfamiliar with HSCI's Program in Ethics and Public Policy might be surprised by the program's range of guest speakers.

In the spring of 2005, Richard Doerflinger, deputy director of pro-life activities for the U.S. Conference of Catholic Bishops, and one of the leading opponents of embryonic stem cell research, was invited to speak at a new undergraduate course titled Ethics, Biotechnology, and the Future of Human Nature. The course, created by Doug Melton, Scientific Co-Director of HSCI, and Michael Sandel, HSCI's Ethics and Public Policy Program Leader, is one of the many outgrowths of the HSCI program. Other guest speakers have included Leon Kass, former chairman of the President's Council on Bioethics, and James Watson, who joined Melton and Sandel in a discussion of the ethical implications of new genetic technologies.

"The program's goal," explains Sandel, "is to foster education and public discussion, not only of stem cell research, but also of other developments in biology and genetics. For instance: What are the ethical implications of our growing ability to manipulate nature, including human nature? Is there a distinction between research and treatments that aim at curing and preventing disease, and those that aim at enhancing human traits? What are the social implications of the progress we're making in genetics and biomedicine?"

The Program in Ethics and Public Policy is designed to reach all of the University's constituencies, from students, to faculty, alumni, and the general public. To accomplish this, the program has developed seminars, lectures, and special dedicated programs that have brought together scientists and humanists; engaged alumni groups and the general public in lively exchanges of ideas with scientists and ethicists; and contributed an overview of ethical issues for science journalists as part of a week-long session co-sponsored with MIT.

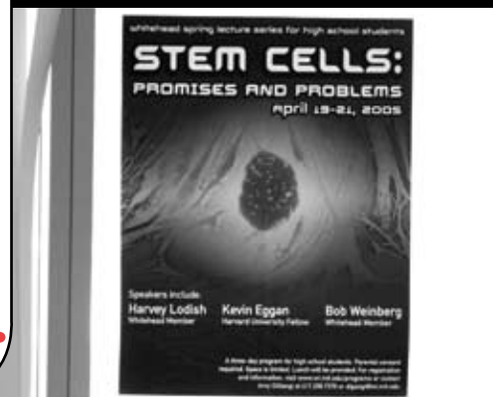
Building links across disciplines, HSCI is working with the existing programs in ethics and health care policy in Harvard's schools of law, medicine, and government. Last year, HSCI teamed up with the Harvard Humanities Center for discussions among scientists and humanists of stem cell research and related topics. And this coming spring, the HSCI Program in Ethics and Public Policy will collaborate with the Harvard Law School's Petrie-Flom Center for Health Law Policy, Biotechnology, and Bioethics on a two-day conference covering the legal, policy, and ethical implications of biotechnology. "Stem cell research has generated an intellectual ferment that reaches beyond the sciences," said Sandel. "Our aim is to foster this engagement and ensure that all voices in these debates are heard."

Core Facilities

One of the ways that HSCI aims to accelerate stem cell research is by providing its community with resources and services that are beyond the means of any individual lab. To accomplish this, HSCI has funded core facilities in two areas that are central to many stem cell scientists' research: conducting flow cytometry experiments and working with human embryonic stem cells.

Flow cytometry cores have been established at Beth Israel Deaconess Medical Center, Joslin Diabetes Center, and Massachusetts General Hospital. The Human Embryonic Stem Cell Facility is located at Children's Hospital Boston.

HSCI will be bringing two new large-scale core operations on-line: the Genome Modification Facility to be directed by Professor Andrew McMahon, and the Therapeutic Screening Center run by Dr. Lee Rubin.



HSCI invested in this specialized equipment to help researchers speed up their work. Because most flow cytometry facilities in general are running at capacity, there are significant wait times associated with their use in addition to the fact that they are typically available only to investigators directly affiliated with that supporting institution. But the HSCI Core Facilities are open to all HSCI members, regardless of specific hospital affiliation, at a discounted rate. This motivates usage and reduces wait time, thus accelerating the "time to answer" for important experiments. Providing a service that is both critical and in demand, these facilities are sought out by researchers from across the HSCI community. As a result, they act as an important connecting point and help foster a culture of interaction and collaboration.

Additionally, since stem cells have specific challenges from unique regulatory requirements to particular cell preparation and culture techniques, having dedicated core facilities like these provides an efficiency of scale and expertise that benefits the entire community. As the field of stem cell research advances, the Institute will continue to provide our members with access to cutting-edge technology.

The hESC facility at Children's provides another sort of leverage and scale to the HSCI community. Having a critical mass of expertise on working with human cells, providing training of personnel, holding seminars and talks on both the science and ethics of working with hESCs, this core is a critical shared resource.

This coming year, HSCI will be bringing two new large-scale core operations online: the Genome Modification Facility to be directed by Professor Andrew McMahon, and the Therapeutic Screening Center run by Dr. Lee Rubin. These new centers are major investments by HSCI in tools and services that no single disease program could invest in on its own and are important to conducting world class science—whether it's readily available custom mouse models or understanding what compounds affect differentiation in specific cell lines. We look forward to telling you more about them next year.

Seed Grants

The purpose of HSCI Seed Grants is to provide early funding for innovative projects in stem cell research that help further the mission of the Institute. The awards put particular emphasis on projects that might be difficult to fund from other sources, either because a project is considered to be "high risk/high reward," or because the research is ineligible for federal funding under the current restrictions on human embryonic stem cell research, or because there is insufficient experimental data to obtain other funding.

Each seed grant provides $150,000 in funding over two years, and is designed to allow researchers to conduct a "proof of concept," or to establish data that may serve as a platform for a larger research initiative or be included in one of the disease programs.

To select each year's seed grant recipients, a multi-institutional panel conducts a vigorous review process. While scientific quality is the primary selection criterion, HSCI looks to fund projects that will advance the field while encouraging younger faculty, enabling collaboration, and supporting its mission of moving stem cell biology into the clinic.

2006 SEED GRANT RECIPIENTS

Raymond Anchan
Brigham & Women's Hospital
Derivation of human embryonic stem cells (hESCs) from blastomere biopsies

Scott Armstrong
Children's Hospital Boston
Development of a hematopoietic stem cell and lineage differentiation map and repository

Bradley Bernstein
Massachusetts General Hospital
Epigenetic mechanisms of ES cell pluripotency

Keith Blackwell
Joslin Diabetes Center
Functions of the oocyte RNA-binding P-body protein CAR-1

David Breault
Children's Hospital Boston
Characterization of putative intestinal progenitor/stem cells using mTert-GFP transgenic mice

Rona Carroll
Brigham & Women's Hospital
Mesenchymal stem cell-based therapy for human brain tumors
Konrad Hochedlinger
Massachusetts General Hospital
Analysis of the pluripotency factors Oct4, Nanog and Sox2 in adult mice
Hanno Hock
Children's Hospital Boston
Deciphering the biology of the transcriptional repressor Tel/Etv6 in hematopoietic stem cells
Charles Lin
Massachusetts General Hospital
In-vivo imaging of hemotopoietic stem cell niche
Anjana Rao
The CBR Institute for Biomedical Research
Identifying DNA demethylases
Rosalind Segal
Dana Farber Cancer Institute
Symmetric and asymmetric proliferation of glioma stem cells
Yaming Wang
Brigham & Women's Hospital
Evaluation of the regeneration capacity of msx1-induced dedifferentiated cells
Jing-Wei Xiong
Massachusetts General Hospital
The hemangioblast development in zebrafish

2005 SEED GRANT RECIPIENTS

Nabeel Bardeesy
Massachusetts General Hospital
The pancreatic adenocarcinoma cell-of-origin
Dong Feng Chen
The Schepens Eye Research Institute
Repairing retinal disease and damage by neural stem/progenitor cell transplantation
Alan Davidson
Massachusetts General Hospital
Functional genomics approach to identify genes expressed in the kidney
Kevin Eggan
Faculty of Arts and Sciences, Harvard University
Derivation of Parkinson's disease specific human embryonic stem cell lines
Niels Geijsen
Massachusetts General Hospital
In vitro germ cell development and epigenetic reprogramming using human and murine ES cells
Rohit Kulkarni
Joslin Diabetes Center
Identification of beta cell growth factor
Jeannie Lee
Massachusetts General Hospital
Analysis of X-chromosome inactivation in human embryonic stem cells
M. William Lensch
Children's Hospital Boston
The analysis of complex genetic syndromes using disease-specific human embryonic stem cell lines
Craig Michelli
Harvard Medical School
Progenitor cells in the adult Drosophila gut: understanding tissue renewal in endoderm lineages
Hanna Mikkola
Dana Farber Cancer Institute
Placenta as a niche for hematopoietic stem cell development
Rosario Sanchez-Pernaute
McLean Hospital
Characterization, transplantation and functional analysis of dopamine neuronal progenitors derived from primate and human embryonic stem cells
Amy Wagers
Joslin Diabetes Center
Biology and function of adult skeletal muscle precursor cells

Education

Education is an essential component of the HSCI mission. Through targeted educational programs, the Institute aims to both inform the public at large and inspire a new generation of scientists, physicians, ethicists, and leaders.

HSCI faculty are involved in teaching more than 18 separate undergraduate and graduate level courses, including a new undergraduate course titled "Ethics, Biotechnology, and the Future of Human Nature," taught by Doug Melton, Scientific Co-Director of HSCI, and Michael Sandel, HSCI's Ethics and Public Policy Program Leader. Professors Melton and Sandel also led a faculty seminar with well-known outside speakers entitled "Between Two Cultures" (to borrow a phrase from C.P. Snow) to get both humanists and scientists to talk about the ethical and policy issues of stem cell science. Graduate and medical school courses range from basic biology and clinical applications to workshops and informal lunchtime seminars on medical ethics.

The HSCI Undergraduate Summer Research Internship Program was established to provide students with an opportunity to gain hands-on experience in stem cell research by working in the labs of HSCI faculty members. In 2005, 26 Harvard undergraduates were selected to participate in the program. This spring, through a generous grant from the Howard Hughes Medical Institute, HSCI was able to expand the program to include nine non-Harvard students, in addition to 25 Harvard undergraduates. The program included a weekly seminar series of lectures and discussion, which was also open to the broader HSCI community. The students concluded their summer work with scientific posters and presentations of their work. Last year's Harvard students were motivated to found their own Harvard Student Stem Cell Society, and we expect that this will spread its reach to other colleges as well.

In November 2005, teachers from the Ephraim Curtis Middle School in Sudbury, Massachusetts visited HSCI for a professional development day. Teachers left feeling confident in their ability to both teach lessons on stem cell science, and engage students, parents, and the broader community about the ethical and policy issues surrounding stem cells in an informed way.

Because much of the public learns about stem cell research through the media, one way of educating the general public is by educating science journalists. In March of 2006, HSCI co-sponsored with the Knight Science Journalism Fellowship Program at MIT a week-long "Stem Cell Boot Camp" for 22 science journalists from around the world. HSCI faculty led discussions on topics from basic science to public policy. A more and better informed public will be good for all of us as we engage in discussions of national importance.

In order to support the training of clinician scientists with expertise in stem cells, HSCI funds a Medical Scientist Training Fellowship for MD-PhD students whose thesis projects or long-term research goals involve stem cells. The first recipient of this award is Ashutosh Jadhav, who has been studying the development of the mammalian retina. Harvard was also happy to announce this year the support of a chair at the Medical School in stem cell biology thanks to a generous donor.

And, or course, our scientists continue to learn much from each other through our Inter-lab presentation series, monthly seminars with external experts, and regular program meetings, some of which are highlighted below in the Events section.

Events

INTER-LAB MEETINGS: Held on a bi-monthly basis, these meetings consist of presentations from three different labs on a common theme. Some themes this past year were "Regulatory and Differentiation Mechanisms" and "Stem Cells and Their Microenvironments." The Inter-labs are specifically designed to provide junior HSCI investigators, postdoctoral fellows, graduate students, and newly appointed faculty the opportunity to share their most recent work with the wider HSCI community. The meetings are moderated by HSCI senior faculty to help foster discussion among researchers and ensure that both progress and issues are shared. Held at the Harvard Medical School, these meetings are typically attended by up to 200 of our community.

MONTHLY SEMINAR SERIES: This year we held a monthly seminar series at the Massachusetts General Hospital Center for Regenerative Medicine, featuring guest speakers from around the world. The series helps to maintain vital connections with the global stem cell research community and ensure that HSCI is connected with leading researchers worldwide. Typical attendance includes about 150 scientists at all levels. Topics this past year included "Self-Renewing Mechanism of Stem Cells in the Germline" and "Aging of Stem Cell Niches," and featured speakers from as far away as Japan.

TONY & SHELLY MALKIN STEM CELL SYMPOSIUM: Funded by a generous donor, the Symposium was developed as a way for the researchers of HSCI to share their work with one another through poster sessions and scientific presentations while also featuring external speakers. The overall topic of this year's symposium was "Stem Cell Biology and Therapy in Organ Systems: Challenges and Opportunities." It included a keynote lecture by Irving Weissman from Stanford University and a dinner presentation by William Sahlman from the Harvard Business School. The symposium also featured speakers from the University of Michigan, Memorial Sloan-Kettering Cancer Center, Massachusetts Institute of Technology, and the London Research Institute. Some 350 HSCI members were in attendance as well as invited members of the public.

HSCI RETREAT: This spring, the first full-day retreat for the HSCI community was held on the Harvard Business School campus. The Retreat was an opportunity for the entire HSCI membership to talk about the mission of the Institute, discuss the accomplishments of the various programs, review plans and investments for the coming year, honor grant recipients, celebrate progress, and talk about how to tackle coming challenges. Scientific poster sessions not only provided a way for labs to showcase their work but also stimulated concrete discussions about project collaborations.

PARKINSON'S THINK TANK: To provide a world-class base for the Parkinson's Disease Program within the Nervous System Disease Program, in June HSCI convened a think tank on the topic of the "molecular development" of dopaminergic neurons with a half-dozen of the world leaders in Parkinson's research. After sharing their work with the community in an open forum, this group of international experts went into closed session to talk about the state of research and the key questions facing the field. This discussion helped define HSCI's focus and initiate project work at HSCI, and collaboratively elsewhere, that will underpin HSCI's Parkinson's disease research efforts.

Each of these events will build upon its success to date and continue this coming year. Additionally, we will hold a few new events this year. One will be a public conference on the politics, ethics, and science of stem cells. We will also broaden our reach by co-sponsoring events with other programs and centers (e.g., a conference on Cellular Treatments for Neurological Diseases with McLean Hospital and HCNR), publicizing related meetings that are important to the stem cell community (e.g., Radcliffe Institute's conference on Tissue Engineering), and hosting visiting speakers from philosophers to scientists.

Selected Scientific Publications

JUNE 2006

Long F, McMahon AP, et al. *Dev Biol.* Independent regulation of skeletal growth by Ihh and IGF signaling

Eggan K, Wagers AJ, et al. *Nature.* Ovulated oocytes in adult mice derive from non-circulating germ cells

Azam M, Daley GQ, et al. *Proc Natl Acad Sci USA.* Activity of dual SRC-ABL inhibitors highlights the role of BCR/ABL kinase dynamics in drug resistance

Wernig G, Gilliland DG, et al. *Blood.* Expression of Jak2V617F causes a polycythemia vera-like disease with associated myelofibrosis in a murine bone marrow transplant model

Inada A, Bonner-Weir S, et al. *Dev Dyn.* Timing and expression pattern of carbonic anhydrase II in pancreas

MAY 2006

Rooke HM, Orkin SH. *Blood.* Phosphorylation of Gata1 at serine residues 72, 142, and 310 is not essential for hematopoiesis in vivo

Lopez-Avalos MD, Weir GC, et al. *Diabetes.* Evidence for a role of the ubiquitin-proteasome pathway in pancreatic islets

Yu J, McMahon AP. *Genesis.* Reproducible and inducible knockdown of gene expression in mice

Clark RA, Kupper TS, et al. *J Invest Dermatol.* A novel method for the isolation of skin resident T cells from normal and diseased human skin

Yen L, Mulligan RC, et al. *RNA.* Identification of inhibitors of ribozyme self-cleavage in mammalian cells via high-throughput screening of chemical libraries

APRIL 2006

Wagner K, Tenen DG, et al. *Proc Natl Acad Sci USA.* Absence of the transcription factor CCAAT enhancer binding protein alpha results in loss of myeloid identity in bcr/abl-induced malignancy

Weinand C, Vacanti JP, et al. *Bone.* Hydrogel-beta-TCP scaffolds and stem cells for tissue engineering bone

Clark RA, Kupper TS, et al. *J Immunol.* The vast majority of CLA+ T cells are resident in normal skin

Honczarenko M, Silberstein LE, et al. *Stem Cells.* Human bone marrow stromal cells express a distinct set of biologically functional chemokine receptors

MARCH 2006

Nishio J, Mathis D, et al. *Science.* Islet recovery and reversal of murine type 1 diabetes in the absence of any infused spleen cell contribution

Yamanaka K, Kupper TS, et al. *Blood.* Skin-derived interleukin-7 contributes to the proliferation of lymphocytes in cutaneous T-cell lymphoma

Balazs AB, Mulligan RC, et al. *Blood.* Endothelial protein C receptor (CD201) explicitly identifies hematopoietic stem cells in murine bone marrow

Huang H, Mathis D, et al. *Proc Natl Acad Sci USA.* Induction of tolerance in arthritogenic B cells with receptors of differing affinity for self-antigen

MacDonald BA, Kalluri R, et al. *Blood.* Zebrafish to humans: evolution of the alpha3-chain of type IV collagen and emergence of the autoimmune epitopes associated with Goodpasture syndrome

Jadhav AP, Cepko CL, et al. *Development.* Notch 1 inhibits photoreceptor production in the developing mammalian retina

FEBRUARY 2006

Bourquin JP, Orkin SH, et al. *Proc Natl Acad Sci USA.* Identification of distinct molecular phenotypes in acute megakaryoblastic leukemia by gene expression profiling

Luckey CJ, Mathis D, et al. *Proc Natl Acad Sci USA.* Memory T and memory B cells share a transcriptional program of self-renewal with long-term hematopoietic stem cells

Steele AD, Macklis JD, et al. *Proc Natl Acad Sci USA.* Prion protein (PrPc) positively regulates neural precursor proliferation during developmental and adult mammalian neurogenesis

Adams GB, Scadden DT, et al. *Nature.* Stem cell engraftment at the endosteal niche is specified by the calcium-sensing receptor

JANUARY 2006

Harpavat S, Cepko CL. *BMC Dev Biol.* RCAS-RNAi: a loss-of-function method for the developing chick retina

Yamanaka K, Kupper TS, et al. *Clin Cancer Res.* Expression of interleukin-18 and caspase-1 in cutaneous T-cell lymphoma

Wang J, Chien KR, et al. *J Biol Chem.* Cardiomyopathy associated with microcirculation dysfunction in laminin alpha4 chain-deficient mice

Deuel TA, Walsh CA, et al. *Neuron.* Genetic interactions between doublecortin and doublecortin-like kinase in neuronal migration and axon outgrowth

DECEMBER 2005

Wang Y, Daley GQ, et al. *Proc Natl Acad Sci USA.* Embryonic stem cell-derived hematopoietic stem cells

Gao X, Kreidberg JA, et al. *Development.* Angioblast-mesenchyme induction of early kidney development is mediated by Wt1 and Vegfa

Sen J, Cepko CL, et al. *Development.* Retinoic acid regulates the expression of dorsoventral topographic guidance molecules in the chick retina

NOVEMBER 2005

Magavi SS, Macklis JD, et al. *J Neurosci.* Adult-born and preexisting olfactory granule neurons undergo distinct experience-dependent modifications of their olfactory responses in vivo

Murtaugh LC, Melton DA, et al. *Development.* Beta-catenin is essential for pancreatic acinar but not islet development

Clark RA, Kupper TS, et al. *J Clin Invest.* Human skin cells support thymus-independent T cell development

Ishii O, Vacanti JP, et al. *J Thorac Cardiovasc Surg.* In vitro tissue engineering of a cardiac graft using a degradable scaffold with an extracellular matrix-like topography

OCTOBER 2005

Mao J, McMahon AP, et al. *Nucleic Acids Res.* An ES cell system for rapid, spatial and temporal analysis of gene function in vitro and in vivo

Grimm J, Weissleder R, et al. *Proc Natl Acad Sci USA.* Use of gene expression profiling to direct in vivo molecular imaging of lung cancer

Kotton DN, Mulligan RC, et al. *Am J Respir Cell Mol Biol.* Failure of bone marrow to reconstitute lung epithelium

Burns CE, Zon LI, et al. *Genes Dev.* Hematopoietic stem cell fate is established by the Notch-Runx pathway

Kang PB, Kunkel LM, et al. *Muscle Nerve.* Variations in gene expression among different types of human skeletal muscle

SEPTEMBER 2005

Honczarenko M, Silberstein LE, et al. *J Immunol.* Complement C3a enhances CXCL12 (SDF-1)-mediated chemotaxis of bone marrow hematopoietic cells independently of C3a receptor

Kotton DN, Mulligan RC, et al. *Blood.* A novel stem-cell population in adult liver with potent hematopoietic-reconstitution activity

Turvey SE, Mathis D, et al. *J Clin Invest.* Noninvasive imaging of pancreatic inflammation and its reversal in type 1 diabetes

Stanger BZ, Melton DA, et al. *Proc Natl Acad Sci USA.* Direct regulation of intestinal fate by Notch

AUGUST 2005

Cowan CA, Eggan K, et al. *Science.* Nuclear reprogramming of somatic cells after fusion with human embryonic stem cells

Terada S, Vacanti JP, et al. *Ann Plast Surg.* In vitro cartilage regeneration from proliferated adult elastic chondrocytes

Carroll TJ, McMahon AP, et al. *Dev Cell.* Wnt9b plays a central role in the regulation of mesenchymal to epithelial transitions underlying organogenesis of the mammalian urogenital system

Nagoshi T, Rosenzweig A, et al. *J Clin Invest.* PI3K rescues the detrimental effects of chronic Akt activation in the heart during ischemia/reperfusion injury

Sanchez-Pernaute R, Isacson O, et al. *Stem Cells.* Long-term survival of dopamine neurons derived from parthenogenetic primate embryonic stem cells (cyno-1) after transplantation

JULY 2005

Rodrigues NP, Scadden DT, et al. *Blood.* Haploinsufficiency of GATA-2 perturbs adult hematopoietic stem-cell homeostasis

Mendez I, Isacson O, et al. *Brain.* Cell type analysis of functional fetal dopamine cell suspension transplants in the striatum and substantia nigra of patients with Parkinson's disease

Duffield JS, Bonventre JV, et al. *J Clin Invest.* Restoration of tubular epithelial cells during repair of the postischemic kidney occurs independently of bone marrow-derived stem cells

** For a complete list of publications by HSCI Principal Faculty, please visit our website at www.hsci.harvard.edu.*

Financials

Overall, HSCI spent $5.3M this past fiscal year. Our single largest increase was in our research programs. Three research funding vehicles (seed grants, core facilities/services, and targeted disease and technology development programs) together represent 76% of total expenses.

In FY06, HSCI sponsored several types of events aimed at building professional networks within the Harvard system that will ultimately lead to new research collaborations; including monthly seminars, an annual symposium, bi-monthly interlab meetings, an annual retreat, and a Parkinson's Disease focused "Think Tank."

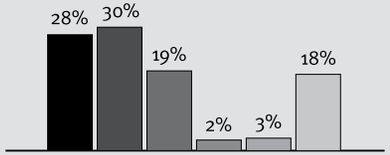
HSCI's educational endeavors have involved Harvard students and trainees and members of the greater community. Specifically, in FY06 HSCI supported a summer undergraduate internship program, a physician-scientist (MD/PhD) fellowship, a faculty seminar program, a co-sponsored stem cell "boot camp" for science journalists, and a stem cell education day for science teachers from an area public school system. Not included in these funds is a chair on stem cell biology at the Harvard Medical School funded by a generous donor.

HSCI's administrative staff structure was established during FY06, with the hiring of several staff including an Executive Director. The development of HSCI's website, an essential tool for community building and information sharing, was a critical FY06 project.

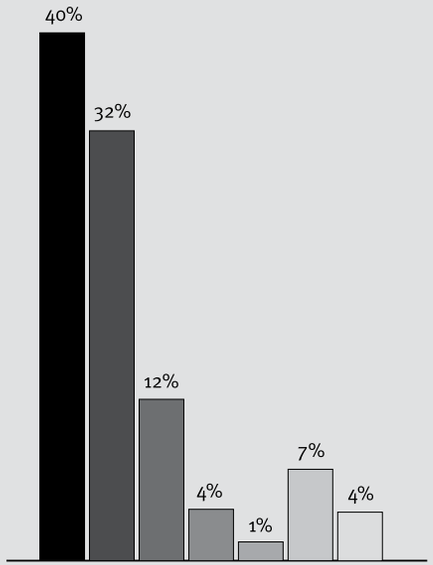
Looking forward to FY07, we expect our actual expenditures to more than triple as we fully fund the research programs including another round of seed grants, invest aggressively in two new major core operations—the Genome Modification Facility and the Therapeutic Screening Center—continue to add on-line collaboration tools to our website, expand our community building events beyond Harvard's walls including collaborative research projects, and develop a broader education offering.

HSCI

FY06 EXPENSES ($5.4 M) *



FY07 BUDGET ($17 M)



- Targeted Research
- Core Facilities & Services
- Seed Grants
- Education & Training
- Events & Community
- Administration & Operations
- Other

unaudited financial statements

Leadership

SCIENTIFIC ADVISORY BOARD

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Paul Berg, Ph.D./ Stanford University School of Medicine
Mark Fishman, M.D./ Novartis Institutes for BioMedical Research
Sir John Gurdon, Ph.D./ The Wellcome Trust, Cancer Research UK Gurdon Institute
Zach W. Hall, Ph.D./ California Institute for Regenerative Medicine
Fiona Watt, Ph.D./ Cancer Research UK

SCIENTIFIC DIRECTORS

Doug Melton/ Harvard University, Molecular & Cell Biology Dept.
David Scadden/ Massachusetts General Hospital

EXECUTIVE DIRECTOR

Brock Reeve/ Harvard Stem Cell Institute

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Keith Blackwell/ Joslin Diabetes Center
Susan Bonner-Weir/ Joslin Diabetes Center
Joseph Bonventre/ Brigham and Women's Hospital
Constance Cepko/ Harvard Medical School
Kenneth Chien*/ Massachusetts General Hospital
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Kevin Eggan/ Harvard University, Molecular & Cell Biology Dept.
Niels Geijsen/ Massachusetts General Hospital
Gary Gilliland/ Brigham & Women's Hospital
Richard Gregory/ Children's Hospital Boston
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Alexander Schier/ Harvard University, Molecular & Cell Biology Dept.
Leslie Silberstein/ Children's Hospital Boston
Daniel Tenen/ Beth Israel Deaconess Medical Center
Joseph Vacanti/ Massachusetts General Hospital
Amy Wagers*/ Joslin Diabetes Center
Christopher Walsh/ Beth Israel Deaconess Medical Center
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Ralph Weissleder/ Massachusetts General Hospital
Leonard Zon**/ Children's Hospital Boston

* *Faculty Executive Committee Member*
** *Faculty Executive Committee Chair*

To Our Donors

We'd like to share three stories of people
who have made important contributions to HSCI.
But first, to everyone who has believed in
what we are doing: Thank you.

Thank you for providing HSCI with $50 million in support over the past two years;

For making possible all that you have read about in the preceding pages;

For helping us to conduct a research aimed at ultimately developing treatments and cures for a wide range of diseases that afflict tens of millions of people in the U.S. and around the globe;

For stepping forward to fill in gaps left by the federal government;

For giving hope to those suffering from diabetes, Parkinson's disease, cardiovascular disease, cancer, ALS, paralysis, and all the other diseases and conditions for which stem cell biology holds so much promise.

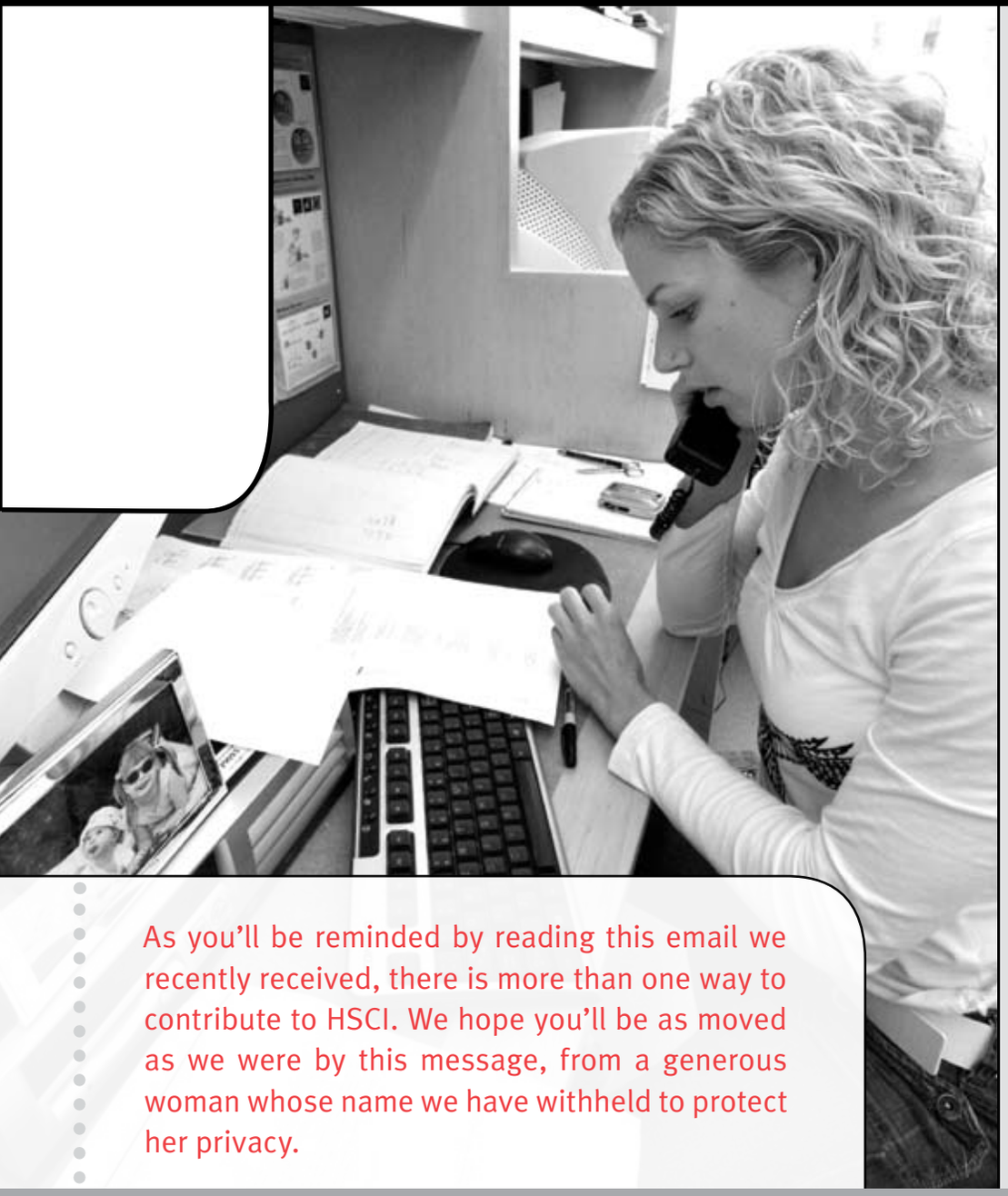
Thank you, whatever your motivation, whatever the level of your gift, for helping us unlock the secrets of human stem cells, and hastening the day when the promise of the science becomes the reality of treatments and cures.

Susan and John Tavela support stem cell research for many reasons, but one trumps them all. "It's about family," Susan says. "My husband's mother died of Alzheimer's. And of course, there's Leslie." Leslie is the Tavelas' daughter-in-law, who suffers from type 1 diabetes. "We want Leslie to be able to have a long life and watch her two children grow up. Supporting stem cell research is the best way to do that." The Tavelas have long supported stem cell research. After reading an article in the Boston Globe about Doug Melton, they sought out HSCI to make a donation. They have made monthly gifts to the Institute ever since. "If people knew as much about stem cell research as we do, everyone would support it in whatever way they could."

"Supporting the HSCI gives us a chance to be close to something that has the potential to change the world," says Alan Washkowitz. He and his wife, Barbara, are inspired by the work being done by HSCI co-directors Doug Melton and David Scadden. "When I first heard Doug and David speak," Alan says, "I was struck by their passion and vision. I may not understand the science that they do, but I know that medicine will be changed by their research." Alan and Barbara have supported HSCI since it was established in 2004. "Giving to HSCI is very worthwhile," Alan says. "We are privileged to be a small part of what Doug and David are doing."

Jerry and Darlene Jordan understand that private philanthropy is critical to moving biomedical research ahead as quickly as possible. This year, they gave a significant gift to the HSCI, endowing a professorship in stem cell research at Harvard Medical School and Massachusetts General Hospital. "Darlene and I feel strongly that our gift will accelerate the research that can positively impact people's lives in the future," Jerry Jordan notes. The Jordans' gift was inspired by the belief that Harvard may help establish Boston as the center of life sciences innovation in the twenty-first century. With the Jordans' help, HSCI is uniquely positioned to achieve its ambitious goals and support remarkable individuals who are at the vanguard of stem cell research.

A Special Kind of Donation



As you'll be reminded by reading this email we recently received, there is more than one way to contribute to HSCI. We hope you'll be as moved as we were by this message, from a generous woman whose name we have withheld to protect her privacy.

To Whom It May Concern:

I am a mother of 3 in Illinois with many frozen embryos that I will not use for conception; may I donate them to your institute? I got your name from a physician in Illinois who was unable to use them because her research is done with public dollars, but suggested I contact you.

I have been extremely frustrated with my inability to donate my frozen embryos (I believe there are 10 1-days and a few blasts) to stem cell research. When this subject comes up in the media, we speak of politicians, ethicists, persons with life-threatening illnesses—but we never discuss the wishes of the women to whom these embryos legally and genetically belong. I am sure that I am not alone in believing this would be a productive, ethical use of these embryos, and it's more than a little ironic that I could elect to have them transferred into my body and then abort them, but can't find a way to donate them to embryonic stem cell research.

In our pursuit of parenthood, my husband and I availed ourselves of much reproductive technology. Three beautiful children later (I'm now 41 years old), I am done child-bearing, and I keep holding these embryos until a friendlier administration will allow me to donate them to stem cell research. May I do so to you? If not, do you have recommendations on how this could be accomplished?

It would give me great peace knowing that these embryos (and I believe there are upwards of 10 of them) were being used to help find answers to debilitating illnesses.

Sincerely yours,

HSCI

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