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### **Stem-cell Science**

WITH AN AMBITIOUS mandate to cure cellular diseases, Harvard has launched an important new scientific enterprise, the Harvard Stem Cell Institute (HSCI). The public announcement was scheduled for April 23, although the news had been previously shared with alumni in a March 2 videoconference that linked sites in New York City, Cambridge, and Florida. Harvard already has outstand-

Scientists have developed 17 new human embryonic stem-cell lines and are making them available to qualified researchers at no charge. Shown are colonies of 50 to 75 stem cells. The cells divide to form new stem cells approximately every 24 hours.

#### JOHN HARVARD'S JOURNAL

ing faculty members and researchers working on stem cells, says Douglas Melton, Cabot professor in the natural sciences and chair of the Life Science Executive Committee for the Faculty of Arts and Sciences, who will codirect the new institute with Dr. David Scadden, professor and director of the Center for Regenerative Medicine at Massachusetts General Hospital (MGH).

HSCI will coordinate the teaching, training, and research of about 25 principal investigators and 64 affiliated member scientists, and will engage seven Harvard schools and six affiliated hospitals, focusing their research and clinical efforts on a singular goal: the use of stem cells to correct organ failure. (Stemcell therapies have the potential to cure many diseases that involve cell loss.) Harvard is al-

ready well positioned to develop therapies in at least four areas: diabetes, blood diseases (including AIDS), neurodegenerative disease, and cardiovascular disease. "These four disease targets will be the initial priorities for the HSCI," says Melton. "Each has a set of [attainable] milestone achievements necessary to realize clinical therapies and a predictable, achievable route to clinical testing."

Melton and Scadden bring together clinical and research expertise in their joint leadership of the new institute. "David and I represent bookends on the problem," says Melton. "He's a clinician, a real doctor...and he works on the stem cell which has been studied the longest and about which the most is known"-the hematopoietic, or adult blood, stem cell used in treating cancer patients through bone-marrow transplants. Notes Scadden, in a separate interview, "Doug is an expert in developmental biology." Melton's laboratory, working in concert with that of Baird professor of science Andrew McMahon and with Douglas Powers of Boston IVF (an in-vitro-fertilization clinic), recently developed and arranged to distribute free to qualified researchers 17 new human embryonic stem-cell lines—more than doubling the number currently available.

Such work is not without controversy. Although adult stem cells, such as the hematopoietic stem cells found in bone marrow, are uncontroversial and are used in treating tens of thousands of patients each year through transplants, they can Type 1 diabetes. Embryonic stem cells, on the other hand, can make any tissue in the body.

Most Harvard research on embryonic stem cells is done in animal models. Making new human embryonic stem-cell lines results in the destruction of a blastocyst, an undifferentiated mass of four to 50 identical cells that forms in the first few days after a sperm fertilizes an egg. Deriv-

ing a new stem-cell line is therefore controversial when performed on a human blastocyst, because some people and certain religious groups hold that this early stage of development represents a human life.

The 17 new Harvard stem-cell lines were therefore all developed—according to earlier National Institutes of Health (NIH) guidelines and in the hope that they will one day help to save human lives—from frozen blastocysts slated to be discarded by an IVF clinic.

(Such clinics store tens of thousands of these early-stage fertilized eggs in a frozen state for implantation in female patients. When a patient's treatment ends, the blastocysts are either discarded, or-with the consent of the couple who owns them-may be used in # medical research.) Because President Bush has banned the use of federal funds for research using stem-cell lines created after his national address of August 9, 2001, any work using these cells

must be supported with private funds. At Harvard, all proposed research involving human embryonic stem cells is subject not only to the customary internal review, but also to scrutiny from a separate committee, headed by Cabot professor of biology Richard Losick, that has representation from throughout the University. Says





Dr. David Scadden (above) and Professor Douglas Melton (top) will codirect Harvard's new Stem Cell Institute to develop treatments for patients with organ disease. Provost Steven Hyman (right) will ensure ethical oversight.

create only the tissue from which they are derived (many claims to the contrary have been disproved in recent years). Blood stem cells can make only blood, for example. Because some tissues, such as the pancreas, do not appear to have an associated adult stem cell, it is impossible to use adult stem cells to treat diseases like Provost Steven E. Hyman, to whom the committee reports, "We really have to be thinking very deeply about the ethical implications of the new science and the new medicine."

Hyman has asked professor of government Michael Sandel, who also serves on the nation's President's Council on Bioethics, to lead a "free and active ethical [discussion], to create the intellectual background [for weighing] these [activities] both in terms of national policy and biomedical ethics." Given the highly politicized and emotional debate engendered by stem-cell research, a first-rate research institution like Harvard, with a tradition of rational, inclusive deliberation and responsible science, would seem well positioned to tackle both the ethical and scientific issues.

The center, one of several large, collaborative science projects announced in the last few years, was created as the result of a "grass-roots faculty effort," Hyman explains. "Science has changed and is changing. The current model, which is the individual laboratory investigator with her students and post docs," he says, "will remain a very important part of science. Having said that, it is really quite clear that much cutting-edge science will depend on large infrastructures...What we see are scientists who are at the cutting edge aggregating into new collaborative coalitions."

Even in that greater context, HSCI seems uniquely positioned to draw on resources from many parts of the University. Stem-cell science will be taught to undergraduates, graduate students, and medical students, and cuts across many areas, including biology, medicine, government and public policy, law, ethics, business, and religion. "We're a university that can cover this whole field," Melton says.

The institute will be "knit together in a very decided and focused way," in order to tackle specific scientific and clinical problems. Melton quickly sketches a matrix. On the horizontal axis he lists a series of disease targets: diabetes, blood disease, neurodegenerative disease, cardiovascular disease, and so on. Down the left axis, he jots some of the stages between isolating a stem cell and actually using it in a patient: self-renewal (keep-



PORTRAIT

HARVARD

## Louis Menand

THOUGH READERS of the New Yorker might identify him as a gifted book critic and stylish essayist—his pieces are 2004 National Magazine Award finalists in both categories—professor of English and American literature and language Louis Menand considers himself an "intellectual historian. I'm interested in where ideas come from, and the influence of one writer on another." His book The Metaphysical Club absorbed 10 years ("It was fun," he says), and won the 2002 Pulitzer Prize for history. It shows how Oliver Wendell Holmes Jr., William James, Charles Sanders Peirce, and John Dewey launched pragmatism and moved "American thought into the modern world." Menand does "a version of American studies," he says. "But nothing before the nineteenth century." Known as "Luke" since childhood (his eponymous father taught political science at MIT), Menand earned a degree in creative writing from Pomona College in 1973, then spent one year at Harvard Law School. "I didn't have the personality to be a lawyer," he says. "I don't like to argue." Instead, he earned a Ph.D. in English from Columbia, then taught at Princeton and CUNY before coming to Harvard last fall. Menand teaches courses on the Jameses (Henry, William, and Alice), and on the art and thought of the Cold War period from 1945 to 1965, the subject of his next book. With his wife, Emily, and two adolescent sons in Manhattan, he commutes between there and Beacon Hill. Menand's elegant prose doesn't emerge from revision: "I don't write drafts," he explains. "My habit is to write one draft, very deliberately." Will there someday be a novel, a screenplay? "Ha!" he says. "I wish."

#### JOHN HARVARD'S JOURNAL

ing it dividing); targeted differentiation (signaling it to make the type of tissue that is desired); scaling up (making lots of the tissue for use in patients); transplantation (getting it into the patient); and clinical studies.

"The way the institute is organized," says Melton, "we might get all the people who are interested in diabetes together and ask how we are going to get a stem cell all the way into a patient." He continues, "Let's say we are stuck on the process of self-renewal. We can now bring together people from all different areas of disease expertise, people who never really talked to each other before-neurologists, endocrinologists, hematologists"to try to solve the problem. A researcher working on Parkinson's disease might have come up with a novel way of ensuring self-renewal that could be applied to other disease targets.

"One of the key things is that people become multilingual," echoes Scadden. "Those who focus predominantly on clinical care will start to appreciate the necessary components of computational science and developmental biology that

are all necessary to take advantage of emerging opportunities in stem-cell science and regenerative medicine." HSCI will have "a very big influence on developing new models of educating people. Having people from Harvard and MIT with training in mathematics and computational science as part of the creative process will be an important part of training the next generation of doctors and scientists so that they are comfortable with spanning these worlds." These new models of inquiry, Scadden hopes, will attract both students and faculty to work in regenerative medicine.

"Harvard [in] its history always has been striving to be a leader in critical areas of knowledge," says Hyman, "and areas like stems cells [are among] the most exciting intellectual challenges in the world today. We would really be abdicating our role as intellectual leaders if we didn't do everything in our power to make it possible for our faculty to engage in these new areas."

## Class-conscious Financial Aid

HARVARD HAS ENHANCED its undergraduate financial-aid program in an effort to make the College more attractive to lower-income students. Beginning this fall, the parental contribution toward tuition, room, and board will be eliminated for entering and continuing students from families whose income is less than \$40,000 per year. That contribution has averaged \$2,300 in the past year. Families with incomes from \$40,000 to \$60,000 will have their expected contribution reduced \$1,250 on average (the University did not quantify their current financial obligation). Students will remain responsible for contributing to their expenses to the tune of \$3,500 next year (met through outside scholarships, term employment, or loans), plus an average of \$2,000 from summer earnings (\$1,850 for freshmen).

The aid enhancements, announced in late February by President Lawrence H. Summers, are expected to assist more than 1,000 families in the next academic



year, when the program will boost Harvard's undergraduate scholarship funding by \$2 million, to nearly \$80 million. (The bill for tuition, room, board, and fees in 2004-2005 will increase by \$1,952, to \$39,880—5.15 percent more than the \$37,928 cost of attending the College during the current academic year.)

At a time of considerable public interest in admissions issues ranging from affirmative action (see "Affirmative Amicus," May-June 2003, page 50, and "Citing Harvard," September-October 2003, page 76, for discussion of the University of Michigan cases decided by the Supreme Court last year) to "legacy" preferences for the children of alumni, Summers defined a new challenge. Speaking before the American Council of Education, in Miami, he said "the most serious domestic problem in the United States today is the widening gap between the children of the rich and the children of the poor, and education is the most powerful weapon we have to address that problem." (The full text is available at www.president.harvard.edu.)

Data released by the University show that measured by family income, parents' education and occupation, and other factors, 73.9 percent of students entering the College come from the highest socioeconomic quartile of society, where family incomes are above \$81,000 (based on 1999 census data). In contrast, just 6.8 percent of entering students come from the first, or lowest, socioeconomic quartile (incomes below \$33,000), and 9.2 percent from the second quartile. By this measure, Harvard actually does a better job of accommodating disadvantaged students than do "highly selective colleges" overall, where just 9 percent of entering students come from the bottom half of the socioeconomic distribution. In other words, Summers said, "Children whose families are in the lower half of the American income distribution are underrepresented by 80 percent" at selective institutions.

The boost in financial aid was shaped in part by interviews with students who said they already shouldered the expected parental