Haute Culture: Tailoring stem cells to make us well

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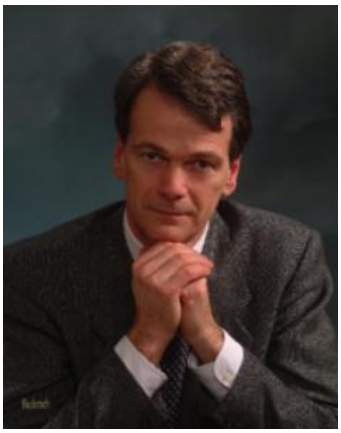
Haute Culture:
Tailoring stem cells to make us well

Moderator



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

Speakers

Chad Cowan, PhD
Assistant Professor of Stem Cell and Regenerative Biology,
Department of Stem Cell and Regenerative Biology,
Harvard University
Massachusetts General Hospital

Fernando Camargo, PhD
Assistant Professor of Stem Cell Regenerative Biology,
Department of Stem Cell and Regenerative Biology,
Harvard University
Children's Hospital Boston Stem Cell Program

About the Speakers

Brock Reeve, MPhil, MBA

Brock Reeve is Executive Director of the Harvard Stem Cell Institute. In partnership with the Faculty Directors, he has overall responsibility for the operations and strategy of the institute whose mission is to use stem cells, both as tools and as therapies, to understand and treat the root causes of leading degenerative diseases.

HSCI is comprised of the schools of Harvard University and all its affiliated hospitals and research institutions. Under the leadership of the Executive Committee, HSCI invests in scientific research in three main areas – seed grants, core facilities and large-scale disease programs. Beyond the science, the institute also has programs to address ethics and public policy issues, provide lab experiences for undergraduates, and to educate high school science teachers, science journalists and the public at large.

HSCI's faculty membership has grown to 80 Principal Faculty and over 150 Affiliated Faculty. The Institute is now engaged with several leading pharmaceutical companies in joint research projects and its faculty have founded five stem cell-related startup companies and serve on leading Scientific Advisory Boards.

In addition to funding its own research programs, HSCI has developed resources for the field including creating more embryonic stem cell lines than any other organization and launching StemBook, the online stem cell journal. The HSCI undergraduate Internship Program includes students from around the world. With a focus on stem cells as tools as well as therapies, unique core operations such as the Therapeutic Screening Center and iPS Core have been created. Programs such as an external speaker series, interlab symposia, annual conferences, public forums have all been developed to accelerate the interchange of ideas among the faculty.

Brock came to this role from the commercial sector with extensive experience in both management consulting and operations for technology-based companies, with a focus on life sciences. Prior to Harvard, Brock was COO and Managing Director of Life Science Insights, an IDC company, a consulting and market research firm specializing in information technology in life sciences. As a consultant, Brock has additional experience in IT and the healthcare/life sciences market with IBM's Business Consulting Services, Viant Corp. and SRI Consulting, where his clients included some of the leading pharmaceutical, biotechnology and medical device companies, and he also has had hands-on operational responsibility in product management and marketing roles in software start-ups.

Brock received a BA and MPhil from Yale University and an MBA from Harvard Business School.

Chad Cowan, PhD

Our goal is to understand how naturally occurring human genetic variation protects (or predisposes) some people to cardiovascular and metabolic disease—the leading cause of death in the world—and to use that information to develop therapies that can protect the entire population from disease. Our strategy is to identify patients, families, and cohorts with disease; to use genetic techniques such as genomewide association studies and exome sequencing to identify novel DNA variants and genes linked to disease; to use human cell-based models and mouse models to understand how the DNA variants affect gene and protein function; and to use these mechanistic insights to begin the process of developing new therapies that will benefit patients and populations. In particular, we are interested in using human pluripotent stem cells to create human-derived tissues, containing specific DNA variants, as genetic disease models in which environmental and epigenetic influences have been minimized. We also aim to use stem cells to enable regenerative medicine, in which a patient's own cells can be genetically cured or made resistant to disease and then transplanted back into the body as a durable treatment.

Chad Cowan received his BA and BS, with honors, from Kansas University. He received his PhD, from the University of Texas Southwestern at Dallas, garnering the Nominata award for most outstanding thesis. He subsequently completed a postdoctoral fellowship with Professor Douglas Melton at Harvard University. He was named a Stowers Medical Investigator in 2006. He currently directs the Harvard Stem Cell Institute's iPS Core Facility and is head of the Diabetes Disease Program.

Fernando D. Camargo, PhD

Fernando D. Camargo, PhD, is an Assistant Professor of Stem Cell and Regenerative Medicine at Harvard University and the Stem Cell Program at Children's Hospital Boston. He is also a principal faculty at the Harvard Stem Cell Institute.

Dr. Camargo studied in the laboratory of Dr. Margaret Goodell for his doctoral work in the Department of Pediatrics at Baylor College of Medicine. In 2005, he was selected for the highly prestigious Whitehead Fellowship at the Whitehead Institute for Biomedical Research, where he directed a laboratory focused on the regulation of stem cell proliferation and differentiation and the mechanisms that control tissue size in mammals. In September 2009, he moved his laboratory to Harvard as a tenure-track professor. In 2010, Dr. Camargo was awarded the NIH New Innovator Award, named a Basil O'Connor Scholar from the March of Dimes, and a Pew Scholar in the Biomedical Sciences.

His laboratory's ultimate goal is to understand the signals that regulate adult stem cell maturation and tissue regeneration for their eventual manipulation and application in the clinic. His lab has been a pioneer in the study of a novel biochemical cascade that controls stem cell numbers and activity. Currently, the main focus of the lab is the study and identification of the signals that regulate organ size and control tissue symmetry. Insight into these processes will shed light on fundamental aspects of tissue regeneration and will facilitate the development of therapeutic approaches based on cellular transplantation. Additionally, our group is investigating the relevance of organ size regulatory mechanisms as components of a novel cancer-suppressing pathway.

Small step forward for stem cells, giant leaps remain

Results from the first-ever trial using stem cells that normally reside in the heart had the scientific community using adjectives like “astounding” and “compelling.” But as encouraging as the findings were, keep in mind that stem cell research is still in its infancy and has a long way to go before yielding effective treatments for heart disease.

Stem cells are “raw material” cells that can develop into other types of cells. Some stem cells, like embryonic stem cells, can become a heart muscle cell, a liver cell, or virtually any other type of cell. Other stem cells have more limited potential, but still can perform vital functions, like producing blood cells. Early stem cell research ignited hope that tissue damaged by a heart attack or other cardiac travail could be regenerated.

Most previous studies of stem cell treatments for heart disease have focused on bone marrow stem cells, and the jury is still out on whether these cells can improve heart function. In the news making SCIPIO trial, researchers tested stem cells taken directly from human heart tissue (see illustration).

The 14 people who got stem cells in the SCIPIO trial were all heart attack survivors with poorly pumping left ventricles (the heart’s main pumping chamber) who’d had recent bypass surgery. Researchers acquired the stem cells from a small piece of tissue removed during the bypass surgery. They grew the stem cells in the lab, and injected them back into the heart about four months afterward.

Safe and effective

SCIPIO’s main goal was to determine whether using heart-derived stem cells was safe. Some types of stem cells used in previous studies induced worrisome heart rhythm abnormalities. No one experienced any such rhythm problems during the SCIPIO trial.

Here’s the astounding part: ventricular pumping power — a measure doctors call ejection fraction — increased from 30% to almost 39% after four months and to 42% after one year in the stem cell recipients. (Normal ejection fractions range from 55% to 70 %.) In addition, MRI scans showed that the size of the scar from heart-attack-related muscle damage decreased in people who received cardiac stem cells. In contrast, researchers saw no such changes among seven people with similar health characteristics who didn’t receive stem cells (*Lancet*, published online Nov. 14, 2011).

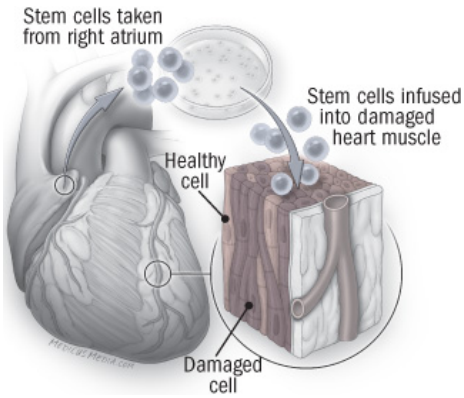
“The 12% absolute increase in ejection fraction after a year is remarkable; we have seen no more than 4% to 5% improvement in the bone marrow studies,” says *Harvard Heart Letter* Associate Editor Dr. Richard Lee. “But SCIPIO is just one small step forward. Often, early results such as these don’t hold up in larger controlled trials.”

The SCIPIO findings raise the question of whether the regenerative power of stem cells derived from heart muscle is potentially greater than that from bone marrow stem cells. In a study of boosting low ejection

fractions with marrow-derived stem cells, researchers observed no difference between heart attack sufferers who received stem cells and those who didn't (*Journal of the American Medical Association*, Nov. 16, 2011).

But even negative findings like that can propel research forward. The people in the *JAMA* study received stem cells two to three weeks after having an angioplasty, reinforcing a hypothesis from prior research that delivery of marrow-derived stem cells between four and eight days after a heart attack is optimal. Why not sooner? Again, prior research suggests that the "microenvironment" of heart tissue immediately after a heart attack is not conducive to stem cells taking root.

Success with stem cells



In the SCIPIO trial, cardiac stem cells taken from the right atrium were multiplied in the lab and then infused into an area of heart muscle damage. After one year, the damaged area was smaller.

Because SCIPIO was the first trial using cardiac stem cells, the best timing for cardiac stem cell treatment remains a wide-open question.

To answer that and other questions, there are many ongoing clinical trials investigating stem cell treatments for heart disease (go to health.harvard.edu/179 for a list). Hope may spring eternal in the human breast, as poet Alexander Pope wrote, but only further research will reveal whether stem cells can mend broken hearts.

To learn more…
This information is prepared by the editors of the Harvard Health Publications division of Harvard Medical School. It originally appeared in the March 2012 issue of the *Harvard Heart Letter* available from http://www.health.harvard.edu/newsletters/heart.

Stem cells and the prostate

Mention stem cells, and many people think of divisive ethical controversies and heated political debates. Indeed, stem cell research has crucial ethical dimensions. Leaving moral complexities aside, though, the basic research is fascinating and important in its own right. And although the prostate lags far behind other areas of stem cell science, reports suggest that stem cells may someday assume a role in the diagnosis and treatment of prostate diseases.

What are stem cells?

Just as the stem of a plant gives rise to other structures, stem cells give rise to all the other cells in the body. Stem cells are undifferentiated, or unspecialized, cells that are able to renew and regenerate themselves through the process of cell division. In addition, if conditions are right, they can differentiate and mature into the specialized cells that make up all of the body's tissues and organs.

There are two main types of stem cells. Embryonic stem cells have the greatest potential to differentiate into specialized cells. Indeed, just a few stem cells present at the very beginning of embryonic life eventually differentiate into cells as different as beating heart muscle cells, nerve cells that generate and transmit vital signals, and pancreas cells that produce insulin. Embryonic stem cells give rise to each and every one of the body's 10 trillion cells.

Adult stem cells play a different role. It now appears that all adult organs contain a small number of stem cells that reside in a special protected region, or niche. Because most cells in a tissue or organ have a limited life span, stem cells function as a reserve of cells that can be moved out of their niche, begin dividing, and differentiate into specialized organ cells to replace dying or injured cells. But unlike embryonic stem cells, which have the potential to morph into any cell type, adult stem cells ordinarily develop only into the same cells as their parent organs. For example, adult stem cells from the liver become normal, functioning liver cells but not brain cells.

Therapeutic potentials

Scientists have the most hope for embryonic stem cells because they are relatively easy to maintain in tissue culture for prolonged periods and because they have the theoretical ability to differentiate into any cell in the body. Researchers hope they will one day be able to stimulate embryonic stem cells to differentiate into healthy nerve cells that could be transplanted into patients to replace nerve cells damaged by Parkinson's disease, strokes, or spinal cord injuries. Similarly, they hope to treat diabetes with pancreas cells, heart attacks with healthy heart muscle cells, and so forth. Although embryonic stem cells hold great promise, actual treatments are a long way off. And current technology relies on obtaining these cells from early embryos that have been produced for in vitro fertilization but are not needed by patients and would be discarded if not used for research.

Adult blood stem cells have been used for some bone marrow transplants in leukemia patients since the 1970s. Until very recently, however, therapeutic adult stem cell research has been thwarted by the difficulty of obtaining these cells and in coaxing them to regain the embryonic stem cells' ability to differentiate into

many types of tissue cells. Scientists are making progress in both areas, but practical treatments are still over the horizon.

Prostate stem cells

Men who have been frustrated by the many aspects of the puzzling prostate will not be surprised to learn that research into prostate stem cells is still in the early stages. Still, new insights are worth considering.

The prostate has only a small number of adult stem cells. They constitute less than 1% of all prostate cells, and they are contained in a niche in the lower, or basal, layer of the prostate's glandular structures. But although these cells are few in number and restricted in location, they do have the potential to proliferate and migrate. In fact, scientists have grown a complete, functioning mouse prostate from a single adult stem cell.

In most organs, stem cells may serve a positive, healthful role by growing into mature tissue cells. But the two most important prostate diseases are characterized by abnormal cell growth; in the case of benign prostatic hyperplasia (BPH), cell growth is excessive, and in prostate cancer, it's uncontrolled. Scientists suspect that prostate stem cells contribute to both problems.

Most cases of BPH begin slowly in middle age. Doctors don't know what causes BPH, but stem cells may play a role. Researchers speculate that stem cells might contribute in two ways. They could divide, proliferate, and differentiate into the excessive glandular and muscle cells that are responsible for the malfunction and enlargement that characterize BPH. Prostate stem cells could also differentiate into stromal (supporting) cells that produce insulin-like growth factor-1 (IGF-1) and other hormones that stimulate the growth of prostate cells. In theory, at least, temporary androgen deprivation therapy combined with a single dose of radiation might target stem cells and provide a durable therapy for BPH.

The possible role of stem cells in prostate cancer is even more theoretical, but just as interesting. Research holds that prostate cancer develops when differentiated, mature prostate cells undergo genetic mutations that permit unrestrained cell multiplication and allow these malignant cells to spread from the prostate to other organs and tissues. These prostate cancer cells have androgen receptors; testosterone and other androgens (male hormones) promote tumor growth, and androgen-deprivation therapy halts that growth. Androgen-deprivation therapy produces great benefit, even when prostate cancer has spread to other organs. But eventually most of these tumors escape from androgen deprivation and begin growing again. Prostate stem cells lack androgen receptors. If these cells constituted even a small portion of the tumor mass, they might be responsible for androgen-independent advanced prostate cancers. If scientists develop new ways to identify and target stem cells, this could lead to new therapy for the men who need it most.

Stem cell science is new, prostate stem cell research newer still. There is no guarantee that laboratory research will produce therapeutic breakthroughs, but without basic research, clinical progress would be seriously impaired.

To learn more…
This information is prepared by the editors of the Harvard Health Publications division of Harvard Medical School. It originally appeared in the January 2010 issue of the *Harvard Men's Health Watch* available from http://www.health.harvard.edu/newsletters/mens.

The Promise of Stem Cells

Studying stem cells will help us understand how they transform into the dazzling array of specialized cells that make us what we are. Some of the most serious medical conditions, such as cancer and birth defects, are due to problems that occur somewhere in this process. A better understanding of normal cell development will allow us to understand and perhaps correct the errors that cause these medical conditions.

Another potential application of stem cells is making cells and tissues for medical therapies. Today, donated organs and tissues are often used to replace those that are diseased or destroyed. Unfortunately, the number of people needing a transplant far exceeds the number of organs available for transplantation. Pluripotent stem cells offer the possibility of a renewable source of replacement cells and tissues to treat a myriad of diseases, conditions, and disabilities including Parkinson's disease, amyotrophic lateral sclerosis, spinal cord injury, burns, heart disease, diabetes, and arthritis.

Scientists have been able to do experiments with human embryonic stem cells (hESC) only since 1998, when a group led by Dr. James Thomson at the University of Wisconsin developed a technique to isolate and grow the cells. Although hESCs are thought to offer potential cures and therapies for many devastating diseases, research using them is still in its early stages.

The National Institutes of Health (NIH) funded its first basic research study on hESCs in 2002. Since that time, biotechnology companies have built upon those basic foundations to begin developing stem cell-based human therapies. There are currently two active clinical trials using cells derived from human embryonic stem cells, both being conducted by a biotechnology company called ACT. The company has laboratories in Marlborough, Massachusetts and corporate offices in Santa Monica, California. ACT has begun enrolling patients for Phase I (safety and tolerability) clinical trials of two hESC-derived stem cell products:

The first ACT trial is testing the safety of hESC-derived retinal cells to treat patients with an eye disease called Stargardt's Macular Dystrophy (SMD).

The second ACT trial is testing the safety of hESC-derived retinal cells to treat patients with age-related macular degeneration.

In January, 2012, the investigators published a preliminary report on the first two patients treated with hESC-derived cells: http://www.ncbi.nlm.nih.gov/pubmed/22281388.

A third clinical trial using hESC-derived cells was halted on November 14, 2011. The trial was being conducted by a biotechnology called Geron, located in Menlo Park, California. Four patients with recent spinal cord injuries had been enrolled for its clinical trial of a hESC-derived therapy. The trial was testing the safety of using hESC-derived cells to achieve restoration of spinal cord function. Oligodendrocyte progenitor cells derived from hESCs were being injected directly into the lesion site of the patient's injured spinal cord. On November 14, Geron announced that it was discontinuing its stem cell programs to concentrate on cancer programs.

Bone marrow contains blood-forming stem cells (hematopoietic stem cells) that have been used for decades to treat blood cancers and other blood disorders. Umbilical cord blood is another source of hematopoietic stem cells that is being used in treatment. You can see a list of diseases that may currently be treated with hematopoietic stem cells at the website of the National Marrow Donor Program.

Scientists are testing the abilities of many different types of stem cells to treat certain diseases. You can search for clinical trials using stem cells (or other methods) to treat a specific disease at ClinicalTrials.gov.

To learn more…
This information was provided by *Stem Cell Information*, the National Institutes of Health resource for stem cell research. You can learn more at http://stemcells.nih.gov/index.asp.

HarvardMedicine

The following articles are selections from *Harvard Medicine* magazine's Spring 2011 issue. Additional content can be found online, please visit: http://harvardmedicine.hms.harvard.edu/

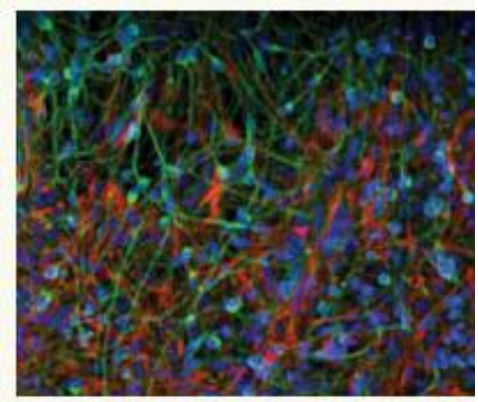
The Twilight Zone

What discoveries were unimaginable even a decade ago?

by Anne Marie Menting

REPROGRAMMABLE ADULT STEM CELLS

Realm of Imagination: *What if the body's cells could be instructed to treat disease or repair damage? The notion of healing at the cellular level has long tantalized researchers. Embryonic stem cells brought promise—then pitfalls. What was needed was a readily accessible supply of adult cells that, like their embryonic progenitors, were willing to assume new roles.*



Courtesy of Rekesh Karmacharya/Broad Institute and McLean Hospital

From Shadow to Substance: Building upon the knowledge that nearly all cells harbor the same genetic code, researchers have searched for ways to reprogram differentiated adult cells. In 2006, they discovered key reprogramming tools: a mere four molecular factors that could take differentiated cells, strip them of their adult identities, and then coax them to develop into new cell types—converting skin cells into liver cells, for example. These induced pluripotent stem, or iPS, cells rocked the world of medical research. "It was a huge, unanticipated breakthrough," says George Daley, an HMS professor of biological chemistry and molecular pharmacology. "The idea that we could turn specialized cells back into embryonic stem cells had been the stuff of science fiction."

The Harvard Dimension: The news that such a small set of factors could alter the fates of cells was met with some skepticism, says Daley. But Konrad Hochedlinger, an HMS assistant professor of medicine, refined the technique, and Daley's lab showed it worked in human cells. Daley's group has also built a large repository of disease-specific cells that can be used to test therapies. Other Harvard researchers are expanding the list of cells that can be reprogrammed and are developing new methods for making cells reprogrammable.

What's Next? "There are so many things going on in stem cell research," says Daley, "that it wouldn't surprise me if in another ten years we achieve something momentous—regenerating an organ, like a heart or liver, or tissue, like bone marrow, which is what we're trying to develop in my lab. And along the way, we might be able to correct any genetic defects in those repurposed cells."

REGENERATIVE CELLS

Realm of Imagination: *When a person's heart, kidney, or lung falters, physicians largely rely on the organ to heal itself, or drugs to boost its function, or transplantation to give new hope. But each carries risks. Wouldn't it be best if organs could reliably repair themselves? Wouldn't it be grand if medicine could harness the body's potential for regeneration?*

From Shadow to Substance: Working with induced pluripotent stem cells, Kenneth Chien, the Charles Addison and Elizabeth Ann Sanders Professor of Basic Science at HMS, has sought to make tissue that mends the muscle of failing hearts. About five years ago, he startled the field of regenerative medicine by discovering a progenitor cell that could generate functioning strips of mature heart muscle tissue. Then he identified a "master" cardiovascular stem cell, one that gives rise to cardiac, smooth muscle, and endothelial heart cells; may help form heart muscle and coronary arteries; and may play a role in the heart's pacemaker system. The value of such a cell is enormous; it holds the potential for uncovering the origins of the human heart as well as for new therapies that repair, replace, or renew damaged tissue.

The Harvard Dimension: One leader in the field, Douglas Melton, co-chair of the Department of Stem Cell and Regenerative Biology at HMS and co-director of the Harvard Stem Cell Institute, provided early inspiration when he generated specific cell types from stem cells. Breakthroughs like Melton's, Chien says, allow investigators to "envision the power that systems for redirecting cell development can have, from their use in modeling human disease, to the most elusive goal of all—personalized regenerative medicine."

What's Next? "Regenerative medicine is between acts, in an intermezzo period," says Chien. "We're moving from stem cell biology toward stem cell therapeutics. We'll no longer just insert cells into the heart and hope they go where we want and do what we want. Instead, I think we'll use pluripotent stem cells to make functioning 'heart parts' that we can simply put into place."

Weapon for Mass Construction

Chemotherapeutic drug activated stem cells that act to regenerate bone in mice
by Ann Marie Menting

Renovation and renewal of bone diminished by age or disease could be just around the corner, according to results from a study by scientists at Massachusetts General Hospital and the Harvard Stem Cell Institute. A team of researchers wrote in the February issue of the Journal of Clinical Investigation that a drug used as a targeted chemotherapy in patients with multiple myeloma helped regenerate bone tissue in mice by activating stem cells critical to the formation of new bone tissue.

The findings could represent a novel therapeutic strategy for bone diseases: targeting stem cells using drugs. If so, this news may one day help put the spring back in the step of postmenopausal women who suffer from osteoporosis or individuals who have lost bone mass because of cancer.

The team of investigators led by Siddhartha Mukherjee ’00, an HMS instructor in medicine at Massachusetts General Hospital’s Center for Regenerative Medicine and Technology, set up their study to examine the effects that the drug bortezamib might have on cells known as mesenchymal stem cells (MSCs). Found in bone marrow, MSCs are multipotent; that is, they can develop into any of several types of cells. If triggered during their more impressionable period, they can become bone, fat, muscle, or cartilage cells that can then grow or repair tissue lost to disease or trauma.

The team selected bortezamib because clinical evidence from multiple myeloma patients taking the drug showed elevated serum levels of alkaline phosphatase and osteocalcin, substances linked with bone formation. Hoping to isolate how the drug’s actions might contribute to increased bone formation, the researchers tested possible targets for the drug. Surprisingly, they found it caused MSCs to form bone tissue.

The in vivo mouse model the scientists used was one developed for menopausal osteoporosis. When they treated these mice with low doses of bortezamib, doses equivalent to between one-fifth and one-third what would normally be considered effective against tumors, they found an increase in bone formation, in the mineralization of spongy tissue matrices that form the ends of long bones such as the femur, and in the production of osteoblasts, the cells that make up bones. Similar results were achieved when the researchers tested the drug in vitro on cultured MSCs derived from human bone marrow and from mouse models.

The authors point out the drug’s potential for people experiencing bone loss. In addition, they note the study offers proof of principle that a drug can harness the inherent power of the body’s stem cells to repair and regenerate tissue—a strategy that might become increasingly key to regenerative medicine. ■

This article appeared in the Spring 2008 issue of *Harvard Medicine.*

Reprogrammed Stem Cells Cling to Past Lives
Harvard Medical School News

Study has significant implications for the use of adult stem cells in research and in cell-replacement therapies

Kit Chellel
September 3, 2010

Some stem cells are unwilling to let go of their past. They cling to traces of a previous life, even after researchers have wiped their slates clean.

In the search for an inexpensive and less controversial alternative to embryonic stem cells, scientists have created induced pluripotent stem (iPS) cells, adult cells that have been reprogrammed for experimental use.

New research has found, however, that iPS cells from adult mice seem to remember what they were before being reset—and therefore remain best suited to carrying out tasks linked to that previous role.

"iPS cells retain a 'memory' of their tissue of origin," said George Daley, senior author of the study, an HMS professor of biological chemistry and molecular pharmacology at Children's Hospital Boston and director of the hospital's Stem Cell Transplantation Program. "iPS cells made from blood are easier to turn back into blood than, say, iPS cells made from skin or brain cells."

The findings, published online July 19 in *Nature*, have significant implications for the use of adult stem cells in research or in cell-replacement therapies. The results are especially noteworthy in light of an August ruling by a federal district court judge that temporarily blocked government funding of research on human embryonic stem cells.

The residual memory comes from epigenetic modification, a means of changing a cell's makeup that does not alter the cell's underlying genetic structure. In the study, residues left behind by a certain type of epigenetic modification called methylation were so distinctive in iPS cells that they could be used to identify where the cells came from.

Daley's team also found that an alternative technique, known as somatic cell nuclear transfer, creates pluripotent stem cells, which are just as good as iPS cells at turning into several different types of tissue—without the residual memory. Somatic nuclear transfer reprograms an adult cell by transferring its nucleus into an unfertilized egg cell, the method famously used to clone Dolly the sheep.

Although nuclear transfer has yet to be successfully used in human cells (the current study used cells from adult mice), Daley believes the findings warrant investigation. "Stem cells generated by somatic cell nuclear transfer are, on average, closer to bona fide embryonic stem cells than are iPS cells," he said.

“This has an important political message,” Daley said. “We still need to study the mechanisms by which nuclear transfer reprograms cells, because the process seems to work more efficiently and faithfully. Learning the secrets of nuclear transfer may help us make better iPS cells.”

Andrew Feinberg, director of the Epigenetics Center at John Hopkins, who worked with Daley on the study, described residual cell memory as “both a blessing and a curse,” adding: “You might want lineage restriction in some cases, but you may also have to do more work to make the iPS more totally pluripotent.”

Another study published online simultaneously in the journal *Nature Biotechnology* supports Daley’s findings. Its senior author, Konrad Hochedlinger, HMS assistant professor of medicine at Massachusetts General Hospital, said, “Our paper comes to a similar conclusion—that a retention of memory reflects the cell of origin and affects the capacity of the iPS cell to differentiate into other cell types.”

For More Information

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Another Set of Fingers
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http://www.scrb.harvard.edu/node/176

Two studies prove value of iPS cells
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Stem cells: Mending a broken heart?
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Stem cell donor and recipient share a special bond: Bob & Annette's story
Dana-Farber Cancer Institute
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Stem cell donors- real heroes in everyday life
Dana-Farber Cancer Institute
http://www.dana-farber.org/Adult-Care/Treatment-and-Support/Patient-Stories/Robert-Soiffer-MD---Stem-cell-donors-everyday-heroes.aspx

Websites:

Harvard University Department of Stem Cell and Regenerative Biology
http://www.scrb.harvard.edu/

Harvard Stem Cell Institute
http://www.hsci.harvard.edu/

iPS Core Facility
http://www.hsci.harvard.edu/node/1005

Chad Cowan HSCI Profile
http://www.hsci.harvard.edu/people/chad-cowan-phd

HCSI Diabetes Disease Program
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Fernando Camargo HSCI Profile
http://www.hsci.harvard.edu/people/fernando-camargo-phd

Fernando Camargo Children's Hospital Boston Research
http://www.childrenshospital.org/cfapps/research/data_admin/Site3108/mainpageS3108P0.html

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