INSTITUT DU MARIAGE ET DE LA FAMILLE CANADA
IMFC
INSTITUTE OF MARRIAGE AND FAMILY CANADA

CANADIAN BUSINESS

The Stem Cell Revolution

Erin Pooley

From the November 20-December 3, 2006 issue of Canadian Business magazine

When Rob McEwen's mother and sister died within a few months of each other just over four years ago, the outspoken gold-mining executive was confronted with a reality many of us would prefer to ignore. "In the space of four or five months, two members of my family went," says the 56-year-old founder and former chairman of Vancouver-based gold-producer Goldcorp Inc. "I suddenly met someone I didn't expect to meet for a long time, and that was mortality."

Preventing death is, ultimately, impossible. Slowing its arrival is not. With that in mind, McEwen and his wife, Cheryl, donated $10 million in 2003 to help establish the University Health Network's McEwen Centre for Regenerative Medicine in Toronto. The centre, launched with much fanfare on Oct. 25, will serve as a hub for top researchers in the field of regenerative medicine. It is here that scientists are hoping to harness the power of embryonic stem cells, which, coupled with their ability to self-renew indefinitely, have an almost magical ability to differentiate themselves into more than 200 specialized cell types.

Stem cells are the precursors to just about every type of specialized cell in the body. They can be found most readily in the umbilical cords of infants and in various adult tissues--the skin, the lining of the gut, the blood. But although they are promising, in terms of possible therapeutic applications, adult and cord blood cells are less malleable than their embryonic stem-cell counterparts, because they are already somewhat specialized and cannot be converted into as many different cell types. The first stem-cell therapy was discovered nearly 50 years ago--when doctors figured out that adult bone marrow contained stem cells that could be transplanted into leukemia patients. However, it wasn't until 1998 that researchers isolated the first line, or colony, of embryonic stem cells from in vitro fertilization.

The promise of these so-called embryonic miracle makers is enormous. By providing an unlimited supply of replacement tissues to help treat everything from diabetes to Parkinson's, embryonic stem cells could completely change medicine. They are more than tools in potentially revolutionary therapies--they also offer a never-before-seen window into the early stages of human development. Stem-cell therapy could also save the Canadian government billions of dollars in chronic health-care costs--and potentially fuel a multibillion-dollar industry in stem-cell therapeutics.

The official launch of the McEwen Centre comes at a crucial time in the history of stem-cell research. On Nov. 7, the Australian Senate voted to lift the country's ban on somatic cell nuclear transfer, or SCNT--the therapeutic cloning of human embryos for research purposes, which is still illegal in Canada. A day later in the United States--just after the U.S. midterm elections, in which Democrats won control of the House of Representatives and the Senate--House Democrat leader Nancy Pelosi vowed that within the first 100 hours of the new Congress in January, she would seek votes on federal funding for stem-cell research. That could reverse a July 2006 veto by President George W. Bush to limit federally funded stem-cell research to stem-cell lines, or colonies, that were derived on or before Aug. 9, 2001.

Those developments followed on the heels of a high-profile spat between Canadian-born sitcom-star-turned-stem-cell-research-advocate Michael J. Fox and right-wing radio commentator Rush Limbaugh, in which Limbaugh had accused the 45-year-old actor of exaggerating his Parkinson's disease symptoms in a campaign-style television advertisement supporting Democratic senate challenger Claire McCaskill. She won,

unseating Missouri's Republican incumbent, and joined newly elected senators from Maryland, New Jersey and Ohio who support stem-cell research.

Embryonic stem-cell research has officially become a cause célèbre--a political and ethical hot potato. The debate that weighs the value of a human embryo against the potential of that embryo to save many more lives is a contentious one. Although the Democrats' sweep of both houses of Congress is likely to intensify that debate, powerful lobby groups from the religious right in the United States have been successful thus far in stunting progress in the field of publicly funded stem-cell research.

But while debate rages on in the corridors of power, progress is being made in a dozen or so research labs around the world. In Canada, where attitudes toward embryonic stem-cell research are generally more liberal, the excitement behind stem-cell research is building. In Toronto, scientists have already been able to grow heart and blood cells in a petri dish using stem cells. In Ottawa, a small Canadian biotech firm called StemPath Inc. is working on producing a drug that will coax a person's existing stem cells in the heart to regenerate themselves, and help repair any damage caused after a heart attack. A group of Edmonton scientists have successfully transplanted pancreatic islet cells from cadavers into diabetic patients.

This is now. In 10 or 15 years, the dream is that doctors will be able to take bags of differentiated stem cells created by biotech companies and transplant or inject them into patients in order to repair damaged tissue. So-called designer drugs, or those that could modulate or target specific stem-cell types in the body toward a particular goal, may also be widely available. These would help patients heal themselves by generating the cells they need to repair damaged tissue. Overall, the worldwide market in stem-cell therapeutics is predicted to reach anywhere between US$10 billion to US$30 billion by 2015.

McEwen, currently chairman and chief executive of Denver-based US Gold, doesn't pretend to be an expert when it comes to the science of regenerative medicine. But the veteran businessman knows a good thing when he sees it. As he points out, there are striking similarities between getting gold out of the ground and harnessing the transformative power of stem cells. First, says McEwen, you need to take a risk. Then, you need patience.

"That, and you need a plan," he says. "Canada needs a plan."

Gordon Keller might be just the man to put that plan into place. Beginning in January, the 54-year-old Saskatchewan native will officially assume the top job at Toronto's McEwen Centre, after a seven-year stint at New York's Mount Sinai School of Medicine. New York magazine recently called Keller "one of the top six medical minds" the city couldn't afford to lose. But lose him it did, and Keller's move to Toronto is likely to draw other top stem-cell researchers to the city to work with his all-star cast. The hope is that the groundbreaking research in regenerative medicine will help propel Toronto--and the rest of the country--into the big leagues of stem-cell research. Keller and his team plan to use mouse and human embryonic stem cells to further understand the process involved in driving one cell type to make another--whether it be a heart, liver or pancreatic cell. In the future, they hope to transplant these cells into patients to treat diseases.

Keller's work is not about cloning--not that he could do that in Canada legally anyway. SCNT is illegal in Canada--the Senate approved Bill C-6, which forbids the cloning of human embryos for either therapeutic or reproductive purposes, in March 2004. As a result, Keller and other Canadian regenerative-medicine specialists must limit their research to both existing and new embryonic stem-cell lines created from embryos left over after in vitro fertilization. In fact, Canada is one of only about half a dozen countries that bans

therapeutic cloning for research purposes. In the United States, researchers can perform SCNT, but only using private funds.

Keller remains unfazed. Regardless of how a stem-cell line is created, he points out, it's likely the science behind its transformation will be similar. Having access to a large number of cells and tissues in culture is proving remarkably helpful for drug companies, which are now starting to test the potential toxic effects of certain molecules on human tissue without harming a patient in the process. These "drug screens," adds Keller, have the potential to revolutionize the way drugs are tested. Such screens could also test the regenerative effects of certain molecules on existing cells. "You could imagine new molecules that induce heart cells to divide, which may provide a new way to regenerate those cells within our own tissue--or the ability to make more in culture," he says.

Researchers in countries such as the United Kingdom, Sweden, China and South Korea, where SCNT is legal for therapeutic purposes, are working on a process that could potentially generate individualized embryonic stem-cell lines that would be genetically identical to each patient, and then be used for transplantation. Unlike the current method of organ transplant, which is limited by supply and by tissue rejection, somatic cell nuclear transfer offers little chance of tissue rejection--and could dramatically improve a patient's chances of survival.

Of course, there are many hurdles--ethical and scientific--still to overcome. In the journal Nature Medicine, researchers at the University of Rochester Medical Center and the Weill Medical College of Cornell University in New York outlined the results of a recent study that looked at using human embryonic stem cells to cure rats with Parkinson's-like symptoms. The treatment stopped the symptoms--but the scientists also discovered the animals had developed the precursors to tumorous masses. While the results inject real caution into the science of stem cells, they also offer a ray of hope.

The challenge of moving stem-cell science from the research bench to the clinic is something Kelly Holman understands well. As a managing director at Toronto-based Genesys Capital Partners Inc.--one of the largest Canadian-based venture-capital firms focused exclusively on the health-care and biotechnology industries--Holman and his partners are in the business of taking risks. To date, there are only three Canadian companies Holman knows of that are working on commercializing stem-cell therapies: Mississauga-based Insception Biosciences, StemPath Inc. in Ottawa and Calgary-based Stem Cell Therapeutics Corp. (TSXV: SSS). Genesys has invested nearly $10 million in the first two.

You can think of stem-cell research as exploring two distinct paths to therapy--the drug model versus what Holman calls the cells-in-a-bag model. The first involves the development of compounds to coax existing stem cells in the body to regenerate themselves. Cells-in-a-bag is direct stem-cell therapy, involving either the injection of stem cells into a patient, or the transplantation of tissue grown in vitro using stem cells.

Insception's bread and butter is the banking of customers' cord blood cells--stem cells found in a baby's umbilical cord--which can be used for a transplant if a child develops a disease. The company is also working on a process to expand the number of blood cells found in the umbilical cord using growth stimulators that, if successful, would produce enough cells to perform many more cord blood transplants in adults. Insception's third, and most exciting platform, involves looking at ways to turn cord blood cells into different cell types. "Coaxing those cord blood cells to become different types of cells has a huge clinical impact," says Holman. "You could come up with a supply of source cells that could help people treat diabetes, vascular disease, spinal cord injury and macular degeneration."

StemPath, on the other hand, is working to advance a drug. The aim of the drug is to coax existing adult stem cells in the heart to regenerate cardiac tissue. "When the heart is insulted, or having a heart attack, a lot of tissue is damaged, which may result in congestive heart failure," says Holman. "StemPath has figured out a biological pathway in the body that will actually activate the cells in the heart. Now they're working on a drug that tickles that biological pathway and then activates those cells post-trauma."

The third company, Stem Cell Therapeutics, is developing drugs that induce a patient's own neural stem cells to multiply and differentiate to form new brain tissue. This could be used to treat patients with strokes or schizophrenia.

"People can get their head around the drug model, because it's pills in a bottle--whereas cells in bags, that's still in the early days," Holman says. "The drug model obviously has some advantages, because that's what drug companies do today. In cell therapy, the risk is the delivery model. How are those therapies ultimately going to be delivered to patients? The pioneers who can iron these issues out could make significant amounts of money."

Vancouver-based biotechnology analyst Brian Bapty of Raymond James Financial Inc. is cautiously optimistic. Stem-cell therapy is "in vogue" right now, he says, but real-world applications are likely at least a decade away, and the market still needs convincing that investing in stem cells will pay off. If research proves successful, though, the commercialization possibilities are very exciting, Bapty says.

Holman envisions a world in which patients will undergo hospital-based stem-cell therapy, involving transplantation of certain cells. Biotechs would supply specific cell types to hospitals. Drug companies might offer a selection of ingestible pills, which would use biological pathways within the body to trigger existing cells to regenerate damaged tissue. But for now, it's hard to tell which model holds the most promise.

How much promise? Well, if you consider the oral diabetic drug market alone was worth almost $7.5 billion in North America last year, according to global health data provider IMS Health, the market potential for various forms of stem-cell therapy is in the billions of dollars. Beyond the evolution of a market that could be worth as much as US$30 billion by 2015, health-care payers stand to save billions more. According to the Ottawa-based Chronic Disease Prevention Alliance of Canada, diabetes and its complications costs $14 billion per year.

In other words, stem cells are a huge market opportunity. By getting into the game early, Genesys is hoping to reap a potential windfall. It is not the only one. South of the border, California-based biotech companies, including Advanced Cell Technology Inc., which trades over the counter (OTCBB: ACTC), and Geron Corp. (Nasdaq: GERN), are pursuing ambitious embryonic stem-cell research platforms. Both saw their stocks rally in the wake of the Democrats' recent electoral sweep. Other U.S. biotech giants such as Amgen (Nasdaq: AMGN) and Genzyme Corp. (Nasdaq: GENZ) are expanding their portfolio of drug candidates that involve therapy using adult stem cells. On Nov. 7, Genzyme snapped up cancer drug developer AnorMED Inc., based in Langley, B.C., for US$584 million after engaging in a heated bidding war with a rival drug company. At stake? AnorMED's promising stem-cell mobilizer, Mozobil. The drug, now in Phase 3 trials, induces the release of adult stem cells from bone marrow; those cells can then be harvested and used for transplants. Analysts predict Mozobil could command annual sales of nearly US$300 million within three years of its launch.

Despite the buzz surrounding companies like AnorMED, Canada's stem-cell industry is still in its infancy. Most experts predict a novel embryonic stem-cell therapy is between 10 to 15 years away. Hundreds of millions of dollars will also be needed to sustain ongoing research at places like the McEwen Centre.

StemPath was formed out of research conducted by Michael Rudnicki and Lynn Megeney, both senior scientists at the Ottawa Health Research Institute. On Nov. 15, Rudnicki also became the director of the Ottawa Hospital's newly launched Sprott Centre for Stem Cell Research, made possible through a $7-million donation from Eric Sprott, chief investment officer and CEO of Ottawa-based Sprott Asset Management Inc., and his wife, Vizma. Rudnicki is also the scientific director and CEO of the Ottawa-based Stem Cell Network, a not-for-profit corporation that brings together more than 70 leading stem-cell experts, with a mandate to advance the science of regenerative medicine--and commercialize any promising therapies or processes.

The momentum behind regenerative medicine is building. But it does not erase the fact that controversy continues to swirl around embryonic stem-cell research. For groups such as the Ottawa-based Institute of Marriage and Family Canada, destroying an embryo to extract stem cells is destroying a human life. The need for large amounts of female eggs to create the embryos has also prompted concerns about the commodification of human reproductive material. Beyond ethical concerns, there are also daunting logistical issues. Just how functional will differentiated stem cells actually be, once they're transplanted into humans? What about unintended side effects? How should stem-cell therapy be delivered, and who will pay for it?

In the meantime, leading stem-cell advocates argue it is important they be permitted to continue their research using the most advanced methods available. In order for Canada to benefit, experts like Rudnicki say the federal government needs to think long and hard about its position on therapeutic cloning when Bill C-6 comes up for review within three years. "The technology is advancing so fast I think it really merits some rethinking," says Rudnicki. "There is an opportunity--we just need to realize it."

Politics aside, there is little disagreement that unravelling the secrets of early biological development using stem cells has the potential to revolutionize the way human disease is treated. In other words, the body of knowledge created by stem-cell research could in the long run be more useful than stem-cell-derived therapy itself. "The information you get out of cell systems is tremendous. Whether or not it leads to a stem-cell-related therapy is a different question," says Bapty. "Once we've learned all we need to know, maybe that's just information that goes into some big book somewhere."

For that reason, Bapty says it's more helpful to think of stem cells not as a panacea, but rather as "participants in a cure." Because in science, as in business, there are no guarantees. Even a gold bug like McEwen knows that.