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STEM CELLS: THEIR PROMISE, THEIR PROBLEMS

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Stem cells have been in the news a great deal recently, both for their medical promise and the difficult ethical questions the use of embryonic stem cells present. Here we discuss some of the science, medical treatments, ethics, IP concerns and business of stem cells.

What are Stem Cells?

There are two general categories of stem cells: embryonic stem cells and adult stem cells. Stem cells are the cells from which all other cells in an organism originate. All the cells in your body, for example, ultimately originated from stem cells. They do this by a process called differentiation, whereby the unspecialized stem cell gives rise to a more specialized type of cell. Stem cells can either multiply to create more stem cells, or they can differentiate into a more specialized cell, such as blood cells.

Embryonic stem cells, first discovered in 1998, are usually retrieved from embryos that were created for in vivo fertilization treatments. The embryos are usually 3 – 5 day-olds and in the blastocyst stage, with approximately 150 cells. Obtaining embryonic stem cells destroys the embryo, however, which some see as morally problematic. While many scientists believe that embryonic stem cells are highly promising for replacing or repairing damaged tissues, researchers have not yet been able to achieve differentiation reliably.

Adult stem cells are undifferentiated cells able to renew themselves and differentiate themselves like embryonic stem cells. Adult stem cells, found among specialized cells in a tissue or organ, allow for its repair or regeneration. Research on adult stem cells began in the 1960s, when researchers discovered that adult bone marrow contains stem cells giving rise to all blood cell types. Adult stem cells are generally thought to be more difficult to work with and less medically promising than embryonic stem cells, because adult tissues contain only a small number of stem cells that tend to remain quiescent for many years until activated by injury or illness. Besides bone marrow, tissues like brain, skin, liver, fat, muscle, blood vessels and peripheral blood contain adult stem cells.

Stem Cells and Regenerative Medicine

Stem cell medical applications are still in their infancy. Most proposed therapies involve replacing specialized cells damaged by disease.

For example, when coronary artery disease affects the heart muscle, muscle cells and blood vessel lining cells can both be lost. Recent studies indicate that stem cells can be coaxed to differentiate into these two types of essential specialized cells, offering the possibility of regenerating the heart muscle and its supporting vascular system.

As another example, to treat diabetes, researchers are actively exploring how to identify and stimulate the cells that give rise to the pancreatic islet cells, the producers of insulin. Such cells could be formed within a patient's own body, or could be formed in vitro and introduced by transplantation. Much research will be required in order to produce a supply (that can be replenished) of stem-cell-derived insulin-producing cells in individual patients, but such cell-based therapy remains a "Holy Grail" for diabetes-sufferers.

Parkinson's disease (PD) may be the first disease for which stem cell transplantation offers clinically meaningful hope. PD results from the degeneration and loss of specialized neurons in the brain that produce dopamine, whose symptoms include tremors, rigidity and decreased mobility. Several laboratories have induced embryonic stem cells to differentiate into dopamine-producing neurons in animal models, which when transplanted into rats with PD-like deficits, reinnervated the damaged brain regions, produced dopamine and improved symptoms. If successful in humans, this therapy could provide significant benefits to those afflicted by PD.

The Ethical Landscape

While the use of adult stem cells has been relatively uncontroversial, a number of moral issues surround the use of embryonic stem cells. These moral issues center around the fact that embryonic stem cells are derived from human embryos, entities that have the potential of developing into human beings.

Ethicists often cite three types of arguments in opposing the use of embryonic stem cells. First, if life begins at conception, one is taking a human life when one harvests embryonic stem cells from a blastocyst. Second, it is morally problematic to damage one person in order to enhance another. Third, a "slippery slope" question arises: if one can produce an embryo to harvest its stem cells, what other uses may be made of these living beings that are human or potentially human? How far down the slippery slope might one slide if it becomes morally permissible to create a living human being in order to use its body parts for the benefit of another, pre-existing human being?

In response, other ethicists who support embryonic stem cell research maintain that the blastocyst, while potentially a human being, is only a collection of cells at this early stage. These scholars argue that a human person does not come into existence with cell fertilization, but rather develops during the course of pregnancy. Moreover, the blastocysts formed during fertility treatment are destined to be discarded in any case, so using these cells allows some good to be derived from them. Stem cell research proponents state that solid moral reasoning can be used to justify the production of embryonic stem cells from blastocysts.

The Political Landscape

The moral debate in scientific circles moved to the political arena on August 9, 2001, when President George W. Bush limited federally funded research on embryonic stem cells to those stem cell lines in existence as of that date. The federal government continues to fund research involving stem cells from other sources, such as umbilical cord blood, placentas, and adult and animal tissues. Private embryonic stem cell research is not prohibited in the United States, and for example, a researcher at Harvard University plans to set up a private institute to study embryonic stem cells.

The President's decision has been criticized for allowing, on the one hand, any embryonic stem cell research at all, and on the other, for severely limiting researchers' options. Regarding the latter position, researchers at the University of California in San Diego and the Salk Institute conducted a study published in January 2005 indicating that methods used to grow a number of the federally approved stem sell lines introduced contaminants that could interfere with using these cells for medical treatments. While some or all of the approved stem cell lines might be salvageable according to the researchers, scientists have pointed to this study as demonstrating the limitations of the current federal policies.

Despite the federal funding restrictions, states are beginning to provide funds for embryonic stem cell research. In November 2004, California passed Proposition 71, which created a $3 billion state taxpayer-funded institute for stem cell research, the California Institute for Regenerative Medicine. Several other states, including New York, New Jersey, Florida, Texas, Illinois, Massachusetts, Wisconsin, Washington and New Hampshire have shown interest in providing their own funding support. Conversely, other states, including Arkansas, Iowa, Louisiana, Michigan, Nebraska, North Dakota, South Dakota, Virginia, Kansas and Missouri, presently have, or are considering, imposing additional restrictions — even complete bans — on embryonic stem cell research.

Due to the controversy surrounding embryonic stem cells, many nations have passed legislation encouraging stem cell research. The U.K. allows the creation of human embryos for stem cell procurement. Other nations that permit stem cell research include Australia, Israel, Singapore, Sweden, Switzerland, Finland, Greece and the Netherlands.

The Stem Cell Patent Landscape

The patent landscape for both adult and embryonic stem cells is very crowded, with hundreds of issued patents having claims to methods of isolating stem cells, methods of propagating stem cell lines, methods of differentiating stem cell lines, and methods of using stem cells in treatment.

On the embryonic stem cell patent front, the University of Wisconsin holds the dominant patent position in primate embryonic stem cell line production. The Wisconsin Alumni Research Foundation ("WARF"), founded to handle the University's patents and technology transfer, holds patents affecting 64 stem cell lines, including extensive rights to five lines.

Among companies, Geron Corporation is a significant player that to date has a portfolio of 240 stem cell patents. Geron obtained an exclusive license from WARF for its human embryonic stem cell technology, which ultimately ended up in litigation that was settled in 2002. Under its present license from WARF, Geron holds exclusive rights to develop certain therapeutic and diagnostic human embryonic stem cell products.

WARF and Geron have agreed to grant research rights to their existing human embryonic stem cell patents and applications to academic and governmental researchers without royalties or fees. Third-party for-profit companies may form collaborations with Geron or obtain licenses to Geron's intellectual property on market terms. WiCell Research Institute, a WARF subsidiary, distributes the cell lines. WARF and WiCell Research Institute agreed to reasonable terms for such distribution in a Memorandum of Understanding with the NIH on September 5, 2001.

The adult stem cell patent landscape is also very crowded, with hundreds of patents directed to various aspects of the technology. For example, Osiris Therapeutics, a clinical stage biotechnology company founded to commercialize adult stem cells derived from bone marrow, has 42 issued patents directed to certain technologies, including methods of isolating and differentiating such cells, and methods of using the cells as immunosuppressants, for cartilage regeneration, and for repair of connective tissue.

Conclusion

Stem cells continue to be the subject of intense focus based on their promise for transformative medical treatments and the ethical dilemmas they present. We expect that this area of research will continue to gather much attention on all fronts. For more information, the NIH maintains an excellent Web site about stem cells, http://stemcells.nih.gov, which provides extensive background information on stem cells as well as bioethical, legal and regulatory information.

If you would like further information about the topics covered in this newsletter, please contact Ethan Horwitz, chair of Goodwin Procter's Intellectual Property Group, at 212.459.7455 or ehorwitz@goodwinprocter.com

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