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Reprogramming the Future of Stem Cell Patents

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Stem cells have the potential to be extremely powerful tools in the medical field. There are two main types of stem cells: somatic stem cells and embryonic stem cells.[1] Somatic stem cells are found in mature organs and tissues and give rise to the cell types of that particular organ or tissue.[2] For example, hematopoietic stem cells give rise to all the blood cell types in the body.[3] Human embryonic stem cells (hESCs) are derived from the inner cell masses of a human embryo.[4] hESCs are pluripotent, which means that they have the ability "to give rise to all of the various cell types that make up the [human] body."[5] This significant characteristic indicates that hESCs have the capability to treat diseases, such as cancer, neurodegenerative disorders, and diabetes, and replace diseased tissues and organs. Further, scientists can use hESCs to study various developmental and biological processes.[6]

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[1] NIH Stem Cell Information, Stem Cell Basics: Introduction, http://stemcells.nih.gov/info/basics/basics1.asp (last visited Oct. 28, 2008).

[2] NIH Stem Cell Information, Stem Cell Basics: What are adult stem cells?, http://stemcells.nih.gov/info/basics/basics4.asp (last visited Oct. 28, 2008).

[3] *Id.*

[4] SCOTT F. GILBERT, DEVELOPMENTAL BIOLOGY 708 (8th ed. 2006); NIH Stem Cell Information, Glossary, http://stemcells.nih.gov/ (follow "Info Center" hyperlink; then follow "Glossary" hyperlink) (last visited Oct. 10, 2008).

[5] NIH Stem Cell Information, Frequently Asked Questions, http://stemcells.nih.gov/research/registry/pluripotent_faq.asp (last visited Oct. 6, 2008).

[6] *See* GILBERT *supra* note 4; NIH Stem Cell Information, Stem Cells and Diseases, http://stemcells.nih.gov/info/health.asp (last visited Oct. 28, 2008); Julia vom Wege Dovi,

Despite the possible benefits of hESCs, President George W. Bush has implemented regulations that restrict the use of these cells in research due to their highly controversial origin. On August 9, 2001, President Bush banned the creation of new hESC lines.[7] His policy also restricted federal funding for hESC research by limiting grants to those researchers who only utilize hESC lines previously derived from embryos obtained with informed consent for reproductive purposes.[8] These moral concerns and changes in policy have motivated scientists to explore alternatives to hESCs.[9]

In November 2007, a major breakthrough in stem cell research was made with the creation of human induced pluripotent stem cells (iPSCs).[10] These stem cells are adult cells reprogrammed to be like an embryonic stem cell by being forced to express certain genetic factors.[11] Compared to hESCs, iPSCs promise similar and additional benefits. Since iPSCs are derived from adult cells, they have the same genetic makeup as the individual from which they were derived.[12] Therefore, medical treatment resulting from the use of the iPSCs can be tailored specifically to that individual's genetic makeup.[13] For instance, the recipient of a donated organ bears the risk of his or her body rejecting the transplant.[14] This

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Speaking Words of Wisdom: Let it be the Reexamination of the Human Embryonic Stem Cell Patents, 12 MARQ. INTELL. PROP. L. REV. 107, 109 (2008); ScienceDaily.com, Module Map Links Embryonic Stem Cells and Cancer Stem Cells, Apr. 9, 2008, http://www.sciencedaily.com/releases/2008/04/080409130711.htm (last visited Nov. 7, 2008).

[7] *See The President's Decision; Bush's Address on Federal Financing for Research With Embryonic Stem Cells*, N.Y. TIMES, Aug. 10, 2001, http://nytimes.com (search "Bush's Address on Federal Financing"; then follow "The President's Decision" hyperlink) [hereinafter *President's Decision*]; NIH Stem Cell Information, Federal Policy, http://stemcells.nih.gov/policy/ (last visited Oct. 10, 2008).

[8] *See President's Decision supra* note 7; NIH *supra* note 7.

[9] Christopher Thomas Scott & Renee A. Reijo Pera, *The Road to Pluripotence: The Research Response to the Empbryonic Stem Cell Debate*, 17 HUMAN MOLECULAR GENETICS R3, R3-R7 (2008); *see* President George W. Bush, *Executive Order: Expanding Approved Stem Cell Lines in Ethically Responsible Ways*, THE WHITE HOUSE, June 20, 2007, http://www.whitehouse.gov/news/releases/2007/06/20070620-6.html.

[10] *See* Yu, et al., *Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells*, 318 SCI. MAG. 1917, 1917-20 (2007); *See* Takahashi et al., *Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors*, 131 CELL 861, 861-72 (Nov. 30, 2007).

[11] *See generally* Yu, et al, *supra* note 10; Takahashi et al., *supra* note 10.

[12] Yu, et al., *supra* note 10, at 1920

[13] *Id*.

[14] *Id*.

complication could be eliminated by creating organs or tissues developed from patient-specific iPSC lines.[15] Also, disease-specific iPSC lines could be derived for drug development and research.[16] Moreover, since iPSCs are not derived from embryos, the ethical concerns that accompany hESCs are not currently at issue.[17] Research using pluripotent stem cells derived from non-embryonic sources has been, and continues to be, eligible for federal funds.[18]

Despite the potential of iPSCs to serve as a replacement for hESCs, the molecular similarities between the two types of stems cells is not yet clear. If iPSCs and hESCs are molecularly similar, then inventors may face the same resistance towards patenting iPSCs that they faced in patenting hESCs. However, if iPSCs and hESCs are not molecularly similar, then inventors may not face as much resistance in patenting iPSCs. Moreover, if obtaining and maintaining iPSC patent rights mirrors what has occurred with hESC patent rights,[19] then researchers may be less inclined to pursue scientific advancements related to iPSCs because their advancements may not be patentable.

Recently, the United States Patent and Trademark Office (USPTO) reexamined several hESC patents[20] developed by James A. Thomson of the University of Wisconsin.[21] The challengers had criticized the patents as being overly broad for claiming the rights to all hESC lines and to the particular method of making them.[22] Despite a preliminary ruling finding that the hESC patents

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[15] *Id.*
[16] *Id.*
[17] *See* Scott & Pera *supra* note 9, at R6.
[18] NIH, *supra* note 5.
[19] Currently, hESCs are patentable subject matter. The USPTO has not deemed hESCs to be the equivalent of a human being, which is precluded from patentability, *see* MANUAL OF PATENTING EXAMINING PROCEDURE §2105 (8th ed., 6th rev. 2007); *see also* Todd N. Spalding & Michele M. Simkin, *How Will Patents Impact the Commercialization of Stem Cell Therapeutics?*, 19 No. 1 INTELL. PROP. & TECH. L.J. 7, 7 (Jan. 2007).
[20] U.S. Patent No. 5,843,780 (filed Jan. 18, 1996); U.S. Patent No. 6,200,806 (June 26, 1998); U.S. Patent 7,029,913 (filed Oct. 18, 2001).
[21] U.S. Patent No. 5,843,780RE (filed July 17, 2006); U.S. Patent No. 6,200,806RE (filed July 17, 2006); U.S. Patent 7,029,913RE (filed July 17, 2006).
[22] *See* '780RE Patent, '806RE Patent, '913RE Patent, *supra* note 21; *see* also Katja Triller Vrtovec & Christopher Thomas Scott, *Patenting Pluripotence: The Next Battle for Stem Cell Intellectual Property*, 26 NATURE BIOTECHNOLOGY 393, 393 (Apr. 2008).

were invalid for being obvious in light of prior art,[23] the USPTO eventually affirmed the validity of the patents.[24]

In addition, the USPTO ultimately rejected a continuation application of one of Thomson's hESC patents for being too broad because it encompassed all human pluripotent stem cells (PSCs), not just hESCs.[25] In its rejection, the USPTO recognized a critical difference between other types of PSCs and hESCs: hESCs produced from the inner cell mass of embryos do not express a specific type of cell-surface marker found on other types of PSCs.[26] Since hESCs do not have this distinguishing cell-surface marker, the USPTO refused to extend the hESC patent claims to include all PSCs because PSCs with the cell-surface marker potentially could be separately patentable.[27]

Conversely, iPSCs might not be patentable separate from hESC patents, because hESC patents might encompass iPSCs. Research shows that human iPSCs and hESCs are similar; however, theorists predict that whether they are so similar that both are encompassed in the hESC patents will depend upon the characteristics of PSCs.[28] Like hESCs, iPSCs do not possess the specific cell-surface marker that other types of PSCs have.[29] Therefore, if the characterization of a hESC depends on the presence or absence of the cell-surface marker, iPSC patents already would be covered by the hESC patents.[30] However, if hESCs are characterized by their origin, then iPSCs may be patentable over hESCs because they are derived from adult cells, not embryos.[31] Other theorists are certain that if the hESC patents were narrowed in scope, then iPSCs would not be covered

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[23] Aurora Plomer et al., *Challenges to Human Embryonic Stem Cell Patents*, 2 CELL STEM CELL 13, 14 (Jan. 2008); Joe Vanden Plas, *Patent Office Upholds Key WARF Stem Cell Patent; Appeal is Likely*, WIS. TECH. NETWORK NEWS, Feb. 29, 2008, http://wistechnology.com/articles/4571.
[24] Vrtovec & Scott, *supra* note 22, at 393.
[25] *Id.* at 393.
[26] *Id.* at 394.
[27] *See Id.*
[28] *Id.*
[29] Vrtovec & Scott, *supra* note 22, at 394.
[30] *Id.*
[31] *Id.*

within the scope of hESC patents.[32] Therefore, iPSCs could be separately patentable, provided they meet all other patentability requirements. [33]

At the end of 2007, both James A. Thomson from the University of Wisconsin and Shinya Yamanaka from Kyoto University in Japan published articles that described the generation of iPSCs from humans.[34] Yamanaka had already obtained a Japanese patent on iPSCs and filed an application for iPSCs with the USPTO in December 2006.[35] In March 2008, Thomson also filed a U.S. patent application for iPSCs.[36] However, it is unclear who will be awarded patent protection in the U.S., because if two different inventors file a patent application in the U.S. for the same invention, then the inventor who proves to be the first to invent will be entitled to the patent.[37] In this case, both applications are currently pending, therefore the USPTO has not resolved the dispute over which party was first to invent, and thus which party is entitled to patent rights, should the patent be granted. Additionally, the iPSCs still need to meet other statutory requirements, such as nonobviousness in light of previous publications by Yamanaka, in order to be patented.[38]

Therefore, if Yamanaka is granted a U.S. patent, then Thomson may face additional patentability issues depending on the breadth of Yamanaka's claims. Yamanaka's Japanese patent is narrow and has claims directed towards reprogramming a cell with four genetic factors.[39] Thomson's published U.S. patent application claims the method of adult cell reprogramming and the reprogrammed cells themselves, but the factors he utilizes do not include two of

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[32] Plas, *supra* note 23.
[33] *Id*.
[34] *See* Yu et al., *supra* note 10 at 1; Takahashi et al., *supra* note 10, at 1.
[35] David Cyranoski, *Japan Fast-Tracks Stem-Cell Patent*, 455 NATURE 269, 269 (Sept. 2008) (the international application is PCT/JP2006/324881); Vrtovec & Scott, *supra* note 22, at 394-95 (Yamanaka filed an international application under the World Intellectual Property Organization (WIPO) Patent Cooperation Treaty (PCT) and lists the U.S. as one of the designated countries).
[36] U.S. Patent Application No. 12/053,440 (filed Mar. 21, 2008).
[37] About.com: Inventors, Information Concerning Patents Interferences, http://inventors.about.com/library/bl/toc/blusptointerference.htm (last visited Oct. 29, 2008).
[38] *Id*.
[39] Cyranoski, *supra* note 35.

Yamanaka's factors.[40] Currently, the claims in Yamanaka's international application are written broadly,[41] however the USPTO might not require the claims to be narrowed in order to obtain a U.S. patent.[42] Therefore, if the USPTO grants Yamanaka a patent in which the claims are broad enough to cover iPSCs from any non-embryonic cell of any species, Thomson's - and future - iPSC patent applications could be affected.[43] A broad patent could preclude the patenting of all iPSCs regardless of whether novel combinations of genetic factors were used to create the cells.[44] However, if Yamanaka's application is restricted to his four factors, Thomson's use of a different set of factors could be separately patentable.[45] Therefore, a narrow interpretation of Yamanaka's application could open the door to future patents on iPSCs.

The potential health benefits conferred from iPSCs is exciting. Since iPSCs are not restricted by federal funding regulations, the ability to patent this technology would greatly spur innovation and research in this area. While there still is a critical need for hESC research, iPSCs offer a very promising alternative without the ethical barrier. Even though stem cell intellectual property is complex due to moral, technical, and legal factors, the future path for iPSCs hopefully will be smoother than that of its predecessor hESCs to allow for the growth and development of this promising scientific discovery. [46]

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[40] *See* '440 Patent, *supra* note 36; *see generally* Takahashi et. al., *supra* note 10.
[41] *See* '440 Patent, *supra* note 36.
[42] *Id.*
[43] Cyranoski, *supra* note 35.
[44] *Id.*
[45] '440 Patent, *supra* note 36.
[46] Plomer, *supra* note 23.