



Stem Cell Patents

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Stem cell research, like other areas of scientific and biotechnological research, leads to innovations, some of which may be protected by intellectual property rights. Patents are one form of intellectual property rights. Intellectual property (IP) includes copyright, trade secrets, patents, industrial design, trademarks and geographical indications. In the stem cell research domain, as in most biotechnology, patents are the most prevalent form of intellectual property protection.

What are Patents?

Patents represent a limited property right that allows the patent holder the right to exclude all others from the use or exploitation of the patentable subject matter. A patent represents a bargain with an inventor in which a time-limited monopoly (usually 20 years) is granted in exchange for public disclosure of the inventor's creation. In this way patents are thought to stimulate research and development, although in the age of biotechnology there is evidence that too much IP can hinder the development of research.¹

Under the *Canadian Patent Act*, to receive a patent, something must be new, useful and non-obvious. For this reason naturally occurring things are not patentable. In Canada, researchers can obtain patent protection for any genetic invention for which they can demonstrate:

- 1) The invention will have *utility* and a clear industrial application;
- 2) It is truly a *novel* invention and not merely a product of nature or one which has been disclosed in a prior publication;
- 3) It displays *inventiveness* and is not just an obvious improvement or alteration on an invention; and
- 4) An ability to *fully reveal (or explain)* their invention in a manner sufficient to allow others to reproduce the patented subject matter.²

The question arises whether man-made reproductions or isolations of naturally occurring things are patentable. This is very relevant to the isolation of naturally occurring animal and human stem cells. Not only is there a question of whether these are non-obvious, but larger ethical questions about the morality of extending property rights to living things have created public outcry at the idea.

Patenting Life Forms

Just as there is controversy over classifying human body parts and tissues as property, the classification of living things or products of nature as property is equally controversial, and some would argue that it is simply a mistake – people are not property. These arguments have been raised in the context of agricultural biotechnology, patents on human genes and patents on animal and human stem cells. Classifying these things as property

¹ Gold, R. et al. *Toward a new Era of Intellectual Property: From Confrontation to Negotiation, A Report from the International Expert Group on Biotechnology Innovation and Intellectual Property 2008*, http://www.theinnovationpartnership.org/data/ieg/documents/report/TIP_Report_E.pdf

² The *Canadian Patent Act*, RSC 1985, c. P-4, s. 2, defines "patentable subject matters" as: "any new and useful art, process, machine, manufacture or composition of matter or any new and useful improvement in any art, process machine, manufacture or composition of matter."

raises issues of commodification, that is viewing or treating something not traditionally thought of as subject to market forces as if it was such a commodity. Where applied to human cells or tissues, property notions are often seen as offensive to human dignity (see Knowles L., “Commercialization and Stem Cell Research” Stem Cell Network).

For the last three decades the long-held tradition of forbidding the patenting of “products of nature” has been under assault. Whereas traditionally animals and plants were not patentable, in 1980 the Supreme Court of the United States opened the gates to the patenting of “non-naturally occurring” living substances in *Diamond v. Chakrabarty*, 447 US 303 (1980). Other countries quickly followed suit, although important differences remain in international patent law, including areas such as the patenting of higher life forms and patenting the products of human embryos. As a result of *Diamond v. Chakrabarty*, since 1980 virtually any living thing that can be reproduced or altered by human intervention has been patentable. This has been contentious for years, but many claim that it forms the backbone of both the biotechnology revolution and the United States’ dominance of the biotechnology industry to date.

The push to globalize the recognition of intellectual property including, where permitted, the patenting of products of nature, hit a zenith with the Trade-related Intellectual Property Rights agreement (TRIPS) of the World Trade Organization in 1995. While international patent laws have been strengthening, European and Canadian experience with patenting of life-forms has been markedly different from the experience in the United States. Greater political ambivalence in Europe led for many years to a moratorium on the patenting of life forms. In the face of American dominance in global biotechnology that moratorium was lifted, although the change in policy continues to be debated, especially in light of patent applications on animal and human stem cells, some of which are have been recently decided.

Canadian case law has been somewhat inconsistent. Case law from the Canadian Supreme Court struck down a patent on a genetically modified mouse engineered to express cancer for research purposes. The court stated that higher life forms could not qualify as a “manufacture”

under the *Canadian Patent Act*.³ By contrast, the same court later upheld a patent on genetically modified plants, extending right to the plants themselves, not just the novel gene sequences.⁴ Where the line should be drawn between that which is nature and therefore, unpatentable and that which is invention and therefore, patentable subject matter continues to be part of the public and policy conversation.

Patents and Human Stem Cells

Given that non-naturally occurring inventions are patentable subject matter, isolated and purified stem cells are patentable as research tools. While patents on animal stem cells might be valid if they are non-obvious, patents on human embryonic stem cells (hES) have been hotly contested. In Europe applications for patents on animal stem cells and hES have been in the courts for years. In May 2008 the United States Patent and Trademark Office (USPTO) issued a patent for the isolation and derivation of hES to the University of Edinburgh. The same patent on a method to isolate stem cells (including hES) using genetic modification had been under review by the European Patent Office (EPO) since 1999. In 2007 the Edinburgh patent was limited to non-human animal ES cells and adult stem cells.

In Europe, the European Patent Convention states that the EPO may deny patents on ethical grounds, if the commercial exploitation of those patents is against *ordre public* (public order) or morality. Examples of things that are against *ordre public* include patents using human embryos for industrial or commercial purposes and patents that modify the inheritable genetic identity of humans. Taken in conjunction with the European Council Directive 98/44/EC which states that elements isolated from the human body may not be subject to patent protection, hES patents look questionable under European Patent law. In fact, for over a decade the patentability of hES lines in Europe has been litigated. As of December 2008, the Expanded Appeal Board of the EPO ruled that hES lines are not eligible for European patent protection.⁵ This ruling differentiates Europe from Japan and the United States. Canada has yet to grant a patent on hES research lines.

3 *Harvard College v. Canada (Commissioner of Patents)*, [2002] 4 S.C.R. 45, 2002 SCC 76.

4 *Monsanto Canada Inc. v. Schmeiser*, [2004] 1 S.C.R. 902, 2004 SCC 34.
5 Gawrylewski, A., “Europe rejects stem cell patent.” *The Scientist Online*, December 1, 2008 <http://www.the-scientist.com/blog/display/55249/>. Many other hES-related processes are subject to European patent protection including processes for the isolation of stem cells from embryos and tissue and process for culturing these cells.

The ethical issue that was paramount in the European decision is the principle of non-commercialization of the human embryo and its products. Other ethical issues raised by the patenting of human stem cells include the barriers to access by other researchers that patents can create through either exclusionary practices or expensive licensing fees (user fees charged by the patent holder). Such research barriers can create obstacles to the development of products and processes that have significant medical benefit. In other words, there are real people who may be harmed by not getting timely access to life-saving treatments or technologies if patent protections are too strong.

In the United States, the Wisconsin Alumni Research Foundation (WARF), a private non-profit foundation that handles IP for the University of Wisconsin-Madison, holds the foundational hES patents. WARF holds three patents from James Thomson's groundbreaking hES research. These patents cover purified preparations of primate ES cells and purified preparations of hES and methods for isolating each type of cell. The patents were issued to Thomson as inventor and assigned immediately by him to WARF. These patents are exceptionally broad and have thus raised concerns about their potential to impede stem cell research in the United States and elsewhere. The patents appear to encompass all hES research no matter how the cells are derived or how they are to be used, and all downstream products including therapeutics.

In 2006 the USPTO received requests to reexamine the WARF patents from the California-based Foundation for Taxpayer and Consumer Rights and the New York-based Public Patent Foundation. These non-profits charged that the cell lines at the heart of the dispute were: non-patentable subject matter, as the isolation of stem cells was obvious given the state of previous scientific discoveries; non-patentable subject matter as contrary to the *Patent Act* provisions on morality, given that they were human cells; and, regardless of the foregoing, the patents were impediments to crucial research in the field of stem cell therapy. Prior to the outcome of the reexamination, WARF announced permanent changes to its access requirements for the stem cells lines under patent. Although academic researchers had been able to use the cell line free of charge, they could not do so if

they were funded by private for-profit money.⁶ Under the new policy, academic researchers using private funding could still use the cell lines free of charge and a licensing fee would only be required if the cell lines went into the private commercial laboratories, or if the academic work was developed into a commercial product or application. Such actions begin to address concerns about the patents blocking the advance of the science and slowing the development of stem cell therapies. Concerns about how the licensing fees would affect pricing of any products or therapies that might be developed still exist. In all likelihood if high licensing fees are demanded by patent holders, those costs will be passed on to the buyers of the therapies and ultimately to patients and insurers.

After long speculation that the WARF patents would be overturned or at least significantly narrowed, in winter 2008 the USPTO upheld the WARF patents.⁷ The rulings mean WARF will continue to control primary IP rights to ES research in the United States. If research using WiCell lines leads to successful medical products or procedures before the patents expire in 2015, the University would likely share in any royalties. At the end of 2008, in contrast to the USPTO decision, the EPO denied the WARF patents on hES for the reasons discussed above.

Other recent developments in stem cell patenting include the granting of the first patent on induced pluripotent stem cells (iPS).⁸ (See Knowles L., "What Are Stem Cells and Where Do They Come From?" Stem Cell Network). Kyoto University in Japan was granted an international patent on a method of cellular reprogramming that enables adult skin stem cells to behave as if they were

6 One particularly contentious piece of WARF's previous licensing policy had been its attitude toward the California Institute of Regenerative Medicine (CIRM). WARF's policy to charge California a commercial license fee was due to a previous decision that any State that stood to benefit from stem cell research was functioning as a commercial actor. California fell under this policy as, under the California stem cell guidelines, a percentage of the money flowing from research funded by the California state/people, must be returned to the state. WARF reconsidered its position and stated that "As a not-for-profit, grant-making organization, CIRM does not require any license or agreement from WARF to pursue its grant making policies. Further, WARF does not expect CIRM to remit to WARF or WiCell [a non-profit foundation holding the Wisconsin cell lines] any portion of payment that CIRM receives from its grantees." (Wisconsin Alumni Research Foundation Changes Stem Cell Policies to Encourage Greater Academic, Industry Collaboration, http://www.warf.org/news/news.jsp?news_id=209)

7 Two more WARF Patents Upheld, http://chronicle.com/news/index.php?id=4122&utm_source=pm&utm_medium=en

8 Cyranoski, D., "Japan fast-tracks stem-cell patent; Kyoto University secures first award for induced pluripotent cells." 2008 *Nature* 455, 269 doi:10.1038/455269b

hES. The claim to the method was put on a fast track by the Japanese Patent Office. The patent application is said to cover the products of cellular reprogramming including iPS from all species. However, the scope of the patent is unclear, since iPS can be created in theory from most adult cells from any type of organism. Depending on how broad the patent claims are, it may suffer from the same legal attacks as the WARF patents. A similar patent in the inventor's name (Yamanaka) is before the USPTO.

Distributive Justice

In the context of hES research the question, "Who profits?" applies first to commercial benefits from the lucrative patents that have been awarded on the hES lines. A second question is who will benefit from the potential medical therapies promised by hES research. Unfortunately, restricted rather than broad access to the benefits of research can be a problem when faced with private funding of research, broad intellectual property protections for scientific innovations, and exclusive licensing agreements for access to that research. There are ways to avoid this restricted access. Some important steps are being taken by private and public funders of scientific research to ensure that broad access to the fruits of the research is part of a funding agreement. Much of this work is done through managing the intellectual property rights that may result from the research, especially through licensing agreements and "humanitarian licensing."⁹

In Canada stem cell lines that are derived using Canadian Institutes of Health Research funding (public) must be listed in a national registry and made available by the researcher to other Canadian academic researchers, subject to reasonable cost-recovery charges. The rationale for the creation of the registry is both efficiency – a reduction in the need to generate large numbers of cell lines – and minimizing the need for donation of large numbers of embryos.¹⁰ The creation of a government-owned and operated stem cell repository is one first step to ensuring that the benefits of stem cell research,

especially those that are publicly funded, are widely available and meet the needs of people all over the world, not just those with the most money. These types of distributive justice concerns form a large part of the ethical backdrop to human stem cell research.

In the United States publicly funded researchers often behave like researchers from the private sector due in large part to a piece of legislation known as the Bayh-Dole Act. The Bayh-Dole legislation encourages commercial products as outputs from publicly funded research. It has been argued that the Bayh-Dole approach brings a private research and development (R & D) mentality into the public research domain. Consequently, university researchers tend to share less with other researchers and keep their research progress and results more secretive than if there were no promise of commercial profits down the road. The result can be more duplication of research efforts than necessary and more restricted access to potentially beneficial research innovations for both other researchers and the public. Both California and Wisconsin, leaders in the US in stem cell research and funding, have created a system based on a "Bayh-Dole model." These States might have chosen an oversight model that attempts to put stem cell lines more into the public science domain. This would have put less emphasis on patents in stem cell lines and more on creating widely accessible and available stem cell repositories or banks. Both Canada and the United Kingdom have created systems that mandate wide access to stem cell lines that have received government licenses or public funding. In the United Kingdom, stem cells that are created pursuant to a Human Fertilisation and Embryology Authority license must be deposited in the UK stem cell bank.¹¹ For further discussion of stem cell banks and registries, see Knowles L., "Stem Cell Banks, Libraries and Registries" Stem Cell Network.

As discussed in the sections on religion and stem cells, (see Knowles L., "Religion and Stem Cell Research" Stem Cell Network) all religions want to ensure that the least fortunate among us (the sickest and the poorest) have equal and perhaps first access to these practices. Public funding agencies also share a significant role in ensuring broad access to therapeutic benefits from stem cell technology. This responsibility is manifest in choosing what

9 Knowles L., Bubela T., "Challenges for Intellectual Property Management of HIV Vaccine-Related Research and Development: Part 1, The Global Context." *Health Law Journal* (in press 2009); Patten S., Bubela T., Knowles L., "Challenges for Intellectual Property Management of HIV Vaccine-Related Research and Development: Part 2, The Canadian Context." *Health Law Journal* (in press 2009).

10 Canadian Institutes of Health Research, Updated Guidelines for Human Pluripotent Stem Cell Research as of June 29, 2007, <http://www.cihr-irsc.gc.ca/e/31488.html>

11 The UK Stem Cell Bank at NIBSC: An Overview at <http://www.nibsc.ac.uk/spotlight/ukstemcell.html> For further discussion of stem cell banks and registries, see Knowles L. and Adair A., "Stem Cell Banks, Libraries and Registries" Stem Cell Network.

research to fund. As in defining most research agendas, the needs of both the few and the many must be taken into consideration. There are areas of research, where the few may have far more resources and the many may represent the poor, in which case principles of distributive justice mandate that the needs of the few not be given higher consideration than the needs of the many.

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Stem cell research holds the potential to give rise to therapies that will be needed in the most and the least developed countries of the world. In many instances these therapies will be beyond the reach of countries that have just pennies to spend on each person for health care every year. Ensuring that the benefits of stem cell research reach as many people as possible is a global ethical imperative.

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