

Stem Cells — Patent Pools to the Rescue?

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This is the third in a series of articles regarding legal issues concerning stem cell research and development. As will be discussed in more detail, any company or research institution that plans to develop stem cells for therapeutic purposes may face a number of blocking patents and applications that will require licenses, if available. We propose the establishment of a stem cell patent pool to allow the development of stem cell therapies without crushing royalty burdens.

Stem cell research is vital to the development of new therapeutic treatments for a multitude of diseases. A result of stem cell research, as with any research program, is that the researchers may seek patent protection for their inventions. Frequently, patents cover complementary technologies (*e.g.*, a product, a method of manufacturing that product or a method of using the product). If owned by different patentees, these complementary technology patents require one to obtain licenses from each patent owner in order to use the technology. A further concern is patents with very broad claims that may block the practice of later discoveries, even if these discoveries are covered by their own implementing patents. These blocking patents may dominate the commercial product, uses or methods of making, thereby requiring one to obtain licenses from multiple patentees so as to avoid infringement.

One might imagine that the massive new funding being provided by California's Proposition 71 will lead to many new discoveries and new patent filings. However, research by SKGF on all U.S. patents that use the terms stem cell(s), progenitor cell(s), precursor cell(s), multipotent cell(s), pluripotent cell(s), or totipotent cell(s) in their claims has resulted in over 1400 patents being identified. These patents were evaluated and classified according to their claims. We identified at least four complementary types of patents relating to stem cell technology. They include patents claiming: (1) preparations of human embryonic stem (hES) cells; (2) methods of culturing hES cells; (3) methods of using hES cells; and (4) tissue-specific stem cells. These patents are owned by Wisconsin Alumni Research Foundation (WARF), Geron Corp. and others. Furthermore, within each type of complementary technology, for example those claiming methods of preparing hES cells, our empirical research indicates that

several patents may exist, not allowing for other patentees or third parties to use that technology without a license.

Patents on the preparation of hES cells are owned by at least three different entities, including Geron Corp., Vanderbilt University and WARF. Reportedly,¹ WARF is asking for a \$100,000 up front fee and a \$25,000 annual maintenance fee from companies that take out a commercial license to its stem cell patents. Geron has secured from WARF exclusive U.S. rights to develop therapeutics and diagnostics from human embryonic stem cell-derived neural, cardiomyocyte and pancreatic islet cells, probably the most valuable types of cells. Research rights have been offered by WARF to academic and governmental researchers without royalties or reach throughs. However, WARF reportedly charges \$5,000 each time its subsidiary, WiCell Research Institute, supplies one of these cell lines to an academic researcher.

We also found hundreds of pending patent applications claiming isolated stem cell preparations, methods for culturing stem cells, methods of preventing differentiation of stem cells, methods of inducing proliferation of stems cells, and methods of treatment with stem cells.

Accordingly, researchers and clinicians who currently study or intend to study hES cells for research and therapeutic purposes may have to obtain a license to multiple blocking patents and complementary patents so as to avoid the risk of infringing these patents. This will most likely lead to a complex licensing scheme and multiple royalty payments. Proposed solutions to this problem include passing a law providing for a stem cell research exemption to patent infringement and compulsory licensing. Instead, we propose the creation of a patent pool to address the issue of multiple blocking and complementary stem cells patents.

A "patent pool" is an arrangement in which "two or more patent owners agree to license certain of their patents to one another and/or third parties." Patent pools structured and implemented in various forms have been used in a variety of industries ranging from sewing machines and aircraft to radio and software. Depending on their structure and implementation, some patent pools have been found to be anti-competitive and objectionable, while others have been found to be pro-competitive and acceptable.

In 1995, the Department of Justice (DOJ) and the Federal Trade Commission (FTC) suggested guidelines to be used in determining when a patent pool is pro-competitive and therefore probably acceptable, and when it is anti-competitive and probably unacceptable.² For example, patent pools may be pro-competitive by: integrating complementary technologies, reducing transaction costs, clearing blocking positions, avoiding costly infringement litigation, and promoting the dissemination of technology. However, patent pools may be found to be anti-competitive if they: constitute methods of fixing prices or allocating customers and markets, exclude or drive competitors from the market or reduce innovation, or discourage the participants

¹ Wadman, W., "Licensing Fees Slow Advance of Stem Cells," *Nature* 272-273 (2005).

² "Antitrust Guidelines for the Licensing of Intellectual Property," issued by the U.S. Department of Justice and the Federal Trade Commission. April 6, 1995.

from engaging in research and development. A result of the DOJ/FTC guidelines has been a spate of approved patent pools, including ones for technology such as MPEG_2, DVD-3, DVD-6 and the 3G platform. Although these approved patent pools are formed in technological areas such as video and audio, patent pools in biotechnology, especially diagnostic genetic testing, have been recently discussed and proposed by others.

For stem cells, a patent pool may be considered especially pro-competitive in view of the recently approved California measure known as Proposition 71. This measure authorizes the state of California to sell \$3 billion in bonds over the next ten years to support stem cell research and "vital" research opportunities. While the implementing regulations are still in the works, any potential license involving a stem cell invention created entirely or in part from these California funds will likely require a royalty payment to the state of California, in addition to any other royalties that must be paid to the patent owners. This may cause a royalty burden far too high for potential licensees. A patent pool with California state participation will help to alleviate this royalty burden.

An important aspect to the creation of any patent pool is the identification of a standard. This standard may have occurred already in the industry without any cooperation among stem cell providers (*de facto*), or, alternatively, it may be created by a standard setting organization (*de jure*) such as a standard development organization or a consortium (*e.g.*, the Stem Cell Consortium at the Columbia University Medical Center, the California Institute for Regenerative Medicine or the FDA). One possible standard may consist of a specified method of preparing hES cell cultures so that consistent results may be obtained by researchers. More specifically, the standard may require culturing the stem cells in the absence of animal feeder cells which can give rise to viral contamination.³ Once a standard has been defined, any patent that is needed to implement that standard would be "essential" to the pool, and, therefore, must be included. In the event that a standard cannot be defined for stem cell technology, a patent pool could still be formed so long as any license offered by the patent pool precisely defines the rights granted by the license and what a licensee needs to practice the technology.

Summary

Patent protection is extremely important to the development of new therapies. Patent protection provides an incentive for innovators to invest large sums of money necessary to bring new therapies to the market. However, blocking and complementary patents claiming stem cell technology may impede the development of stem cell research and therapeutic uses because of the multiple licensing schemes needed by both researchers and clinicians. A collection of patents that are essential to a stem cell standard and complementary patents would allow for a "one-stop" license. This would certainly benefit the companies bringing stem cell therapies to

³ The stem cells approved for use by the Bush Administration reportedly were grown on mouse feeder cells and carry a risk of viral contamination. Geron's U.S. Patent 6,642,048 claims a method of proliferating human blastocyst-derived pluripotent stem cells in substantially undifferentiated form in a growth environment substantially free of any such feeder cells.

the market as well the patentees themselves. However, any such scheme must be carefully constructed so that the patent pool is pro-competitive.

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