Wiggin & Dana

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INTELLECTUAL PROPERTY RIGHTS AND LICENSES MAY DETERMINE THE FUTURE OF U.S. STEM CELL RESEARCH

Although the recent debate on the use of human embryonic stem cells for research purposes centers on the ethical dilemma, the true extent of future stem cell research that will be done in this country may be determined largely by patent law and contractual arrangements.

Human embryonic stem cells are thought to have the ability to regenerate healthy tissue to replace tissue damaged by disease or injury, and may offer treatments for degenerative diseases such as Alzheimer's or Parkinson's disease. Investigators from the following 10 laboratories in the United States, Australia, India, Israel and Sweden reported to the NIH that they derived stem cells from 64 individual, genetically diverse blastocysts:

Name	**Number of existing stem cell lines reported to NIH**
BresaGen, Inc., Athens, Georgia	4
CyThera, Inc., San Diego, California	9
Karolinska Institute, Stockholm, Sweden	5
Monash University, Melbourne, Australia	6
National Center for Biological Sciences, Bangalore, India	3
Reliance Life Sciences, Mumbai, India	7
Technion-Israel Institute of Technology, Haifa, Israel	4
University of California, San Francisco California	2
Göteborg University, Göteborg, Sweden	19
Wisconsin Alumni Research Foundation, Madison, Wisconsin	5

The Wisconsin Alumni Research Foundation (WARF www.wisc.edu/warf) is the owner of two U.S. Patents on embryonic stem cells: U.S. Patent No. 5,843,780 directed to primate embryonic stem cells, and U.S. Patent No. 6,200,806 directed to human embryonic stem cells. While there are many patents covering stem cells of other organisms, the two Wisconsin patents are unique in that they are the only patents claiming human embryonic stem cells. Both of these patents have been licensed to Geron Corporation (www.geron.com), which has the exclusive right to develop the stem cells into six cell lines: hepatocytes, myocytes, neural cells, pancreatic islet cells, hematopoietic cells, and osteoblasts.

Funding Limitations: Effect on Research

The recent announcement by the Bush Administration limiting federal funding for embryonic stem cell research, coupled with the WARF/Geron patent position, will most likely have significant consequences for research companies and academic research institutions in the U.S. The Bush Administration's directive not to fund any new embryonic stem cell lines with federal money limits resources, and therefore reduces the likelihood that other scientists will develop new, derivative lines that could challenge the WARF/Geron proprietary position in this field. Without federal funding, researchers at public universities will have to look to private capital to fund this research. This is a significant disadvantage because public institutions typically receive less than $1 from private sources for every $10 obtained from the government.

In addition, the patents owned by WARF are broad and arguably could be interpreted to include all human embryonic stem cells. A court could determine that any use of any type of human embryonic stem cells claimed in the WARF patents by an unauthorized user could result in infringement of the patents. Moreover, Geron's license from WARF on the six cell lines means that anyone wishing to develop stem cells in the six cell lines must negotiate with Geron, and Geron will undoubtedly protect its proprietary position. For example, Geron (or other private institutions or companies controlling additional stem cell lines) could impose significant restrictions on the types of research performed with any of the human embryonic stem cells that are transferred to other researchers, or claim ownership of products resulting from

the research. Geron has indicated that academic scientists would be free to convert stem cells into derivative cells of the types covered by its agreement with WARF, but would not be permitted to commercialize such derivative cells. WARF, on the other hand, has established the WiCell Research Institute (www.wicell.org) to distribute stem cell lines to researchers. The cells are given to research companies and academic research institutions under a material transfer agreement, and each institution must agree not to use the cells for therapeutic or diagnostic purposes. However, such use restrictions are generally unacceptable in the academic community, and could hinder development of cures for many degenerative diseases.

The limitations imposed on stem cell research in the United States resulting from the funding, patent, and license situation could benefit research centers outside the U.S., and possibly cause U.S.-based embryonic stem cell researchers to move overseas. Other countries have fewer restrictions on use or development of embryonic stem cells, and those governments are more willing to fund this type of research. England, for example, recently legalized the creation and destruction of embryos and embryonic clones for stem cell research. Moreover, since the U.S. Patents licensed to Geron are enforceable only in the U.S., research institutions and companies in other countries, and U.S. companies operating overseas, may use the human embryonic stem cells claimed in the U.S. patents without fear of infringement (or at least until WARF obtains patent protection in other countries, or a product made from one of the patented processes is imported into the U.S.).

Congressional Involvement

Because human embryonic stem cell research is in its early stages, there is no universally accepted standard for determining what characteristics will predict the ability of such cells to be useful for research purposes. This issue was raised at the September 5, 2001 hearing of the Senate Health, Education, Labor and Pensions Committee. Critics, including Sen. Arlen Spector and Committee Chairman Sen. Edward Kennedy, noted that many of the cell lines cited by the President were in varying stages of development, and questioned whether the few lines of the 64 that are actually ripe for research are enough to make the research worthwhile. Secretary of Health and Human Services, Tommy Thompson, said that it takes time for a line to develop, and estimated that some 24 or 25 lines of cells were now ready for researchers.

Accessibility of Human Stem Cell Lines

Also on September 5, the NIH and the WiCell Institute announced an agreement for research use of WiCell's existing five human embryonic stem cell lines. Pursuant to this agreement, scientists at the NIH will be able to access these cell lines to explore new avenues of research in this field, and freely publish the results of their research. The NIH will retain its ownership of any new intellectual property that might arise from its research. WiCell will retain commercial rights to its materials and will receive a fee to cover its handling and distribution expenses in supplying these cell lines. WiCell also agreed to make stem cell lines available for use by non-profit institutions that receive NIH grants under the same terms and conditions as those available to NIH scientists.

While the long-term consequences of the stem cell research situation remain to be seen, WARF and Geron have differing views on the scope of their license agreement. WARF recently filed a declaratory judgment action in federal court against Geron to ensure broad research access to the stem cell lines that are already developed. Geron feels that WARF is obligated to add additional cell types to Geron's license agreement on an exclusive basis. WARF does not share this view, and has sought legal intervention to resolve the issue. The declaratory judgment seeks to have the court declare that Geron has no right to add additional cell types to its license agreement with WARF. WARF's position is that Geron's exclusive use of additional cell types would preclude the use of important stem cell types by other researchers in the pharmaceutical, medical, and scientific communities. On September 25, WARF filed an amended lawsuit that seeks to include any research products that might be developed. This expanded lawsuit would prevent Geron from using any WARF stem cells to develop potentially commercial products such as drug tests.

Wiggin & Dana Clients in the News

Wiggin & Dana represented **Pharmacia Corporation** (Peapack, NJ) in connection with Pharmacia's spin-off of a majority interest in Biovitrum AB, a Stockholm-based biotechnology company involved in, among other activities, the discovery of compounds for the treatment of metabolic diseases, initially financed by a $130 million investment from a consortium of investors, co-led by MPM Capital and Nordic Capital.

Wiggin & Dana is currently representing **Lifecodes Corporation**, a leading provider of identity genomics testing for forensics and paternity, in a stock for stock tax-free exchange with Orchid BioSciences.

Wiggin & Dana represented **Karo Bio AB** (Stockholm, Sweden) in connection with Karo Bio's collaboration with American Home Products Corp. to develop a new treatments for atherosclerosis based on modulators of the liver X receptor (LXR). Under the agreement, Karo Bio has the potential to receive up to $100 million (if two compounds are developed) in up front, R&D and milestone payments in addition to royalties.

Wiggin & Dana acted as counsel to **Cellular Genomics Inc.** (New Haven, CT) in connection with Cellular Genomics' recent $22 million round of private equity financing led by MPM Capital, together with AGTC Funds, Inc., Vector Fund Management, and existing shareholders CHL Medical Partners and Connecticut Innovations, Inc.

Wiggin & Dana acted as counsel to **Protometrix, Inc.** (New Haven, CT), a new biotechnology company using a method of high-speed protein analysis developed at Yale University, in connection with its first round of venture capital financing with Collinson, Howe and Lennox (CHL Medical Partners II, L.P.) and OrbiMed Associates.

Wiggin & Dana represented **Biacore International AB** (Uppsala, Sweden) in its acquisition of an exclusive license to Axiom Biotechnologies' cell-based technology for drug discovery.