



The Stem-Cell Market — Patents and the Pursuit of Scientific Progress

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University of Wisconsin researcher James Thomson and his colleagues wowed the scientific community when they reported in November 1998 that they had isolated and cultured human embryonic

stem cells.¹ They also precipitated intense debate. Although moral dilemmas and federal funding of stem-cell research have received the most media attention, behind-the-scenes concern has centered on the market for stem cells — the ownership, control, pricing, and availability of stem-cell lines. For many academic researchers hoping to build on Thomson's discovery, the difficulty of obtaining stem cells was immensely frustrating.

This difficulty arose because not only did Wisconsin have material rights to the cell lines its researchers generated, but Thomson had filed U.S. patent applications on his discoveries, resulting in intellectual property rights. These latter rights, owned by

the University of Wisconsin and managed by its technology-transfer office, the Wisconsin Alumni Research Foundation (WARF), encompassed both Thomson's stem cells and the core techniques used to develop them. For this reason, these rights governed research on almost all available human embryonic stem-cell lines.

These patents have now been reexamined by the U.S. Patent and Trademark Office, thanks to a challenge brought by a consumer watchdog group. The preliminary decision of the Patent Office, issued in April 2007, is that the patents should be revoked, on the grounds that Thomson's invention was not a significant advance beyond already published work. Whatever is ultimately de-

cided, this case provides important lessons about universities' use of material and intellectual property rights to shape the future of scientific research.

Traditionally, there have been two separate markets for scientific knowledge.² Knowledge generated in academia has been governed by norms facilitating full and rapid publication, disclosure, and sharing; in addition to publishing, academic scientists are generally expected to comply with requests for their materials and methods, and few restrictions are placed on colleagues after materials are shared. In return, scientists receive recognition for scientific priority and rewards for publishing their findings. In contrast, knowledge generated in the private sector has been governed by property rights protected by patents. Knowledge is disclosed in patent applications in exchange for temporary monopolies, whereby scientists prohibit

others from using their materials while they, through commercialization, capture the value created. If private-sector scientists choose to share their materials or methods with colleagues outside their organization, they can craft a contract allowing them to reap part of any future profits.

As academic research began increasingly to produce knowledge of interest to the private sector, many universities responded — especially after the Bayh–Dole Act of 1980 streamlined the rules for academic patenting — by publishing and patenting ideas simultaneously. As originally conceived, such patents would permit academic scientists to provide the private sector with incentives to “buy” and commercialize academic discoveries without detrimental effects on the academic market. Lately, these systems have started to impinge on each other, with potentially serious consequences for scientific progress. In the 1980s, firms such as Cetus and DuPont attempted to impose stringent contractual terms on academic scientists who used the companies’ basic research tools. Universities, in turn, increasingly sought contracts from scientists at other universities who pursued research using materials their employees had produced.

Human embryonic stem cells, with their potential both for expanding our understanding of biology and for commercial use, represent a classic example of knowledge that should be accessible to both academia and industry. Although it ought to be possible to create a stem-cell market that provides both rapid, unconditional access to academic researchers and more circumscribed access to commercial scientists, along with higher prices and profit sharing, the University

of Wisconsin has instead imposed terms and conditions on academic researchers that, I believe, represent an encroachment of private-sector barriers on the free exchange of scientific ideas.

As the developer of human embryonic stem cells, the university



has the same rights over its materials that academic institutions have always held. Thomson and his colleagues may keep these materials proprietary or share them on any terms they wish. If their research had been funded by federal grants, they would have been subject to the National Institutes of Health guidelines promoting wide and rapid exchange of materials. Having been funded by Geron, the research was not subject to such strictures. Because they published their findings in an academic journal, Thomson and his coauthors were, however, subject to the journal’s requirements to make their materials available. The policy at *Science*, which published the 1998 study, precludes publication of articles that come with “unreasonable restrictions”; the journal has little recourse, however, if restrictions are imposed after publication.

In addition to material rights, the Patent Office granted WARF three extremely broad patents covering the stem cells and the methods for creating them. In the decade before these patent rights were (preliminarily) deemed invalid, they permitted WARF to prohibit any U.S. researchers, in the pub-

lic or private sector, from “making, using, selling, offering to sell, or importing” what it had patented and from using its patented idea as the basis for another invention without a contractual agreement. WARF could, if it chose, control any research involving its human embryonic stem cells as well as the use of any other human embryonic stem cells made through its methods — which, with a few recent exceptions, encompassed all available cell lines.

Armed with these rights, WARF has used two forms of contracts to control the human embryonic stem-cell market: licenses governing the use of patented material or technology, which typically define the scope of use and require payment of an up-front fee plus royalties from sales of any products derived from the licensed technology, and material transfer agreements governing the transfer of tangible research materials, with negotiable arrangements regarding the scope of research use, publications, transfer to third parties, and ownership of any technology developed.

WARF signed a license agreement with Geron, giving it exclusive rights to develop therapeutic and diagnostic products from neural stem cells, cardiomyocytes, and pancreatic islet cells and nonexclusive rights to develop products and commercialize research products that are based on other cell types.³ Other companies could obtain only nonexclusive rights. WARF’s agreements with academic researchers included critical limitations on the purposes for which stem-cell lines could be used and on the sharing of cells with other researchers, allowing WARF to propagate its contractual conditions throughout future commercial and academic development alike.

WARF has been accused of “stifling” the market for stem cells, particularly for academic researchers. It has responded, in essence, that because Thomson’s research was privately funded, WARF is being generous to share at all.³ But this argument fails to recognize that most universities continually strive to ensure that corporate funding does not conflict with their academic mission, of which the wide dissemination of knowledge is surely a part.

WARF has also argued that it was “learning” how to establish appropriate market conditions, having repeatedly tried to reshape the stem-cell market by changing its contractual terms, partly in response to objections from the scientific community.⁴ In January 2007, for example, WARF began to permit industry-sponsored research involving its stem cells to be pursued at academic institutions without a license, and it eased restrictions on stem-cell transfers among researchers. It has gradually loosened its control, simplified its practices, and reduced its prices. Such evolution makes it clear that it is not the

patents themselves but the contracts through which patent rights are imposed that can impede the advancement of science. If replicated elsewhere, restrictive practices could balkanize research, causing experimental designs and collaborations to be driven by legal rather than scientific choices.

By contrast, one can envision an open commons for human embryonic stem-cell research, combined with strong incentives for commercial research investments. Such a scheme would not mean eschewing patent rights. Rather, it would require a commitment by academic institutions to allow a wide-reaching reciprocal exemption for the free exchange of materials for research purposes, with relevant stipulations built into commercial licenses. These terms could be extended to for-profit researchers while they conducted research, with an agreement to negotiate effective commercial terms if and when products were identified. At the same time, federal agencies could expand their investments in institutions that facilitate the rapid exchange, validation, and comparative analysis

of stem cells as envisioned by the International Society for Stem Cell Research. Such a scenario would be in the long-term best interests of science.

The challenge for universities today is not so much to choose whether or not to patent their ideas, but rather to determine how best to control their discoveries and whether their technology-transfer policies advance their broader mission.

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3. Stem cell deal reached. Press release of the Wisconsin Alumni Research Foundation, Madison, January 9, 2002. (Accessed May 17, 2007, at <http://www.news.wisc.edu/packages/stemcells/6949.html>.)

4. Wisconsin Alumni Research Foundation changes stem cell policies to encourage greater academic, industry collaboration. Press release of the Wisconsin Alumni Research Foundation, Madison, January 23, 2007. (Accessed May 17, 2007, at http://www.warf.org/news/news.jsp?news_id=209.)

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Expanding the Black Box — Depression, Antidepressants, and the Risk of Suicide

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On May 2, 2007, the Food and Drug Administration (FDA) ordered that all antidepressant medications carry an expanded black-box warning incorporating information about an increased risk of suicidal symptoms in young adults 18 to 24 years of age. Since October 2004, antidepressants have been required to have a black-box warning indicating that they are associated with

an increased risk of suicidal thinking, feeling, and behavior in children and adolescents.

The new warning also states that there is no evidence of an increased risk for adults older than 24 years of age and that the risk is actually decreased for adults 65 years of age or older. Strikingly, the label states that “depression and other serious psychiatric disorders are themselves

associated with increases in the risk of suicide,” which makes it the first black-box warning to note that a disease itself carries risk — and implies that there is risk in not using the very medication being warned about.

The new warning was developed in the wake of a December 2006 meeting of the FDA’s Psychopharmacologic Drugs Advisory Committee, which focused on the