

Obvious? Some say Thomson (right) didn't invent anything.



STEM CELLS

Prominent Researchers Join the Attack on Stem Cell Patents

James Thomson's work deserves praise but no patents for doing what others could have achieved with the proper resources, critics say

Four prominent stem cell scientists have filed "declarations" in support of a citizens' group that is trying to break the University of Wisconsin's hold on patents for human embryonic stem (ES) cells.

Joining the fray are Harvard researchers Chad Cowan and Douglas Melton, as well as Alan Trounson of Australia's Monash University. A new statement was also submitted by Jeanne Loring of the Burnham Institute for Medical Research in San Diego, California, who has been advising the Foundation for Taxpayer and Consumer Rights, which filed the initial complaint last July.

In April, the U.S. Patent and Trademark Office (PTO) issued a preliminary ruling upholding the taxpayer foundation's challenges to three existing patents (*Science*, 13 April, p. 182) covering primate and human ES cells, which are based on the work of University of Wisconsin, Madison, researcher James Thomson and held by the Wisconsin Alumni Research Foundation (WARF). WARF narrowed its claims in response to the ruling, excluding human ES cells from sources other than fertilized eggs, such as cloning. But WARF is standing pat in face of the latest onslaught. Spokesperson Andrew Cohn says it will have no response to the statements, which contain "nothing new."

The scientists' statements reiterate the taxpayer foundation's central arguments: that the feat by Thomson—who announced the first successful cultivation of human ES cells in

1998 (*Science*, 6 November 1998, p. 1145)—was "obvious" and therefore unpatentable since it was the outcome of using already-known technology.

The four scientists emphasize that Thomson deserves all the accolades he has received. But they argue that he was just lucky in having access to abundant funding (from Geron Corporation in Menlo Park, California) and fresh frozen human embryos (from Israel). "I believe that had any other stem cell scientist been given the same starting material and financial support, they could have made the same accomplishment," stated Melton.

WARF argues that for 2 decades after the discovery of mouse ES cells, people "repeatedly tried and failed" to cultivate sustainable lines from other mammals including sheep, pigs, hamsters, cows, and humans. But none of these efforts was successful until Thomson reported the first monkey ES cell line in 1995. WARF cites Ariff Bongso at the National University of Singapore as a researcher who tried and failed to cultivate human ES cells pre-Thomson. Bongso derived a human cell line in 1994 but was unable to maintain it. WARF also emphasizes that Thomson was the first to report that Leukemia Inhibitory Factor, or LIF, although necessary for cultivating mouse ES cells, is not needed with human cells.

The challengers counter that "not a single scientist in the field tried and failed to achieve Thomson's accomplishment"—not for lack of know-how but because they did not have the

proper resources. They also cite Bongso's work, arguing that with a little more time he would have gotten it right. Trounson says he had "work in progress" cultivating human ES cells at the time Thomson reported his breakthrough (Trounson's work was published in 2000). Melton points out that his team in the past few years has successfully isolated human ES cells "by simply following ... methods taught for deriving mouse, rat, pig, and sheep ES cells. We did so without recourse to Dr. Thomson's publications. ..."

Colin Stewart, a stem cell researcher at the Institute of Medical Biology in Singapore, is the only outside expert who has offered a declaration to the PTO in support of WARF's position. Stewart, co-discoverer of the role of LIF in mouse ES cell culture, basically argues that existing methods for cultivating mouse cells did not provide adequate guidance for cultivating human ones. (Stewart was not available for comment.)

Some lawyers have gone to bat for WARF. In a blog posted on 4 July, Chicago, Illinois, biotech lawyer Kevin Noonan points out it is difficult to maintain that the invention was anticipated by "prior art" given the acknowledged "absence of appropriate starting materials"—human embryos. "The best the art could provide is a suggestion about how human stem cells *might* be produced," he writes. Madison, Wisconsin, patent attorney Grady Frenchick is confident the patents will hold up. "Everybody's going to use [Thomson's] method of isolation and cultivation. That's truly the breakthrough," he says.

But it is difficult to find a stem cell researcher other than Stewart or Thomson who thinks WARF's patents are justified. "I know of no one other than the folks ... associated with WARF and these patents who is in favor of how they are handling this," says Fred Gage of the Salk Research Institute in San Diego, California.

Johns Hopkins University stem cell researcher John Gearhart agrees with the challengers. "The procedure James [Thomson] used to generate human ES cells was one that had been basically reported [back in the '80s] for generating mouse ES cells," says Gearhart. The LIF argument is a red herring, he adds. Even though Thomson found it was not necessary for growing human cells, its presence does not interfere with culturing them.

Gearhart says he doubts "whether the patent office really understood what was going on" when it issued WARF's patents. "They were not very rigorous." But with so many eyes now on it, the PTO is presumably giving the issue more than routine scrutiny.

—CONSTANCE HOLDEN

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