

Massachusetts General Researchers Discover Stem Cell that Makes Eggs

By Carolyn Y. Johnson, Globe Staff

Massachusetts General Hospital researchers reported today they have discovered a rare stem cell in women's ovaries that they hope one day might be used to make eggs, a claim already generating vigorous debate among scientists familiar with the research.

For decades, it has been thought that women are born with a finite supply of eggs, limiting their reproductive years. Doctors have sought ways of extending the fertility of women, especially as many wait later in life to begin having children.

The research, led by Jonathan Tilly of Mass. General and appearing in the journal [Nature Medicine](#), opens the door to the possibility of taking tissue from a woman's ovaries, harvesting stem cells from that tissue, and then creating eggs.

But scientists not involved with the Mass. General research said such an approach -- if it is even possible -- sits far in the future and will require considerably more work. Several scientists said Tilly, who co-founded a company focused on developing novel infertility treatments, had not yet made a convincing case that the stem cells he discovered can yield viable eggs, a critical first step.

Tilly has been a lightning rod in the field of fertility medicine since 2004, when he challenged the orthodoxy that women do not produce new eggs. In a research paper published that year, Tilly laid the foundation for the findings reported yesterday.

"There was a lot of backlash. It wasn't surprising, given the magnitude of the paradigm shift that was being proposed -- this was one of the fundamental beliefs in our field," Tilly said. "The subsequent eight years have been a long haul."

In his new study, Tilly extended research by Chinese scientists published in 2009. He developed a technique that allowed scientists to sift out rare stem cells within the ovaries of mice that were tagged and implanted into the ovaries of normal mice. In the mouse ovaries, the stem cells produced eggs, which were removed and fertilized in a laboratory dish. They developed into embryos, although scientists did not use the embryos to produce mice.

Tilly and his team then wanted to know if such cells existed in humans, too.

The research team obtained ovarian tissue removed from young women undergoing sex change operations in Japan and performed the same experiment they'd done with the

mouse ovaries. Much to their excitement, they discovered the rare, egg-producing cells in humans.

In later experiments, the human stem cells were used to produce cells that appeared to be eggs. In part because of ethical limitations, researchers were not able to show that the eggs could be used to create human embryos.

Tilly said that he has patented the stem cells and licensed the technology to OvaScience, the startup he co-founded.

Outside researchers described the findings as intriguing and provocative but also raised many questions. Scientists said it was still far from certain that the eggs created in the experiments could be used to produce babies. And they expressed concern that the findings could falsely inflate the hopes of women struggling with infertility.

Dr. David Keefe, chairman of obstetrics and gynecology at New York University Langone Medical Center, said he and other clinicians who see patients would like more than anything to have greater options for women to overcome infertility. But he said the Mass. General researcher had a history of leaping ahead from basic research findings to suggest clinical possibilities.

“Those of us who take care of patients are extremely protective of their hopes,” Keefe said. He noted that a few years ago, he saw half-a-dozen patients who wanted to delay their fertility decisions because of earlier research at Mass. General.

Even if the new findings are immediately replicated in labs around the world, Keefe said, “it’s so far from being clinical that it’s predatory to not be circumspect about it. Humility is an absolute requirement in this field. You’re dealing with people’s hopes and dreams.”

A 2005 study led by Tilly and done in mice suggested bone marrow transplants might offer a way to restore fertility. A year later, a separate group of Harvard researchers showed that this was unlikely to be true. Tilly himself no longer believes this is a way to restore fertility.

“The big difference in that work, now in retrospect, is these non-ovarian sources [of stem cells] don’t appear to do the job,” he said.

Tilly’s work in the past has divided researchers and failed to persuade many in the field that his interpretations are correct.

Teresa Woodruff, a professor of obstetrics and gynecology at the Feinberg School of Medicine at Northwestern University said she had already drawn up a chart of the claims made in the paper, the evidence to support those claims, and the questions they raise. Still,

she said, “I do think he’s pushing the envelope in a way that does push all of us to think more broadly.”

Evelyn Telfer, a cell biologist at the University of Edinburgh, who criticized some of Tilly’s earlier work, said she is excited about the new findings. Tilly said that next month, he will fly to Scotland to begin a collaboration with Telfer.

“What he’s saying is we can get these cells,” Telfer said, “and I think it’s pretty convincing.”

The new paper doesn’t offer evidence that such stem cells are active in the ovary, supplying eggs during a woman’s lifetime. But the powerful cells could provide new insights into the important and poorly understood process in biology of egg-formation and allow scientists to look for drugs that might increase the activities of these stem cells, in order to overcome fertility problems.

Skeptics and supporters agreed on one thing: much work lies ahead.

“That’s science,” said Hugh Clarke, a professor in the department of obstetrics and gynecology at McGill University. “Of course, dogma should be challenged, but we shouldn’t assume dogma has been overturned based on a single report.”

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