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Stem-cell era reaches age 10

Setbacks and controversy haven't stopped progress in the field since UW researcher James Thomson's breakthrough in 1998

BY MARK JOHNSON

Ten years ago today, human embryonic stem cells entered the popular vocabulary. The world hasn't been the same.

The first report that the human cells had been isolated and grown by scientists at the University of Wisconsin-Madison appeared in the journal *Science*, triggering a decade of fierce debate and great hope.

The report may not have seemed revolutionary from the dense headline: "Embryonic Stem Cell Lines Derived from Human Blastocysts." The report's last sentence, however, made clear the importance of the discovery:

"Progress in basic developmental biology is now extremely rapid;" James Thomson and his co-authors wrote, "human (embryonic stem) cells will link this progress even more closely to the prevention and treatment of human disease."

"My first reaction was: I knew it," said Robert Lanza, who was working with a tissue engineering firm back in 1998 and now serves as chief scientific officer for Advanced Cell Technology in Worcester, Mass. "I was trying to tell everybody for a year that there was this cell, this master cell, out there. And it was going to revolutionize regenerative medicine."

Although the revolution has yet to reach patients, it has already reshaped regenerative medicine, a field built around the idea of growing new tissues and organs to replace those lost or damaged. Today, major avenues of research center on stimulating adult stem cells already in the body, or using stem cells in laboratory dishes to make more specific varieties needed to help the brain, heart and other organs.

Because of their ability to make all other cell types and survive indefinitely in a lab dish, embryonic stem cells have become both a source of other cells and a tool for the study of human development.

"It was a monumental discovery. It was a giant step forward and obviously put Wisconsin at the forefront of the world," said Leo T. Furcht, head of the University of Minnesota's department of laboratory medicine and pathology, and co-author of the 2008 book "The Stem Cell Dilemma."

A new front

The intense interest in the discovery would change the fundamental conditions of research, as embryonic stem cells became a new front in the nation's long-running debate on the nature and sanctity of life. In August 2001, the same month that Time put Thomson on its cover, President Bush put restrictions on the stem cell field. Federal funding was limited to work on the stem cell lines already in use before his announcement - a policy that frustrated scientists.

Despite funding difficulties, the number of stem cell researchers has risen sharply. In 2002, the International Society of Stem Cell Researchers formed with an initial membership of 150. By the end of the first year, the society was up to 600 members, and today it boasts more than 2,600 from 45 countries.

Over the last decade, researchers have learned how to turn embryonic stem cells into heart, brain and pancreatic cells - some of the types doctors will need in order to study diseases, test drugs and develop therapies.

"There's been good progress," Thomson said recently. "The whole field has actually moved along at a reasonable pace."

Scientists have also learned much about the genes that play a powerful role in allowing embryonic stem cells to retain their potential. This knowledge set the stage for last year's announcement that the labs of Thomson and Japanese scientist Shinya Yamanaka had discovered a possible alternative to the human embryonic stem cell.

The two labs were able to turn back the developmental clock, reprogramming human skin cells to make them look and act like embryonic stem cells. The scientists infected the cells with a virus carrying four genes that play major roles in embryonic stem cells.

"The discovery of how to reprogram cells probably would not have been possible without the knowledge of embryonic stem cells," said Mark Magnuson, director of Vanderbilt University's Center for Stem Cell Biology.

Thomson, Yamanaka and others have cautioned that much work remains to establish that the new cells have all of the same abilities as embryonic stem cells. Both scientists have disagreed strongly with suggestions that reprogramming removed any further need for research involving human embryonic stem cells.

For one thing, the methods used to create the new cells risk causing cancer, though in recent months scientists have made considerable progress in reducing this risk.

Still no treatments

Despite the advances, embryonic stem cells have yet to be used for human treatments. And that has put researchers in a difficult position with the patients who have looked to the cells for hope.

Beverly Torok-Storb, co-head of the Stem and Progenitor Cell Biology Program at Fred Hutchinson Cancer Research Center in Seattle, said it is important that the public appreciate how "painstakingly slow everything is" in science. A few years ago she was at a forum where a patient with Lou Gehrig's disease spoke.

"He was hoping something could be done for him before he died," Torok-Storb said, recalling that she sat there knowing how unlikely it was that scientists would be able to help the man. "It was very painful."

A decade after Thomson's isolation of human embryonic stem cells, the questions surrounding possible therapeutic applications remain to be answered, as do more fundamental questions about our biology.

Thomson continues to seek the answer to one very basic question.

"It's the one we've been nudging at the whole time," he said. "We still can't articulate why one cell can make anything in the whole body and another can't. We know a lot about the particular factors that are important to this one cell, but I can't write you a simple paragraph explaining why that's true.&ensp.&ensp.& I can't write a little &ensp. story around it, and I'd like to be able to do that."