

## STEM CELLS SIDESTEP CONTROVERSY

K. Gorbatyuk, *IN-01*,  
N. I. Mulina, *ELA*

Science and technology have utterly transformed human life in the past few generations. But big changes arrive faster and faster these days. Now we're right on the verge of some extraordinary stuff. New techniques will circumvent ethical concerns, and maybe lead us to the Medical Holy Grail: the ability to grow new tissue and organs from the patient's own cells, virtually eliminating the possibility of rejection.

During 2012, two scientific teams announced, in separate studies, that they had transformed ordinary adult skin cells into neural cells, a breakthrough that could change the course of human stem cell research. Stem cells hold enormous potential for medicine because they can develop from undifferentiated cells into a variety of specialized ones. Studying stem cells will help us understand how they transform into the dazzling array of specialized cells that make us what we are. Some of the most serious medical conditions, such as cancer and birth defects, are due to problems that occur somewhere in this process. A better understanding of normal cell development will allow us to understand and perhaps correct the errors that cause these medical conditions. But their use has been stymied by ethical concerns, because most of stem cells are harvested from human embryos, which are destroyed in the process.

In 2006, Shinya Yamanaka of Japan's Kyoto University figured out a way to bypass embryonic cells. He generated stem cells from skin cells, a discovery for which he shared with John Gurdon the 2012 Nobel Prize in medicine. These cells are called iPS cells. Induced pluripotent stem cells (iPSCs) are adult cells that have been genetically reprogrammed to an embryonic stem cell-like state by being forced to express genes and factors important for maintaining the defining properties of embryonic stem cells. Although additional research is needed, iPSCs are already useful tools for drug development and modeling of diseases, and scientists hope to use them in transplantation medicine. Perhaps the most important potential application of human stem cells is the generation of cells and tissues that could be used for cell-based therapies. Today, donated organs and tissues are often used to replace ailing or destroyed tissue, but the need for transplantable tissues and organs far outweighs the available supply. Stem cells, directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat diseases

including Alzheimer's diseases, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis.

For example, it may become possible to generate healthy heart muscle cells in the laboratory and then transplant those cells into patients with chronic heart disease. Preliminary research in mice and other animals indicates that bone marrow stromal cells, transplanted into a damaged heart, can have beneficial effects. In addition, tissues derived from iPSCs will be a nearly identical match to the cell donor and thus probably avoid rejection by the immune system.

However, the process of obtaining induced pluripotent stem cells is extremely inefficient. Complete reprogramming of somatic cells in iPSCs can take a month, while only one of the thousands of cells will become pluripotent. Moreover, the results of several studies suggest that, for all its plasticity iPSCs are not absolute equivalent of embryonic stem cells. Despite this, Japanese researchers hope to test iPS cells in clinical trials for a form of blindness as early as next year - catching up with recent successful eye trials using embryonic stem cells. Gurdon played down such worries and said regulatory authorities and governments should take a step back and let patients assess the potential benefits and risks for themselves. "If you explain to a patient what can be done, and what might be the downside - then you should let the patient choose. Don't have ethicists or ... doctors or whoever say you may or may not have replacement cells," he told reporters.

To summarize, stem cells offer exciting promise for future therapies, but significant technical hurdles remain that will only be overcome through years of intensive research.

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