Cloned stem cells prove identical to fertilized stem cells

January 18 2006

Scientists generally agree that all cloned animals are biologically flawed. But they don't agree about what that means for stem cells derived from cloned embryos, the basis for therapeutic cloning.

Also known as somatic cell nuclear transfer, therapeutic cloning is a promising approach to creating individually customized cellular therapies for treating certain disorders. Demonstrated in mice but not in humans, it begins with stem cells derived from a cloned embryo. But if cloned embryos can't produce normal organisms, how can they produce normal stem cells?

Analyzing the complete gene-expression profiles of both cloned and fertilization-derived stem cells in mice, scientists at MIT and the Whitehead Institute for Biomedical Research now have concluded that the two are, in fact, indistinguishable.

"This paper demonstrates clearly that it doesn't matter if a stem cell has been derived from a cloned embryo or from a fertilized embryo," says Whitehead member and MIT biology Professor Rudolf Jaenisch, senior author on a paper that will appear online the week of Jan. 16 in the Proceedings of the National Academy of Sciences. "Both can be equally good for therapy."

To create a clone, a scientist removes the nucleus from a donor cell, then places it into an egg from which the nucleus has been removed. The researcher then tricks the egg into thinking it's been fertilized. The egg

develops into a blastocyst, an early-stage embryo consisting of no more than 100 or so cells. The scientist can then either remove the stem cells from this blastocyst, or place it into a uterus where it has the potential to develop into a fetus.

Here's where things get complicated. The original donated nucleus may have come from, say, a skin cell. For a viable fetus to develop, the egg needs to reprogram the genome of the skin cell, shutting off genes specific for skin tissue and turning on genes needed for embryonic development, genes that are normally dormant in tissue-specific cells. In other words, the egg needs to erase all tissue-specific memories from the skin cell and revert it into a genomic blank slate.

But this entire process is almost never perfect, and nearly all cells in a cloned blastocyst retain some memory of their original source. As a result, the developing fetus inevitably has some degree of genetic abnormality. Most clones, in fact, die in utero or at birth. The few clones that make it into adulthood are often plagued by bizarre health complications. This is one reason why scientists generally believe that attempting to clone a human being is morally reprehensible.

But are the cloned embryo's stem cells beleaguered by the same defects?

Studies have demonstrated that a small number of stem cells in the blastocyst appear to be spared this faulty reprogramming. When stem cells from a cloned blastocyst are removed and placed into a dish, most die. A few, however, survive and give rise to an embryonic stem cell line, and these appear to be thoroughly reprogrammed.

Researchers have tried to test the integrity of these surviving stem cells by transplanting them into fertilized blastocysts and then observing the overall health of the resulting animal. Although these animals generated entirely from cloned stem cells appear to be fine, many scientists don't

accept this result as definitive.

Tobias Brambrink, a postdoctoral researcher in the Jaenisch lab, tried a different approach, comparing gene expression in cloned and fertilization-derived stem cells. With a series of microarray chips, Brambrink measured which genes were active and which were silent in both kinds of cells. To ensure the accuracy of his results, he compared five lines of cloned stem cells with five fertilization-derived stem cell lines.

"The results are very clear," says Brambrink. "If a gene is active in fertilized stem cells, it's also active in cloned stem cells, and at the same level of activity. The same goes for genes that are silent. There is really no significant molecular difference between both kinds of stem cells."

"In my opinion, these results solidify the argument that while a cloned animal is abnormal, a cloned stem cell is perfectly normal," says Jaenisch.

Source: MIT (by David Cameron)