Therapeutic cloning gets a boost with new research findings

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A paper by San Antonio and Honolulu researchers offers the first direct demonstration that cloning by somatic cell nuclear transfer does not lead to an increase in the frequency of point mutations.

Germ cells, the cells which give rise to a mammal's sperm or eggs, exhibit a five to ten-fold lower rate of spontaneous point mutations than adult somatic cells, which give rise to the body's remaining cell types, tissues and organs. Despite their comparatively higher mutation rates, however, adult somatic cells are used as the donor cells in a cloning process called somatic cell nuclear transfer (SCNT). This made researchers wonder if cloning by SCNT leads to progeny with more mutations than their naturally conceived counterparts. Also, would cloned fetuses receive DNA programming predisposing them to develop mutations faster than natural fetuses of the same age?

Those scenarios are simply not likely, say researchers at The University of Texas at San Antonio, The University of Texas Health Science Center at San Antonio and The University of Hawaii at Honolulu's John A. Burns School of Medicine. The team, which spent more than five years analyzing mutation rates and types in cloned Big Blue® mouse fetuses recently published its findings in the online Early Edition of the Proceedings of the National Academy of Sciences in a paper titled "Epigenetic regulation of genetic integrity is reprogrammed during cloning."

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John McCarrey, professor of cellular and molecular biology at UTSA and the study's principal investigator, suggests a "bottleneck effect" is partially responsible for the observations his team recorded. "To create a cloned fetus by somatic cell nuclear transfer, only one adult somatic cell -- one donor cell -- is needed," he explains. "Because a random cell population exhibits a low mutation rate overall and only one cell from that population is used for cloning, the likelihood is remote that the cell chosen to be cloned will transfer a genetic mutation to its cloned offspring. Therefore, the bottleneck effect limits the transfer of mutations from donor cells to cloned offspring."

Not only did the researchers find that SCNT does not lead to an increase in the frequency of point mutations in cloned mice, the team also found that naturally conceived fetuses and cloned fetuses that are the same age have similar rates of spontaneous mutation development. They attribute this finding to epigenetic reprogramming.

It is known in the scientific community that germ cells contain an epigenome, a programmed state of the genome, that keeps mutation rates low. They suggest this type of epigenome is found in germ cells because those cells are responsible for contributing genetic information to subsequent generations. Adult somatic cells (the donor cells in SCNT) have higher mutation rates and less stringent epigenetic programming to avoid mutations than germ cells, but offspring produced from somatic cells by cloning have mutation rates similar to those in offspring produced by natural reproduction, suggesting that the epigenome of an adult somatic cell is reprogrammed during cloning to maintain the genetic integrity of that cell's progeny.

Source: University of Texas at San Antonio