World's first chimeric monkeys are born

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Roku. Image: OHSU

Researchers have produced the world's first chimeric monkeys. The bodies of these monkeys, which are normal and healthy, are composed of a mixture of cells representing as many as six distinct genomes. The advance holds great potential for future research as chimeric animals had been largely restricted to mice, the researchers say. The report, published online ahead of the release of the January 20th issue of *Cell*, also suggests there may be limits to the use of cultured embryonic stem cells.

The chimeric monkeys were born after the researchers essentially glued cells from separate rhesus monkey embryos together and successfully

implanted these mixed embryos into mothers. The key was mixing cells from very early stage embryos when each individual embryonic cell is totipotent, capable of giving rise to a whole animal as well as the placenta and other life-sustaining tissues. (This is in contrast to pluripotent stem cells, which can differentiate into any tissue type in the body, but not extra-embryonic tissues or entire organisms.)

"The cells never fuse, but they stay together and work together to form tissues and organs," said Shoukhrat Mitalipov of the Oregon National Primate Research Center at Oregon Health & Science University. "The possibilities for science are enormous."

Roku & Hex. Image: OHSU

Initial efforts by Mitalipov's team to produce living monkey chimeras by

introducing cultured embryonic stem cells into monkey embryos -- a well-established means to produce chimeric mice -- failed. Chimeric mice have been extremely important to biomedical research by enabling the production of transgenic "knock-out" mice carrying deletions of targeted genes, Mitalipov explained.

Mitalipov says it appears that primate embryos prevent cultured embryonic stem cells from becoming integrated as they do in mice. Their study also suggests that cultured primate and human embryonic stem cells, some of which have been maintained in lab dishes for as long as two decades, may not be as potent as those found inside a living embryo.

"We need to go back to basics," Mitalipov said. "We need to study not just cultured embryonic stem cells but also stem cells in embryos. It's too soon to close the chapter on these cells." For instance, he added, cultured embryonic stem cells are now considered the "gold standard" for comparisons to induced pluripotent stem (iPS) cells made by treating adult cells with relatively simple cocktails.

"We cannot model everything in the mouse," Mitalipov continued. "If we want to move stem cell therapies from the lab to clinics and from the mouse to humans, we need to understand what these primate cells can and can't do. We need to study them in humans, including human embryos." He emphasized, however, that there is no practical use or intention for anyone to produce human chimeras.

More information: Tachibana et al.: “Totipotent but not pluripotent primate embryonic cells contribute to chimeras.” DOI:10.1016/j.cell.2011.12.007

Abstract
Totipotent cells in early embryos are progenitors of all stem cells and are

capable of developing into a whole organism, including extraembryonic tissues such as placenta. Pluripotent cells in the inner cell mass (ICM) are the descendants of totipotent cells and can differentiate into any cell type of a body except extraembryonic tissues. The ability to contribute to chimeric animals upon reintroduction into host embryos is the key feature of murine totipotent and pluripotent cells. Here, we demonstrate that rhesus monkey embryonic stem cells (ESCs) and isolated ICMs fail to incorporate into host embryos and develop into chimeras. However, chimeric offspring were produced following aggregation of totipotent cells of the four-cell embryos. These results provide insights into the species-specific nature of primate embryos and suggest that a chimera assay using pluripotent cells may not be feasible.

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