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Researchers replace organ in adult mice using 'single-parent' stem cells

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Researchers at the University of Pennsylvania School of Veterinary Medicine have derived uniparental embryonic stem cells - created from a single donor's eggs or two sperm - and, for the first time, successfully used them to repopulate a damaged organ with healthy cells in adult mice. Their findings demonstrate that single-parent stem cells can proliferate normally in an adult organ and could provide a less controversial alternative to the therapeutic cloning of embryonic stem cells.

"Creating uniparental embryonic stem cells is actually much more efficient than generating embryonic stem cells by cloning," said K. John McLaughlin, an assistant professor in Penn's Department of Animal Biology and researcher at the Center for Animal Transgenesis and Germ Cell Research at Penn's New Bolton Center. "The fact that we are not destroying a viable embryo in the process also avoids certain ethical issues that currently surround embryonic stem cell science."

McLaughlin and his colleagues report their findings in the Feb. 15 issue of the journal *Genes & Development.*

"While previous research has approached the possibility of using a woman's egg cells to create therapeutic stem cells, we discovered that we could actually repopulate an adult organ. To our surprise we also found that by using male-only derived embryonic stem cells, we could do the same," McLaughlin said. "In humans, this could provide a therapeutic route for both genders; members of either sex can use this technique to

produce compatible stem cells, much like you might donate blood for your own use in advance of an operation."

Parthenogenesis, the act of creating an embryo without fertilization, is common in some plants, insects and animals, including the recent and celebrated case of the "virgin birth" of a komodo dragon in England. Humans and all other mammals, however, require two sets of chromosomes - one from each parent - to create a functioning embryo.According to McLaughlin, this is because mammalian embryos rely on a process called genomic imprinting, where cells will read certain genes from only one parent. Imprinting failures could lead to the death of an embryo and are frequently associated with some forms of cancer and other genetic disorders.

"There was considerable doubt that uniparental stem cells would work since the lack a balanced set of chromosomes from both parents would interfere with the natural outcomes of genomic imprinting," McLaughlin said. "It turns out that genomic imprinting may be more a concern for developing stages and not so much a factor in the routine function of adult tissue, which was the ultimate goal for deriving these stem cells."

To study uniparental stem cells and the possible effects of genomic imprinting, McLaughlin's team created an experiment in which they would attempt to reconstitute the hematopoietic, or blood-producing, stem cells that were destroyed in mice exposed to radiation. The Penn researchers first created gynogenetic (egg-based) and androgenetic (sperm-based) embryonic stem cells and then injected those into blastocysts, a pre-embryonic clump of cells from a fertilized egg. The researchers could then harvest fetal liver cell precursors for transplant. Ultimately, the scientists found that uniparental cells, regardless of parent of origin, were able to functionally replenish the entire blood-producing system of adult mice.

The scientists were able to maintain animals for more than 12 months with entirely uniparental blood and were able to rescue other irradiated mice with bone marrow transplants from these animals. It is clear proof, according to McLaughlin, that uniparental cells could produce hematopoietic stem cells. In addition, McLaughlin's group found no evidence of disease linked to the transplanted cells.

In another finding critical for any clinical approach using embryonic stem cells, the researchers were able to reproduce much of their findings by producing blood stem cells from embryonic stem cells entirely in the culture dish before transplanting them.

The Penn researchers believe that using uniparental embryonic stem cells as a tissue source could provide a major advance in the alleviation of human disease, provided these results can be translated into human studies.

Source: University of Pennsylvania