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Mouse study looks at safety of stem cell therapy for early menopause

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Now that we know that egg-making stem cells exist in adult rodents and humans and that these cells can be transplanted into mice with premature ovarian failure to produce offspring, the next question is to assess whether the offspring from the egg-making stem cells of a single adult mouse are biologically normal compared to natural births. On May 18 in the journal *Molecular Therapy*, researchers in China show that female mice with early menopause that receive egg-making stem cells from another mouse are capable of producing healthy pups 2 months later with no observable genetic malfunctions.

"One of our aims is to cure the disease of premature ovarian failure using female germline stem cells," says senior author Ji Wu, a reproductive biologist at Shanghai Jiao Tong University. "Before this treatment can be applied to humans, we need to know the mechanism of female germline stem cell development and safety after transplantation of single mouse female germline stem cells."

Premature ovarian failure, also called early menopause, is the loss of normal ovarian function, and thereby the release of eggs, before the age of 40. The condition is rare, affecting 200,000 women in the United States per year, and is incurable, although it can be treated with hormone supplements. Multiple groups are now looking at whether stimulating tissue regeneration or using stem cell transplants could help.

In the *Molecular Therapy* study, Wu and her colleagues isolated and characterized female germline stem cells from a single transgenic mouse

with cells that show green fluorescence when activated by a blue laser. This allowed the researchers to observe and analyze the development of the transplanted stem cells, which were introduced to the ovaries of other mice using a fine glass needle.

Wu and colleagues found that the transplanted egg-producing stem cells exhibited a homing ability and began to differentiate into early-stage oocytes when they reached the edge of the ovary. The oocytes spent a few weeks maturing and yielded offspring within 2 months. The researchers then demonstrated that the developmental mechanisms of eggs derived from transplanted germline stem cells were similar to that of normal eggs.

"The results are exciting because it's not easy to get offspring from female germline stem cells derived from a single mouse," Wu says.

Wu's lab is also working to establish female egg-producing stem cell lines from scarce ovarian tissues derived from follicular aspirates—the leftover cells gathered when a clinician searches a patient for oocytes—that are produced and discarded in in vitro fertilization centers worldwide. These aspirates can yield stem cells that differentiate into eggs in the lab, with the potential to be transplanted. The study not only provides a new approach to obtain human female germline stem cells for medical treatment, but also opens several avenues to investigate human oogenesis in vitro.

More information: *Molecular Therapy*, Wu et al.: "Tracing and characterizing the development of transplanted female germline stem cells in vivo" www.cell.com/molecular-therapy … 1525-0016(17)30180-6 , DOI: 10.1016/j.ymthe.2017.04.019

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