REPRODUCTIVE BIOLOGY

Mouse eggs made in the lab

First eggs created wholly in a dish raise call for debate over technology's use in humans.

BY DAVID CYRANOSKI

In a tour de force of reproductive biology, scientists in Japan have transformed mouse skin cells into eggs in a dish, and used those eggs to birth fertile pups. The report marks the first creation of mouse eggs entirely outside the animal. Researchers hope the process could be adapted to produce lab-grown human eggs too.

Katsuhiko Hayashi, a reproductive biologist at Kyushu University in Fukuoka, led the group that announced the breakthrough on 17 October in *Nature* (O. Hikabe *et al. Nature* http://doi.org/brxt; 2016). In 2012, when at the University of Kyoto, he and stem-cell biologist Mitinori Saitou reported taking skin cells down the pathway towards eggs: reprogramming them to embryonic-like stem cells and then into primordial germ cells (PGCs). These early cells emerge as an embryo develops, and later give rise to sperm or eggs. But to get the PGCs to form mature eggs, the researchers had to transfer them into the ovaries of living mice. The next advance came in July 2016, when a team led by Yayoi Obata at the Tokyo University of Agriculture reported transforming PGCs extracted from mouse fetuses into oocytes (egg cells) without using a live mammal. Working with Obata, Hayashi and Saitou have now completed the progression: from skin cells to functional eggs in a dish. With the use of *in vitro* fertilization techniques, 26 healthy pups were born, and some of them have given birth to offspring.

"This is truly amazing," says Jacob Hanna, a stem-cell biologist at the Weizmann Institute of Science in Rehovot, Israel. "To be able to make robust and functional mouse oocytes over and over again entirely in a dish, and see the entire process without the 'black box' of having to do any of the steps in host animals, is most exciting." The procedure is technically challenging, Hayashi says, but different groups in his lab have reproduced it. Although the team did not need to implant PGCs into living mice, they did have to add cells from ovaries of other mouse fetuses, effectively creating an ovary-like support in which the eggs could grow.

Hayashi says the work will help him to study egg development; he is not trying to make functional human eggs in the lab. But he suspects that others will try. "I do not think it is going to prove much more complex," says Hanna. Hayashi thinks that "oocyte-like" human eggs might be produced within ten years, but doubts that they will be of sufficient quality for fertility treatments. In his study, only 3.5% of the early embryos created from artificial eggs gave rise to pups, compared with 60% of eggs that were matured inside a mouse.

Debate over the ethics of the technology should begin now, says Azim Surani, a pioneer in the field at the University of Cambridge, UK. "This is the right time to involve the public in these discussions, long before the procedure becomes feasible in humans," he says. ■