Researchers claim to have made artificial mouse sperm in a dish

But some scientists are not convinced by the report.

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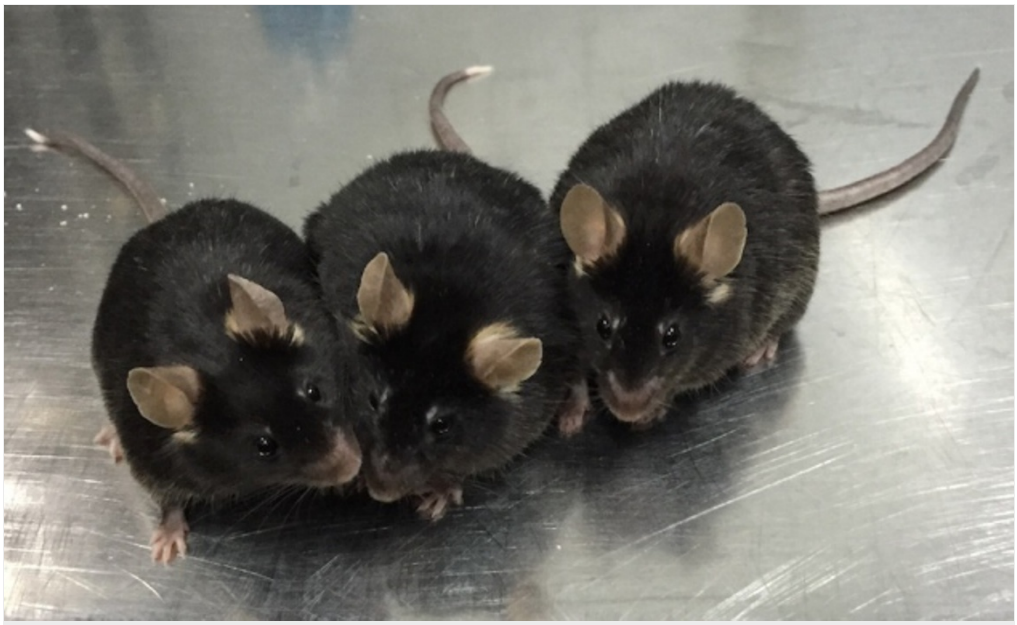


Xiao-Yang Zhao/Qi Zhou/Jia-Hao Sha

These mice, each about 12 months old, were born from eggs fertilized with artificial spermatids made in a dish, Chinese scientists say.

Researchers in China say that they have discovered a way to make rudimentary mouse sperm in a dish, and used them to produce offspring.

If the claim stands up to scrutiny, it could point the way to making human sperm in the lab for fertility treatments. But some scientists are not convinced by the report, which is published today in *Cell Stem Cell*[1].

“The results are super-exciting and important,” says Jacob Hanna, a stem-cell scientist at the Weizmann Institute of Science in Rehovot, Israel. But Takashi Shinohara, a reproductive biologist at Kyoto University in Japan, is among researchers who have doubts about the work: he notes that scientists have struggled to replicate several previous claims that sperm can be made in a dish.

In 2011, molecular biologists led by Mitinori Saitou at Kyoto University reported that they had managed to recreate the first stages of sperm development in a dish[2]. They coaxed mouse embryonic stem cells to become cells that resembled primordial germ cells (PGCs) — an

important stage in the development of both eggs and sperm.

Stem cells: Egg engineers

Saitou's team then implanted the artificial PGCs into a mouse: when implanted in testes, they grew to become sperm; in ovaries, they matured into eggs.

Now, Xiao-Yang Zhao, a development biologist at the Southern Medical University in Guangzhou, and Qi Zhou, a cloning specialist and stem-cell biologist at the Institute of Zoology in Beijing, along with colleagues from Nanjing Medical University, say that they have trumped Saitou's work by carrying out more of the process in a dish.

Recipe for sperm

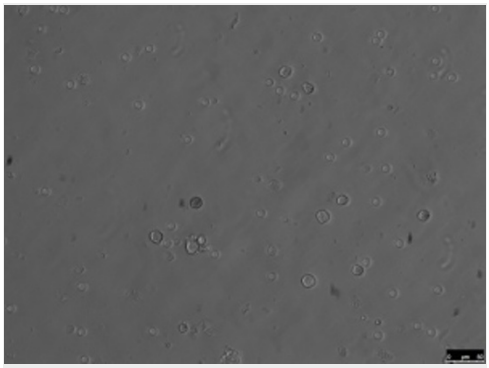
The team first made mouse PGCs, and then added cells taken from the testicular tissue of newborn mice, as well as other biological molecules.

After 14 days, they report, spermatid-like cells developed. Spermatids are not mature sperm: they are round, rather than having sperm's elongated shape, and cannot swim. But they do have only one set of chromosomes, showing that (unlike PGCs) they have passed the critical developmental stage of meiosis, in which a cell's chromosome pairs split up.

The researchers injected the spermatids directly into mouse eggs; this led to offspring which, at 15 months, appear healthy, says Zhao. The animals were able to give birth to a next generation of mice.

"The fact that the resulting cell could be injected into an egg and produce a viable animal is a stringent test," says Allan Spradling, a reproductive biologist at the Carnegie Institution for Science in Baltimore, Maryland. But the mice that were produced "might still contain defects or problems that do not manifest themselves until later", he adds.

Azim Surani, a developmental biologist at the University of Cambridge, UK, says that the results are "encouraging", although he cautions that it is hard to know whether the artificial spermatids do behave exactly like their natural counterparts.



Xiao-Yang Zhao/Qi Zhou/Jia-Hao Sha

The mouse spermatid-like cells as they appear under a microscope.

Cautious reception

Other scientists raise specific concerns that mainly relate to the timing of the processes that lead to the sperm cells. For example, Zhou and Zhao report that, on the basis of a genetic analysis, their artificial PGCs were similar to mouse cells at 12.5 days of development. But Saitou and others say that artificial PGCs should look more like 9.5-day-old cell.

And other stages of germ-cell development occurred unexpectedly quickly: in a real mouse, it takes more than 4 weeks for the PGC to become a spermatid, for example, but the Chinese team reports a 14-day interval between artificial PGC and spermatid.

"You have to be very cautious about the implications of this paper," says Saitou. Shinohara says that the researchers' scenario is "practically impossible", and Takehiko Ogawa, a reproductive biologist at Yokohama City University in Japan, says that the results are so surprising he "cannot yet believe it". He plans to try to reproduce the results.

Zhou says that the researchers are "very confident" that their protocol can be repeated in other laboratories — and that it would be normal for there to be variations between creating sperm in a dish and the process in live mice. He says that part of the acceleration could be because the cells seemed to have skipped an 'arrested' state that PGCs normally pass through. But Saitou counters that this state is crucial for PGCs to develop properly; at this accelerated pace, he says, the spermatids might not be normal.

From mice to men?

Applying the same concept to try to make human sperm is the next step, says Zhao. A year ago, Hanna and Surani reported making human PGCs in a dish from reprogrammed skin cells. But for ethical reasons, they didn't try to reintroduce them into humans[3].

Zhao says that his team is already trying to make human PGCs mature in a dish, using human testicular tissue from patients. And Hanna, who says that such tissue is hard to come by, has been using cells from testicular tissue of mice, pigs and monkeys to attempt the same

thing.

Still, there are important differences between the way in which sperm develop in mice and in humans, warns Yi Zhang, a geneticist at Harvard Medical School in Boston, Massachusetts. “It may not be as straightforward as people hope,” he says.

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References

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