BIOTECHNOLOGY

# Synthetic embryos have been implanted into monkey wombs

Embryos made from stem cells, rather than an egg and sperm, appear to generate a short-lived pregnancy-like response in monkeys.

By Jessica Hamzelou

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**Embryos made from stem cells—instead of a sperm and egg—have been created from monkey cells for the first time. When researchers put these "synthetic embryos" into** the uteruses of adult monkeys, some showed the initial signs of pregnancy. It's the furthest scientists have ever been able to take lab-grown embryos in primates—and the work hints that it may one day be possible to generate fetuses this way.

"This is amazing," says Susana Chuva de Sousa Lopes, a developmental biologist at Leiden University in the Netherlands, who was not involved in the study. "It's the first time I've seen [synthetic embryos] developed so far, and with such good quality." It is also the first time such embryo-like structures have been implanted in monkeys.

The team behind the research, Zhen Liu at the Chinese Academy of Sciences in Shanghai and his colleagues, started with embryonic stem cells originally taken from macaque monkey embryos. These cells have been grown in labs for multiple generations and, given the right conditions, have the potential to develop into pretty much any type of body cell, including those that make up organs, blood, and nervous system.

## Lab-grown embryos

The team used a set of lab conditions, which they tweaked and improved, to encourage embryonic stem cells to develop further. Over several days, the cells began developing in a very similar way to embryos. The resulting blobs of cells are called blastoids, because they look like early embryos, which are called blastocysts.



After the blastoids had been growing in a dish for seven days, the researchers put them through a series of tests to figure out how similar they were to typical embryos. In one test, the team separated the individual cells in the blastoids and checked to see which genes were expressed in each one. The team analyzed over 6,000 individual cells this way.

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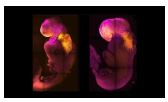

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The stem-cell-derived embryos could shed new light on the earliest stages of human pregnancy.

These tests revealed close similarities between the stem-cell-derived embryos and conventional monkey embryos. "The … analysis is simply mind-blowing," says Chuva de Sousa Lopes. "These blastoids seemed to transition to something that really looks like an embryo. And that is really amazing."

Some of the blastoids were grown for longer—up to 17 days. These structures looked very much like typical embryos, the researchers say, although other scientists not involved in the study say more evidence is needed to prove just how similar they are.

The only way to find out how embryo-like these blastoids really are is to test whether they can develop in a monkey's uterus. So the team put between eight and 10 seven-day-old blastoids into the uteruses of each of eight adult monkeys. The researchers then monitored the transferred blastoids for three weeks.

The researchers believe that in three of these monkeys, the blastoids successfully implanted in the uterus and appeared to generate a yolk sac—one of the very first signs of pregnancy. These monkeys also had elevated levels of pregnancy hormones. In other words, they would have had a positive pregnancy test.

The presence of these hormones is not surprising, says Nicolas Rivron at the Austrian Academy of Sciences in Vienna, who has done similar research in mice. It is a set of cells in the developing embryo that produce these hormones, whether or not the embryo is going to develop further, he says. As part of his own past research, Rivron and his colleagues grew human blastoids in a dish. When they dipped a pregnancy test into this dish, it gave a positive result.

But within 20 days of transfer, the monkey blastoids stopped developing and seemed to come apart, say Liu and colleagues, who



That might be because a typical embryo is generated from an egg, which is then fertilized by sperm. A blastoid made from stem cells might express genes in the same way as a normal embryo, but it may be missing something crucial that normally comes from an egg,

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says Martinez Arias.

There's also a chance that the team might have seen more progress if the experiment had been done in more monkeys. After all, of the 484 blastoids that were developing at day seven, only five survived to day 17. And getting an embryo to implant in the uterus is a tricky business, says Chuva de Sousa Lopes. "Even when you do IVF in humans, it's one of the bottlenecks in getting pregnant," she says. "Perhaps if you did this with 100 monkeys, you would have two that would get pregnant further."

Monkey lives are precious, though, says Martinez Arias, and such large experiments would probably not be considered ethical.



### A model embryo

None of this means that the blastoids are not useful. They still provide a good model of what happens in the earliest stages of embryo development in monkeys—and potentially in humans.

Researchers hope that monkey blastoids will help us learn more about human embryos. We know very little about how the union of sperm and egg eventually leads to the development of our organs and nervous system—and why things can sometimes go wrong. Scientists are generally not allowed to study human embryos in a lab beyond 14 days after fertilization. And recently published international guidelines stress that human blastoids should never be implanted into a person or any other animal.

"We want to understand human development, and it is not safe to transfer human blastoids [into people]," says Rivron. "We have to find an alternative. And nonhuman primates are the closest relatives to humans."

Scientists hope that this type of research can tell us more about human pregnancy, including why some people struggle to conceive and why some miscarriages happen. Because scientists could generate infinite numbers of blastoids, they wouldn't need to rely on animals as embryo donors. And they would be able to test drugs on hundreds or thousands of blastoids in the hope of discovering ways to improve IVF, says Naomi Moris, who researches embryo development at the Crick Institute in London.

### Stem-cell babies?

As the technology advances, it's likely that researchers will find ways to use stem cells to create more mature embryos, and potentially fetuses and baby animals. "There seems to be some kind of race to see who is first to get something out of these blastoids," says Martinez Arias.

As things stand, there's no way one of these blastoids could develop into a fetus or, eventually, a baby monkey. But the technology is improving all the time. Research into synthetic embryos has really taken off only in the last five to 10 years, and a huge amount of progress has been made in that time, says Moris.

"We're definitely moving very fast, and developments are being made really, really rapidly in this field," she says. We need to make sure that laws keep pace with developments "to make sure we're not pushing ahead too fast," she says.

"One day, will someone get a monkey from a blastoid? Probably," says Martinez Arias. "But I don't see that happening anytime soon."

**by Jessica Hamzelou**



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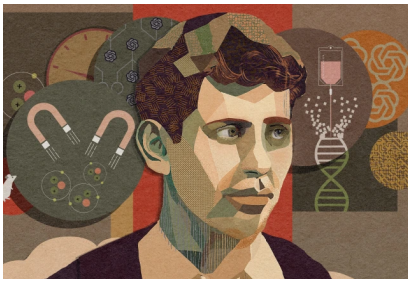

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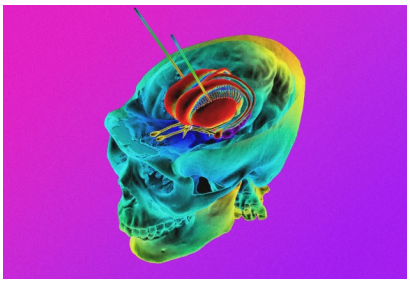

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