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NEWS

24 January 2018

First monkeys cloned with technique that made Dolly the sheep

Chinese scientists create cloned primates that could revolutionize studies of human disease.

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Zhong Zhong, one of the cloned macaque monkeys. Credit: Qiang Sun and Mu-ming Poo, CAS

Biologists in Shanghai, China, have created the first primates cloned with a technique similar to the one used to clone Dolly the sheep and nearly two dozen other species. The method has failed to produce live primates until now.

Researchers hope to use this revised technique to develop populations of genetically identical primates to provide improved animal models of human disorders, such as cancer. The technology, described in *Cell*¹ on 24 January, could also be combined with gene-editing tools such as CRISPR–Cas9 to create genetically engineered primate-brain models of human disorders, including Parkinson’s disease.

“This paper really marks the beginning of a new era for biomedical research,” says Xiong Zhi-Qi, a neuroscientist who studies brain disease at the Chinese Academy of Sciences Institute of Neuroscience (ION) in Shanghai. He was not involved in the cloning project.

But the achievement is also likely to raise some concerns among scientists and the public that the technique might be used to create cloned humans. “Technically, there is no barrier to human cloning,” says ION director Mu-Ming Poo, who is a co-author of the study. But ION is interested only in making cloned non-human primates for research groups, says Poo: “We want to produce genetically identical monkeys. That is our only purpose.”

Primates have proved tricky to copy, despite many attempts using the standard cloning technique. In that method, the DNA of a donor cell is injected into an egg that has had its own genetic material removed.

ION researchers Sun Qiang and Liu Zhen combined several techniques developed by other groups to optimize the procedure. One trick was to undo chemical modifications in the DNA that occur when embryonic cells turn into specialized cells. The researchers had more success with DNA from fetal cells, rather than cells from live offspring.

Using fetal cells, they created 109 cloned embryos, and implanted nearly three-quarters of them into 21 surrogate monkeys. This resulted in six pregnancies. Two long-tailed macaques (*Macaca fascicularis*) survived birth: Zhong Zhong,

now eight weeks old, and Hua Hua, six weeks. Poo says that the pair seem healthy so far. The institute is now awaiting the birth of another six clones.

Cloning specialist Shoukhrat Mitalipov of the Oregon Health and Science University in Portland says that the Chinese team should be congratulated. “I know how hard it is,” says Mitalipov, who estimates he used more than 15,000 monkey eggs in cloning attempts in the 2000s. Although he was able to produce stem-cell lines from cloned human and monkey embryos, his team’s primate pregnancies never resulted in a live birth.

Cloned animals offer some significant advantages over non-clones as models for studying human disease. In experiments with non-cloned animals, it is difficult to know whether differences between the test and control groups were caused by the treatment or genetic variation, says Terry Sejnowski, a computational neurobiologist at the Salk Institute for Biological Studies in La Jolla, California. “Working with cloned animals greatly reduces the variability of the genetic background, so fewer animals are needed,” he says.

Parkinson’s studies

Sejnowski also says that primate brains are the best model for studying human mental disorders and degenerative diseases. The ability to clone monkeys might revive primate studies, which have declined in most countries, says Poo. Parkinson’s disease experiments that currently use hundreds of monkeys could be done with just ten clones, he says.

Neuroscientist Chang Hung-Chun, also at ION, says that primate-cloning technology will soon be combined with gene-editing tools to study human genetic disorders in primate brains. Gene editing is already used on developing monkey embryos, but that leaves open the possibility that some cells are not edited, which then affects the results, says Chang.

With cloning, the donor cell can be edited before it is injected into the egg. Within a year, Poo expects the birth of cloned monkeys whose cells have been genetically edited to model circadian-rhythm disorders and Parkinson’s disease.

Spurred by the promise of primate research, the city of Shanghai is planning major funding for an International Primate Research Center, expected to be formally announced in the next few months. The centre will produce clones for scientists around the globe. “This will be the CERN of primate neurobiology,” Poo says. There’s already high demand from pharmaceutical companies that want to use cloned monkeys to test drugs, he says.

Although most reproductive biologists are unlikely to consider using the technique to clone humans because of ethical objections, Mitalipov worries that it might be attempted in a private clinic.

China has guidelines that prohibit reproductive cloning, but no strict laws. It also has a weak record of enforcement of its rules on the use of stem cells for therapy. Some other countries — notably the United States — do not prohibit reproductive cloning at all. “Only regulation can stop it now,” says Poo. “Society has to pay more attention to this.”

Nature **553**, 387–388

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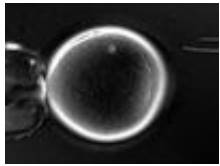
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