QIANG SUN/MU-MING POO/CAS

A baby long-tailed macaque, named Zhong Zhong, is one of the first cloned monkeys.

GENETICS

Monkeys cloned in China

Genetically identical animals promise improved models of human disease, but raise concerns about reproductive cloning of humans.

BY DAVID CYRANOSKI

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* on 24 January (Z. Liu *et al. Cell* http://dx.doi.org/10.1016/j.cell.2018.01.020; 2018), 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." ■

GERMANY

Incoming government set to splurge on science

German spending may reach 3.5% of gross domestic product.

BY QUIRIN SCHIERMEIER

German politicians seem close to agreeing on a coalition government that would further boost federal funds for research — cementing the country's status as one of the world's biggest science spenders.

Political negotiations have been ongoing for four months since an inconclusive general election last September. In that election, Chancellor Angela Merkel's centre-right Christian Democratic Union (CDU) gained the largest share of seats but no outright majority, and the Social Democratic party (SPD) — Merkel's coalition partner in the last government — came second, and vowed to oppose the CDU rather than support it in government. After talks between the CDU and smaller parties broke down, the SPD voted on 21 January to seek to enter a coalition government again.

The parties have already set out the cornerstones of their coalition agreement in a paper leaked to the press on 12 January. These include injecting at least an extra €2 billion (US$2.5 billion) of federal spending into Germany's science system over the coming years, in a bid to increase the country's overall research spending from just under 3% of gross domestic expenditure to 3.5% by 2025. This would bring Germany into third place globally on the proportion spent on research and development, behind only Israel and South Korea. However, the German goal relies on contributions from the nation's 16 state governments and industry to increase spending, as well as the federal government.

During Merkel's 12-year chancellorship, federal science spending has almost doubled. Moreover, an agreement in 2005 between the federal government and state governments guaranteed annual budget increases of at least 3% to the country's main science organizations — including the Max Planck Society, the Helmholtz Association of German Research Centres and the German Research Foundation (DFG), Germany's main grant-giving agency for university research.

"All the indications are that research support remains a top government priority in many fields," says Otmar Wiestler, president of the Helmholtz Association in Berlin. "That's very encouraging. Planning security is a prerequisite for us to be able to develop strategic research activities in key areas, such as mobility, climate change, energy supply, personal medicine and information technology."

However, low public acceptance of genetic engineering in plants and the use of genetically modified organisms in agriculture remains a concern, says Jörg Hacker, president of the Leopoldina, Germany's National Academy of Sciences in Halle. "Germany needs a bioscience agenda," he says. "A technology-friendly society should be open to the potential of advances such as CRISPR–Cas technology."

The coalition partners promised to improve funding opportunities for basic research into pressing societal challenges, including energy, health, mobility and security. Details have yet to be announced, but many scientists hope that the government might create a federal funding agency for blue-skies research.

The parties have also already set out plans to increase wind and solar energy capacity by about 10% by 2020. Germany currently meets about one-third of its electricity demand from wind, solar, hydro and biomass sources. However, it is currently expected to miss its goal of reducing carbon dioxide emissions by 40% relative to 1990 levels by 2020. Coalition partners have said that they will strive to produce at least 65% of Germany's power generation with renewable energy sources by 2030 — twice current levels — and they have announced a legislative initiative to make Germany's climate and energy targets legally binding. ■