NEWS IN FOCUS

INSTITUTE OF NEUROSCIENCE, CHINESE ACADEMY OF SCIENCES

These cloned macaque monkeys share a mutation that disrupts their sleep cycle.

CHINA

Gene-edited monkey clones stir excitement and debate

Genetically identical primates offer the best models of human disease, but raise ethical issues.

BY DAVID CYRANOSKI

Researchers interested in unravelling the mechanisms of complex human disorders, such as Alzheimer's disease, could soon visit China to access cloned monkeys with genomes that have been edited to display these conditions.

On 24 January, scientists at the Institute of Neuroscience (ION) in Shanghai reported that they had used gene editing to disable a gene in macaque monkeys (*Macaca fascicularis*) that is crucial to their sleep–wake cycle. The scientists then cloned one of those monkeys to produce five primates with almost identical genes (P. Qiu *et al. Natl Sci. Rev.* **6**, nwz002; 2019 and Z. Liu *et al. Natl Sci. Rev.* **6**, nwz003; 2019).

It is the first time that researchers have cloned a gene-edited monkey, and proof of principle for the researchers' plan to create populations of genetically identical primates that they say will revolutionize research.

Some of the researchers are part of the new International Centre for Primate Brain Research, which is funded by the Chinese government and wants to create such populations.

Monkey models of diseases such as sickle-cell anaemia and cystic fibrosis "would be incredibly helpful to allow humanity to treat or cure these illnesses", says Mitchell Lazar, who studies metabolic disease at the University of Pennsylvania in Philadelphia.

Primates are also the best animal model for studying higher cognitive functions and brain disorders in humans, says neuroscientist Mu-ming Poo, the ION's director ▶

and co-founder of the 720-million-yuan (US$106-million) centre. His group was the first to clone primates, two identical macaque monkeys, last year. Other groups have edited the genomes of monkeys to create models of diseases, such as Huntington's disease and immune disorders.

But primates are expensive, and many people object to their use in research. The advantage of creating cloned monkeys is that it reduces the number of animals needed for certain types of experiment, such as testing whether a drug works, says Poo. Researchers typically need large numbers of animals to determine whether the effects they see are because of the drug or due to genetic variation between the animals. By using genetically identical animals, such uncertainty can be eliminated, reducing the number of animals required, he says.

Poo is planning to first create models of brain diseases, such as Alzheimer's disease and Parkinson's disease, followed, over the next few years, by primate models of metabolic and immune-deficiency disorders and cancer that scientists could use in research in China.

In Europe and the United States, research using non-human primates increasingly faces regulatory hurdles, high costs and bioethical opposition. This stands in contrast to Chinese research; the country's 2011 five-year plan set primate disease models as a national goal, and in 2014, the science ministry invested 25 million yuan in the endeavour.

But the process of cloning monkeys is inefficient and expensive. To create the 5 cloned macaques, the team started with 325 cloned gene-edited embryos, which it implanted into 65 surrogate monkeys. The process cost about $500,000, estimates Poo.

The team used the standard cloning technique: DNA from a donor cell — in this case taken from an adult monkey with an edited genome — is injected into an egg that has had its own genetic material removed. The DNA reprograms into an embryonic state, allowing specialized cells to form.

"Monkey models would be incredibly helpful to allow humanity to treat or cure these illnesses."

Poo's team is the first to clone primates using DNA from adult cells. The two macaques the group cloned last year came from fetal DNA. The success with adult DNA means that the group can check whether gene edits made to an embryo produce desirable traits in an adult monkey before scientists clone it.

That monkeys can be cloned from other living monkeys is an exciting proof of principle, says reproductive biologist Shoukhrat Mitalipov, from the Oregon Health and Sciences University in Portland. Mitalipov expects that the costs of cloning primates will come down, and that the animals will probably be a good model for researchers to study genetic diseases.

But some scientists think that experiments using monkeys should be a last resort because of the animals' high levels of cognition. Lazar says that some experiments — for example, research into the genes behind human diseases — "are equally appropriate scientifically" in mice. Research in mice is also cheaper and more accepted by the public. Lazar worries that if scientists have ready access to gene-edited monkeys, they might use them for experiments that are conventionally done in rodents. Poo says that mice are not a good substitute for studying higher cognitive functions and brain disorders in humans. The ION follows strict international guidelines for animal research, he says.

Poo's team will continue to study the effect of gene editing on the five cloned macaques. The group disabled *BMAL1*, a gene that helps to maintain circadian rhythm, the internal clock that facilitates a healthy sleep–wake cycle, and found that the monkeys moved more at night and slept less overall, signs of circadian-rhythm disorders.

The research was published in *National Science Review*, for which Poo is executive editor-in-chief. Poo says he did this because the journal needs publicity. But he says the papers were reviewed by international experts and he was not involved in their processing. ■

PARTNERSHIPS

Berkeley bans new research funding from Huawei

Moratorium comes after United States charges Chinese firm with stealing trade secrets.

BY ELIZABETH GIBNEY

The University of California, Berkeley, will not enter into new research collaborations with the Chinese telecommunications firm Huawei, after the US Department of Justice brought criminal charges against the company on 28 January.

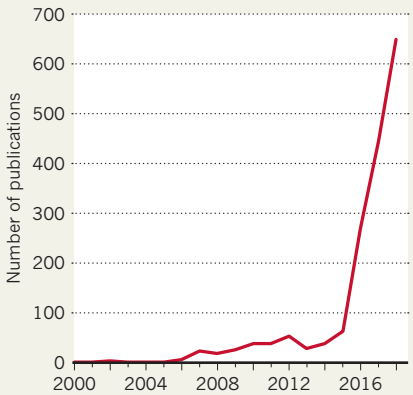
The University of Texas at Austin has also confirmed to *Nature* that it is reviewing its relationship with the company — which is a major investor in research worldwide.

The move comes two weeks after the University of Oxford, UK, said that it would stop seeking new funding from the firm, citing "public concerns raised in recent months surrounding UK partnerships".

Since late 2018, Huawei — a major electronics manufacturer headquartered in Shenzhen — has been under mounting scrutiny from international governments. Several countries have raised security concerns over its devices and over the company's involvement in developing their telecommunications networks.

HUAWEI-FUNDED RESEARCH

Scholarly articles and conference papers acknowledging the Chinese firm Huawei as a funding source shot up in 2016.



SOURCE: SCOPUS

The US charges against Huawei include theft of trade secrets, violations of economic sanctions, wire fraud and obstruction of justice.

In a statement published on its website, Huawei said it was "disappointed" to learn of the indictments, which includes individual charges against the firm's chief financial officer, Wanzhou Meng.

It added: "The Company denies that it or its subsidiary or affiliate have committed any of the asserted violations of U.S. law set forth in each of the indictments, is not aware of any wrongdoing by Ms. Meng, and believes the