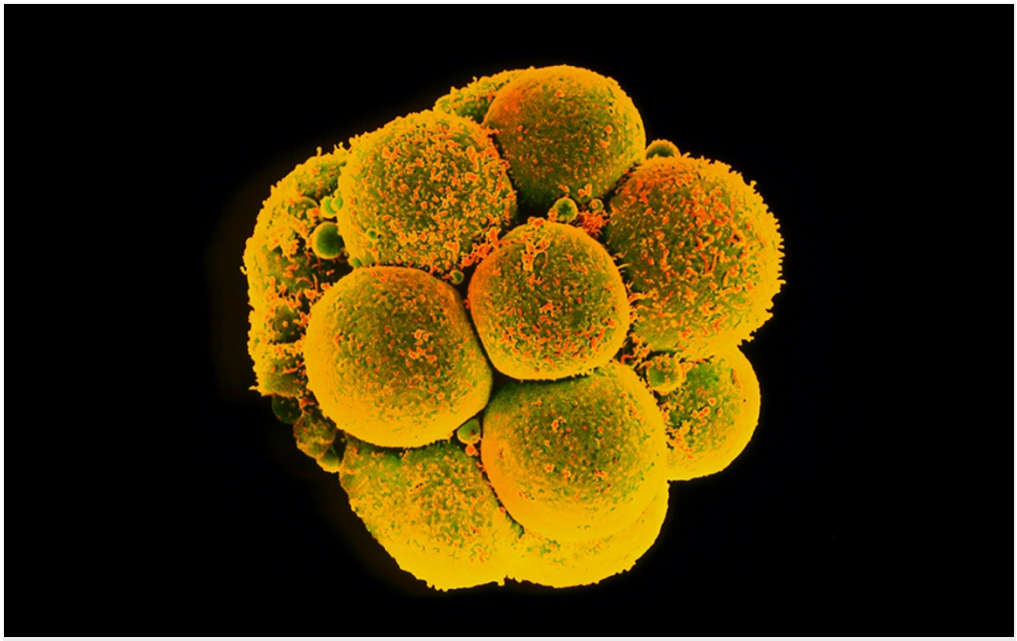
NATURE | NEWS

Second Chinese team reports gene editing in human embryos

Study used CRISPR technology to introduce HIV-resistance mutation into embryos.

Ewen Callaway

08 April 2016



Yorgos Nikas/SPL

Early-stage human embryos have been edited by scientists.

Researchers in China have reported editing the genes of human embryos to try to make them resistant to HIV infection. Their paper[1] — which used CRISPR-editing tools in non-viable embryos that were destroyed after three days — is only the second published claim of gene editing in human embryos.

In April 2015, a different China-based team announced that they had modified a gene linked to a blood disease in human embryos (which were also not viable, and so could not have resulted in a live birth)[2]. That report — a world first — fuelled global deliberations over the ethics of modifying embryos and human reproductive cells, and led to calls for a moratorium on even such proof-of-principle research.

Where in the world could the first CRISPR baby be born?

At the time, rumours swirled that other teams had conducted similar experiments. Sources in China told *Nature*'s news team that a handful of papers had been submitted for publication. The latest paper, which appeared in the *Journal of Assisted Reproduction and Genetics* on 6 April, might be one of these. *Nature*'s news team has asked the paper's corresponding author, stem-cell scientist Yong Fan, for comment, but had not heard from him by the time of this report.

HIV resistance

In the paper, Fan, who works at Guangzhou Medical University in China, and his team say that they collected a total of 213 fertilized human eggs between April and September 2014. The fertilized eggs, donated by 87 patients, were unsuitable for implantation as part of *in vitro* fertility therapy, because they contained an extra set of chromosomes.

Fan's team used CRISPR–Cas9 genome editing to introduce into some of the embryos a mutation that cripples an immune-cell gene called *CCR5*. Some humans naturally carry this mutation (known as *CCR5*Δ32) and they are resistant to HIV, because the mutation alters the CCR5 protein in a way that prevents the virus from entering the T cells it tries to infect.

Genetic analysis showed that 4 of 26 human embryos targeted were successfully modified. But not all the embryos' chromosomes harboured the *CCR5*Δ32 mutation — some contained unmodified *CCR5*, whereas others had acquired different mutations.

George Daley, a stem-cell biologist at Children's Hospital Boston in Massachusetts, says that the paper's main advance is the use of CRISPR to introduce a precise genetic modification successfully. "This paper doesn't look like it offers much more than anecdotal evidence that it works in human embryos, which we already knew," he says. "It's certainly a long way from realizing the intended potential" — a human embryo with all its copies of *CCR5* inactivated.

CRISPR: gene editing is just the beginning

"It just emphasizes that there are still a lot of technical difficulties to doing precision editing in human embryo cells," says Xiao-Jiang Li, a neuroscientist at Emory University in Atlanta, Georgia. He thinks that researchers should work out these kinks in non-human primates, for example, before continuing to modify the genomes of human embryos using techniques such as CRISPR.

Ethics of experiments

Tetsuya Ishii, a bioethicist at Hokkaido University in Sapporo, Japan, sees no problem with how the experiments were conducted — a local ethics committee approved them, and the egg donors gave their informed consent — but he questions their necessity. "Introducing *CCR5*Δ32 and trying repair, even in non-viable embryos, is just playing with human embryos," Ishii says.

Fan's team writes in the paper that proof-of-principle experiments for human-embryo editing such as theirs are important to conduct while the ethical and legal issues of germline modification are being hashed out. "We believe that any attempt to generate genetically modified humans through the modification of early embryos needs to be strictly prohibited until we can resolve both ethical and scientific issues," they write.

Don't edit the human germ line

Daley sees a stark contrast between Fan's work and research approved in February by UK fertility regulators that will allow CRISPR genome editing of human embryos. Those experiments, led by developmental biologist Kathy Niakan at the Francis Crick Institute in London, will inactivate genes involved in very early embryo development, in hopes of understanding why some pregnancies terminate. (The work will be done in viable embryos, but the researchers' licence requires that experiments be stopped within 14 days.)

Earlier this year, developmental biologist Robin Lovell-Badge, also at the Francis Crick Institute, told *Nature* that he thought that the carefully considered UK approval might embolden other researchers who are interested in pursuing embryo-editing research. "If they've been doing it in China, we may see several manuscripts begin to appear," he said.

Whereas Niakan's work is answering questions intrinsic to embryology, Fan's work is establishing proof of principle for what would need to be done to generate an individual with resistance to HIV, Daley adds. "That means the science is going forward before there's been the general consensus after deliberation that such an approach is medically warranted," he says.

Nature | doi:10.1038/nature.2016.19718

References

1. Kang, X. *et al. J. Assist. Reprod. Genet.* http://dx.doi.org/10.1007/s10815-016-0710-8 (2016).
2. Liang, P. *et al. Protein Cell* **6**, 363–372 (2015).