Precise gene editing in monkeys paves the way for valuable human disease models

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Researchers achieved precise gene modification in monkeys. Credit: *Cell*, Niu et al.

Monkeys are important for modeling diseases because of their close similarities to humans, but past efforts to precisely modify genes in primates have failed. In a study published by Cell Press January 30th in the journal *Cell*, researchers achieved precise gene modification in monkeys for the first time using an efficient and reliable approach known as the CRISPR/Cas9 system. The study opens promising new avenues for the development of more effective treatments for a range of human diseases.

"Our study shows that the CRISPR/Cas9 system enables simultaneous disruption of two target genes in one step without producing off-target mutations," says study author Jiahao Sha of Nanjing Medical University. "Considering that many human diseases are caused by genetic abnormalities, targeted genetic modification in monkeys is invaluable for the generation of human disease models."

The CRISPR/Cas9 system is a gene editing tool capable of targeting specific DNA sequences in the genome. Cas9 proteins, which are directed by molecules called single-guide RNAs to specific sites in the genome, generate mutations by introducing double-stranded DNA breaks. Until now, the CRISPR/Cas9 system and other targeted gene editing techniques were successfully applied to mammals such as mice and rats, but not to primates.

Sha teamed up with Xingxu Huang of Nanjing University and Weizhi Ji of the Yunnan Key Laboratory of Primate Biomedical Research and Kunming Biomed International. The researchers injected messenger RNA molecules encoding Cas9, in addition to single-guide RNAs designed to target three specific genes, into one-cell-stage embryos of cynomolgus monkeys. After sequencing genomic DNA from 15 embryos, they found that eight of these embryos showed evidence of simultaneous mutations in two of the target genes.

The researchers then transferred genetically modified embryos into surrogate females, one of which gave birth to a set of twins. By sequencing the twins' genomic DNA, they found mutations in two of the target genes. Moreover, the CRISPR/Cas9 system did not produce mutations at genomic sites that were not targeted, suggesting that the tool will not cause undesirable effects when applied to monkeys. "With the precise genomic targeting of the CRISPR/Cas9 system, we expect that many disease models will be generated in monkeys, which will significantly advance the development of therapeutic strategies in biomedical research," Ji says.

More information: *Cell*, Niu et al.: "Generation of gene-modified cynomolgus monkey via Cas9/RNA-

mediated gene targeting in one-cell embryos."
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