Chinese team uses base editing to repair genetic disease in human embryo

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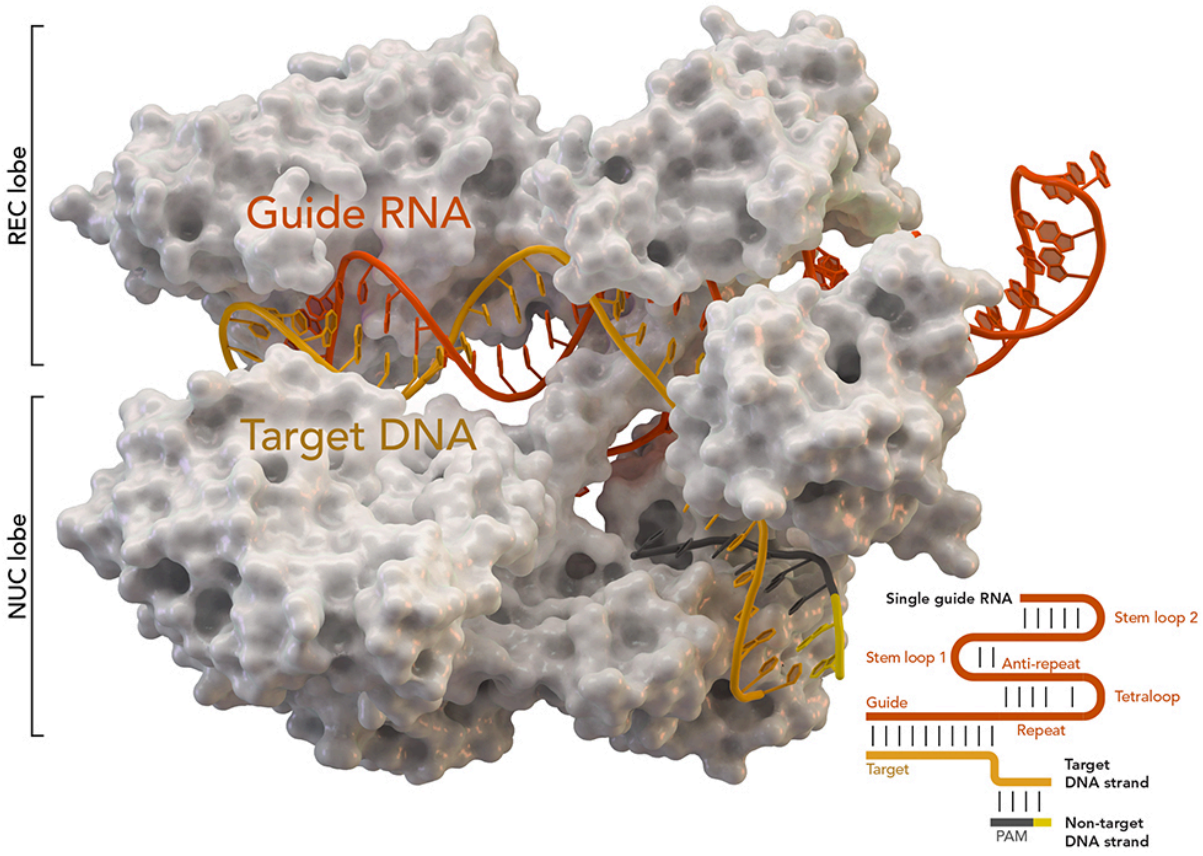

CRISPR-associated protein Cas9 (white) from Staphylococcus aureus based on Protein Database ID 5AXW. Credit: Thomas Splettstoesser (Wikipedia, CC BY-SA 4.0)

A team of researchers in China has used a form of the CRISPR gene editing technique to repair a genetic defect in a viable human embryo. In their paper published in the journal *Molecular Therapy*, the group describes their work and how well it worked.

Only three years ago, CRISPR was first used on a human embryo. In that work, a Chinese team attempted to use the technique to repair a genetic fault. Though the work made headlines around the world, it had a low success rate—just four out of 54 embryos that survived the technique carried the repaired genes. Since that time, a new variation of CRISPR has been developed—it is called base editing, and works in a more efficient way. Instead of snipping DNA strands and replacing removed bits with desired traits, the new method does nothing more than swap DNA letters—trading out an A for a G, for example. In this new effort, the researchers used this new method to correct a gene mutation that results in humans having a condition called Marfan syndrome, in which people have an A instead of a G in the FBN1 gene. It is a disorder that causes problems with connective tissue, leading to a myriad of problems for those born with it.

The new research is unique in that the scientists used viable embryos created using in vitro fertilization. The team could have implanted these viable gene-edited embryos into a woman's uterus, had they chosen to do so.

The researchers report that they conducted the procedure on 18 embryos, and in all of them, the intended letters were swapped as planned. However, in two instances, other letters were swapped unintentionally, as well. They claim their work provided proof of concept for the technique—in a real-world IVF clinic, the defective embryos would have been found and discarded. They do acknowledge, however, that the field is still very new, and that a lot more work is required before attempts are made to use such techniques in embryos

that are allowed to develop into fetuses.

More information: Yanting Zeng et al. Correction of the Marfan Syndrome Pathogenic FBN1 Mutation by Base Editing in Human Cells and Heterozygous Embryos, *Molecular Therapy* (2018). DOI: 10.1016/j.ymthe.2018.08.007

Abstract

There are urgent demands for efficient treatment of heritable genetic diseases. The base editing technology has displayed its efficiency and precision in base substitution in human embryos, providing a potential early-stage treatment for genetic diseases. Taking advantage of this technology, we corrected a Marfan syndrome pathogenic mutation, $FBN1^{T7498C}$. We first tested the feasibility in mutant cells, then successfully achieved genetic correction in heterozygous human embryos. The results showed that the BE3 mediated perfect correction at the efficiency of about 89%. Importantly, no off-target and indels were detected in any tested sites in samples by high-throughput deep sequencing combined with whole-genome sequencing analysis. Our study therefore suggests the efficiency and genetic safety of correcting a Marfan syndrome (MFS) pathogenic mutation in embryos by base editing.