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WHAT IS GENOME EDITING?

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There Are Four Different Types Of Nucleotide Possible In A Dna Sequence: Adenine, Cytosine, Guanine And Thymine Symbolized With A, C, G And T. The Order Of These Nucleic Acids Form The Genetic Code.

What is it?

In a first, researchers from the Oregon Health and Science University along with colleagues in California, China and South Korea repaired a mutation in human embryos by using a gene-editing tool called CRISPR-Cas9.

The mutation seen in the MYBPC3 gene causes a common heart condition called hypertrophic cardiomyopathy, which is marked by thickening of the heart muscle.

The mutation is seen in about one in 500 people and can lead to sudden death later in life. It is an inherited cardiac disease and the presence of even one copy of the gene can cause symptoms, which usually manifest as heart failure. Correcting the mutation in the embryo ensures that the child is born healthy and the defective gene is not passed on to future generations. There is currently no cure for the condition.

How did it come about?

CRISPR-Cas9 is a system used by bacterial cells to recognise and destroy viral DNA as a form of adaptive immunity. Using components of the CRISPR system, researchers can remove, add or alter specific DNA sequences in the genome of higher organisms.

The gene editing tool has two components — a single-guide RNA (sgRNA) that contains a sequence that can bind to DNA, and the Cas9 enzyme which acts as a molecular scissor that can cleave DNA. The genetic sequence of the sgRNA matches the target sequence of the DNA that has to be edited. In order to selectively edit a desired sequence in DNA, the sgRNA is designed to find and bind to the target.

Upon finding its target, the Cas9 enzyme swings into an active form that cuts both strands of the target DNA. One of the two main DNA-repair pathways in the cell then gets activated to repair the double-stranded breaks. While one of the repair mechanisms result in changes to the DNA sequence, the other is more suitable for introducing specific sequences to enable tailored repair. In theory, the guide RNA will only bind to the target sequence and no other regions of the genome.

But the CRISPR-Cas9 system can also recognise and cleave different regions of the genome than the one that was intended to be edited. These “off-target” changes are very likely to take place when the gene-editing tool binds to DNA sequences that are very similar to the target one. Though many studies have found few unwanted changes suggesting that the tool is probably safe, researchers are working on safer alternatives.

Why does it matter?

Along with sperm from a man with hypertrophic cardiomyopathy, the gene-editing tool was also introduced into eggs from 12 healthy women before fertilisation. In normal conditions, a piece of

DNA with the correct sequence serves as a template for the repair to work, although the efficiency can be significantly low. Instead of the repair template that was provided by the researchers, the cells used the healthy copy of the DNA from the egg as a template. This came as a big surprise.

Normally, if sperm from a father with one mutant copy of the gene is fertilized in vitro with normal eggs, 50% of the embryos would inherit the condition. When the gene-editing tool was used, 42 out of the 58 embryos did not carry the mutation. The remaining 16 embryos had unwanted additions or deletions of DNA.

Thus the probability of inheriting the healthy gene increased from 50 to 72.4%. There was no off-target snipping of the DNA. According to Nature, “the edited embryos developed similarly to the control embryos, with 50% reaching an early stage of development (blastocyst). This indicates that editing does not block development.”

What next?

Clinical trials are under way in China and in the U.S. to use this tool for treating cancer. In May this year, it was shown in mice that it is possible to shut down HIV-1 replication and even eliminate the virus from infected cells. In agriculture, a new breed of crops that are gene-edited will become commercially available in a few years. In February this year, the National Academy of Sciences (NAS) and the National Academy of Medicine said scientific advances make gene editing in human reproductive cells “a realistic possibility that deserves serious consideration.”

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