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Hope of safer cure for genetic diseases

Tom Whipple Science Editor

Diseases such as muscular dystrophy, kidney failure and diabetes could be treated more gently after scientists developed a tool that "switches on" genes rather than cutting them.

In the past decade, genetics research has been revolutionised by a technique called Crispr Cas9 that uses a molecule to find a specific stretch of DNA. It then harnesses an enzyme to snip it and so delete or edit it.

The powerful technology poses serious safety concerns if used in humans because of the potential for it to go wrong. Many researchers are wary of cutting DNA because they could accidentally target the wrong bit.

American researchers, however, say they have found an alternative by modifying the Crispr Cas9 system. They describe a safer approach in a paper in the journal *Cell*.

"Cutting DNA opens the door to introducing new mutations," Juan Carlos Izpisua Belmonte, from the Salk Institute for Biological Studies, said. "That is something that is going to stay with us with Crispr or any other tool we develop that cuts DNA. It is a major bottleneck in the field of genetics — the possibility that the cell, after the DNA is cut, may introduce harmful mistakes."

Professor Belmonte and his colleagues use the same molecule to guide the enzyme to the target bit of DNA. Rather than cut it, though, they boosted it. They argued that this meant that they could amplify the signal from genes that combat diseases.

To test the theory, they used mice genetically modified to suffer from diabetes, kidney failure and muscular dystrophy. They then tried to reverse the progress of the diseases by activating genes to mitigate the effects.

It worked. They boosted insulin production, the mice's kidneys improved, and those with muscular dystrophy saw muscle growth.

"We are not fixing the gene; the mutation is still there," the professor said. This means it is not a cure, in the way that true gene editing would be. He said, however, that it was sufficient to harness the power already dormant in the genome to reverse the symptoms.

Other scientists welcomed the research. Helen Claire O'Neill, from University College London, said that the research was exciting. "This paper clearly shows the potential therapeutic viability of this technology in human disease models," she said.

Alena Pance, from the Wellcome Sanger Institute, said that more work was needed to make sure it was safe.

"These results bring hope for a targeted gene therapy and widen the application of the technology," she said.

"But it is a proof of principle where follow-up of longer term effects . . . are not examined. These issues would need to be investigated in depth before any application in humans is considered."