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# Unexpected outcomes sound warning for treatment of genetic diseases using gene editing in embryos

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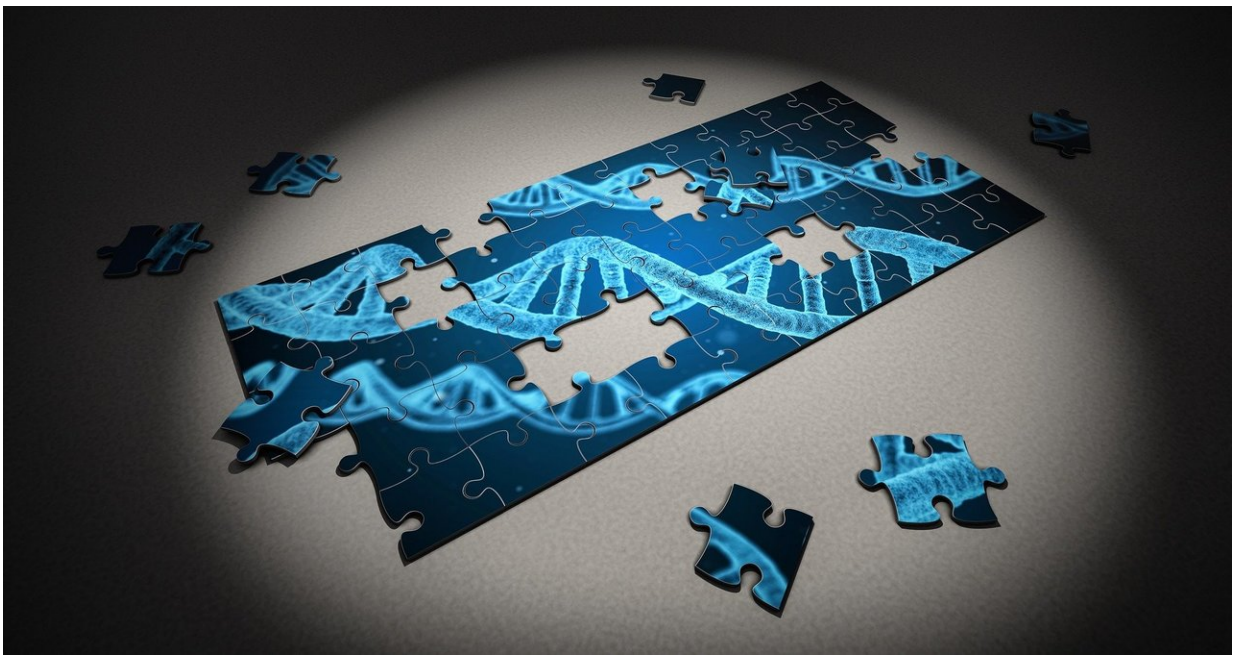

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New research led by the South Australian Health and Medical Research Institute (SAHMRI) and the University of Adelaide has uncovered a significant hurdle for realising the potential benefits of gene editing in embryos.

The team, led by Professor Paul Thomas, investigated North American research published last year that seemed to demonstrate that gene editing in human embryos was highly effective in repairing a defective gene in a majority of the embryos.

Professor Thomas says their research provides an alternative explanation for the apparent gene correction, demonstrating that rather than the gene editing technology fixing small errors, much larger errors were being created.

"Gene editing technology is still relatively new, and part of this field of research includes understanding the flaws, which will ultimately allow us to develop the safest possible therapies for genetic conditions," Professor Thomas said.

Professor Thomas and the research paper's first author, Dr. Fatwa Adikusuma, replicated the North American study with preclinical animal models. Australia has strict legislation restricting gene editing in human embryos.

"We looked beyond the small deletions, exploring larger areas of DNA," Dr. Adikusuma said.

"When we searched a wider area, we found that repair of the DNA break generated by 'molecular scissors' resulted in deletion of large stretches of DNA."

The molecular scissors, or CRISPR-Cas9 as they are scientifically known, are a tool utilised by scientists to cut specific regions of a cell's genetic material (DNA). Repair of the cut can alter the target DNA sequence, resulting in a specific change or "edit". Faulty genes can theoretically be repaired by cutting them using CRISPR scissors. However, as Professor Thomas and his colleagues have shown, DNA can

sometimes be lost during the repair process, resulting in large deletions that would not restore function to the faulty gene.

"CRISPR-Cas9 technology is very exciting, with researchers already using it to cure muscular dystrophy in mice, and a number of clinical trials are underway to test gene editing therapies for several cancers as well as blood diseases," Professor Thomas said.

"Understanding the fundamental mechanisms by which these tools work are important advancements for research and for clinical translation to treat a host of genetic diseases."

The research findings were published online today in the British multidisciplinary science journal *Nature*.

**More information:** Fatwa Adikusuma et al. Large deletions induced by Cas9 cleavage, *Nature* (2018). DOI: 10.1038/s41586-018-0380-z

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