

Here I list ten ethical principles that He violated through his interviews, website, meeting presentation and the accompanying news reports in China and the United States that featured him.

A first problem is that He's work is a violation of an international consensus on if, whether, or when the editing of human embryos should be permitted. At the First International Summit on Human Gene Editing in 2015 in Washington, DC, the organizing committee released a statement¹ that it would be "irresponsible to proceed with any clinical use of germline editing unless and until (i) the relevant safety and efficacy issues have been resolved, based on appropriate understanding and balancing of risks, potential benefits, and alternatives, and (ii) there is a broad societal consensus about the appropriateness of the proposed application." Thus far, these conditions have not been met². He has published his own ethical guidelines³ on the justification for his clinical research (some of which he himself has broken).

Second, He has not reported prior studies of CRISPR edits on embryos of mice, primates and humans. There is a void in the scientific literature as to He's prior work on editing embryos. His English language publications (19 in PubMed) list only a single publication involving CRISPR editing.

Third, reporting of off-target effects and highlighting of the risks of gene-editing embryos was insufficient. Off-target and undesirable 'on-target' effects are commonplace with the use of CRISPR-Cas9 and represent the most prevalent risks to an organism. He acknowledged such risks in his public statements but falsely reports that he has determined how to eliminate them or interpret them as irrelevant to the functioning organism.

Fourth, He failed to gather sufficient information and follow scientific consensus on the minimal risks that would make gene-editing of embryos permissible. No references are given in He's writings, website or public statements on the consensus or lack thereof that there are

minimal risks in undertaking gene editing of embryos at the current state of knowledge.

Fifth, He did not comply with the national ethical guidelines in China for embryo research. In 2003, China issued guidance to IVF clinics that prohibits the implantation of embryos used in research. He's clinical trial was removed from China's Clinical Trial Registry for not providing data on safety and validity of his work.

Sixth, He failed to work within the ethical framework of his own university. The Southern University of Science and Technology disassociated itself from He's clinical trials and did not give ethical approval for his embryo-editing experiments.

Seventh, enhancement—widely acknowledged as the most ethically problematic frontier of germline gene editing—took precedence in He's experiments over curing a life-threatening disease. All evaluations of human germline gene modification agree that, if there is ever to be a justification for such experiments on human beings, they should focus on curing a life-threatening or debilitating disease for which there is no alternative therapy⁴. He rationalized his experiments as potentially protective against HIV infection, which can be prevented in ways other than embryo gene editing.

Eighth, He engaged in undue inducement of parents. Ethical guidelines on recruiting people into clinical trials recognize the problem of extravagant inducements. He communicated to prospective parents that his trial would cover IVF payments, supportive care and a daily allowance. The amount adds up to about \$40,000, which can be considered a sufficiently high inducement that it would cloud the parents judgment in making a reasoned decision about risks and benefits⁵.

Ninth, He was at fault for not providing an acceptable informed consent document. The informed consent form that he submitted to his research subjects was a 23-page document. It contained many technical terms, had no discussion about the meaning and significance of off-target effects or undesirable on-target

changes on the child, and protected his team from responsibility for unforeseen risks. It also failed to inform the parents of alternative methods of preventing HIV infection. There was no evidence that the university or a government ethics body reviewed and approved the informed consent form.

Finally, He did not inform parents in the trial of his conflicts of interest. He has roles in several companies in Guangdong Province and Beijing as an active board member or investor⁶. Such involvement requires disclosure for an individual participating as principal investigator in a clinical trial. There were no such disclosures in the informed consent form.

On the basis of the above, I contend that the ethical infractions in this work are among the most egregious that have been recorded in modern medical history since the Second World War. There is every reason for researchers across the world to be embarrassed and for the scientific community to speak of this work as "reckless."

COMPETING INTERESTS

The author declares no competing interests.

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