Brave new dialogue

The development of CRISPR–Cas technology and its applications in biomedical research have generated much excitement. If fully realized, this technology has the potential to help treat or prevent severe diseases. However, these tools also carry considerable risk if improperly used. The scientific community must promote constructive dialogue among its members and within society at large to ensure that research on genome editing is conducted responsibly.

Genetic manipulation of human preimplantation embryos for research purposes has been ongoing for only a few years.

In 2015, a group of Chinese researchers led by Junjiu Huang announced that they had used clustered regularly interspaced short palindromic repeats (CRISPR) technology in human tripronuclear zygotes (Liang, P. et al., *Protein & Cell* **6**, 363–372; 2015). Two years later, in the United States, Shoukhrat Mitalipov and colleagues reported that they successfully corrected a pathogenic mutation in human embryos (Ma, H. et al., *Nature* **548**, 413–419; 2017). In another pioneering effort in the United Kingdom, Kathy Niakan's group genetically modified human blastocysts (Fogarty, N. M. E. et al., *Nature* **550**, 67–73; 2017).

However, in November 2018, a report took the scientific community, and indeed the world, by surprise when Jiankui He claimed to have helped generate the first genetically modified human babies.

Nature Genetics was fortunate to be represented at the Second International Summit on Human Genome Editing, where He presented his work. The lecture room was crowded with journalists and tense with anticipation. Although the discussion session was well conducted and informative, He did not adequately address several important questions. There was an immediate call for a formal investigation and for independent corroboration of He's claims.

It is clear that He's research did not have suitable ethical oversight and did not fully ensure the safety of the procedure and the future well-being of the newborn twins. Additionally, the motivation for such an endeavor is poorly justified, because the editing strategy aimed to genetically 'enhance' the babies rather than to modify an existing disease-causing mutation. Scientifically, there are also major concerns, because the mutations may have undesired pleotropic effects, and the existence of off-target genomic alterations remains uncertain.

To date, no peer-reviewed paper has been published reporting He's results.

Indeed, *Nature Genetics* was asked by some Summit participants whether we would review or publish research on human germline genetic editing. We have published several papers on the use and development of CRISPR tools. Any manuscript reporting genetic modification of human embryos or gametes would need to follow strict scientific and ethical guidelines; more details can be found in a recent *Nature* Editorial (*Nature* **557**, 6; 2018). On the basis of the available information, He's research would not have met the editorial criteria adopted by *Nature* journals.

A key outcome of the first International Summit on Human Genome Editing was the recommendation for a global moratorium on human germline editing. A noteworthy criticism that emerged following He's announcement is that the scientific community has failed to respect this self-imposed moratorium and that there is a need to further regulate the use of CRISPR tools and increase societal and legal oversight. To this point, George Daley, a member of the Summit's organizing committee, indicated during his lecture that—even though He's conduct was reprehensible, and germline editing should not be permitted at present—we should remain open to the possibility of future use of CRISPR tools to treat or avoid genetic disorders in cases in which there are no viable alternatives, and the benefits clearly outweigh the risks. Such examples might include highly penetrant rare Mendelian disorders.

Human genome editing is a subject that merits careful and broad discussion across different branches of society. It should include research institutions and learned societies, patient-advocacy groups, ethicists, healthcare providers and scientists (biomedical and social); in addition, moral and religious traditions that differ among nations should be taken into account.

A coordinated worldwide discussion on this topic would be ideal. We should be mindful that, as with 'stem cell tourism', individuals might possibly try to cross borders to seek CRISPR treatments that are unauthorized in their countries of residence. Indeed, global efforts, such as an initiative launched by the World Health Organization, should help to establish international standards for the governance of human genomic editing.

Going forward, even if scientists and physicians are able to ensure minimal medical risk, should society allow human germline editing? And, if so, for what traits or diseases? One could argue that traits and diseases exist in a phenotypic continuum and that, for specific cases, the boundary has shifted over time and across cultures. What some consider an enhancement, others might see as undesirable.

Events such as the Summit on Human Genome Editing provide important forums for the scientific community to grapple with this complex debate, and we look forward to participating in the next meeting.

Germline editing has profound implications for the future of humanity. The ongoing dialogue will therefore need to be a brave one and to include voices from diverse parts of society and the global community. ❐

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