PERSPECTIVE

Embryo editing needs scrutiny

Genome-editing presents many opportunities. But the advent of human-germline editing brings urgency to ethical discussions, says **Jennifer Doudna**.

Modern molecular biology arose in the 1970s when researchers realized that they could use bacterial enzymes, which evolved to defend bacteria against pathogens, to modify DNA in other organisms. That breakthrough initiated an active discussion about the safety and ethics of these 'recombinant DNA' technologies, and highlighted the importance of transparency and open discourse in fostering public trust in the scientific community. Some 40 years later, we have the latest evolution of this technology: CRISPR–Cas9. The system makes genome engineering even easier, and in doing so opens it up to many more stakeholders. This once again raises fundamental questions about appropriate use of a powerful technology, made more urgent by a recent demonstration of human-germline editing. At least one thing is clear at this stage — we do not yet know enough about the capabilities and limits of the new technologies, especially when it comes to creating heritable mutations.

In response to these fundamental ethical questions, the US National Academies of Sciences, Engineering, and Medicine, Britain's Royal Society and the Chinese Academy of Sciences will co-sponsor an international summit in December to consider the scientific and societal implications of genome editing. The issues up for discussion span clinical, agricultural and environmental applications, but most attention will focus on human-germline editing, owing to the potential for this application to eradicate genetic diseases and, ultimately, to alter the course of evolution.

The rapid development and widespread adoption of easy-to-use, inexpensive and effective genome-editing methodologies has changed the landscape of biology. The simplicity of the CRISPR–Cas9 system allows researchers and students to make precise changes to genomes, thereby enabling many experiments that were previously difficult or impossible to conduct. For example, CRISPR–Cas9 can be used to precisely replicate the genetic basis for human diseases in model organisms, leading to unprecedented insights into previously enigmatic disorders. The Cas9 enzyme can also be used to precisely alter epigenetic signatures, providing a means to manipulate the products of transcription without changing the DNA code. Moreover, the technology makes it easier to correct genetic defects in whole animals and in cultured tissues produced from stem cells — strategies that could eventually be used to treat or cure human disease.

When genomic changes are made in fully developed non-reproductive cells, they affect only the treated organism or person and do not become heritable. But if genomic changes are made to germ cells such as those that develop into eggs or sperm, or to developing embryos, the changes are incorporated into the cells of the organism that grows from them — including its own germ cells. Hence the changes can be passed on to future generations. We know that CRISPR–Cas9 technology works in both non-reproductive cells and germ cells, and in both primate and human embryos. The publication of human-embryo editing experiments in May (P. Liang *et al. Protein Cell* **6,** 363–372; 2015) by researchers at Sun Yat-sen University in Guangzhou, China, lends a sense of urgency to December's meeting. Although those experiments were carried out on embryos that could not develop into a baby, the study nonetheless underscored the fact that this is a technology that could have profound implications for permanent alteration of the human genome.

Opinion on the use of human-germline engineering varies widely. Some scientists favour the rapid development of the technology, whereas others advise banning it for the foreseeable future. In my view, a complete ban might prevent research that could lead to future therapies, and it is also impractical given the widespread accessibility and ease of use of CRISPR–Cas9. Instead, solid agreement on an appropriate middle ground is desirable. In addition, future discussions that build on this December's meeting should address other potentially harmful applications of genome editing in non-human systems, such as the alteration of insect DNA to 'drive' certain genes into a population.

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As the public conversations proceed, five specific steps, which should be taken to ensure a prudent path forward, have emerged.

First, safety: the global community of scientists and clinicians needs to adopt standard methods for measuring genome-editing efficiency and off-target effects, so that researchers find it easier to compare and evaluate the results of different experiments for clinical relevance. Second, communication: the December summit should stimulate further forums in which experts from the genome-editing and bioethics communities provide information and education for the public about the scientific, ethical, social and legal implications of human-genome modification. Third, guidelines: there should be international cooperation by policymakers and scientists to determine a shared path forward and to provide clear guidance about what is and is not ethically acceptable research. Fourth, regulation: out of this cooperation, appropriate oversight should be organized and applied to laboratory work that aims to evaluate the efficacy and specificity of genome-editing technologies in the human germ line. And fifth, caution: human-germline editing for the purposes of creating genome-modified humans should not proceed at this time, partly because of the unknown social consequences, but also because the technology and our knowledge of the human genome are simply not ready to do so safely.

The December summit is an important opportunity for China, the United Kingdom and the United States to lead the global discussion, and for the genome-editing community to renew its commitment — which began more than 40 years ago — to wholeheartedly engage with the public. ■

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