Responsible Use of Human Gene-Editing Technologies

Victor J. Dzau[1] and Ralph J. Cicerone[2]

[1]President, National Academy of Medicine; [2]President, National Academy of Sciences.

Over the last 40 years, a remarkable series of technological developments have greatly advanced scientists' ability to manipulate genetic material. Current techniques for genome editing allow for more highly specific and efficient modification of DNA than previous editing tools.[1] Researchers can investigate gene function in various organisms, such as plants, insects, mice, zebrafish, and even human cell lines *in vitro*. In theory, the technology is capable of introducing or correcting single point mutations,[2] regulating transcription,[3] or even epigenetic modifications,[4] and therefore holds great promise for medicine.

One powerful and efficient tool for genome engineering uses the clustered regularly interspaced short palindromic repeat (CRISPR) nuclease Cas9 to cut sequences specified by guide RNA molecules. This technique is in widespread use in research and has already engineered the genomes of more than a dozen species. In April, a Chinese research team[5] reported editing the genomes of human embryos using the CRISPR/Cas9 system. However, there are significant scientific and technical questions about the efficacy and risks of these technologies. The Chinese research team reported that the embryos were "mosaic," meaning that only some cells had the desired changes, and there were a large number of "off-target effects" or mutations in nontargeted genes that were likely to be harmful if the embryos had been viable. Their work also raised significant concerns on the social and ethical aspects of human gene editing, especially on human embryos.

Gene-editing technologies hold great promise for advancing science and improving human health. For instance, the genomes of plants and animals could be modified to boost agriculture and food production, and the technology potentially could be used to edit somatic cells to cure genetic diseases such as sickle cell disease.[6] However, these technologies also raise a number of ethical and social considerations. Of particular concern is the potential to make permanent modifications to human DNA in the nuclei of cells in eggs, sperm, or human embryos that are then passed down to succeeding generations. This is known as human germline editing.

As a result, the National Academy of Sciences and the National Academy of Medicine are launching a major initiative to guide decision making about research involving human gene editing.[7] We have appointed a multidisciplinary advisory group that will help steer our initiative. This fall, we will host an international summit to assemble researchers and other experts to explore the scientific, ethical, and policy issues associated with human gene-editing research. In addition, the academies will convene a multidisciplinary, international committee to undertake an in-depth study to examine the scientific underpinnings; clinical implications; and ethical, legal, and social aspects of the use of current and developing human genome editing technologies in biomedical research and medicine. The study will take a global perspective, and committee members will represent a wide range of expertise from diverse disciplines such as bioethics.

The academies have a history of providing leadership on emerging and controversial technologies. In 1975, the National Academy of Sciences convened the Asilomar conference, a landmark turning point for recombinant DNA research that resulted in guidelines for recombinant DNA research.[8] Our

Correspondence: Victor J. Dzau, National Academy of Medicine, 500 5th Street, NW, Washington, DC 20001. E-mail: vdzau@nas.edu; Ralph J. Cicerone, National Academy of Sciences, 500 5th Street, NW, Washington, DC 20001. E-mail: naspresident@nas.edu

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1988 study on mapping the human genome helped steer what has become an incredible source of new scientific advances.[9] In 2005, we issued guidelines[9] for human embryonic stem cell research, which were widely adopted by research institutions and international scientific societies. In keeping with these efforts, we are prepared to undertake this initiative to provide a comprehensive understanding of human genome editing and its implications.

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REFERENCES

1. Esvelt K, Wang H. Genome-scale engineering for systems and synthetic biology. Mol Syst Biol 2013; 9:641.
2. Inui M, et al. Rapid generation of mouse models with defined point mutations by the CRISPR/Cas9 system. Sci Rep 2014;4:5396.
3. Gilbert LA, Larson MH, Morsut L, et al. CRISPR-mediated modular RNA-guided regulation of transcription in eukaryotes. Cell 2013;154:442–451.
4. Hilton I, et al. Epigenome editing by a CRISPR-Cas9-based acetyltransferase activates genes from promoters and enhancers. Nat Biotechnol 2015;33:510–517.
5. Liang P, Xu Y, Zhang X, et al. CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes. Protein Cell 2015;6:363–372.
6. Zou J, Mali P, Huang X, Dowey S, Cheng L. Site-specific gene correction of a point mutation in human iPS cells derived from an adult patient with sickle cell disease. Blood 2011;118:4599–4608.
7. Institute of Medicine of the National Academies. Announcement: National Academy of Sciences and National Academy of Medicine announce initiative of human gene editing. www.iom.edu/Global/News%20Announcements/NAS-NAM-Human-Gene-Editing.aspx (accessed on June 19, 2015)
8. Berg P, Baltimore D, Brenner S, et al. Summary statement of the Asilomar Conference on recombinant DNA molecules. *Proc. Nat. Acad. Sci.* 1975;72:1981–1984.
9. National Research Council. *Mapping and Sequencing the Human Genome*. The National Academies Press, Washington, DC. 1988.
10. Institute of Medicine and National Research Council. *Guidelines for Human Embryonic Stem Cell Research*. The National Academies Press, Washington, DC. 2005.