

Conclusions of the NAS Committee on Human Gene Editing: reflections of a committee member

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Genome editing is a new tool for making precise alterations to an organism's genetic material. Recent scientific advances have led to the advent of CRISPR-Cas9, a more efficient, precise, and flexible method. This new technique has, quite normally, provoked a flurry of interest from around the world regarding the possible ways in which genome editing could improve human health. It has also sparked controversy over the ethical issues that are inherent to the act of editing the human genome.

As a response to the global reaction of the discovery and use of CRISPR-Cas9, the US National Academy of Sciences, Engineering, and Medicine, the Chinese Academy of Sciences and the UK's Royal Society organized an international summit to address both the scientific pertinence of CRISPR-Cas9 and more especially the ethical and moral issues this technique engenders. Indeed, the rapidity with which this technology developed and was then applied has led many associations, policymakers and stakeholders to express deep concern about whether or not appropriate systems are in place to frame these technologies, and if not what new forms of regulation are required, and especially how the public should be engaged in making these decisions.¹

One of the conclusions of the "International Summit on Human Gene Editing" was to launch an independent working committee whose mission was to produce a comprehensive study of the scientific underpinnings of human gene-editing technologies, their potential use in biomedical research and medicine – including human germline editing – and the clinical, ethical, legal, and social implications of their use.²

Hence began a year-long encounter of our multidisciplinary working committee (8 social scientists, one patient's group director whose group represents several genetic diseases³ and 12 'hard' scientists). Our objective was to respond to the Statement of Task through our own independent and in-depth review of the science and policies of human gene editing by reviewing the literature and holding data-gathering meetings in the U.S. and abroad to solicit extensive input from re-

searchers, clinicians, policymakers, and the public. We also constantly kept abreast of the latest scientific achievements in this rapidly developing field.

Not only was there the desire from the outset to include experts from different disciplines, the group was also made up of people from several countries around the world: China, France, Egypt, to name but a few. In addition, it was important from the start for our committee to hold our meetings abroad, and we did so in Paris in April 2016 thanks to the generous invitation of the French National Academy of Medicine with whom one of the meetings was held in collaboration with the Federation of European Academies of Medicine.⁴ Last but not least, we auditioned many persons speaking for the associations they represent, and consistently organized public debates both *in situ* and online.

The result of our deliberations, debates, auditions, and exchanges culminated in our Consensus Study, *Human Genome Editing*, released on February 14th, 2017.⁵ The Report takes into account important questions about the human application of genome editing including: balancing potential benefits with unintended risks, governing the use of genome editing, incorporating societal values into clinical applications and policy decisions, and respecting the inevitable differences across nations and cultures that will shape how and whether to use these new technologies. We also propose criteria for heritable germline editing, provide conclusions on the crucial need for public education and engagement, and present several general principles for the governance of human genome editing.

The Report's main messages are: 1) Genome editing in the context of basic research and somatic gene therapy is valuable and adequately regulated; 2) Somatic therapy should be used only for treatment and prevention of disease and disability; it should not be tried for enhancement at this time; public engagement and input are needed; 3) Heritable genome editing needs much more research before it might be ready to be tried; also, public input and engagement are vital; 4) When tried, heritable genome editing must be approached cautiously; it must be used only for treating or preventing severe diseases and according to strict criteria accom-

1 See Summit website for further information and videos of all the presentations and public debates: <http://nationalacademies.org/gene-editing/Gene-Edit-Summit/> (accessed 2/8/2017).

2 See Statement of Task at: www8.nationalacademies.org/onpinews/newsitem.aspx?RecordID=12082015 (accessed 2/8/2017).

3 See www.geneticalliance.org (accessed 2/8/2017).

4 All videos and slides of all public meetings are available at: <http://nationalacademies.org/gene-editing/consensus-study/meetings/index.htm> (accessed 2/8/2017).

5 See <http://nationalacademies.org/gene-editing/consensus-study> (accessed 2/8/2017).

panied by stringent oversight, no enhancement allowed.

Addressing more specifically the issue of heritable genome editing, indeed the most controversial of all topics, the report also lays out very strict conditions:

1. Clinical trials of heritable germline editing are not to be permitted if they do not meet the appropriate risk and benefit standards for clinical trials. Indeed, currently much more research is needed before any such trial goes forward.
2. We also lay out specific criteria that would have to be met before a germline clinical trial be permitted: (a) absence of reasonable alternatives; (b) restriction to editing genes that have been convincingly demonstrated to cause or to strongly dispose to a serious disease or condition (for example, any dominant genetic affliction such as Huntington's Disease); (c) credible pre-clinical and/or clinical data on risks and potential health benefits; (d) ongoing, rigorous oversight during clinical trials; (e) comprehensive plans for long-term multi-generational follow-up; and (f) continued reassessment of both health and societal benefits and risks, with wide-ranging, ongoing input from the public.
3. Extensive and broad public discussion is needed before allowing human genome editing for any purpose other than treating or preventing disease or disability.

In conclusion, it is important to mention additional points. The Committee was made up of a broad and diverse panel of experts. Each and every one of the 21 members came to the Committee and entered this

year-long process of debate and discussion with our own personal viewpoints and beliefs. As a group, yet from an individual standpoint as well, we were especially eager to hear from patients' groups, disability groups, and social scientists. We were also extremely focused on grasping the full spectrum of risks and benefits from the standpoint of the scientific technique itself, and were enlightened on this topic not only from the 'hard scientists' on the Committee but from others outside of our group of experts.

This input, both rich and varied, led to different rationales and arguments for each one of us, and also influenced the way we formulated and expressed our personal position on each of the tasks we were asked to address. In the end, and following lengthy debate – not only during the meetings but throughout the entire drafting of the report – we all came to a full consensus on the Report's conclusions and recommendations. The future now belongs to further and intensified international discussion, increased public engagement and continued careful and well-regulated research in the realm of human gene editing.

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