Genome Editing for Human Benefit: Ethics, Engagement and Governance

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Guidance and policy paper: Research governance of heritable genome editing rooted in salient value sharing

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Brief description of the context

The announcement by Jiankui He, in which he claimed he had genome-edited human embryos that led to the birth of twin girls in 2018, reinforced the need of governance and regulation that promote responsible research globally on the use of genome editing technology in human reproduction. At the same time, this announcement indicated the fact that many international statements about the risks of heritable/germline genome editing are not being implemented effectively.[1, 2, 3]

According to national guidelines in Japan, research involving the genome editing of surplus human blastocysts is allowed only for the purpose of 1) contributing to the understanding of embryo development and embryo implantation and 2) contributing to assisted reproduction technologies. Transplantation of the genome-edited blastocysts into a human/animal womb is prohibited. On the other hand, clinical applications using genome editing is not covered by the national guidelines. In other words, it is possible for infertile couples to use genome editing for reproductive purposes. Currently, the National Committee is discussing whether to propose a new law that bans the use of genome editing technology for reproductive purposes.

Under this context, this article discusses the proper research governance of heritable genome editing and does not focus on basic research for the two purposes explained above.

Commentary

The discussions by the National Committee in Japan and several international statements about heritable genome editing focus on the "how-to" or “conditions” for using this technology to produce a baby.[4,5] “How to” includes establishing a law/guideline or review system such as a research ethics committee. “Conditions” include safety, researchers’ capacity building, social acceptance, and social welfare. In my impression, these discussions and statements are made under the assumption that researchers and clinicians aim to conduct heritable genome editing clinically, but not until the conditions above are established.

However, even if all the conditions are cleared, should society permit heritable genome editing? To answer this question, stakeholders, including scientists, clinicians, regulatory authorities, and the public must deliberate prudentially.

Recommendations

In that deliberation, I recommend the following:

1) Defining quality of life, welfare, and health

The fundamental question to be deliberated is whether humans should use heritable genome editing in human reproduction.[6]

While heritable genome editing may be able to “cure” an anticipated disease or disability, existing discussions give little consideration to other means that could also provide a higher quality of life. Generally, quality of life assumes good health, and most existing discussions about germline genome editing aim to improve physical health. However, quality of life also includes other aspects, including mental and social aspects. In addition, quality of life is affected by welfare, which is more than ‘good health’.[7]

In addition, everyone has mutations in the genome, some of which are actually beneficial. For example, the person who has a homozygous mutation in the hemoglobin beta gene suffers from sickle cell disease, but the person who has a heterozygous mutation does not develop the disease and has tolerance for malaria. Similarly, cystic fibrosis results when a person inherits homozygous mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, but people with heterozygous mutations do not develop the disease and may even be protected against Typhoid Fever.[8] These reports teach us that mutations have the potential to benefit quality of life, welfare and health.

In other cases, some people in Japan think that having a disease is simply part of their identity. In this context, they think that diseases are not something that should be removed, and that treatment should be for improving quality of life.

These perspectives lead us to the basic question, "what is a disease or disability?”

2) A grand design for the research governance of heritable genome editing

A grand design for research governance constitutes hardware, software, and heartware. Hardware includes research infrastructure, such as buildings and instruments. Software refers to regulations and education. Finally, heartware describes how to apply one’s own principles to professionalism conduct.[9]

Almost all existing discussions relate to hardware and software. These discussions are important for research governance. From the perspective of heartware, regulation may work as a deterrent, especially when it includes punishment. Punishment assures the public that misbehaving researchers will not continue with inappropriate conduct, but it does not build trust between the public and research community.[10] Good research governance must build and sustain trust. This is where heartware is key. Heartware is how guidelines incorporate ethical challenges. In order to motivate researchers to conduct responsible research, it is important to make a standard of conduct that is devised voluntarily and includes the mission and values of the research to provoke thought about one’s principles (e.g. the Japanese Society for Regenerative Medicine “Standards of Conduct for Researchers related to Regenerative Medicine”).[11]

We have proposed a set of principles to assist researchers to consider professional and ethical behavior in their research.[12] Research regulation in most high-income countries includes a framework for a research ethics review system and for informed consent. However, based on our observations of Japanese researchers, many researchers do not understand the reason why a research ethics review system is needed.[12] In addition to the regulatory framework, explaining the reason why researchers should conduct their research based on their own principles will encourage responsible research.

3) Sharing salient values: The role of professionals and the general public

It is important to share salient values regarding what kind of society we want. In this regard, consensus is not the primary goal. Rather, stakeholders must clearly state their own values and respect those of others. Based on the understanding of differences (dissensus), stakeholders are to share salient values to establish their ideal society. The public plays the role of describing the expectations or concerns of this ideal, whereas professionals, which include scientists, clinicians, and regulatory authorities, make proposals for measures that realize the ideal.

In addition, when we think of the ideal society, the reasoning or justification should be considered. For example, informed consent from the patient should not be sufficient justification for conducting heritable genome editing. Rather, it is a precondition for providing the technology. Further, if clinicians/researchers decide to use a cutting-edge technology, including genome editing, based on only patient or public needs and preferences, then they are merely technology providers. It is important that the clinicians/researchers as professionals consider the conflict between respecting and curing the patient and preserving the diversity of the human genome.

4) Deliberation independent of economic benefit

When stakeholders consider and decide the governance and regulation, it is critical to minimize economic and government influence. Any new technology comes with the expectation of economic opportunity. However, economic motives could dampen protection of the patient/public.

Conclusion

In summary, my recommendations for governance of heritable genome editing, are 1) rethinking quality of life, welfare, and health, 2) developing a grand design, 3) sharing salient values, and 4) deliberation independent of economic benefit.

References

1. International Society for Stem Cell Research. ISSCR Statement on Human Germline Genome Modification. 2015. https://www.isscr.org/professional-resources/news-publicationsss/isscr-news-articles/article-listing/2015/03/19/statement-on-human-germline-genome-modification (accessed 24 October 2019)
2. The Academy of Medical Science, the Association of Medical Research Charities, Biotechnology and Biological Sciences Research Council, Medical Research Council and the Wellcome Trust. Genome editing in human cells – initial joint statement. 2015. https://acmedsci.ac.uk/file-download/37773-55e6b4e90f49c.pdf (accessed 24 October 2019)
3. National Academies of Sciences, Engineering, and Medicine. International Summit on Human Gene Editing: A Global Discussion. Washington, DC: The National Academies Press. 2015. https://doi.org/10.17226/21913. (accessed 24 October 2019)
4. National Academies of Science, Engineering, and Medicine. Second International Summit on Human Genome Editing: Continuing the Global Discussion: Proceedings of a Workshop-in Brief. Washington, DC: The National Academies Press. 2019. https://doi.org/10.17226/25343 (accessed 24 October 2019)
5. The U.S. National Academy of Medicine (NAM), the U.S. National Academy of Sciences (NAS), and the Royal Society of the U.K. International Commission on Clinical Use of Heritable Human Genome Editing. http://nationalacademies.org/gene-editing/index.htm (accessed 24 October 2019)
6. Hurlbut J. B. Human genome editing: ask whether, not how. Nature. 2019. 565. 135.
7. The Nuffield Council on Bioethics. Genome editing and human reproduction: social and ethical issues. 17 July 2018.
8. EurekAlert! Cystic fibrosis gene protects against typhoid fever. PUBLIC RELEASE: 6-MAY-1998. https://www.eurekalert.org/pub_releases/1998-05/NIoA-CFGP-060598.php (accessed 24 October 2019)
9. Harashina S. Environmental planning on urban level-Towards sustainable development-. Discussion Paper 96-6. Department of Society Engineering, Tokyo Institute of Technology. 1996.
10. Nakayachi K, Cvetkovich G. Trust of risk managers: An integration of the SVS model and the traditional view of trust. The Japanese Society of Social Phycology. 2008; 23(3): 259-268. [in Japanese]
11. Suzuki M, Sato K. Developing a program to foster professionalism for stem cell research, Uehiro Carnegie Oxford Conference 2014 ETHICS FOR THE FUTURE OF iPS / STEM CELLS. 2016; 153-159.

12. Suzuki M, Sato K. Description and evaluation of the research ethics review process in Japan: Proposed measures for improvement. Journal of Empirical Research on Human Research Ethics. 2016; 11(3): 256-266.