Recommendations for Legal Regulation on Clinical Applications of Human Germline Genome Editing

Summary

1. Background to formulation of the Recommendations

Genome editing is a technology that allows specific regions of the genome, the blueprint that contains all of the genetic information for an organism, to be modified at will. Its clinical applications to human somatic cells are already in progress. However, concerns have been raised about its clinical applications[1] to fertilized human embryos and germ cell lines in terms of safety and ethical issues, as genome editing is relatively inexpensive and does not require advanced technology. It is against this background that a pair of genome-edited twins were born in China in 2018. Genome editing of human embryos and germ cell lines for clinical purposes needs to be regulated effectively because of the dangers of unexpected side effects in the unborn child, the inheritance of genetic modifications, and the possibility that genome editing could lead to eugenic selection of humans.

In September 2017, the Committee on Genome Editing Technology in Medical Sciences and Clinical Applications of the Science Council of Japan released the results of its deliberations during the 23rd term as recommendations titled, “Genome Editing Technology in Medical Sciences and Clinical Applications in Japan”. In these recommendations, the Council prescribed the need for a legal framework for regulating the clinical application of genome editing in human embryos and germ cells. However, specific discussions on the structure of such a framework were left as an issue for the future.

[1]The transfer of fertilized human embryos into the uterus which could result in the birth of individuals with edited genome.

2. Current status and issues

The G7 countries other than Japan, i.e., the United Kingdom, the United States, France, Germany, Canada, and Italy, all have legal restrictions in place regarding the clinical application of genome editing technology to human embryos and germ cells. In particular, a number of countries prohibit the genetic modification of human embryos or human cloning through comprehensive laws on bioethics and laws on the use of human embryos. Japan, on the other hand, does not have any laws that describe general rules related to research using human embryos, and only a general clause related to clinical practice in the Medical Practitioners' Act apply (warnings, suspension of work, or revocation of license in cases of misconduct). In addition, although several guidelines have been developed by government agencies, most of the guidelines related to human embryos are not based on laws. Consequently, while administrative sanctions such as the suspension of public funding can be imposed against parties that violate these guidelines, such violations are not subject to criminal penalties. It is particularly concerning that even if the birth of genome-edited children that occurred in China in 2018 were to occur in Japan, the act of genome editing would not be punishable by law.

Furthermore, consideration of such regulations in only one country is insufficient in today's globalized society in which people and goods can move relatively freely across national borders. The World Health Organization (WHO) and international academic organizations are making efforts to strengthen regulations and governance at the international level. Japan has committed to these activities, but it is important that Japan's own domestic regulations are consistent with these international rules.

Japan has previously regulated activities in the absence of laws for extended periods, bringing into question the country's credibility from a perspective of democracy and its role in international rulemaking.

3. Key points of the Recommendations

(1) Legal regulations pertaining to the clinical application of genome editing technology should be promulgated at an early stage. It is essential that regulations based on law are promulgated as early as possible in order to ensure that punitive measures have been put in place for preventing clinical applications of genome editing technology to human embryos. For the time being, it would be appropriate to include in the scope of such

regulations all operations that have a long-term effect on gene function.

(2) Structure of legal regulations on the clinical application of genome editing technology
In view of (1) above, and considering the urgent need for regulation, the following two options are proposed:
(a) The Act on Regulation of Human Cloning Techniques (enacted in 2000), which is the only law to include the term “human embryo,” enshrines in law the protection of “human dignity” besides that of “safety for human life and body” as well as “public order.” With the emergence of genome editing technology, the definition of human dignity in the Act should be expanded to include the maintenance of human biological diversity so that it will serve as a basis of regulations. Or,
(b) A compact law should be enacted that focuses on the clinical application of genome editing to human embryos from the perspective of human dignity, including the maintenance of human biological diversity.
In either (a) or (b), it would be desirable for the law to prohibit clinical applications in principle, but to do so in a way that does not preclude exceptions from being made in the future if deemed necessary. Thus, when implementing regulations, consideration should be given to the methods by which clinical applications are regulated, such as regulating the handling of specified embryos, and imposing penalties if the regulations are violated (e.g., administrative sanctions and criminal penalties) rather than directly subjecting clinical applications to criminal penalties.

(3) Domestic and international rulemaking
International collaboration is essential for the formulation of regulations on genome editing. Therefore, in addition to (2) above, it is essential that Japanese representatives from expert groups participate in international activities led by the WHO and the academic community, and that Japan commits to international rulemaking. The representatives need to contribute to the international community by sharing with other countries the experiences gained through examination of the issues domestically, while at the same time the Japanese government needs to collaborate internationally by reflecting the outcomes of international discussions in the development of domestic regulations and review systems.

4. Future issues

The Recommendations propose a specific modality for laws and regulations under the current legal system. Nonetheless, ideally, the way forward would still be to enact a comprehensive law on the bioethics associated with human embryos and germ lines, even though this would take time. It is also necessary to consider that laws and regulations aimed at clinical applications should not hinder basic research using human embryos and germ lines that does not lead to the production of individuals. Instead, it is hoped that appropriate fundamental research into human embryos and germ lines using genome editing technology will lead to the development of new treatments that, to the maximum extent possible, do not require genome editing technology.