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Governance of Human Genome Editing and the Role of Interdisciplinary Collaborations

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Abstract

Making possible the easy and effective modification of genes, genome editing has become an indispensable tool for basic and applied medicine and life sciences. Since 2015, when a research paper describing basic research work on genome editing in human embryos was published, there has been extensive discussion on the use of the technology in humans. In particular, the question regarding whether the technology can be applied to the human germ line through which modified genes are passed on to the next generations has been hotly debated. In this article, by analyzing various events and discourses during this period, some crucial issues and lessons for the future have been highlighted and examined. During the analysis, it became clear that, while the scientific community played an important role in stimulating public discussions, its self-regulation was not sufficient to prevent incidents like the birth of twin babies through genome editing. In the future, it will be crucial to deepen more interdisciplinary and global-scale discussions through the participation of non-medical and scientific specialists, citizens, patients, etc. Bioethicists and ELSI (Ethical, Legal, and Social Issues or Implications) specialists are also expected to play an important role in facilitating such discussions.

Keywords

Genome editing
Genetic modification passed on to next generations
Scientific research community
World Health Organisation
Interdisciplinary collaboration

1. Introduction

Life science is a research field that aims to understand life phenomena and develop applied technologies, and developed dramatically since the second half of the 20th century. One of its characteristics is that new experimental techniques have been developed in basic

research aimed at understanding life phenomena and later applied to medicine and industry.

Genome editing emerged as an extension of such life science research. Genome editing is a technology that can modify genes in the same way as genetic recombination technology, but it is characterized by its ability to modify genes more easily and precisely. In particular, CRISPR-Cas9, which was announced in 2012, is even simpler and more efficient and quickly became a fundamental technology used extensively in both basic and applied research [1].

The advent of genome editing has once again raised widespread questions about the pros and cons of applying trans-generational genetic modification to humans, which had previously been considered impermissible due to its simplicity and efficiency, and also the question of how should society tackle this.

With these questions in mind, this paper sets and examines two objectives. The main objective is to review and critically examine domestic and international discussions and responses to human genome editing, focusing on its clinical application to germ line cells (fertilized eggs, sperm, eggs, etc.) since 2015, when it first became a major topic. Another objective is to discuss the role to be played by interdisciplinary research fields such as bioethics and Ethical, Legal, and Social Issues or Implications (ELSI) research. By doing so, it aims to present knowledge that will be useful in addressing the aforementioned questions.

Note that the author of this article has been directly or indirectly involved in many of the events discussed, and the descriptions and discussions will be from the perspective of those involved. Reference is also made to the process of preparation and publication of the statement on genome editing published by the Board of Directors of the Japanese Society for Bioethics in December 2018 [2].

2. History to date

First, a brief review of the history from the 1970s to the present (spring 2020) is given in **Table 1** to gain an understanding of historical trends.

In the late 1980s, genome research began to decode the entire genetic information of living organisms (i.e. the genome), and in 1990 the Human Genome Project was launched, and the human genome was decoded for the first time in history over a period of 13 years until 2003. At that time, the Human Genome ELSI Programme was launched to address ELSI associated with the decoding of the human genome [3]. In 1997, the United Nations Educational, Scientific and Cultural Organisation (UNESCO) adopted the Universal Declaration on the Human Genome and Human Rights. Article 1 of the Declaration states that 'the human genome is the heritage of humanity' and Article 24 states that manipulation of the genome of the germ line is 'an act that may be contrary to human dignity' [4].

It was around this time (1990s) that the technology known as genome editing first appeared [1]. However, until around 2010, the idea of genetic modification of the germ line was widely accepted.

In contrast, the introduction of a new type of genome editing technology, CRISPR-Cas9, in 2012 led to a renewed and active debate on the pros and cons of germline genome modification. In addition, by this time, assisted reproductive technologies had become widespread and a large number of human embryos created for reproductive purposes but not used had been preserved.

In April 2015, basic research by Chinese researchers on genome editing of human embryos (embryos containing two sperm during IVF that do not develop normally [5]) accelerated the debate. In July, the Specialist Committee on Bioethics of the Council for Science, Technology, and Innovation of the Cabinet Office began to consider the issue [6], and in December, the First International Summit on Human Genome Editing was held in Washington, USA [7].

Over the following three years, various organizations considered the issues and published reports, while at the same time, technical improvements

Table 1. Background to date

	Overseas or World	Japan
1970s	Genetic modification technology	
1990	Human Genome Project launched	Japan participates in the Human Genome Project
1997	UNESCO Universal Declaration on the Human Genome and Human Rights	
2002		Guidelines for Gene Therapy Clinical Research
2012	CRISPR-Cas9 announced.	
April 2015	Basic research paper on human embryos in China	
August 2015	US-Japan Society for Gene and Cell Therapy Statement	Statement of the US-Japan Society for Gene and Cell Therapy
December 2015	1st International Summit on Human Genome Editing, Washington	
April 2016		Cabinet Office, Expert Committee on Bioethics, 'Interim Summary'
February 2017	Report of the National Academy of Sciences of the United States of America	
September 2017		Science Council of Japan recommendations
July 2018	Nuffield Ethics Council Report	
November 2018	2nd International Summit on Human Genome Editing (Hong Kong)	
February 2019	WHO Commission established	
April 2019		Cabinet Office, Expert Committee on Bioethics, Second Report on the Review of the Basic Approach to the Handling of Human Embryos, Revised Guidelines on Clinical Research, including Gene Therapy
May 2019	International Commission (American-British Academy) established.	
January 2020		Ministry of Health, Labour and Welfare Expert Committee, "Discussion Paper"
March 2020		Science Council of Japan Recommendations

Note: Matters relating to the clinical application of genome editing primarily to the human germ line.

in genome editing were made [1]. Then, in November 2018, at the 2nd International Summit on Human Genome Editing held in Hong Kong, a Chinese researcher (He Jiankui; hereafter referred to as HJ) announced that by applying genome editing to human embryos, twin girls with a low susceptibility to human immunodeficiency virus (HIV) were born. However, it became clear that there were various procedural problems [8,9]. The unethical procedure of what many experts consider to be premature action has accelerated the debate on the regulation and governance of genome editing, which has continued to the present day.

3. Issues that have been identified

The challenges that have been identified for genome editing in germ cell lines are divided into two categories: basic research and clinical applications.

In basic research, human embryos are subjected to genome editing and analyzed in the early embryonic period (usually within 14 days after fertilization) without being returned to the mother's womb to obtain research results [9-11]. There are ethical issues such as the pros and cons of using human embryos for research. In Japan, the UK, China, and other countries, it can be carried out under certain objectives and regulations, while in Germany and France, it is currently not permitted [10,11].

Clinical application, on the other hand, refers to the implantation of genome-edited human embryos into the mother's womb, leading to birth as an individual. Numerous challenges have been pointed out [9]. One is scientific and technical challenges, such as off-targeting (where non-purposive sites are modified) and mosaicism (where only some cells undergo genome

editing after the fertilized egg divides). The second, which is both an ethical and a scientific challenge, is that the effects of genome editing on the individuals whose genomes have been edited and on future generations who will inherit the modified genome cannot be predicted.

The challenge for society as a whole is the pros and cons of human beings modifying their own genomes. This was pointed out in the statement of the First International Summit on Human Genome Editing, which stated that clinical application should not proceed at present unless sufficient debate has been exhausted along with other issues [7,9]. In Japan, in a statement issued jointly by the Philosophical Society of Japan, the Japanese Society of Ethics, and the Japanese Association for Religion in response to the announcement of the birth of twins by Chinese researcher HJ in December 2018, it was stated that "genetic modification is irreversibly transmitted to offspring over generations and could be the beginning of changing the human species at the genome level". The statement added: "If a situation such as designer babies develops, it will lead to human breeding or eugenic modification. If it is possible in the future that this could be done, e.g. for the treatment of certain diseases, it would have to be in very narrow and exceptional cases" [12].

Other issues that have been raised include the possibility that the clinical application of genome editing could undermine the value of those who have not undergone genome editing or who have not chosen to have their children's genomes edited, and the disparity caused by economic power. Yet another issue is the regulation of human genome editing. This involves the issue of how regulation should be done in each country, for example, whether it should be through laws or guidelines, and how substantive regulation can be done at the international level in addition to regulation at the national level.

4. Efforts that have been made

Four categories of efforts made since 2015 to address the challenges posed by human genome editing are discussed in this section: national governments, the scientific research community, international organizations, and others.

4.1. Actions taken by national governments

Governments have responded in their own way to the regulation of the clinical application of genome editing to human embryos. **Table 2** is taken from a research study conducted in the UK, USA, Germany, France, and China, for which the author was Principal Investigator in 2019 [11]. Each country currently prohibits clinical applications, either by law or by administrative guidance.

The UK, Germany, and France have laws on the handling of human embryos and assisted reproduction in general that existed before human genome editing became a hot topic and have responded to this situation. They all prohibit, with penalties, the use of genome editing on human embryos and their return to the mother's womb to give birth to an individual. In China, there has been no law with penalties so far, only a ban through administrative guidance, but an amendment to the Civil Law is planned [13].

The situation in the USA is more complex than in the aforementioned three European countries and there is no uniform legislation at the federal level covering human embryos or assisted reproduction. However, a ban has been in place since 2016 in the form of a prohibition on clinical research involving the application of genome editing to human embryos from being reviewed by the US Food and Drug Administration (FDA). Direct clinical application as a medical treatment is also prohibited by law with penalties, as medical care cannot be provided without clinical research if it involves genetic modification.

Table 2. Country-specific regulations on the clinical application of genome editing to human embryos

	Japan	United States	United Kingdom	Germany	France	China
Laws and regulations	Guidelines on gene therapy and other clinical research (administrative guidance)	No legislation regulating at the federal level Calculation Budget Act Supplementary Dicky-Wicker Amendment	Human Fertilization and Embryology Act (HFE Act).	Law on the protection of embryos	Article 16-4 of the Civil Code Article L.2151-2 of the Public Health Code	Code of Management of Assisted Human Reproductive Technologies (administrative guidance)
Clinical research on genome editing in human embryos	Prohibited by the Guidelines on Clinical Research on Gene Therapy (Clinical research aimed at genetic modification of human germ cells or embryos and clinical research that may result in genetic modification of human germ cells or embryos is prohibited)	(1) Congress prohibited the Food and Drug Administration (FDA) from reviewing for approval clinical trials that "intentionally create or alter human embryos, including genetic modifications" (2) Prohibits federal funding for research involving the creation of human embryos or the loss or damage of human embryos	(1) Criminal penalties are imposed for artificially mutating the genetic information of human germ cells (for clinical applications using genome editing, although basic research is not prohibited) and for using gametes with artificially mutated genes for fertilization (2) Prohibits, in effect, the implantation in utero of human fertilized embryos that have undergone germline genome editing	Any person who artificially alters the genetic information of a human germline cell and any person who uses a human germline cell with artificially altered genetic information for fertilization shall be punished, even if they have not attempted to do so	(1) Prohibits the intrusion into the integrity of the human species, the selection of humans through eugenic movements, and the transformation of genetic characteristics that would cause any change in offspring (2) Prohibits the creation of human embryos by embryo creation or cloning for research purposes and the creation of transgenic or chimeric embryos	Use of oocyte and nuclear transfer techniques for reproductive purposes and manipulation of gametes, zygotes, or embryos' genes for reproductive purposes are prohibited (no penalties)
Medical provision of genome editing for human embryos.	(1) No legal regulation as of March 2020 (2) The Ministry of Health, Labour, and Welfare's expert committee clearly stated the need for legal regulation in its "Summary of Discussions" published in January 2020	According to the Federal Food Drug and Cosmetic Act (FDC Act), FDA approval is required for the application of novel medical technologies such as human genome editing. However, due to the above-mentioned regulations on clinical research*, applications for human genome editing are not permitted. Violations are punishable under the FDC Act				

Extracted and partially revised from the report of the 2019 Health and Labour Science Special Research Project "Research on legal systems and the latest trends related to the handling of human embryos using genome editing technologies, etc. in other countries and on the public regulations in Japan that should be in place" [11]. In some countries, descriptions of basic research are also included.

In Japan, clinical research involving trans-generational genetic modification has been prohibited since government guidelines were established in 2002; in 2015, a new guideline was set out, known as the 'Guidelines for Clinical Research on Gene Therapy and Other Clinical Research' for reasons such as consistency with other guidelines, but in 2019, to ensure that genome editing is covered [14]. On the other hand, despite Japan having the largest number of assisted reproductive technologies in the world, there is no law on the medical application of genome editing to human embryos (directly, not through research), although there are self-regulations by academic societies [15]. As a result, the unethical application of genome editing to human embryos, as in the case of HJ, resulting in the birth of a child, cannot be penalized. In response to such a situation, the Expert Committee on Bioethics and the Expert Committee established by the Ministry of Health, Labour and Welfare in August 2019 examined the situation and published a report in January 2020 that a law banning the clinical application of genome editing to human embryos is needed [16].

4.2. Movements by the scientific research community

The scientists who created the new technology of genome editing and their communities have played a major role in the movement since 2015. Three cases are discussed here.

One is that the scientist who created CRISPR-Cas9, Jennifer Doudna herself, has played a major role in stimulating the social debate on genome editing in the US and the international community. She recognized the need for policy, ethical, and regulatory discussions on genome editing around 2014, shortly after the publication of CRISPR-Cas9 in 2012, and in January 2015, being one of the organizing committees for two International Summits on Human Genome Editing, with the participation of Nobel laureate David Baltimore, and held a meeting with 15 experts [17]. A summary of the discussions was published in Science in March of the same year [18], allowing leading scientists and experts around the world to recognize the importance and urgency of the issue.

In addition, Doudna's 2017 book describes how, as a basic scientist who had been working towards the beneficial use of genome editing in life sciences and medicine, she suddenly realized that the technology she had created could lead to a misuse that would go down in history alongside the atomic bomb, and was distressed and acted to stimulate social debate is described [17]. The significance of the fact that the scientists who created the technology themselves have led the social debate is discussed in the discussion. The second point is that these developments eventually led to organized action by the scientific research community, creating a global forum for discussion, including international summits in 2015 and 2018. The first international summit was jointly organized by the US National Academy of Sciences and Academy of Medicine, the Royal Society, and the Chinese Academy of Sciences, and brought together about 500 people from around the world to discuss a diverse range of scientific and medical topics, as well as the history of eugenics and presentations from the perspective of patient groups and disabled people [7]. Subsequently, in 2017, the US National Academies of Sciences and Medicine published a report [19].

For the second international summit in Hong Kong in 2018, the Hong Kong Academy of Sciences, rather than the Chinese Academy of Sciences, was the co-organizer, and the author was an organizing committee member. The summit was also broadcast live on the web, with 80,000 independent accesses from 190 countries [20]. The final day's statement condemned the actions of the HJ and stated that it would be irresponsible to pursue clinical applications at this time point, but that a pathway for responsible clinical applications in the future needed to be discussed. In response to the latter, the US Academy of Medicine and Science, together with the Royal Society in the UK, formed an 'International Commission' in May 2019,

with members from 10 countries, including Japan, to recommend the requirements and systems needed to proceed to clinical application [21].

Third, a diverse range of activities has spread, with academies and societies around the world compiling reports and organizing symposia. In Japan, the Science Council of Japan compiled recommendations on genome editing technologies in the medical and healthcare fields in 2017 and published recommendations on legal regulations in March 2020 [13,22]. The latter states that a law is needed in Japan to prohibit the clinical application of genome editing in human germ line cells, and describes a specific proposed form of law.

4.3. Response by international organizations

The question of whether or not humanity should alter its own genome in a trans-generational manner cannot be decided by a single country alone but must be considered in an international forum. The United Nations is a well-known international forum, and the United Nations Educational, Scientific and Cultural Organisation (UNESCO) and the World Health Organisation (WHO) are working on the aforementioned question.

UNESCO has a long history of addressing bioethics, having established the International Bioethics Commission (IBC) in 1993. As already mentioned, in 1997, the 29th General Conference adopted the Universal Declaration on the Human Genome and Human Rights [4]. The Declaration set out principles on human dignity and the human genome, the rights of the parties, including the prohibition of discrimination, and the conditions under which medical and scientific research involving the human genome may be conducted. Furthermore, in 2015, the IBC presented principles and ideas to be respected for various medical and advanced scientific technologies, called the IBC Report on the Human Genome and Human Rights [23]. It stated that the human genome is a 'heritage of humanity' and, like world heritage such as cultural and natural heritage, should be 'protected and passed on to future generations'. It then advocates the need for a moratorium for the time being on genetic modification of the germ line and activities to discuss and establish standards at the global level.

Meanwhile, in its 13th General Programme, which sets the basic policy for the five-year period from 2019, WHO states that advanced technologies will contribute to improving people's healthcare by preemptively addressing the ethical challenges of advanced technologies such as genome analysis, genome editing, AI, and big data. Based on this idea, in February 2019, WHO established an advisory committee consisting of 18 members from 15 countries (WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing) with 18 members from 15 countries [24]. The committee includes not only members from Western Europe and North America, but also Eastern Europe, Africa, the Middle East, Asia, and Oceania, and the committee members' fields of expertise are diverse, ranging from medicine and biology to humanities and social sciences such as philosophy and law.

The committee is tasked with examining the scientific, ethical, social, and legal issues related to human genome editing and proposing the principles and mechanisms needed to strengthen governance of genome editing from the institutional level to national, regional, and global levels over a period of about one and a half years until around autumn 2020. Although the final report is still in the preparatory stage, the draft Governance Framework, published in July 2020, includes a variety of proposed measures, such as the strengthening of regulations by national governments and relevant organizations, with an awareness of international cooperation, and the imposition of certain obligations on researchers when publishing articles in specialized journals [25]. The aim is for governance to be strengthened across the world through the introduction of diverse mechanisms by countries and relevant organizations around the world.

In addition, WHO has long operated the

International Clinical Trials Registry Platform (ICTRP), an international clinical trials registry platform that connects databases of clinical trials and research from around the world and enables interdisciplinary searches. Approximately 15 primary registries in Japan, the US, and other countries are participating [26]. At its first meeting in 2019, the Committee asked the Director-General of WHO to improve the registry in line with genome editing and to establish a system for registering clinical research using genome editing technologies and basic research involving human embryos (trial version in operation in 2020). The aim is to ensure research transparency and deter problematic research. In addition, the committee is also considering measures to prevent researchers from relocating from countries with strict regulations to countries with less stringent regulations to conduct ethically problematic research.

4.4. Activities by other stakeholders

In addition to the activities described in the previous sections, a wide range of other stakeholder activities are taking place.

One is to think together with the public at large and with patient groups. Discussions involving citizens and patients, who are the ultimate stakeholders, are essential for social decision-making on issues such as how genome editing should be used and whether trans-generational genome modification of germ line cells is acceptable. As far as the author can see, there does not necessarily seem to be a lot of activity in Europe and the USA, and it is not yet active in Japan either. In this context, the National Museum of Emerging Science and Innovation (Miraikan) in Odaiba, Tokyo, has been holding talk events for visitors and high school students to discuss genome editing since 2016. It has also created opportunities for dialogue with patients and people involved in patient associations [27].

Meanwhile, in the United States, even before the first international summit in 2015, several opinions have been expressed, questioning the discussions led by the government and the scientific community and arguing for the need for discussions involving a wide range of stakeholders, including citizens.

Widely known are the arguments of Sheila Jasanoff of Harvard University and Benjamin Hurlbut of Arizona State University, among others. After commending scientific leaders for creating a space for social discussion to advance responsible science, they argued that the human genome does not belong to any particular culture, country, or religion, much less science, and therefore cannot be adequately discussed at an international summit [28]. Hurlbut also criticized the 1975 Asilomar Conference, often cited as a model for the consideration of new technologies, where experts limited their agenda to the safety of recombinant DNA and failed to incorporate the diverse perspectives of society, and the same for the 2015 International Summit on Human Genome Editing for not incorporating the diverse perspectives of society [28], and proposes a new mechanism (the Global Observatory) for this purpose [29].

5. Consideration

The following four points are discussed regarding what can be learned from the history and events mentioned in previous sections, and what suggestions can be made for the future.

5.1. Changes from 2015 to 2020 - three phases

A great deal has happened in five years, from spring 2015 to 2020, which can be divided into three phases:

(1) The period from spring to the end of 2015 was a time when the problem was recognized all at once and a list of issues began to be enumerated, while the clinical application of germ lines was banned 'for the time being' as an emergency response. Academic societies and governments recognized the problem, statements were issued, committees such as Japan's Expert Committee on Bioethics and the Academy began to consider the issue, and an international summit was held in Washington in

December.

(2) The three years between the beginning of 2016 and the 2nd international summit in November 2018 was a period of progress in sorting out the scientific, ethical, and social issues and the beginning of consideration of cases in which genome editing could be used with the question of "in what cases can clinical applications of germline lineage be implemented". With technological advances such as base editing (a more precise technique that can alter only a single base of double-stranded DNA without completely cutting it), there was a widespread impression that the technical challenges of genome editing would eventually be resolved. Reports published by the US National Academies of Sciences and Medicine in 2017 and by the UK Nuffield Council on Bioethics in 2018 concluded that there are cases where the clinical application of germline lineage should proceed [19,30]. Specific examples included cases where both members of a couple carry the gene for a dominant (manifest) genetic disease or where both members of a couple homozygously carry the gene for a recessive (latent) genetic disease. In these cases, pre-implantation diagnosis does not result in a child without the disease gene. It was during this period that these studies were conducted in more detail. At the same time, however, there were those, such as Jasanoff and his colleagues, who argued that scientific considerations alone were not sufficient and that more open discussions were needed with the participation of stakeholders from all over the world.

(3) The period from the 2018 International Summit to spring 2020 had a simultaneous movement toward more concrete pathways for clinical application that began in early 2016–2018 and a movement that, following the announcement of the twins' birth by HJ, should ban clinical application and have more social discussion. These two different directions of movement appear to be even more polarized than at the time of 2016–2018.

It is speculated that those who are trying to promote it are likely having the US scientific community (or part of it) as their center. They have included the need for a "pathway to responsible clinical application" in the statement of the 2nd international summit, while envisaging the aforementioned specific cases where genome editing is needed, and have also led the formation of the International Commission since then. The intention behind this is likely to ensure that the US, which has always had a scientific and technological advantage in genome editing, takes the lead in the world. Another possibility may be the idea that if the scientific reasons are good enough, then it should move forward on that basis.

In any case, it is believed that the current situation is problematic and is not without some sense of urgency. Only a few people in the world are willing to promote clinical applications on scientific grounds. In many countries and regions, there is still not enough social discussion, and Japan is one of them. It is essential that a time-consuming dialogue involving the majority of the world's organizations and people is necessary, and that even if a complete agreement is difficult, the possibilities for clinical application are fully discussed in an international forum and, in the process, examined from multiple perspectives.

5.2. The role played by the scientific research community and its limitations

Looking back over the five years since 2015, it is clear that the scientific research community has played a major role in creating and stimulating international debate.

In particular, it is commendable that Jennifer Doudna, the discoverer of CRISPR-Cas9, has personally recognized the importance of the issue and involved many people and organizations in creating a space for discussion, despite being a basic scientist. At the 1st international summit, experts not only from the scientific side but also from history and sociology

were on the stage to share the breadth of the issue. It was precise because the scientists who developed the technology themselves participated in the discussions so that they could share and discuss the current state of the art of the latest scientific research.

However, after four years, it has become apparent that there are challenges and limitations to scientist-centered discussions. Two points should be noted:

(1) Even if experts in the humanities and social sciences, citizens, and patients participate in the discussion, scientists still pull the discussion toward the use of technology. This is obvious without having to point it out again, but as mentioned in the previous section, the discussion on advancing clinical applications is now starting to take on a life of its own and is becoming increasingly disconnected from other people and organizations. Stakeholders, both internal and external, should be more strongly aware that discussions among scientists alone are not sufficient.

(2) It has become clear that self-regulation by scientists is not sufficient for the governance of technology. At the 1st international summit in 2015, the scientific community that developed the technology took the lead in discussions together with people from various fields and agreed that the clinical application of germline concluded that the clinical application of the technology was prohibited until a social consensus was reached [6]. However, the HJ event made it clear that such a scientist-led consensus alone is not enough to stop unethical practices. In the future, non-scientist-led activities will be more important than ever. UNESCO, WHO, and the governments that work with them will also play a greater role.

5.3. Initiatives and challenges in Japan

In Japan, the scientific community moved quickly. In August 2015, the Japanese Society for Gene Therapy, together with the American Society for Gene and Cell Therapy, issued a joint statement containing opposition to the clinical application of genome editing in germline lineage and has since held public forums [31]. The Science Council also issued recommendations in 2017 and 2020. Several medical and scientific societies also issued statements after the HJ event, and the three aforementioned humanities societies issued a joint statement at the end of December 2018 [12].

Furthermore, on 9 December 2018, the Japan Society for Bioethics decided to publish a statement on the announcement of the birth of twins from human fertilized eggs using genome editing technology [2]. The statement stated that “the clinical application of trans-generational genome editing on human subjects should be prohibited at present, based on a synthesis of (among other) various perspectives”, and that the society will continue to work towards social discussion and the development of appropriate regulations to prevent the recurrence of unethical practices.

Here, the circumstances leading up to the publication of the statement are briefly explained. The 30th annual conference in 2018 was held in Kyoto on 8 and 9 December, immediately after the international summit in Hong Kong on 27–29 November, and the statement had already been published by the Japan Medical Association, the Medical Association, and others. It is believed to be important for interdisciplinary societies such as the Society for Bioethics and Humanities and social sciences societies to raise their voices, and consult informally with several board members during the 8 December conference. As a result, it was decided to propose the idea to the Board of Directors, who hastily prepared a draft and presented it to the Board of Directors the following day. At the board meeting, all board members agreed with the proposal, and some amendments were incorporated into the final draft, but as there were a few opinions at the general meeting that were against the society expressing its opinion on social issues, the board members decided to make it public. It is hoped that the various activities described in the second half of the statement will be implemented in concrete terms

in the future.

Meanwhile, with regard to Japanese government-related organizations, the Expert Committee on Bioethics of the Cabinet Office and the Expert Committee of the Ministry of Health, Labor, and Welfare have been taking up the issue of genome editing at appropriate times, and a certain level of response has been achieved. The opinion that a law is needed regarding the regulation of the clinical application of genome editing of germ cell lines has also been compiled, and a concrete draft law will be considered in the future. In that case, it would be better to prohibit clinical applications for the time being, but to open the way for clinical applications in the future, depending on the social debate. This is because the direction of the debate is not set at the moment. It is also undeniable that the debate so far has been limited to specialists, and a more open discussion is needed in the future.

5.4. The importance of cross-sectoral collaboration

Looking back at the various activities on human genome editing described so far, it is clear that almost all of them involve people from a large number of disciplines in an interdisciplinary manner. These include researchers and specialists in science and medicine, experts in the humanities and social sciences, government officials, patients, patient organizations, and other civil society sectors.

Dialogue and debate between people from different perspectives will become increasingly important as humanity as a whole grapples with the question of whether trans-generational genetic modification should be applied to humans in the future. It is obvious that all people should listen to different points of view, but there are two additional views to point out in this article:

(1) Scientists who understand the latest developments in genome editing research should involve and communicate with people in other fields, and at the same time have a flexible attitude to listen to the views of other fields. In the author's experience, scientists such as Robin Lobelbadge of the Francis Crick Institute in the UK (a biologist who chaired a session at the international summit in Hong Kong where HJ was speaking [32]) and Janet Losan of Canada (former president of the International Stem Cell Society) have a professional understanding of science and a broad perspective to contribute to the debate. In a field such as genome editing, where the scientific aspects are changing rapidly, it is essential for scientists to participate in the debate. However, if those scientists impose their views on the scientific community, social discussion cannot take place. The author feels that the participation of scientists with both expertise and flexibility is still low in Japan, and hopes that it will increase in the future.

(2) It is expected that experts who can connect the natural sciences with the humanities and social sciences in an interdisciplinary manner will play an important role. Experts in bioethics and ELSI research are constantly pursuing issues in medicine and life sciences while analyzing things from the perspective of the humanities and social sciences and can be expected to play a role in promoting discussion among diverse groups of people and in stopping scientists from running amok. Among them, ELSI research is based on connecting diverse fields and working across them [33], and the author believes that it will become an essential field for the governance of science and technology in the 21st century [34]. The importance of ELSI research has been increasingly recognized in recent years, and in April 2020, Osaka University will establish a specialized organization (Research Centre for Co-Creation of Social Technology, abbreviated as ELSI Centre) [35].

In the future, each country will need to deepen discussions in their own countries, as well as actively

participate in discussions on the global stage and promote activities to reach a global agreement. The question of whether there are any cases in which clinical application of germline genome editing should be permitted. It is necessary to consider the scientific feasibility and social necessity in concrete terms, with a ban for the time being. In doing so, it is expected that scientists, medical professionals, experts in the humanities and social sciences, government officials, citizens, patients, and experts in different disciplines will all participate and collaborate in the examination process.

6. Conclusion

In the next few years to a decade or so, human societies are likely to make important choices about their own genomes that will go down in history. To ensure that people around the world do not regret that choice, there needs to be a full international forum for discussion across diverse disciplines. From the review in this paper, it appears that only a few experts may proceed to make critical decisions. Efforts need to be made to stimulate further discussion within and across countries and to ensure that decisions are made by the people of the world as a human community. Experts in bioethics and ELSI research are expected to play a central role in this.

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