

Report

International Workshop on the Ethics of Genome Editing

2015.11.22

Project: “Toward Constructing an
Interdisciplinary Platform for Bioethics”

International Institute of Advanced Studies
Center for Applied Philosophy & Ethics

1. Introduction: Workshop Objectives

2015 was a year full of news on genome editing. April 18, 2015 saw the publication of a report on Chinese researchers performing genome editing on human embryos.¹ Because word of this article spread among researchers even before it was published, however, declarations by scholarly associations and others regarding the propriety of genome editing research began to appear before the article was published.² Declarations by groups such as the United States National Institutes of Health (NIH) and the US-Japan Gene Therapy Conference continued to appear even after the article was published.³ Many stressed the need for a ban or moratorium on the use of genome editing on human embryos.⁴

Against this backdrop, this November 22, 2015 workshop at the International Institute for Advanced Studies, which was a continuation of the first workshop held on August 5, carried out discussions on the ethics of genome editing. Yet, the scope of debates was not limited to applications of genome editing on humans, but also encompassed discussions of various ethical issues created by this technological feat, including the genetic modification of animals and plants. Specifically, through six reports and three group discussions, the following three questions were examined in detail, and views of participants about other concerns were collected as well. Among these, the problem of whether or not genome editing of human embryos should be permitted was addressed directly through question 2 below, and in a number of reports.

Three Questions Examined at the Workshop
--

¹ Liang, P. et al. CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes, *Protein & Cell*, 6(5):2015;363-372.

² For example, this was true for the statement released by the International Society for Stem Cell Research on March 19. The ISSCR Statement on Human Germline Genome Modification (<http://www.isscr.org/home/about-us/news-press-releases/2015/2015/03/19/statement-on-human-germline-genome-modification>)

³ Statement on NIH funding of research using gene-editing technologies in human embryos (<http://www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-nih-funding-research-using-gene-editing-technologies-human-embryos>), ASGCT and JSST Joint Position Statement on Human Genomic Editing (<http://jsst.jp/INFORMATION/mt2015118a.pdf>)

⁴ Also, on December 3, the International Summit on Human Gene Editing was held in the United States, and a statement was released which permitted basic research on and clinical application of human somatic cells under certain conditions, and permitted genome editing on human embryos only for basic research. Japanese texts of this and other major reports were published on the website of the Kyoto University Center for Applied Philosophy & Ethics. <http://www.cape.bun.kyoto-u.ac.jp/project/project02/>

Furthermore, on December 17, *Science* chose genome editing using CRISPR as the number one Breakthrough of the Year for 2015. 'And Science's Breakthrough of the Year is ...' <http://news.sciencemag.org/scientific-community/2015/12/and-science-s-breakthrough-year>

- (1) Is there a moral difference between only cutting DNA, and the cutting and insertion of DNA? In other words, are there fewer issues with cutting DNA alone through genome editing technologies relative to inserting genes after cutting?
- (2) Is the position that “modification of human germline cells is impermissible, but the modification of somatic cells is allowable” morally defensible? If so, on what principle?
- (3) Is the differential treatment of humans and non-human animals in the context of genetic modification defensible? In other words, is it possible to justify a position that “modification of human embryonic cells is impermissible, but the modification of somatic cells is allowable, and the modification of both embryonic and somatic cells is permissible in the case of non-human animals”?

Below, we provide a concise overview of the six reports, the discussion of the three questions above, and other concerns raised by participants. It should be noted at the outset, however, that the objective of this workshop was to identify the various arguments pertaining to these questions, and not to reach a consensus.

This report is a draft based on the notes of Satoshi Kodama, which were expanded and revised by Soichiro Tanaka, Keiko Sato, and Mika Suzuki, and subsequently confirmed by all Japanese participants. The English edition was composed thereafter.

Finally, this workshop was made possible by research grants from the International Institute of Advanced Studies and Kyoto University (SPIRITS, <http://research.kyoto-u.ac.jp/service/topic/spirits/>). We express our gratitude for this support. We also express our profound thanks to all project members and guest participants who took part in the workshop and contributed to the lectures and lively discussion.

Satoshi Kodama
Project Representative

Participants

- “Toward Constructing an Interdisciplinary Platform for Bioethics” Project Members
- | | |
|-------------------|--|
| Satoshi Kodama | (Graduate School of Letters, Kyoto University) |
| Ryuichi Ida | (Graduate School of Global Studies, Doshisha University) |
| Shinya Saito | (Graduate School of Health Sciences, Okayama University) |
| Keiko Sato | (Kyoto University Hospital) |
| Mika Suzuki | (Center for iPS cell Research and Application, Kyoto University) |
| Sayaka Takenouchi | (Graduate School of Medicine, Kyoto University) |
| Takahiro Hattori | (Institute for Liberal Arts and Sciences, Kyoto University) |
| Jin Higashijima | (Faculty of Global and Science Studies, Yamaguchi University) |
| Jusaku Minari | (Graduate School for Medicine, Osaka University) |

Kojiro Shimozuma	(Department of Biomedical Sciences, Ritsumeikan University)
Noriko Nagao	(Graduate School of Health Sciences, Kobe University)
Soichiro Toda	(Graduate School of Medicine, Kyoto University)
Soichiro Tanaka	(Graduate Student, Graduate School of Letters, Kyoto University)

• Guest Participants

Yutaka Hishiyama	(Japan Agency for Medical Research and Development)
Minori Kokado	(Graduate School of Medicine, Osaka University)
Masato Kinoshita	(Graduate School of Agriculture, Kyoto University)
Robert Sparrow	(Faculty of Arts, Monash University)
Catherine Mills	(Faculty of Arts, Monash University)
Justin Oakley	(Faculty of Arts, Monash University)
Tamra Lysaght	(Centre for Biomedical Ethics, National University, Singapore)

2. Overview of Six Reports

(1) Yutaka Hishiyama

“What Countermeasures for Genome Editing Can be Taken—From the Perspective of Public Policy”

The recent rise of genome editing has made it possible to insert and delete genes with high accuracy. One can now manipulate genes from reproductive or embryonic cells, which used to be very difficult. This technology may bring about major developments in basic life sciences, pharmaceuticals, and food production. There are, however, technical problems that have not been resolved, including off-target mutations and mosaics. In terms of ethical, legal, and social concerns, the problem of reproductive gene modifications being inherited by the next generation has been raised. There also exist the theoretical possibility of genetically modifying human embryos, as well as the possibility that genetically-modified organisms might affect the ecosystem. Finally, while there are regulations on recombinant DNA technology in Japan, it is possible that genome editing technology would fall outside the scope of these regulations. These concerns require conscious and comprehensive consideration not merely for the life sciences, but as important industrial technologies. Furthermore, human appetite knows no limits, and it is not possible to give a definitive answer to the question about whether genetic modification of embryos might be permitted for some purposes. Based on experiences dealing with the ELSI (ethical, legal, and social implications) surrounding cutting edge technologies of the past, one can expect that at the very least genome editing may be regulated for efficacy and safety.

(2) Mika Suzuki

“Genome editing –How should we understand this technology?”

In this presentation, I introduce points of discussion about the ethics behind genome editing technology in humans and non-humans. One focus point is the distinction between mutations caused by genome editing and those from genomic mutations (imperfect DNA repair) or environmental insults (chemical radiation, etc.) A second focus point considers the distinction between manipulation of the genome through cutting and inserting. The final point considers the attitude of the general public towards genome editing, especially with regards to in which species and in which purpose it is acceptable or not. Throughout my presentation, I connect these points to what kind of society we want and leave for future generations.

(3) Masato Kinoshita

“Characteristics of the Products of Genome Editing With or Without Exogenous Gene Insertion”

This report presents an overview of the differences between previous breeding methods and breeding methods using genome editing. Because breeding methods that make use of spontaneous mutations and induction of mutations require the selection of individual

organisms with desirable traits, these might be called passive breeding methods. On the other hand, gene recombination and genome editing do not require waiting for desirable mutations. These methods can be carried out in a substantially shorter amount of time and more effectively than passive breeding methods. The difference between older gene recombination methods and genome editing methods is that, while in the former the position of inserted genes is random, in the latter it can be accurately designated. Finally, the report pointed out that mutations through genome editing that does not involve gene insertion cannot be distinguished from spontaneous mutations. Considering that, naturally, varieties bred using spontaneous mutations have been accepted as food products, it is likely that those developed by genome editing without exogenous gene insertion could also be accepted by the public if accurate information is provided.

(4) Robert Sparrow
“Editing genomes, designing people”

In this presentation I argue that concerns about the safety of editing the human germline are unlikely to render it unethical. All reproductive technologies developed to date have been radically experimental when first trialled, suggesting that scientists’ concerns about risk and safety will inevitably dissipate when the technology is closer to fruition. Moreover, coming into existence is itself risky regardless of the means by which it occurs. Worries about future generations can always be met by the person with the edited germline deciding — or being compelled — not to reproduce. A more serious objection to germline genome editing for the purposes of human enhancement, however, which was famously made by Habermas, is that it establishes a radically asymmetric relation between the “designers” and the “designed.” Those who have had their genomes edited will reflect the intentions of the parties that initiated the editing. Moreover, unlike the relation between parent and child, the relation between designers and designed is essentially instrumental, rather than dialogical, in nature. Considering the ways in which individuals born with edited genomes may become “obsolete” may usefully illustrate the ethical perils of this relation.

(5) Catherine Mills
“Intergenerational relations and the ethics of gene editing”

According to a number of bioethicists and philosophers, gene editing techniques have the potential to profoundly alter intergenerational relations in ways that may prove ethically deleterious. In this presentation, I discuss three such attempts to understand the ethics of gene editing: Sandel’s critique of a drive to mastery and corresponding formulation of an ethics of the gift; Habermas’s concern that genetic engineering threatens to transform the ethical self-understanding of the species; and Baylis et.al.’s argument for the use of an heuristic of ‘radical rupture’ in discussions of the ethics of inheritable genetic modification. I suggest that while these approaches do well to focus on intergenerational relations, none offer particularly compelling accounts of the morally important features of intergenerational relations.

(6) Keiko Sato

“How Far Will Genome Editing Go?”

Discussions on genome editing have tended to consider it an aspect of gene modification technologies. As a fundamental principle for using these technologies, we would like to adopt the following: “We use these technologies only to the extent that they do not alter the essential traits of living organisms.” This principle is inspired by the Japanese concept of “*hitozato*” (human dwellings). This concept holds that humans will coexist with nature, leave areas of nature untouched by human hands, and not use them more than necessary. Key points that must be kept in mind with respect to applying genome editing to germlines include the risks, benefits, other values, and the distinction between clinical application and basic research. In particular, it is currently not possible to assess all risks, or even to predict what risks might be inherited after the next generation. Even if, hypothetically, safety could be guaranteed, the clinical application of genetic modification to zygotes should be prohibited given the risk that it will harm the “natural” “integrity” of humans and cause them to lose their sense of humility. However, because the development of genome editing in and of itself is desirable, basic research should not be prohibited. It will be necessary to institute comprehensive governance to prohibit clinical application and allow basic research.

3. Three Questions and Views on Them

(1) Is there a moral difference between only cutting DNA, and the cutting and insertion of DNA? In other words, are there fewer issues with cutting DNA alone through genome editing technologies relative to inserting genes after cutting?

This issue is an active area of discussion, particularly with respect to the application of genome editing to animals and plants. For example, in the Science Council of Japan report “The Current State and Issues of NPBT (New Plant Breeding Techniques)” (August 8, 2014)⁵, the problem is raised in the following manner:

“In the case of genome editing that does not result in the insertion of new genes, it is thought that there is no way to distinguish these from spontaneous mutations, i.e., non-recombinants. It is necessary to give due consideration to the problem of to what extent these mutations should be regarded as the same as spontaneous mutations, and what to do to detect and control these mutations.” (p. iv)

According to Kinoshita’s report at the workshop, it is possible to create useful animals through the cutting of DNA alone (the manufacture, for example, of more muscular organisms by disabling myostatin-inhibiting genes). Moreover, if these are mutations that can also occur naturally, then there is no need to regard these techniques as the same as previous gene recombination technologies, because no exogenous genes have been introduced. This, in turn, supports the argument that regulation of these techniques should be less stringent. In fact, when genome editing that only involves DNA cutting is used on animals and plants, it is not clear whether these correspond to genetically modified organisms (GMOs) regulated under the Cartagena Protocols (p 11). This issue requires immediate discussion.

Furthermore, a point raised in Suzuki’s discussion is that, if “mutations that also occur naturally are exempted from regulations on GMOs,” it may become necessary to examine the consistency of regulations in comparison with those on methods previously used for breed improvement (through induction of spontaneous mutations, etc).

Needless to say, we think this point is not limited to animals and plants, but may also be relevant to the application of genome editing to human subjects. In clinical research on gene therapy using genome editing, for example, the question has arisen of whether the current Guidelines for Clinical Research on Gene Therapy apply when DNA is only cut and exogenous genes are not inserted.⁶ If new regulations for clinical research on gene therapy

⁵ <http://www.scj.go.jp/ja/info/kohyo/pdf/kohyo-22-h140826.pdf>

⁶ These guidelines define gene therapy as “the administration within the human body of genes or cells with introduced genes for the purposes of curing or preventing diseases. The text of the guidelines (enacted October 1, 2015) can be viewed at the URL below:

are created, there will likely be debates about whether to make distinctions between techniques that only cut DNA and those that involve cutting DNA to insert new genes, when it comes to approaches of risk assessment and informed consent.

This workshop, however, discussed general issues expected to arise as points of debate in any country, rather than examining the consistency of current laws in detail. The views expressed at the workshop are introduced below.

Views that this distinction is not important:

- Even in cases of DNA cutting alone, there is the possibility of dramatic changes in the functions of living organisms, which could result in major damage to the environment. Even if the off-target issue is resolved, shouldn't questions about whether there is an impact on the somatic gene network or epigenetics be assessed similarly for both types when it comes to the safety of the final product? In the fields of food products and medical treatment in particular, aren't cases of DNA cutting alone and cutting and inserting DNA the same when one considers the use of existing systems to verify efficacy and safety? Thus, careful environmental and safety assessments in cases of both DNA cutting alone and DNA cutting and insertion are necessary. (Because the issues of environmental risk and safety are complex and have long-term implications, however, some questioned whether it is really possible to assess them. Furthermore, if it is deemed that no distinction exists between the techniques, there is the issue of how to maintain consistency with current regulations on breeding methods (irradiation, tetraploid method)).
- It is not viable to adhere to binary thinking that holds that DNA cutting is safe because it is natural, but inserting DNA is risky because it is human-induced. In either case, the consequences of such genetic changes must be assessed. For instance, in developing measures against infectious diseases, there is monitoring of natural mutations that may pose a major threat to humans, and no one argues that these mutations are safe because they occur naturally. It should also be noted that things currently assumed to be "natural" may include elements that are human-induced (in the case of so-called "natural foods," for example). Conversely, if one considers the use of genome editing to treat conditions such as single nucleotide polymorphisms by replacing a base, this constitutes using "artificial" means to restore a "natural" state (the way things should be), and there is no reason such means should be regulated more strictly than techniques that only cut DNA.
- It is possible that attempting regulation based on the distinction between whether the means used are artificial or not could lead to confusion. For example, when one compares single nucleotide replacement by genome editing or caused by radiation exposure to single nucleotide replacement that occurred naturally as a spontaneous mutation, and categorize the first two as "artificial" and the last as not "artificial," this

could result in a situation whereby regulations differ even though the end product is the same.

- Distinguishing between “artificial” and “natural” will also likely be extremely difficult in practice. Considered in the context of breeding (breed improvement), there is the problem of whether it is possible to define the extent the following three are natural and to what extent they are artificial: (1) selection based on natural crossbreeding; (2) selection based on induced mutations; and (3) selection based on genome editing.
- Some expressed the view that there are more limitations on what can be done through genome editing in cases of DNA cutting alone compared to DNA cutting and insertion. In response, some put forward the view that, in principle, to the extent that bases are made up of only 4 types (ATGC), the same things can be accomplished with DNA cutting alone as with DNA cutting and insertion if ingenuity is exercised in how the DNA is cut. Although this view is speculative, some pointed out that if correct, then all genetic recombination can be done of its own accord (i.e., by DNA cutting alone), and the very concept of “exogenous genes” would become meaningless.
- Some expressed the opinion that viewing genome editing with DNA cutting alone as different from genetic recombination has a transparently political motive. In other words, the motivation is to make genome editing more socially acceptable, by claiming that it is a new technology, while also emphasizing that this mutation can also occur naturally. Similarly, it was suggested that the question of whether a genetically-mutated animal or plant should be evaluated based on the technology (means) of genetic mutation or the resulting product might end up becoming a political decision made based on “which is more profitable for industry.”

Views That This Distinction is Important:

- If one follows the spirit of “conservation of the ecosystem,” which is one of the goals of the Cartagena Protocols, then the concept of DNA cutting alone, without inserting exogenous genes, is likely important.
- It is meaningful to treat the technology of DNA cutting alone, which in light of the history of social reception of genetically-modified crops is likely to be accepted by society, differently from techniques that insert DNA.

Other Views

- Some pointed out that while considerations of safety and short- and long-term risks to the environment are certainly of importance, these are not ethical issues in and of themselves.⁷

⁷ In the Hinxton Group’s ‘Statement on Genome Editing Technologies and Human Germline Genetic Modification’ (http://www.hinxtongroup.org/hinxton2015_statement.pdf), it is similarly pointed out that, when it comes to interventions in human germline cells, there should be a rigorous distinction made between reflecting concerns about technological aspects and safety, on the one hand, and “moral concerns,” on the other, in the enactment of policy and regulations. A Japanese overview of the Hinxton Group’s ‘Statement is accessible at the following URL: <http://www.cape.bun.kyoto-u.ac.jp/wp-content/uploads/2015/10/e3a4d999fe834ea41dfa5b9a875a88d81.pdf>

- There was also the view that we must take into consideration the costs of not using genome editing and not taking on those risks, in other words, the costs of doing nothing. For example, these include costs incurred if agricultural crop improvements and gene therapy do not advance because regulations on genome editing are made excessively strict.
- It was pointed out that the distinction between cutting DNA alone and cutting and inserting DNA only makes sense when taking into account what specifically is being regulated. Discussing the differences between the two without this dimension is not productive.

(2) Is the position that “modification of human germline cells is impermissible, but the modification of somatic cells is allowable” morally defensible? If so, on what principle?

In the many past reports and declarations pertaining to the use of genome editing on humans, the general framework accepted, in the context of medical applications at least, is the position that “modification of human germline cells is impermissible, but the modification of somatic cells is allowable.” At the research meeting held by the International Institute of Advanced Studies in August of this year⁸, there were discussions of the pros and cons of using genome editing techniques that target human germline cells. It was confirmed at that meeting that, according to current social consensus, there is a sharp distinction between genetic intervention in germline cells and somatic cells, and that “modifications that are carried over into the next generation should not be performed.” As background reasons for this, the following were discussed: the uncertainty of the risk of modification, the inability to take responsibility for carrying out the modification, the impossibility of undoing the modification, and damage to the dignity of the next generation.⁹

On the other hand, imagine that in the near future it becomes possible to perform gene therapy on mutations such as BRCA1/2 using genome editing at the zygote stage. One view was that, in this case, it would be better to intervene at the germline cell stage rather than treat breast cancer or perform preventive resection each time as the next generation

⁸ For details on the August research meeting, see pages 7-8 of the following URL:
http://www.iias.or.jp/research/project/pdf/2015_01.pdf

⁹ Regarding human dignity, UNESCO’s Universal Declaration on the Human Genome and Human Rights, adopted in 1997, makes the following point in Article 24: “It should make recommendations, in accordance with UNESCO’s statutory procedures, addressed to the General Conference and give advice concerning the follow-up of this Declaration, in particular regarding the identification of practices that could be contrary to human dignity, such as germ-line interventions.” See the following MEXT site for the original declaration: <http://www.mext.go.jp/unesco/009/005.htm>. Furthermore, in an October 2, 2015 UNESCO report that follows the spirit of this declaration, they propose a moratorium on genome editing on human embryos because of the potential impact on future generations, noting that it could “jeopardize the inherent and therefore equal dignity of all human beings and renew eugenics.” For more information, see: <http://en.unesco.org/news/unesco-panel-experts-calls-ban-editing-human-dna-avoid-unethical-tampering-hereditary-traits>; <http://unesdoc.unesco.org/images/0023/002332/233258E.pdf>

become adults. Another view was that there was more room to examine whether the concept of “dignity” should be used because people’s interpretations of it are divided.

In the case of interventions in germline cells, the focus has been on the issue of inheritability by the next generation. Yet, what is the reason that inheritability by the next generation should never be permitted? At least to the extent that genetic modification is conducted for the purpose of therapy or prevention, it is possible to argue that there is no problem if the effects of therapy or prevention are inherited by the next generation. For example, as a result of humanity eradicating smallpox in the latter half of the 20th century, the effects were inherited by the next generation, but few would take issue with this. For the same reason, couldn’t one also argue that wiping out genetic illnesses, even if humanity cannot completely eradicate them, is the present generation’s obligation to future generations?

Based on this problem consciousness, we set aside the present social consensus in order to discuss by which principles it would be possible to draw a line between intervention in germline cells and somatic cells. The views expressed at the workshop are presented below.

Views that it is possible to justify the position that “modification of human germline cells is impermissible, but the modification of somatic cells is allowable”

- As already discussed in reports by Sparrow and Mills, some believed that genetic modification of germline cells (particularly zygotes) requires more cautious consideration because it has the potential to cause major changes in the relationship between parent and child. In short, it is necessary to examine the impact of the relationship between the one who designs the genes (the parent) and the one who has genes designed (the child) on the parent-child relationship.
- Furthermore, it is also important to examine the impact of modification of the child’s genes on social equality. This applies especially to the use of gene modification for purposes of enhancement.
- In the case of intervention in germline cells, there is the issue that the child cannot consent even if the parent can. On this point, however, some expressed the view that, when one considers that treatments given shortly after birth are performed without the child’s consent, it may be difficult to make the child’s consent a necessary condition.
- Regarding modification of germline cells, because of problems such as genotype, phenotype, epigenetics and, more broadly, the interaction between the environment and genes, it may be more difficult to assess the risks of this compared to the modification of somatic cells.

Views that it is not possible to justify the position that “modification of human germline cells is impermissible, but the modification of somatic cells is allowable”

- In theory, the difference between germline cells and somatic cells is the size of the risk. It is simply that, to the extent that there is more research on somatic cell gene therapy,

the risks of gene modification in somatic cells is better understood. But there is no essential difference between the two.

- Even in germline cells, it should be permitted if done for treatment purposes, e.g., for severe genetic illnesses. Enhancement is not permitted, but this also applies to somatic cells. Again, there is no essential difference.
- Considering that, currently, therapy during the fetal period is more realistic, if this is done earlier at the stage of germline cells, isn't it true that there is essentially no difference?

Other Views

- Originally, with pre-implantation diagnosis (PGD) or the like, most cases can be addressed without using genetic modification of germline cells. Some expressed the view that in exceptional cases that cannot be treated, sperm or eggs from a third party should be used.
- For parents who value blood relations, however, alternative methods such as PGD or use of third party sperm or eggs may not be an option. Some asked what grounds could be used to deny such parents the opportunity to use genome editing. Even if there are alternatives such as third parties, shouldn't genome editing be developed as another new alternative? It was also pointed out that if one's position is to advise parents who value blood ties to use other methods such as PGD or third party sperm or eggs, one should simultaneously examine the allowed scope for using such techniques, because the use of PGD and third party sperm and eggs is also considerably restricted in Japan.
- The rejoinder to this was that claims that "I want to value blood relations" might not reflect the parent's true wishes, and declarations that "it is to help patients" might just serve as an excuse for technological development.
- The stance that "basic research on human germline cells is fine, but clinical application is wrong" was criticized.¹⁰ As can be understood if one considers the example of atomic energy, the "development" of scientific technology is intricately tied to its "use." If basic research is permitted, it should be expected that this is premised on clinical application. Put another way, if there are no imaginable clinical applications, then basic research would never be accepted.
- Furthermore, if at the point that a certain technology is developed, the way the technology will be used has not been adequately discussed, this will result in an extremely dangerous situation. In particular, the line currently drawn on human embryos, which states that "research is allowed within 14 days of fertilization," blurs the line between basic research and clinical application. It must be considered that permitting research on fertilized eggs could lead to a slippery slope of allowing use for treatment and then even for enhancement. It is too simplistic to propose permitting

¹⁰ This could be said to represent the stance of the statement from the International Summit on Genome Editing.

only basic research for the time being without fully discussing for what purposes clinical application might be allowed.¹¹

- Some asked if it wasn't possible to imagine members of the children's or grandchildren's generation suing the present generation because they could have used genome editing to perform therapy on zygotes, but did not. This could be considered a type of "wrongful life" lawsuit.
- With respect to gene therapy in general, there was also a view that we should reconsider the value of disabilities. For example, if there is a culture of hearing impaired people, would it really be a good thing to use gene therapy to treat this ailment?
- Some also expressed the view that, because the birth of new technologies increases the responsibility carried by individuals and society, we must give more thought to what obligation the current generation owes toward the next generation of children and grandchildren (inter-generational obligation).

(3) Is the differential treatment of humans and non-human animals in the context of genetic modification defensible? In other words, is it possible to justify a position that "modification of human embryonic cells is impermissible, but the modification of somatic cells is allowable, and the modification of both embryonic and somatic cells is permissible in the case of non-human animals"?

One feature of genome editing is the breadth of its scope.¹² It is applicable not only to humans, but more broadly to animals and plants as well. Currently the regulations on genetic modification vary greatly depending on whether it is applied to humans, or non-human animals and plants, which is due to a number of factors including: the long history of breed improvement of animals and plants, the understanding in the Cartagena Protocols that restricting human behavior is not appropriate¹³, and the limited applications of past

¹¹ The statement from the Hinxton group divides basic research into four types: "1) research to understand and improve the technique of genome editing itself, 2) genome editing used as a tool to address fundamental questions of human and non-human animal biology, 3) research to generate preliminary data for the development of human somatic applications, and 4) research to inform the plausibility of developing safe human reproductive applications." In this manner, it is important to debate the types of basic research that could be considered allowable by organizing the concepts of basic research.

¹² This point is also emphasized in the background paper by the UK's Nuffield Council, 'Identifying key developments, issues and questions relating to techniques of genome editing with engineered nucleases.' (<http://nuffieldbioethics.org/wp-content/uploads/Genome-Editing-Briefing-Paper-Newson-Wrigley.pdf>). See paragraphs 29 and 30. The Japanese summary can be accessed at the following link:

<http://www.cape.bun.kyoto-u.ac.jp/wp-content/uploads/2015/08/506407081c856c824256cb6178e89c15.pdf>

¹³ Biosafety Clearing House "Explanation of Laws Related to Preserving Biodiversity through Regulations on the Use of Genetically Modified Organisms." See page 3.

http://www.bch.biodic.go.jp/download/law/060606law_manual_ver3.pdf

"For human cells, because it is not appropriate to restrict human behavior, even in a case where the use of gene therapy on humans makes them fit the definition of genetically modified organisms in this law, humans are excluded from the definition of organisms under this law."

recombinant DNA technologies.¹⁴ Yet, if it were possible to apply genome editing to humans, animals, and plants in the same way (relative to recombinant DNA technologies), then it would only be a matter of time until it will be necessary to discuss to what extent there are grounds for these regulatory differences. Although it was not possible to discuss this point as much as the preceding two points due to time restrictions, the following views were expressed.

- While eugenics is thought to be unethical, breed improvement of animals and plants, which is also a form of eugenics, is performed as a matter of course. Shall we accept the idea that it is fine to only find problems with how humans are treated and do as we please with plants and animals, even though these are also forms of life (living organisms)?
- It is possible that genome editing will hasten the process by which animals and plants are reduced to tools (or means to an end). It may not be possible to protect each and every animal and plant, but it is necessary to examine the impact on species conservation and biodiversity.
- It is also necessary to discuss why we permit animals and plants to be treated as tools. It is necessary to examine whether there is a basis for asserting that one can easily make a distinction with humans because animals and plants do not have cognitive abilities or (in the case of plants) senses that are developed as much as in humans.

4. Other Issues and Concerns Expressed

Finally, workshop participants were given the opportunity to freely raise arguments or concerns related to the ethics of genome editing that did not fit into the preceding three points.

- Importance of Understanding Genome Editing, and Roles of Citizens and Specialists: Regarding the ethics of leading edge technologies, because it is difficult to assess the risks and benefits without adequate knowledge of the technologies, participants in the debates must share a common knowledge. There is also the question of how much to value the judgments of members of the general public, who do not necessarily possess sufficient knowledge about the technology. Citizens' consensus is important for democracy, but it is also necessary for specialists to explore the issues and present options. It is important to reconcile the views of specialists and the public.

¹⁴ For example, it was thought that application of recombinant DNA technology to human embryos was in fact technically impossible. See the following US government report, pp 46-47. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. *Splicing Life: A Report on the Social and Ethical Issues of Genetic Engineering with Human Beings*. Washington, DC: President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, 1982. In addition, the use of recombinant DNA technologies on human germline cells was not examined at the 1975 Asilomar conference because it was "not realistic." See the following article. Amy Maxmen, 'Easy DNA Editing Will Remake the World. Buckle Up.' WIRED, July 2015. (<http://www.wired.com/2015/07/crispr-dna-editing-2/>)

Furthermore, if a certain technology benefits only a minority of citizens, how should the views of that minority be taken into account?

- Dealing with the Yuck Factor: People tend to experience a sense of discomfort when they hear about the genetic modification of zygotes. It is important to create a space in which the benefits, risks, and other ethical issues can be discussed without relying on this image.
- Dealing with Citizen and Patient Needs: Can these technologies be implemented if average people agree and accept them? Can just about anything be performed if the desire and need is there? This should be thought of as a responsibility of the specialists who provide the technology.
- Economic and Industrial Perspectives: It is also necessary to examine the application and regulation of genome editing from the perspectives of its economic aspects and market principles (industry).
- Neutrality and Reliability of Statements from Specialists: Who will explain that “genome editing technologies are safe”? If someone with a neutral stance does not explain this, the general public is unlikely to believe it. Also, there is a possibility that the notion that “it will be useful for therapy” will be used as a means to obtain research funding. This could raise issues with the reliability of assessments of technologies and research.
- Need for Discussion of Chimera Animals: Discussion of chimera animals is also necessary. For example, there has been talk of using genome editing to create human organs in pigs (xenotransplantation). If it were possible to create a pig that produced human eggs, there would be prospects for its use in research.

This concludes the workshop report.