JST-RISTEX Forum on Genome Ethics

Case Study 2024

Report

March 2025

JST-RISTEX Forum on Genome Ethics

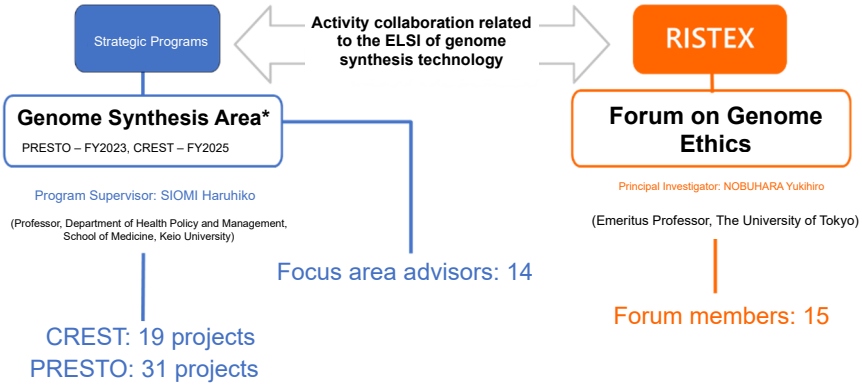
Contents

1. Preface

With R&D on genome-related technologies advancing rapidly, we have entered a new era of artificial designing and synthesizing of genome sequences at our will, including the decoding of human genome sequences and the emergence of CRISPR-Cas9 genome editing technology. While such technical advances could significantly benefit many focus areas, they could also negatively impact life, species, and even ecosystems because genomes are the Blueprint for Life. Under such circumstances, promoting R&D on new technologies related to genomic information requires the consideration of ELSI/RRI perspectives and the establishment of underlying norms and values.

In this context, the Research Institute of Science and Technology for Society (RISTEX) of the Japan Science and Technology Agency (JST) established and operates the Forum on Genome Ethics to solve envisioned ethical, legal, and social issues/implications (ELSI) associated with the R&D and social implementation of emerging technologies. Also, RISTEX set up the Forum as part of the initiative to contribute to responsible research and innovation (RRI) through approaches to ELSI. Through the Forum, RISTEX discusses ethics-related considerations for genome-related technologies and social ethics and implements survey/research activities. Additionally, the Forum on Genome Ethics is engaging in activities to examine and experiment with what ELSI/RRI should be from the upstream of R&D through online seminars and joint workshops (hereinafter “WS”) in collaboration with Large-Scale Genome Synthesis and Cell Programming, a focus area of the JST Strategic Basic Research Programs CREST/PRESTO) (hereinafter "Genome Synthesis Area"). The Programs aim to create essential technologies for cell utilization based on interpreting the principle of genome operation and the knowledge thereof.

Figure/table 1: ELSI initiatives related to genome synthesis technology (FY2019–)



(*Focus Area of Large-Scale Genome Synthesis and Cell Programming)

This fiscal year, the Forum on Genome Ethics held case study workshops to discuss ELSI issues and major perspectives and conducted surveys to raise public awareness for a project in the JST-CREST Genome Synthesis Area (see the figure/table below).

Figure/table 2: Target case study project

Research on Introduction and Manipulation Technology of Long-chain DNA Using Electric Field-Induced Microbubbles and DNA Nanoparticle Crystals **Principal Investigator: YAMANISHI Yoko (Professor, Graduate School of**

	Engineering, Kyushu University) Co-researchers: SUGANO Shigeo (Senior Research Scientist, Bioproduction Institute Plant Gene Regulation Group, National Institute of Advanced Industrial Science and Technology) TAGAWA Miho (Professor, Institute of Materials and Systems for Sustainability, Nagoya University) TSUBOUCHI Tomomi (Associate Professor, Laboratory of Stem Cell Biology, National Institute for Basic Biology, National Institutes for Natural Sciences)

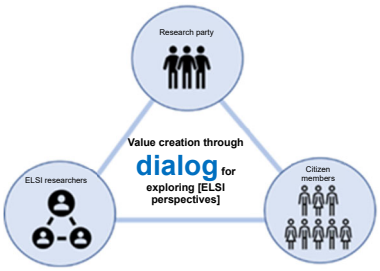
2. Planning

(1) Objectives of Case Study 2024

FY2024's case studies (hereinafter “Case Study 2024”) were conducted with the following objectives.

Figure/table 3: Objectives of Case Study 2024

- To explore “(ELSI) perspectives to be discussed together” through dialog while understanding the differences in positions and knowledge among the three parties: research parties, ELSI researchers, and citizen members.
- To hold Forum WS and Citizens WS alternatively, share the outcomes from the two parties, and continue the discussion.
- To summarize the discussion results in an easy-to-understand manner and publish them along with the discussion process.
- The activities above are expected to lead to the following additional objectives: (1) the participant researchers contribute to the promotion of research activities with ELSI taken into consideration by feeding back the outcomes to their activities, and (2) disseminating this information, including the process involved, gets the initiative referenced in other initiatives as an example of the response to ELSI.



(2) Organization for Case Study 2024

Six Yamanishi Project (hereinafter “Yamanishi PJ”) members and four core forum members led this case study. Also, CREST Program Supervisor Prof. Siomi and the forum members participated in each WS.

Figure/table 4: Case Study 2024 core members

(3) Setting the attributes of citizen members

We considered appropriate candidates for citizen members who can engage in dialog related to genome ethics based on the following conditions. Eventually, we chose to collaborate with the National Institute of Technology, Ichinoseki College (hereinafter “Ichinoseki Kosen”), which appeared to have focused on entrepreneurship education in recent years and has a relatively large number of students interested in the social implementation of technology.

Figure/table 5: Image of citizen members who want to promote dialog in Case Study 2024

[1] **Citizen members must have some understanding, interest, and knowledge of science and technology**

[2] While maintaining a sense of general citizenship, some citizen members **can express a measure of opinions concerning genome synthesis**(Not everyone needs to satisfy the requirement, and those who are capable do not have to be experts in that field. Instead, those speaking from a citizen member's perspective are more desirable.)

[3] What is more desirable is that each group has only **a few participants (two or three)** **who have an interest in ELSI** about cutting-edge research, while maintaining a sense of general citizenship

[4] Also recommended are **citizen members who candidly express their feelings** (without trying to adapt to the surveyor's side)

[5] Considering the long-term impact (positive/negative) on cutting-edge research, **younger generations** should be included.

3. Implementation process of WS and results

(1) Holding of Forum WS and Citizen WS

[1] Holding of Forum WS

We held three rounds of Forum WS in Case Study 2024. In the 1st Forum WS, the Forum members visited the Yamanishi Laboratory at Kyushu University, where they learned about the Yamanishi PJ's research through a research lab tour and other activities. We also coordinated the production of videos and preparation of explanatory materials from the standpoint of how we should explain the research of the Yamanishi PJ to the citizen members during the 1st Citizen WS. In the 2nd Forum WS, we shared the opinion from some citizen members during the 1st Citizen WS: "Discussing ELSI perspectives would be difficult since we cannot fully understand them just by viewing videos and reading explanatory materials." This was followed by our discussion of possible improvement measures. We also shared the thoughts of the four core forum members on the Yamanishi PJ's ELSI perspectives, which was followed by an exchange of opinions. In the 3rd Forum WS, we shared a revised version of reference materials for citizen members, which was prepared mainly by the core members after repeated trial and error. We then selected two of the ELSI perspectives the core members had raised during the 2nd Forum WS. All members were divided into two groups to delve further into the ELSI perspectives. Lastly, all members had a plenary session to share each group's major discussion points, which were followed by an exchange of opinions.

Figure/table 6: Schedule of Forum WS such as dates and agenda

Round	Date and venue	Agenda and others
1st	October 2, 2024 Kyushu University	• Learned about the Yamanishi PJ through a research site visit (Kyushu University) • Considered the direction the Yamanishi PJ's ELSI perspectives should take • Considered explanatory materials for citizen members for the 1st Citizen WS
2nd	November 22, 2024 Online	• Shared and interpreted citizen members' opinions obtained from the 1st Citizen WS • Considered how to respond to citizen members (such as revision of explanatory materials for citizen members) • Consolidated the thoughts of the four core forum members on the Yamanishi PJ's ELSI perspectives
3rd	January 27, 2025 Online	• Shared citizen members' opinions obtained from the 2nd Citizen WS and considered how to respond to them • Delved further into the Yamanishi PJ's perspectives. After discussion in two separate groups, a plenary session was held for further discussion. ➢ Perspective 1: Will the very nature and concept of living things change by the ability to insert long-chain DNA into their cells? ➢ Perspective 2: What is the range of diseases for which introducing long-chain DNA and chromosomes is permitted?

In addition to the above, planning meetings led by the core members were held as needed. The main meetings were as follows.

Figure/table 7: Forum on Genome Ethics: Case Study 2024 core member meetings

Date	Agenda and others
2024 September 24	• Made final checks about the procedure for the 1st Forum WS, and explanatory materials, and others • Planned the Citizen WS

October 25	• Checked and corrected the videos to be used in the 1st Citizen WS (Prof. Yamanishi participated)
November 14	• Shared the opinions received from the citizen members in the 1st Citizen WS • Considered how to respond to the citizen members' opinions from now on • Considered the procedure for the 3rd Forum WS
December 6	• Corrected the Yamanishi PJ's explanatory materials for the citizen members • Prepared explanatory materials for the 2nd Citizen WS
December 17	• Checked the corrected content of the Yamanishi PJ's explanatory materials for the citizen members (Prof. Yamanishi participated)
2025 January 17	• Considered the procedure for the 3rd Forum WS • Checked the corrected content of the Yamanishi PJ's explanatory materials for the citizen members (Prof. Yamanishi participated)

[2] Holding of Citizen WS

The Citizen WS was held three times. The first Citizen WS was held at Ichinoseki Kosen with 17 participants. As observers, one member of the Forum on Genome Ethics participated in the WS onsite, with another joining the WS online. The citizen members, divided into three groups, viewed the Yamanishi PJ's explanatory videos. Each group then exchanged opinions about the Yamanishi PJ's ELSI perspectives from a citizens' viewpoint for two hours. The participants concluded that, "Discussing ELSI perspectives would be difficult since we cannot fully understand them just by viewing videos and reading explanatory materials." They then proposed what should be improved to enable them to discuss the Yamanishi PJ's ELSI perspectives from a citizens' viewpoint in future. The 2nd Citizen WS was held online with six members: some were citizens who had participated in the 1st Citizen WS, with the rest being forum management staff. In addition, the four core forum members also participated online. After reviewing the discussion in the 1st Citizen WS, the citizen members re-expressed their opinions from a citizens' viewpoint concerning the conditions required for them to consider the Yamanishi PJ's ELSI perspectives. Furthermore, the four forum core members shared with the citizens the current status of the Forum on Genome Ethics' response to the discussion in the 1st Citizen WS. The core members then explained the Yamanishi PJ's ELSI perspectives from their respective standpoints. The 3rd Citizen WS was held at Ichinoseki Kosen, inviting 13 citizen members, four researchers from the Forum on Genome Ethics, two researchers from the Yamanishi PJ (subject to Case Study 2024), and a representative (Program Supervisor) from the CREST to which the Yamanishi PJ belongs, totaling 20 people. They exchanged their opinions over three hours. After a lively discussion, we introduced a video of a futuristic novel created using an SF prototyping technique, which the Forum on Genome Ethics produced based on Prof. Yamanishi's presentation to the citizen members and the citizen members' discussion in the Citizen WS. Dialog between the citizen members and researchers followed.

Figure/table 8: Schedule of Citizen WS such as dates and agenda

Round	Date and venue	Agenda and others
1st	October 30 and	• Explained the research summary of the Yamanishi PJ

	31, 2024 Ichinoseki Kosen	➢ Viewed explanatory videos at the venue after reading the Yamanishi PJ's reference materials (such as press releases) in advance. • Opinions from the citizen members ➢ After reading the research materials for the Yamanishi PJ, what words or explanations caught your attention, and what points did you want to know more about? ➢ What should the citizen members discuss further for society as a whole to utilize the Yamanishi PJ's research outcomes appropriately in society? (similar to the ELSI perspectives) ➢ What is the significance/approach of the citizens becoming involved in ongoing cutting-edge research like the example of the Yamanishi PJ? • With 17 citizens divided into three groups (the details are described later), the Citizen WS conducted two-hour discussions for each group on separate occasions.
2nd	December 18 Online	• Re-checked the points considered important after reviewing the discussion in the 1st Citizen WS • The four core forum members participated and advised that they were revising the explanatory materials for the citizen members, and then explained the then-latest version. • The core members introduced their thoughts on the Yamanishi PJ's ELSI perspectives
3rd	February 28, 2025 Hybrid online and onsite meeting at Ichinoseki Kosen	• Based on the past discussions in each Citizen WS, the citizen members, the research party (Prof. Yamanishi), and the Forum on Genome Ethics answered the questions asked. • Viewed a video of a futuristic novel created using an SF prototyping technique • Exchanged opinions. The exchange of opinions started in two separate groups, becoming plenary sessions later. ➢ Perspective 1. How should we consider the Yamanishi PJ's ELSI perspectives? ➢ Perspective 2. What should we do to proceed with ELSI-related discussions with the citizen members on cutting-edge research?

(2) Results of each Forum/Citizen WS

[1] The 1st Forum WS

(Explanation of research details by Prof. Yamanishi)

Aiming to introduce large substances like long-chain DNA into cells, Prof. Yamanishi divides research elements into long-chain DNA encapsulation, cell-introduction, and functional expression technologies, engaging in interdisciplinary research with multiple research collaborators who specialize in engineering, biotechnology, and other fields. Prof. Yamanishi said she was striving for a long-chain DNA delivery system's practical application and social implementation as one of her research outcomes.

Prof. Yamanishi is responsible for researching and developing cell-introduction technology that requires much engineering knowledge. During a lab tour, she showed the forum members the latest experimental equipment, which uses micro-bubble knives to inject micro

bubbles into cells and microfluidic chips manufactured to perform cell fusion efficiently.

(ELSI perspectives related to the Yamanishi PJ)

The Forum WS first discussed the unease we would face and importance when considering ELSI applied to essential technologies. The Yamanishi PJ is implemented to develop a technology incorporating long-chain DNA into cells. However, a member said determining the scope of ELSI considerations is puzzling because we are not sure whether we should consider various ELSI perspectives for incorporating long-chain DNA into cells or whether we should consider ELSI perspectives with a view to their wide range of possibilities by regarding the technology Prof. Yamanishi developed as a (general-purpose) technology that can incorporate substances other than long-chain DNA into cells.

On the other hand, some members pointed out that determining its “exit” (how it should be utilized in society) is required and that the exit side would likely lead the discussion on regulations, among other things. One member said it might be possible to proceed with ELSI discussion by using a broader range of imagination as the basis for discussion, for example, “If inserting an entire complex as (artificial) chromosomes instead of DNA into cells were possible, we wonder how this world would change.”

Regarding technology-derived risks, the Forum WS shared the need to recognize the concern that highly versatile technologies might have significant impacts and inevitably carry higher risks. The Forum WS also agreed that many stakeholders must advance technological development by considering various aspects, including whether we can limit such risks within a controllable range, how we can better estimate the significance of those risks, and how we can come up with a control mechanism in society to prevent misuse of technologies.

Lastly, considering the broad range of applications for the Yamanishi PJ, we can assume that introducing non-life matter into life is technically possible. In this respect, the Forum WS reached a common understanding that if this assumption is correct, discussions about how much of life and non-life can be fused, what it means for humans and machines to become united, and what life is after all must be deepened further as ELSI perspectives.

(Dialog with the citizen members)

Concerning cutting-edge essential technologies, the Forum WS discussed the significance of promoting dialog with the citizens and the procedure for the dialog. Because essential technology is “fundamental,” as the term implies, particularly when research and development is underway, we have no clear answers to what kind of products and services will be created using those essential technologies. Even in this situation, the Forum WS reconfirmed the importance of exploring possibilities for dialog with the citizens. Based on that, a member said they could see the significance of dialog with the citizens because how to show information, such as reference materials and videos, could change the citizens’ opinions, and because such dialog helped collect supporters of a particular research. A member commented that the dialog procedure should be designed to extract diverse opinions from the citizen members by showing a 10-minute video introducing our research and then receiving feedback from them. The member added that carefully checking the citizen members' responses is vital.

(Comment from Program Supervisor Prof. Siomi)

Before closing the 1st Forum WS, Prof. Siomi made the following comment, looking back

on the overall discussion. “From the researcher’s perspective, we cannot help but resist the feeling that we should only research what we want. At the same time, we cannot survive without strong support from many other people. The researcher does not know how to obtain support well, but I saw something gradually appear during today’s discussion. This is a wonderful learning experience, so I want many researchers to get involved in such events, learn how others see their research, and learn how they can get support. In my opinion, acquiring such ways of thinking is very important.”

[2] The 1st Citizen WS

(Participants, procedure, etc.)

With cooperation from Ichinoseki Kosen, the Citizen WS gathered participants from Kosen students, local members of society selected through open recruitment, and individuals approached by the WS. The table below lists the final participants (17 people). The target students were in the 5th grade regular course or above (equivalent to the age group of college sophomores or above).

Figure/table 9: Attributes of participants in the 1st Citizen WS

Group 1	Group 2	Group 3	Total
Five students from chemistry and biotechnology courses at Ichinoseki Kosen	Seven students from machinery and intelligence courses and information and software courses at Ichinoseki Kosen	Five members of society (working for local financial institutions, commerce and industry associations, teachers, administrative staff, etc.)	12 students and 5 members of society 17 people in total

The Citizen WS checked the citizen members’ impressions and opinions after they read the reference materials and videos described below.

Figure/table 10: Information provided to the participants in the 1st Citizen WS

[Materials distributed in advance: Part 1] Six days before the WS

- Press release [Promotion of Molecular Introduction into Cells by Electromechanical Perforation (Electromechanical Poration)]: https://www.jst.go.jp/pr/announce/20221021-2/pdf/20221021-2.pdf
- CREST report on “Large-Scale Genome Synthesis and Cell Programming” (already published), FY2019 and FY2020
- Yamanishi Laboratory website, Research page: https://bmf.mech.kyushu-u.ac.jp/researches/

[Materials distributed in advance: Part 2] The day before the WS

✓ Prof. Yamanishi’s explanatory materials for the citizen members (PowerPoint)

[A video message from Prof. Yamanishi was shown at the venue on the day]

(Comments on the Yamanishi PJ’s explanatory materials for the citizen members)

The Citizen WS asked the citizen members to express their opinions based on what they had realized from the following three major perspectives.

- Words and explanations that caught the citizen members' attention after reading the research materials for the Yamanishi PJ, and what points they wanted to know more about
- Things that should be discussed further throughout society as a whole to utilize the Yamanishi PJ's research outcomes appropriately in society (this is nearly equal to ELSI)
- The significance/approach of the citizens becoming involved in ongoing cutting-edge research, as exemplified by the Yamanishi PJ

As a result, the majority of opinions concerned the preconditions for considering ELSI perspectives in the Yamanishi PJ. We also divided the participants into several groups depending on their attributes to see the differences in reactions. As we had expected, the students from chemistry and biotechnology courses approached this WS more proactively and expressed opinions more specifically than those from machinery and intelligence courses and information and software courses. Meanwhile, the members of society expressed opinions somewhat different from those of the students, based on their position (finance background, housewives, etc.) and influenced by the media. Despite such differences, the three groups had many things in common, including comments like: "I cannot find any connection between myself and the materials and videos related to the Yamanishi PJ." The table below summarizes seven major opinions that were common among the three groups.

Figure/table 11: The 1st Citizen WS: Citizen members' reactions to the Yamanishi PJ's explanatory materials for the citizens

Foundations that allow the citizen members to participate in ELSI discussion	**1. Citizen members want to know the connection between the Project and them, based on the technology's specific application examples**	• In considering ELSI, expressing my opinions as a citizen would be difficult without understanding how that technology is utilized in society.(Because the connection between the technology and myself is unknown.) • The technology appears to have the potential for various applications, but I do not need an exhaustive list of that potential. I would be fine with knowing just the applications with high feasibility and the things Prof. Yamanishi wants to realize.
	2. Citizen members want to know the background and objective of the research and its relationship with other studies	• I want to know the first part of the story about why the Yamanishi PJ was needed. What brought the development of a device to deliver long-chain DNA in the first place? With such information, I could at least imagine the technology's impact on society (though I have no idea right now). • Since CREST probably set the internal division of research roles, I could not understand what CREST wants to accomplish in this research without knowing the overall picture, including the division of roles for other studies. (I could not understand it by looking at Prof. Yamanishi's research alone.)
	3. Citizen members need the creation of bases where their ELSI discussion can be encouraged	• In the first place, imagining the ethical issues is difficult without knowing how the technology is utilized in society. This point is essential if citizens are involved in the discussion. • Undoubtedly, the aim of developing this technology is to improve society, but it must also have its negative aspects (regardless of whether or not we are aware of them). I first felt the need to build bases for the discussion (made available for citizens) by organizing the advantages and disadvantages. • This goes back to pre-ELSI days, but we first need to get citizens interested before they get involved.

	4. Citizen members want to see relevant experts collaboratively disseminate their discussion	• I understand that the medical field is an area where Prof. Yamanishi's research is applied practically. So I want her to collaborate with the medical field (i.e., doctors and medical researchers) as users of her research to discuss practical applications and related ethical issues. • The above effort must be made first before starting the dialog with citizen members. I felt that disseminating practical, specific applications and ethical issues discussed in that field (by experts) would deepen the discussion in society as a whole, where citizen members also participate.
	5. Citizen members want to have reference materials they can understand	• I want the overall course of events, such as the flow and story, taken into consideration. I wanted Prof. Yamanishi's reference materials to first specifically explain what the introduction of long-chain DNA into cells with the help of this technology would change after all. I just wanted to understand the flow of this story. For example, because existing technologies did not work for some reasons, Prof. Yamanishi and her team devised and developed this technology. The story flow may or may not come with the details of Prof. Yamanishi's technology, but just a reference version would suffice. • I got stuck whenever I encountered a word I did not understand. I could not even understand the title of this research.
	6. Citizen members want the timing of their involvement in ELSI discussion taken into consideration	• There is significance in citizens participating in ongoing research. Doing this could improve the likelihood of the research moving in a direction favorable to society. • We should consider whether citizens' involvement in basic research always ensures a good result.(For example, there is a risk that the freedom to research will be lost due to citizens' opinions.) • It is also essential to determine at which stage of research citizens should get involved, though it depends on the field and research.
Assignment of responsibilities	**7. Citizen members may think ethical issues in research lie on the user side**	• First, regardless of who explains it, evaluating challenges such as risk accountabilities and responsibilities is difficult unless the person can describe the research's applications to some extent. • The researcher must also be knowledgeable about the risks their research carries. Therefore, I want Prof. Yamanishi to explain or enlighten the risks brought by her research as a leading researcher in this field. However, I am not saying Prof. Yamanishi needs to disseminate her views on ethical issues. I felt that the government (which adopted the research) should disseminate information about ethical issues to the public. • Whether good or bad, technology is all about how it will be utilized. Risks and their responsibilities are issues that must be handled by the technology user/application side, not by the researchers who developed the technology.

*For details of the discussion at the 1st Citizen WS, see "Reference Material: Citizens' Opinions on Initial Materials for the Yamanishi PJ at the 1st Citizen WS," which is described later in this document.

[3] The 2nd Forum WS

(Sharing the 1st Citizen WS results)

The Secretariat of Forum on Genome Ethics (hereinafter “Secretariat”) introduced the citizen members’ main opinions confirmed at the 1st Citizen WS (see the table on the previous page). The Secretariat reported those opinions by broadly classifying them into seven categories. As an important point underlying all opinions, the Secretariat pointed out that the citizen members wanted specific examples of research details for social implementation presented as a precondition for considering ELSI perspectives. It was particularly emphasized that a significant precondition for their ELSI discussion would depend on the likelihood of assuming how the research will become interrelated with them to some extent.

The background to this situation was confirmed to include: a) The Yamanishi PJ, the theme of the Forum on Genome Ethics for FY2024, involves the research and development of essential technologies, making the identification of specific, practical examples that citizen members can access difficult at this point; b) the nature of mechanical engineering, the field of expertise of Prof. Yamanishi; c) the development of the device is part of an overall research project of CREST. The Forum WS then discussed the necessity of informing the citizen members about the above background and the research’s positioning.

(Efforts to promote constructive discussion with the citizen members)

Based on the challenging results from the 1st Citizen WS, the Forum WS discussed various ideas for specific approaches to promote the discussion while gaining the citizen members’ understanding.

First, a member said that “the world we live in today has been built thanks to past technologies” and that acknowledging the fact might trigger our imagination about the future. It might be possible to argue what would happen when new technologies emerged in the biotechnology field, recalling how the world had changed before and after the advent of mobile phones and Zoom video conference technology. The idea helped facilitate the discussion on the future by drawing a simple projection line.

Another member suggested explaining this situation using analogies from technology areas, such as information and telecommunications, which the citizens find easy to understand. The Yamanishi PJ's development of a technology that can introduce long-chain DNA into cells, which has been difficult in the past, is expected to dramatically increase the amount of information that can be transmitted into cells. However, a question has arisen whether the introduction of genetic information (manipulation) is reversible, although false information can be corrected relatively easily in the world of the Internet.

In addition, a member said there is a technique to activate the discussion by presenting conflicting positions to the citizen members to argue the extreme possibility of applications and asking them to imagine which position is closer to theirs. Taking that suggestion further, the member presented the idea that the citizen members would find the discussion easier when the main perspective is social inequality that may arise from the spread of that technology into society, rather than discussing the safety and morality of that technology.

From a broad perspective, today’s humanity does not know about the introduction and driving of long-chain DNA pursued by this research project, which is applicable as the precondition for ELSI discussion involving Citizen WS and researchers from diverse fields. This is precisely why another member pointed out that humanity first needs to develop a common view that research aimed at filling in the blank is necessary. The research party recognized the need to advise many people of the current situation, namely, “We are doing

this research to understand what humanity has not understood." and confirmed that it wanted to improve this situation.

(Brushing up The Yamanishi PJ's explanatory materials for the citizen members)

Based on the 1st Citizen WS results, the Forum WS shared opinions on how to revise the Yamanishi PJ's explanatory materials for the citizen members. As well as discussing ideas on how the Yamanishi PJ's technology is used, it introduced and discussed the four core members' opinions on the Project's ELSI perspectives.

Figure/table 12: Proposals of how to brush up the Yamanishi PJ's explanatory materials for the citizen members – Proposed by the core members

Policy	✓ At the 1st Citizen WS, the citizen members claimed that the Yamanishi PJ's explanatory materials were difficult to understand. To verify how we could have prepared more easily understood materials, the core forum members **tried to organize a revised version** in coordination with Prof. Yamanishi.
Points for improvement	1. Simply explain **the objective of CREST [Genome Synthesis] Large-Scale Genome Synthesis and Cell Programming** Define where **the role of the Yamanishi PJ** is positioned. 2. With CREST Genome Synthesis understood as an **essential technology development**, concisely describe its **ultimate social applications (such as the medical and biotechnology industries or agriculture).** 3. Present **what is new and what is challenging about the EMP technology in the Yamanishi PJ** so that **the citizen members can understand its significance in comparison with conventional technologies.**(The comparison should include: how long-chain DNA differs from short-chain DNA, the significance and difficulty of introducing long-chain DNA into cells, and the appealing points of EMP technology.) 4. In proceeding with the Yamanishi PJ, provide images of **how far genome synthesis-related technologies have progressed so far and what will become possible based on the technology in what timeframe in the future.** 5. Show what kinds of images various stakeholders have in mind **concerning specific methods for utilization** after the Yamanishi PJ's advanced technical developments become available. To that end, the forum members **first exchange their opinions about what they think and include appropriate examples in the Project's reference materials.** 6. **Imagine a society where the Yamanishi PJ's advanced technologies are ready for use. It will present the citizen members with the kinds of advantages and problems that can exist** and summarize them in a form so that the citizen members can consider ELSI issues.

(Thoughts of the four core forum members on the Yamanishi PJ's ELSI perspectives)

The four core members explained the proposal for the Yamanishi PJ's ELSI perspectives they had considered. When we consider the possibility of creating new or unexpected living organisms, should we define areas that humans cannot control? To what extent should

manipulation of cells be permitted from the standpoint of respect for life? Should multi-stage perspectives exist depending on the technology's readiness? In addition to the above, the Forum WS presented proposals for ELSI perspectives, such as aversion to introducing animal chromosomes into human cells, animalizing human cells and humanizing animal cells, and the possibility of new animal species emerging. Opinions were exchanged following the presentation.

Figure/table 13: Ideas for methods for utilization related to technologies developed in the Yamanishi PJ

- Observation of the expression of cell functions by introducing human genes into chimpanzee cells (basic research)
- Genome replacement enabling the animalizing of human cells and humanizing of animal cells (cell engineering)
- Designer babies (fertility treatment)
- Highly accurate DNA insertion technologies enabling the best possible treatment depending on each patient's condition and requests (personalized medicine)
- Health promotion, beauty care, and aging prevention, as well as illness treatment (health promotion and beauty care)
- Enhancement of biological functions such as gene doping (enhancement)
- Manufacturing of pharmaceuticals, supplements, probiotics, etc. (drug development)
- Use in food, agriculture, livestock, fisheries, forestry, etc. (agriculture, forestry, and fisheries industries)
- Applications in the environment and energy fields (biotechnology industry)

Figure/table 14: The Yamanishi PJ's ELSI perspectives – Consolidated by the core members

- This technology can be used to treat diseases but changes the very nature of living things
- What is the range of diseases for which long-chain DNA and chromosome introduction are permitted?
- Are there inviolable areas that humans must not manipulate? Is it acceptable to retain areas where there is no manipulating technology?
- Just as a digital divide has emerged in the world of the Internet, a genome divide may also occur
- Arguments on gene modification need to be reconsidered (how should we consider regulations against genome manipulation?)
- We should depart from the binary opposition of good versus evil utilization
- We do not yet know how long-chain DNA is driven. How should we deal with things we don't know or understand?
- How should we put in order what we are ready for and not prepared for?
- Creating useful devices and deciding what we use them for are separate things, which must be discussed by the concerned parties
- We do not want this technology's methods of utilization limited (the direction of development should be decided through discussion)

[4] The 2nd Citizen WS

(Participants, procedure, etc.)

The 2nd Citizen WS assembled six citizen members, consisting of participants and forum management staff from the 1st Citizen WS (five students and one member of society), together with four members from the JST Forum on Genome Ethics. They exchanged

opinions on how citizen members and researchers can collaborate to engage in constructive dialog concerning the ELSI of cutting-edge research, its possibilities, and the challenges to be overcome.

(Matters we must discuss to ensure that cutting-edge research will be appropriately accepted and utilized in society)

The participants expressed opinions on points considered particularly important when teams involved in academia-led research on cutting-edge technology developments and citizens proceed with constructive dialog aimed at ensuring that the research will be appropriately accepted and utilized in society. Based on the discussion at the 1st Citizen WS, the six citizens presented the following points, which they considered important in considering the Yamanishi PJ's ELSI perspectives. These reconfirmed what was discussed at the 1st Citizen WS. Once the use of the Yamanishi PJ's technology is defined and the social advantages and disadvantages are organized, the citizen members will realize for the first time that ELSI issues are their problems. As a result, the citizen members will likely become interested in and concerned about the Yamanishi PJ's research. This suggests that if their situation improved that much, the citizen members would be ready to discuss the Yamanishi PJ's ELSI perspectives. Separately, a member said that when it comes to dialog with citizens, complete attention should be paid to who the citizens are in the first place and who determines that definition. This opinion argued that ELSI discussion is expected to include, in particular, citizens who may oppose the research subject for discussion and the views of minorities whose voices are not loud enough.

Figure/table 15: Matters required when the citizen members consider the Yamanishi PJ's ELSI perspectives (the citizen members' opinions)

- Many citizens should be considered to have no knowledge about cutting-edge research, such as that of the Yamanishi PJ. Thus, considering ELSI with those citizens would require them to become interested and concerned in the research.
- To get the citizens interested in cutting-edge research, it may be essential to make them interested in the associated ELSI issues as their problems by organizing the advantages and disadvantages that may impact society.
- In the real world, it must be difficult for general citizens to understand the details of cutting-edge research. Researchers may be expected to tell citizens what the research can be used for and how society will change eventually, rather than asking them to understand the research details. If the citizen members can see how the research is used even without understanding its details, they should be able to have a variety of opinions on the associated ELSI issues.
- What types of citizens are they when we say dialog with citizens? The kinds of citizen we should engage in dialog with may be one of the critical ELSI discussion points. For example, engaging in dialog with citizens who seem unfriendly to the research currently under discussion may be necessary. We also want to consider how to check the voices of minorities from an ethical awareness standpoint.

In response to the opinions above, the forum core members thought it extremely important that the citizen members considering ELSI issues as their problems could be a precondition for considering those issues. As another approach to get the citizen members to take the ELSI issues as their problems, the forum core members provided an idea that highlighting the viewpoint of being a sponsor of research projects through their tax payment could be one of the available directions. On the other hand, the core members said that the citizen members wanted an explanation of the impact of the research's advantages and disadvantages on society. The core members then asked whether it makes sense to judge

that this one is worth researching because of its advantages and that one is not because of its disadvantages. This opinion pointed to the importance of looking further into the future to pursue the wide range of possibilities that research can open up. Furthermore, one of the core members pointed to trends in the citizen members' thinking related to the ELSI discussion of the Yamanishi PJ. This raised the question about the citizen members having gone too far into a belief that they cannot or must not discuss ELSI issues without correctly understanding the research content and its impact. The person who raised the question often disseminates his opinions and interacts with society concerning cutting-edge research on space and genome synthesis. According to that person, many people engage in discussions without necessarily understanding the associated issues correctly in real society. An important point is that many researchers move forward by disseminating their thoughts and opinions while misunderstanding things and making mistakes in the reality of society, rather than concluding that something is incorrect or inadequate. In his opinion, acknowledging the reality first is important. His point was that even if it takes a lot of time, researchers who discuss diverse issues according to such acknowledgment can discover various possibilities.

(Response from the Forum on Genome Ethics members to the citizen members: Revisions to the Yamanishi PJ's explanatory materials)

In response to the citizen members claiming that the research details presented at the 1st Citizen WS were difficult to understand, the forum members explained the status of revisions to the explanatory materials currently underway.

- An overview of CREST was added to clarify the positioning of the Yamanishi PJ. CREST is a framework that promotes team-based research to create seeds for innovative technologies. CREST has research areas inside that framework to establish genome-scale DNA synthesis and functional expression technologies. The forum members then stressed that under those research areas, the Yamanishi PJ proceeds with research aimed at introducing large, chromosome-level DNA into cells for cell function expression.
- The following was explained to improve the citizen members' understanding of the current situation: a) The Yamanishi PJ set the goal of developing essential technology, and its research is ongoing. Therefore, it would be difficult for Prof. Yamanishi to explain specifically how the research will be used in society, b) it would take some time before this research can be applied to medical and industrial fields, and c) discussing the research's potential now would end up with fictional stories after the research has progressed further. We have no idea what will happen right now.
- The forum members presented specific examples of the potential use of this technology based on their thoughts.
- Aiming to activate ELSI-related discussions, the forum members wrote futuristic newspaper articles about the Yamanishi PJ's impact on society.

The citizen members responded to the above explanation by the forum members as follows.

- I felt that the explanation was much more reader-friendly than the materials presented at the 1st Citizen WS. I understood the research's current positioning and status, including that even researchers find it difficult to tell what this research will be used for. Once recognizing such preconditions, the citizen members' side finds engaging in discussion easier.
- The simple description of the relationship between CREST's whole image and direction and the Yamanishi PJ was good. However, the forum members' response presented just a simple list of application examples for what might eventually happen

from the research, making it still hard for the citizen members to imagine the relationship with us. For example, the citizen members can better understand this explanation if it covers the potential risks that may eventually arise from this research. I am concerned about the possibility of bioterrorism due to research like the Yamanishi PJ. However, the following explanation, for example, would be instructive in correctly understanding such a risk: “That possibility is virtually zero because we have a safety assurance system in place. On the other hand, this research carries a higher risk of creating designer babies.” Such concrete statements would allow the citizen members to be ready to discuss potential ELSI issues and hold them responsible for such discussions.

- On the other hand, the government should more seriously consider how to foster citizens who can participate in such discussions. It is time to start implementing specific societal measures, such as incorporating them into elementary to high school curricula and mandating participation in town meetings on next-generation science and technology, just like the lay-judge system.
- I had thought that understanding the research should precede discussing it. However, when a forum member made a comment earlier to the effect that “ambiguity opens up possibilities for communication,” I thought it was a great insight for me. When I participated in the discussion at the 1st Citizen WS, I felt that the researchers and citizen members should come to a compromise more. But I later thought ambiguity might be the key to improving the opposing discussion. If there had been a precondition for allowing ambiguity on both sides, the citizen members could have spoken up more freely, and the researchers could have discussed all kinds of things. I feel that they might have bound themselves by “correctness.”

The forum members shared part of their efforts to consolidate the ELSI issues related to the Yamanishi PJ.

- First, it is important to create a common language that allows the research party, researchers from various fields, and the citizen members to discuss issues on common ground.
- When conducting cell manipulation like large-scale DNA introduction, we must consider the issue of technological acceptability relating to what kind of manipulation can be applied to which cells and to what extent society can permit such manipulation from the perspective of respect for life. In doing so, we must also consider what kind of future we expect.
- Is it really a good thing that advances in technology allow us to manipulate life at will? While some argue that inappropriate manipulation should be restricted, we must consider every possible option, including suspending technological development at its preliminary stage.
- For example, if someone replicates animal chromosomes in human cells, how will society react? If people feel a sense of aversion about it, why is that? It would be great if we could engage in ELSI discussions with the citizen members this way.
- The more advanced the research becomes, the more critical it becomes to clearly define the incremental positioning of the research subject to the discussion. Moreover, we may be expected to become more creative in selecting participants and preparing the procedure for ELSI discussions to extract the appropriate perspectives for each stage.

[5] The 3rd Forum WS

(Sharing the 2nd Citizen WS results)

First, the Secretariat reported the main points of discussions raised by the citizen members at the 2nd Citizen WS to the forum members. Specifically, the Secretariat reported the following four points: [1] The Citizen WS wants the forum members to start to get the citizen members interested/concerned about the research details; [2] The Citizen WS wants the forum members to organize the technology's advantages and disadvantages that impact society, making the citizen members take them as their problems; [3] The Citizen WS wants the forum members to tell the citizens what the research is used for and what kind of impact it will have, rather than having them understand the research details; [4] Attention should be paid to how the target citizens are selected because there are many different types of citizens.

(Delving further into the Yamanishi PJ's ELSI perspectives)

Next, the forum members selected two critical perspectives from the proposed ELSI perspectives of the Yamanishi PJ, which were repeatedly discussed at the 1st and 2nd Forum WS. Prof. Yamanishi and the forum members were then divided into two groups to delve further into those perspectives. The two ELSI perspectives selected were as follows.

> **[Perspective 1]** Will the very nature and concept of living things change by the ability to insert long-chain DNA into their cells?
> **[Perspective 2]** What is the range of diseases for which introducing long-chain DNA and chromosomes is permitted?

(Delving further into Perspective 1)

- The ability to introduce substances with various functions into cells at will, including long-chain DNA, could replace cellular functions beyond our imagination. If that happens, the concept of living things may come to include hybrids with artificial objects.
- This drastic change in the concept of living things might blur the boundaries between natural and artificial objects, leading us to discuss ELSI issues with the citizen members by possibly asking, "How do you usually distinguish between living things and objects?" or "If the concept of living things changes, is that something important to you?"
- That argument may vary depending on how that person daily acknowledges the concept of living things, or it may be an opportunity to reaffirm that recognition. For example, people often say, "This wheat is not genetically modified." However, the question is whether or not we recognize only living organisms that have not been genetically modified as ones in their original form.
- There was an argument in the past about what would change if a new living organism were created by combining different species, but we do not want to just repeat that argument. Therefore, it is essential to consider how to discuss the image of how much introduction of long chain DNA can change a cell into a different one, the unique technology developed by the Yamanishi PJ.
- We have already entered an era where a considerable amount of genome editing can be done using CRISPR-Cas9. The Yamanishi PJ aims to do similar genome-editing using long-chain DNA, but our concern is how well the gene editing using long-chain DNA can compete with or can be differentiated from CRISPR-Cas9. The ELSI perspectives of CRISPR-Cas9 have already been discussed, with some overlapping with those of the Yamanishi PJ. However, we believe the technically

different portions require another round of discussions.

- The Yamanishi PJ aims at megabase DNA insertion, with 10 kilobase DNA insertion already possible today. Once this method is commercially available, the genome-editing of living organisms can be done on a larger scale than by conventional methods. Just as advances in molecular biology have dramatically changed evolutionary trees, classifying living organisms based on their genes, not based on their appearance, may become possible. In the future, we may see living organisms classified as close in appearance but distant in DNA structure. Human genomes consist of approximately 3 billion base pairs. One can argue whether we should regard one living organism and another as the same based on similarity in the number of their base pairs. For example, if two living organisms have up to 99.99% of their genomes in common, are they the same organisms? Conversely, if they have 99.98%-or-less genomes in common, are they different organisms? Where is the threshold between same and different? We may ask the citizen members such a question.
- Thinking about the advantages and disadvantages accurately and logically is critical to discussing ELSI issues with the citizen members. In addition, the emotional aspects of the research, such as which parts of the research the research party (researchers involved in the Yamanishi PJ) finds interesting, may sometimes spark lively discussion.
- It may be important for the citizen members to consider the social impact and value of the Yamanishi PJ's technology instead of waiting for the researchers to tell them its significance. When people in various circumstances look at this technology, what kind of value do they find? We understand that citizen members' opinions play an important role in promoting broad discussions, whether they relate to business or ethical values.
- As one of its possible future goals, the Yamanishi PJ's technology could become an application that introduces objects, which are not necessarily genes, into cells. It suggests the possibility of a new form of intracellular symbiosis occurring.
- Even if introducing microorganisms and artificial objects into cells is possible, the citizen members may find it difficult to imagine the benefits unless they are clearly explained. It would be great to show what kind of future we can expect from intracellular symbiosis when it becomes technically possible.
- It is essential to consider ELSI perspectives as something we should handle step-by-step. If we suddenly start talking about inserting long-chain DNA into cells, many people would be frightened and react strongly against it. We need to discuss and define the necessary perspectives before arguing whether we should insert long-chain DNA or not, including whether we can trace the state of the inserted long-chain DNA, whether we can create a mechanism similar to a marker that allows everyone to recognize that long-chain DNA is present, and whether we can restore/remove the inserted object. Continuing discussions like this would mean re-examining the very nature of existing living things, including ourselves, before deciding whether or not to transplant the organs of other animals into humans. After completing this process, we should consider process designs that encourage bolder discussions.
- In the plant world, there is a method called cell fusion. We usually see new agricultural efforts progressing, such as producing interspecific hybrids by interbreeding Chinese cabbage and regular cabbage, and growing bigger strawberries from regular-sized strawberries. We eat them without worrying about how they were made. One can argue how far we can apply what we already do for plant production to mammals. How much will society permit such genetic

modifications? What should be done if someone wants to keep a new living organism as a pet (one that transcends a species boundary)? There is a possibility of more and more people wanting to create things like this.

- From the viewpoint of moving toward blurring species boundaries, Japan has been making genetic modifications to fish, which we accept as the norm. We feel Japanese people are lax about their understanding of this issue. In Japan, there is a belief in reincarnation. For example, they tend to believe, “I might be reborn as a turtle next time.” In this sense, one can say that Christian societies, which believe God created species boundaries, differ considerably from Japanese society.
- For example, just like aortic valve replacement using biological valves (from cows and pigs) is covered by health insurance, crossing species boundaries is already accepted by society in medical applications.
- When viewed on a scale of millions of years, the genes of living organisms have undergone significant changes in nature. When the Yamanishi PJ is regarded as a technology that accelerates those changes, it leads to the ELSI discussions on the main perspective: “This project may change the very nature and concept of living things.” We think this is an essential perspective on how fast we should develop cutting-edge technologies and how we can adjust the speed.

(Delving further into Perspective 2)

- If asked what kinds of diseases are acceptable for gene modifications, we would point to life-threatening diseases or those with no alternative therapies. If parents are told during prenatal testing that their baby is missing a chromosome or has an extra one, they will be faced with a difficult decision. If a DNA modification is an option, they would consider it. On the other hand, where no life-threatening disease is involved, society would hardly accept a gene modification as an option. Drawing the line between what is life-threatening and what is not is very difficult. For example, some patients can only survive with 24-hour support. In such a case, one can argue that intervention is permissible if that condition can be improved.
- It may be necessary to ensure whether the destination of long-chain DNA insertion is in a germ cell or somatic cells. This technology will probably be tried first in an area where its evaluation is relatively easy (e.g., introducing long-chain DNA into a somatic cell), which is followed by a societal acceptance process. Please note that we (personally) oppose inserting DNA into fertilized eggs, at least for now.
- From the standpoint of inserting large DNA, people with Duchenne muscular dystrophy and mitochondrial disease are included as candidates for long-chain DNA insertion treatment. Because this treatment requires two to three megabase genes, the existing methods (such as replacement therapy) have been unsuccessful. For this reason, many people would be delighted if the Yamanishi PJ’s technology becomes available as an optional treatment. This technology also applies to Parkinson's disease because its genes are sufficiently large. The citizen members may be able to understand the Yamanishi PJ’s technology more easily when described as having the potential to cure such diseases. Regarding the discussion on enhancement, inserting this long DNA into cells might enable something we have not seen before. We remember that conventional short-chain DNA insertions were also intended for plant species protection, with a technology to integrate traceable DNA barcodes developed.
- We believe that diseases caused by a single gene are curable using CRISPR-Cas9 even today. With the spread of CRISPR-Cas9, it is essential to consider what contributions can be made solely by a technology that introduces long-chain DNA

into cells. For example, while chimpanzees and humans have almost the same genetic sequence, they are entirely different living organisms. The reason why they are entirely different living organisms despite their nearly identical genes may be attributed to the difference in their gene expression. Accumulating research in such fundamental areas may create the possibility of an ultimate solution (treatment) being developed. This technology that introduces whole long-chain DNA into cells should increase human knowledge of genome dynamics, which may play the role of a contributor as a powerful tool for conducting basic research. Likewise, CRISPR-Cas9 underwent 20 to 30 years of basic research before finding its way to today's application research. We believe it is necessary to understand the Yamanishi PJ's technology from a similar perspective.

- As we are also involved in plant research, we know that crossbreeding plants takes a lot of time. We do not know yet about the gene regions important for plants (although we can infer their correlative relationships), and experimentally shaping their causal relationships requires a technology that can stably introduce long-chain DNA into cells. So we are working on plant research with the understanding that such technological development is necessary. Combining a technology to accelerate the speed at which the introduced cells are multiplied and incorporated into individual cells, and a technology that can insert an object the size of a chromosome, has the potential to lead us to various discoveries. On the other hand, some researchers around us engage in microbial symbiosis. The Yamanishi PJ's technology may contribute also to the reconstruction of microbial symbiosis, although it broadens the scope of the research. (Research on sea slugs that steal chloroplasts from algae to produce their own energy is becoming a hot topic.) We believe the Yamanishi PJ's technology has potential beyond gene insertion, making it very interesting.

[6] The 3rd Citizen WS

(Participants, procedure, etc.)

The 3rd Citizen WS was held at Ichinoseki Kosen inviting the following 20 people: 13 citizen members consisting of the nine students and two members of society who participated in the 1st Citizen WS and one student and one member of society who joined Citizen WS for the first time, four researchers from the Forum on Genome Ethics, two researchers from the Yamanishi PJ for Case Study 2024, and a representative (Program Supervisor) from the CREST to which Yamanishi PJ belongs. They exchanged their opinions over three hours.

As shown in the following table, the program for the day included ELSI discussions from the citizens' viewpoint based on the discussions held at the last two rounds of Citizen WS, the second presentation on the research details from the research party to the citizen members, and the thoughts of the Forum on Genome Ethics on the Yamanishi PJ's ELSI perspectives (see Response 1 through 3). After that, the Citizen WS viewed a video entitled "Futuristic Novel" created using an SF prototyping technique. Lastly, the researchers and citizen members had the second round of discussions on the Yamanishi PJ's ELSI perspectives and the significance of the citizens' involvement in cutting-edge research from various aspects.

Figure/table 16: Program for the 3rd Citizen WS

[Response 1]	**Citizen members' perceptions of ELSI discussions on cutting-edge technology development (Facilitator: Yutaro Ueno, Advanced Engineering Course, Ichinoseki Kosen**） • Issues raised by the citizen members – What is needed for the citizen members to participate in ELSI discussions on cutting-edge research
[Response 2]	**Presentation by Prof. Yoko Yamanishi, (Kyushu University)** • Introduction: The significance of citizens' voices for me • Presentation: Further explanation on the research details of the Yamanishi PJ
[Response 3]	**Thoughts of the Forum on Genome Ethics on the Yamanishi PJ's ELSI perspectives(Nariyoshi Shinomiya, Former President, National Defense Medical College / Visiting Researcher, National Institute of Infectious Diseases)** • Introduction of a futuristic novel created using an SF prototyping technique • The Forum on Genome Ethics' consolidation of the Yamanishi PJ's ELSI perspectives
[4] Opinion exchange	**Facilitator: Yukihiro Nobuhara, Emeritus Professor, The University of Tokyo** **(Perspective 1) How should we consider the Yamanishi PJ's ELSI perspectives?** **(Perspective 2) What should we do to proceed with ELSI-related discussions with the citizen members on cutting-edge research?** First half: Group discussion Latter half: Plenary discussion

■ Response 1. Citizen members' perceptions of ELSI discussions on cutting-edge technology development

Two citizen members who participated in the 1st and 2nd Citizen WS (Mr./Ms. Kurosawa and Mr./Ms. Sasaki from Ichinoseki Kosen) delivered a presentation on the significance and issues of the citizen members participating in ELSI discussions on cutting-edge research

based on the discussions thus far. The main points of that discussion are as follows.

(About the Yamanishi PJ)

- We viewed the video and read the preparatory materials at the 1st WS, but found it difficult to understand the technology's novelty and strength.
- We could not understand the meaning of the words in the sentences. Even imagining what was meant was difficult. The analogy of a cargo-loaded ship passing through gateways gave us a specific image and was easily understood.
- If the explanation of the research had been consistent throughout the Citizen WS, we could have better understood the research details.

(About the Yamanishi PJ's ELSI perspectives)

- It was difficult to imagine how the technology would be used in various fields, making it difficult to estimate the benefits and damage that could arise from citizens' use of the new technologies.
- We wanted to know potential societal advantages and disadvantages instead of the researchers unilaterally explaining their research details. Unless the citizen members become interested, the Citizen WS will not be ready to consider ELSI issues. We would be afraid if the researchers proceeded with ELSI discussions on their own, leaving the citizen members ignorant.
- We understand that the Yamanishi PJ is developing a technology that enables long-chain DNA insertion into cells. We felt uneasy about how far human cell manipulation would be permitted.
- If we assume that ELSI issues arise in the context of technology use, it was unclear to what extent the researchers involved in the Yamanishi PJ should be held responsible for the consequences. We felt it unreasonable to get the researchers to take full responsibility.
- We felt it was necessary to create guidelines for the appropriate use of new technologies in society.

(Measures to facilitate citizens' participation in ELSI discussions on cutting-edge research)

- Above all, communicating why the research must be done is essential. General citizens, particularly those not involved in research, cannot understand research details. If the researchers can communicate what they are passionate about, citizens can recognize the positioning of this research, though the level of understanding varies depending on each citizen.
- The researchers must clarify what they expect from citizens. The researchers must change the opinions they want to obtain and how they interact with citizens, depending on the stage of research. While understanding that certain and uncertain factors exist depending on the research stage, we wonder if it is meaningful to consider ethical perspectives in the early stages, when how the research will be utilized is unknown. The significance of citizens participation and the content of discussions should change depending on the research stage, so we want the researchers to customize the interaction with citizens for each stage.
- The researchers do not have to share all research details with citizens. Even if they are explained, we cannot understand them anyway. Conversely, we want the researchers to consider further which part of the research citizens should know.
- In addition, since uncertainties always accompany research, the scope of its application methods should have its limitations. In that case, speculating about future stories may fan anxiety. Therefore, it is important to clearly communicate what is confirmed at the present research stage and what can be explained.
- One option is to advise citizens on a research overview without asking for a detailed

technical understanding. Citizens can actively participate in discussions if they become interested in something without specialized knowledge or the ability to understand technical terms. One such example is animation as an effective communication tool.

(Significance of citizens participating in ELSI discussions on cutting-edge research)

- Citizens' participation should help obtain diverse perspectives and a wide range of opinions. Exchanging opinions and engaging in conflicting arguments with citizen members who live under various circumstances may create new insights.
- Dialog with citizens could align research policies with social needs. Dialog with citizens could improve their technical literacy, and the researchers teaching citizens could improve their own.
- When researchers and citizens work together on ongoing research, they may encounter challenging aspects. However, even if the citizens cannot understand many things at the research stage, they can catch up with the researchers by the time the implementation stage starts, which increases the likelihood of the ongoing research progressing smoothly.
- Sharing the issues raised by cutting-edge research with citizens at an early stage is meaningful. We consider that in the event of a problem with research outcomes, not only should the researchers consider how to deal with it, but the citizens who accept the research outcomes must also be held responsible.

Response 2. Presentation by Prof. Yamanishi

At the 1st Citizen WS, Prof. Yamanishi, the leader of the Yamanishi PJ, delivered her presentation on "Explanation of Research" on a video screen (a PowerPoint presentation by the professor). However, the citizen members claimed that the presentation was difficult to understand. Based on that feedback, the forum members and Prof. Yamanishi had brushed up the explanatory materials over several months. This time, Prof. Yamanishi passionately spoke about her research directly to the citizen members, using the latest version of explanatory materials.

The citizen members' response to this presentation was completely different from the video presentation at the 1st Citizen WS. Some of the citizen members' reactions are listed below.

- (Student A) Compared with the one for the 1st Citizen WS, this presentation is so easy to understand, which makes me wonder if it discusses the same subject. Gold nanoparticle crystals are wrapped up with something like the nucleus' cousin because a foreign substance is ejected when it enters a nucleus. Is my understanding correct?
- (Prof. Yamanishi) Gold nanoparticle crystals look like those made from DNA in appearance. The idea is to encapsulate a substance in the nanoparticle crystals. We probably can say DNA is close and familiar to cells, but it has not been proven yet.
- (Student B) My level of understanding has improved drastically since the 1st Citizen WS. I am now convinced of how important it is to listen to others directly. In electric field-induced microbubbles, the microbubbles are applied to a cell membrane to induce and massage the membrane and open an entrance hole for DNA introduction. Is this a correct statement?
- (Prof. Yamanishi) Elastic bubbles approach the site where DNA-suspended solution is dispersed. Due to the relatively large size of the microbubbles, you can imagine

this process better by interpreting that the bubbles distort the site rather than move toward a specific target. We also use a method for injecting microbubbles through a needle. However, when introducing electrically induced microbubbles, the cells are too small for the microbubbles to open a hole, so we vibrate and stimulate the cells using relatively large microbubbles.

Response 3. Thoughts of the Forum on Genome Ethics on the Yamanishi PJ's ELSI perspectives

Dr. Shinomiya explained the outline and production intent of the futuristic novel created using an SF prototyping technique. He produced it to consider the Yamanishi PJ's ELSI perspectives with the citizen members.

- SF prototyping is a method of imagining the future after cutting-edge research, such as the Yamanishi PJ, has been implemented in society.
- This time, the novel envisioned a future 40 years away based on the awareness that the ability to insert long-chain DNA into cells could change the very nature and concept of living things. This story is based on the following scenarios. Genome editing therapy for critical illness will be approved in the 2030s, with extensive genome editing spreading throughout society. Then, platforms for distributing genome editing products will be established between the 2040s and the 2050s. In the 2060s, voluntary editing of human cells will be approved. People can purchase genome editing products from platforms, embed those products into their bodies, and turn on the expression of cell functions when they choose. In the 2070s, the second generation of those who received voluntary gene editing begins to emerge.

*For the content of the novel (the narration of the video), please see "Reference Material: Futuristic Novel Created Using an SF Prototyping Technique," which is described later in this report.

Response 4. Opinion exchanges

Prof. Nobuhara explained the main points of discussion from the opinion exchanges. The Citizen WS formed two citizen/researcher mixed teams, and the respective teams started team discussions based on these points. These meetings were followed by a plenary session where all members shared each team's discussion results and discussed them further.

Perspective 1. How should we consider the Yamanishi PJ's ELSI perspectives?	Will the very nature and concept of living things change by the ability to insert long-chain DNA into their cells? • What kinds of new living things do you want/not want to emerge? • If you could change into a new living thing, what kind of living thing would you want to become? • Are changes in the very nature and concept of living things good or bad? • How can we control the positive and negative sides of these changes?
Perspective 2. What should we do to proceed with ELSI-related discussions with the citizen members on cutting-edge research?	How and to what extent should we communicate cutting-edge research to citizens? • How and to what extent should we communicate the impact of research on society? How can SF prototyping and fictional articles about the future help society? • Would it be better for us to communicate the details of cutting-edge research to citizens? If so, how and to what extent should we share it with citizens? What is it for? Is it to satisfy the intellectual curiosity of citizens?

The main opinions related to [Perspectives 1] were as follows.

(At what timing should we do ELSI discussions on cutting-edge research? What is the significance of citizens' participation?)

- A citizen member expressed an opinion about whether we can question the ethical issues of technology itself. We should consider that the technology to insert long-chain DNA into cells, which the Yamanishi PJ is developing, is not an ethical issue. Instead, we should understand that ethical issues will arise later when utilizing that technology in society. This opinion meant that we do not need to consider ethical issues regarding technology at a stage when its practical application is not yet determined.
- A researcher (humanities) responded to these questions as follows. History teaches us that accomplishments in scientific research and technological development may sometimes bring unexpected disasters to humanity after they leave the hands of researchers and begin to walk on their own. The development of atomic bombs is a typical example. There is a question about whether we can appropriately control ethical issues by arguing about the problems of new technologies after their practical applications in society have become known. History shows that this is a difficult task. If that is the case, adequate decisions must be made, such as stopping the research at the technical development stage.
- Another researcher (medicine) expressed the following opinion. The research party does not know how its technology will be utilized in society. And society will attempt to utilize such technology depending on its interests and concerns. This means that society is integrated into the process of determining how the technology will be utilized. I consider it a good thing that the diverse perspectives of citizens will be reflected in that process in some way. If that is the case, the participation of citizens in ELSI discussions before the technology's application is determined makes a lot of sense.

(ELSI perspectives that may arise in future society – [1] Loss of the concept of effort)

- Researchers (medicine, engineering) talked about a future society where the Yamanishi PJ and related research are implemented. In biological experiments currently underway, we can embed a device into genes to enable the expression of some gene functions at a specific point in time (just like we press switches). However, unlike robots, the expression of gene functions does not occur immediately after the switch is pressed. The time scale for biological processes is longer: you will see the change happen slowly over a whole day. The future in which such technology becomes a reality may be just around the corner.
- Responding to the opinion, a student said, "If such a future comes, we may lose the concept of effort."
- The researcher (engineering) responded, "In such a future, we may be discussing what are the things people get through their efforts, just as humans have been doing till today, what are the things people get through genome editing technology, as if they shop around, and how such values are going to change."

- The researcher (medicine) added the following comment. “Although discourses like genetic fundamentalism, which claim that the genome determines everything, are often seen in the media, they are untrue. For example, the arguments over designer babies, created through genome manipulation to produce superior humans, are unrealistic. If you want to design humans, you must control their genomes and the upbringing environment 100%. That is impossible, and you will never get the humans you envisioned. However, this does not mean you can rest easy. Genetic fundamentalism could go too far, leading to the misuse of genome technology based on excessive social expectations. This situation may need the perspective of managing society's expectations of technology.”

(ELSI perspectives that may arise in future society – [2] Loss of individuality)

- A student asked the following question. “I think our society today is built on disparity. For example, the Olympic games are sustained by disparities in athletes’ physical abilities. Everyone would start setting high expectations when genome editing technology becomes readily available. As a result, their capabilities will reach the maximum level, gradually eliminating the disparities among people. I cannot imagine such a future without disparities. The existence of disparities is a beauty in our lives. The loss of all disparities might collapse the social order and cause fragility and the meaning in life to disappear. Such a society in the future might be perfect strictly from an efficiency standpoint, but how would we feel about it?”
- A researcher (engineering) responded, “It may be a question about how we should choose our individuality. This is an issue that requires us to consider carefully a future in which technologies that can change ourselves continue to develop. For example, what individuality is in the first place, including whether it is something we should/could choose.”
- A researcher (medicine) asked, “If there are technologies that can enhance your various capacities, do you want them?” A student replied, “Not in Japan, but if you ask this question of people from developing countries, most would want them.” Other students said, “It is better not to want them. It will make our life uninteresting.”

(ELSI perspectives that may arise in future society – [3] Range of diseases)

- In response to a question about how far society should permit genome editing technology, a student said, "It is acceptable to use the technology to restore something negative to zero, such as removing disabilities. Conversely, improving zero to something positive would require a separate discussion.”
- In contrast, other students added, “The question is how to draw the line,” and “We may draw a distinction between medical treatment and anything beyond that, for example.”
- A researcher (medicine) commented, “There are also various problems in the medical field. The cases of severe genetic diseases are easy to understand. Such cases include modifying genes vulnerable to cancer. The question is how much editing is

permissible? How to consider illness is also a point of contention."

- A student said, "Drawing a line based on the availability of insurance coverage may be one option. If that method is used, guidelines can be created relatively easily." The student also said, "It may be easier to draw a distinction using, for example, a survival rate of five years or the life expectancy."
- A member of society commented, "If you feel desperate, you would take risks. Your judgment would vary depending on the situation you are in and the magnitude of the risk." The Citizen WS shared the need to add and consider the perspective that how to draw the line also depends on the situation where the person is placed.

(ELSI perspectives that may arise in future society – [4] Controlling the positive and negative sides of technology

- The SF novel does not mention the potential negative side of technology. A researcher (engineering) pointed out that controlling the negative side would be the key.
- A student said that if someone created a powerful military force using genome editing technology, we would not have a chance against it. Therefore, we must control the technology to prevent such a possibility. The student wondered if we can keep the technology under control when it becomes so generalized and liberalized that everyone can use it.
- A researcher (medicine) said, "Japan used to have a law called the Eugenic Protection Act. This did not allow people with negative genes to have children." This researcher commented that using genome editing to move things in a positive direction might lead to the exclusion of people with negative genes. The Citizen WS participants realized that not only technology but also the act of legal control may actually have dangerous aspects. The members acknowledged that enforcing appropriate legislation to control the negative side of technology does not necessarily mean the end of ELSI discussions.

The main opinions related to [Perspectives 2] were as follows.

(Efforts to discuss ELSI issues on cutting-edge technology with citizens)

- In response to a question about how and to what extent we should communicate cutting-edge research to citizens, a student said, "I would point to animation if I am asked to pick out one, though the method should not be limited to one."
- Someone pointed out that SF prototyping is a method that presents one extreme scenario as a starting point intended to draw out many other opinions. The person added that although that intent makes sense in some cases, citizens may feel they are being imposed with a one-sided view.
- Meanwhile, a student expressed an opinion about the appropriate amount of information we should communicate to citizens: "It is not necessary to explain everything to citizens, and we should share only key perspectives with them. Vaccination is a method of introducing weakened viruses into the body, which sounds scary to everyone. But vaccination is essential in that the vaccine creates antibodies to protect the body. However, citizens do not know how much vaccine should be injected into their bodies. This example shows that explaining everything to citizens may sometimes become counterproductive."

- A researcher (medicine) said that those who want to recommend some research can emphasize its positive aspects, and those concerned about that research may stress its negative aspects. In response, a student responded, “The citizens’ side also tries to understand some research at a time convenient for them. So, focusing only on researchers in this context seems inappropriate. The timing of trying to understand research depends on the citizens. Whether citizens begin to understand the research when it comes closer or at the principle-building stage varies depending on the individual citizen. Also, citizens are not always allowed to say things that are convenient for them.”

- A student pointed out the importance of passion. “Today, Prof. Yamanishi spoke passionately about her research. When a teacher explains topics by linking them to everyday life, his/her classes are interesting. On the other hand, when a teacher speaks straightforwardly, we find it difficult to understand him/her. If the teacher is not passionate about the lesson or teaches in an uninteresting way, the students will not be motivated. In this Citizen WS, Prof. Yamanishi spoke passionately and interestingly, engaging the participants in the subsequent discussion very effectively.”
- In response to a question about how we can stave off bad ideas and misuse of this research, the Citizen WS expressed opinions as follows: “Every technology could be misused, so we must accept it as a necessary evil to a certain extent,” “There is no option but to regulate it by law,” and “It may be better to solve the problem when it arises, rather than imposing regulations prematurely.”

Summarized below are the main opinions expressed by the participants at the end of this Citizen WS based on the discussions in [Perspectives 1 and 2].

(Role expected of genome ethics researchers)

- We can understand the content of discussions from the researchers' and the citizen members' positions. There are things only we can discover because of our hybrid perspectives. One of our roles is to demonstrate such perspectives. Being conscious of various perspectives is important to us.(a researcher of genome ethics)
- This is my first time participating in Citizen WS, so I cannot compare this event with the first one. However, today's discussions taught me that there are many things I did not know. When the topic of designer babies came up, I thought of versatile, brilliant humans like Superman, but I realized I was creating my own image of designer babies. The existence of genome ethics researchers is significant in bridging the gap between researchers and the general public. As a citizen, I am very grateful of their presence. (a student)

(Science of the future)

- The way of thinking characteristic in Japan is based on pursuing the middle ground rather than considering things from a binary opposition standpoint. Japan is always

searching for the middle ground. This will build the Japanese science of the future. In the future, it will become more important to consider intermediate positions instead of choosing between the two. I want to pursue that kind of science. I have missed that point until now. I only did the easy parts. I will pursue the middle ground that I have missed. In doing so, dialog between science and society will become increasingly important. Philosophy is good at this in academic fields. (a researcher of medicine)

- Western philosophy emphasizes logical reasoning, concluding that something has or has not been clarified. A moderate spirit leads to the Buddhist spirit of moderation. The only way to satisfy all people is to get them moderately satisfied. We have reached an era where scientists must consider this type of approach. (a researcher of scientific philosophy)

(Looking back on the dialog between the citizen members and the researchers)

- After listening to the students, I thought that involving people like them in ELSI discussions would lead to a brighter future. They raised various ELSI perspectives. Considering negative aspects is an eternal question, and I think about it daily. When it comes to communication, solving all issues in a single event is difficult because the participants are all different: some are animation fans, and others are not. It seems important to sporadically throw ideas across various channels, hoping some of them will hit the mark. The original ideas may solidify as a multi-layered thought in the long run. To make it happen, you need to increase the number of palettes for your paintings. I recommend increasing the variety of your specialized fields and lowering the thresholds across them, such as animation, music, or novels, for those who are good at each field. I believe fostering such a culture is an critical step forward. (a researcher of molecular biology)
- When I observed the 1st Citizen WS, I was pleased to hear the citizen members honestly say they did not understand it. That happening urged the forum members to include the citizen members' viewpoints in Prof. Yamanishi's research and the related ELSI perspectives. (a researcher of scientific philosophy)
- After participating in this Citizen WS, I realized how important it is to repeat this kind of discussion. I have learned a lot about Prof. Yamanishi's research over the past five years, but I could first understand some points much better at this opportunity. The citizen members who participated in the 1st Citizen WS candidly said, "We do not understand this." Prof. Yamanishi then delivered a revised version of her presentation, from which I discovered something new. Although researchers seldom have such opportunities, I thought again about how critical candid feedback is when someone needs additional explanation. (a researcher in medicine)

- Lastly, I want to re-emphasize the significance of continuing such initiatives on a regular basis. By interacting with citizens, researchers can learn

what they do not know. Getting citizens to tell how they can better understand something unclear is essential, and accumulating such interactions may change society. Even if someone thinks something is good, it does not necessarily mean everyone else does. For example, while vaccines save millions of lives, some people oppose them. I wonder why that is as a researcher. People who lost their lives due to vaccination are reported in the media, but millions of people are saved behind the scenes. How will society accept such situations? It can only be done through dialog like today's. People who vigorously oppose something have a firm conviction, and it is difficult to explain using logic alone. Therefore, it is important to create opportunities like this and engage in repeated dialog so that we all work together to build a society where everyone feels happy. (a researcher in medicine)

(3) Post-Case study questionnaire

[1] Planning and procedure for Case Study 2024: [Positive points]

- **Cooperation of the Yamanishi Team; Participation of Prof. Siomi, CREST Program Supervisor**
  - One of the most significant achievements of Case Study 2024 was the cooperation from Prof. Yamanishi and other researchers of the Yamanishi PJ. We initially suspected they might feel this engagement was a burden while being busy. However, after repeating various meetings, they have increasingly recognized the importance of the workshops and have become quite proactive in the latter half.
  - We usually have only few opportunities to listen to the citizen members' candid opinions on our research. However, the citizen members gave us their valuable opinions this time, which helped us learn various standpoints, including how to communicate our research better to them. It turned out to be an outstanding experience.
  - At the same time, Professor Siomi, CREST Program Supervisor, often participated in workshops to deepen our discussions. His contribution was significant. His participation in the last Citizen WS onsite at Ichinoseki Kosen marked one of the significant successes of this case study.
- **Independent operation by the Forum on Genome Ethics; Coordination made by RISTEX**
  - It was good that the case study's annual schedule was set up at the initial stage.
  - Everyone responded proactively to in-process adjustments thanks to the high awareness among concerned parties, including Prof. Yamanishi.
  - Thanks to the RISTEX team, which took the lead in planning these case studies, we had the chance to participate in these discussions that researchers alone would find difficult to organize.
  - We carefully made preliminary preparations for each of the three case studies through up-front discussions among the Forum on Genome Ethics, the Japan Research Institute, and the Yamanishi team.
- **Procedure for discussions at workshops and other events**
  - It was a good idea to divide the members into small groups for discussion. Discussion with many people makes us feel passive, preventing active thinking.
  - It was a good idea to divide the members into small groups for discussion.

Discussion with many people makes us feel passive, preventing active thinking.

- **Preparation of reference materials**
  - The general introduction slides for the Yamanishi PJ have been revised repeatedly to make them easier for general citizens to understand.
  - The SF prototyping novel created by the Forum on Genome Ethics served as an excellent stimulus for general citizens to consider the Yamanishi PJ's ELSI perspectives.

[2] Planning and procedure for Case Study 2024: [Points for improvement]

- **Planning and consensus building**
  - Before asking the researchers for cooperation in this case study, we should have explained more about the intention of this WS and the activity plans for the whole year so that they could better understand the situation. In addition, we regret that we had abandoned our exhibit at the Science Agora because our feasibility study indicated that the level of our initial burden would be unacceptable.
  - We did not understand what was expected of us, particularly in the first half of the presentation (I thought the presentation talked about two separate points: CREST genome synthesis in general and the Yamanishi team's technology. However, I saw them mixed up right up to the end). I thought it would be better if we started explaining the research details to the RISTEX team in an easy-to-understand manner, followed by ethics experts raising some potential issues. This approach could have narrowed the ELSI perspectives early on, leading to more in-depth discussions.
  - The case study started late and slipped into the end of the fiscal year. We want to advance the start of future case studies by a month or so.
  - We could not set aside enough time to discuss the Yamanishi PJ's ELSI perspectives professionally and thoroughly. The Forum on Genome Ethics should have challenged the Yamanishi team by providing an opportunity to raise and discuss specific ELSI perspectives.
  - It feels as if we have just completed a full warm-up, so I wish we could continue this discussion a little longer.
- **Process of dialog with citizens**
  - A more understandable dialog with the citizens might involve the researchers first approaching them to communicate about the research and then expanding the interpretation of the research through science communicators, novels, and animations.

[3] Planning and procedure for Citizen WS for FY2024: [Positive points]

- **Participation of students and others from Ichinoseki Kosen**
  - One of the main factors in this workshop's significant success is the involvement of people from Ichinoseki Kosen. The Forum on Genome Ethics selected Ichinoseki Kosen as the target audience of the Citizen WS. What were the circumstances or preliminary survey results behind the decision? The reasons would help us select the target audience of the next Citizen WS. Young people, mainly students from Ichinoseki Kosen, proactively participated in the Citizen WS. I learned that their

attitude contributed to the discussion's progress.
  - The students had various perspectives and were extremely proactive.
  - The Citizen WS was conducted by inviting a limited target audience, primarily students from Ichinoseki Kosen. Despite that, they expressed candid and lively opinions, making the event meaningful.
  - Notably, many students candidly stated that the Yamanishi PJ's introductory slides were difficult to understand and that supplemental information was needed to explain technical terms and explicitly present examples of potential social utilization. Those statements led to significant improvements in the introductory slides and the production of SF prototyping, which were evaluated as extremely instructive.
- **Self information dissemination by researchers**
  - Prof. Yamanishi showcased her research using revised slides at the 3rd Citizen WS (at Ichinoseki Kosen), which impressed the students significantly. As was expected, that scene demonstrated the importance of researchers actively disseminating their own information.
  - I realized that the effect of presenting and communicating something face-to-face is several times greater than that obtained through online and video communications. I want the Forum on Genome Ethics to continue face-to-face workshops like this in the future.
- **Collaboration between the forum members and the Yamanishi team**
  - The forum members and Prof. Yamanishi were actively creating various content for the presentation for the citizen members. I was impressed by that scene.
- **Dialog methods and tools**
  - Many research projects have mysterious titles. Thus, using techniques such as novels and animation was very helpful in expanding the imagination of citizen members.
- **Dialog continuation and expansion**
  - Based on feedback from each Citizen WS, our issues gradually became clear, and appropriate measures were taken accordingly. As a result, I finally felt that we were connected with the citizen members.
- **Procedure for discussions at workshops and other events**
  - Through small group discussions, which provided a discussion-friendly atmosphere, we could listen to candid opinions from the citizen members. Based on such discussions, we sought opinions from experts about expected ethical and other issues. As a result, we learned many things.

[4] Planning and procedure for Citizen WS for FY2024: [Points for improvement]

- **Planning**
  - In the first half of FY2024, we did not necessarily have accurate goals presented or the items to be implemented selected. In the latter half, we also saw many new attempts being scheduled one after another (such as the introduction of the SF prototyping novel). So, we felt as if we had left something unfinished. Unfortunately, due to unavoidable schedule constraints, we did not have enough time to thoroughly discuss all agenda items at the 3rd Citizen WS. We should have planned

the annual schedule more deliberately in the first half of FY2024.
  - The participants had limited time, and the discussion would have been more productive with a little more time.
  - It feels as if we have just completed a full warm-up, so I wish we could continue this discussion a little longer.
- **Setting the attributes of citizens**
  - Many young people participated in the Citizen WS. However, the discussion would have gone differently with people in their 40s or older.
- **Procedure for discussions at workshops and other events**
  - The 2nd Citizen WS was held online. As expected, the online discussion lacked excitement, and we prefer face-to-face onsite discussions to the extent possible. When an online workshop cannot be avoided, we should thoroughly concentrate the workshop's content in advance. We expect the participants to consider what they want to say in online meetings relatively clearly.
  - At least, the introductory discussion should have been held face-to-face to make it more effective.

[5] Activities of the Forum on Genome Ethics in FY2025 and later: [Should we conduct case studies?]

- **It is desirable to continue case studies. However, there is room for improvement in their procedure.**
  - FY2025 is the final year for the activities of the Forum on Genome Ethics. Therefore, we must summarize the activities of the Forum on Genome Ethics up to now. The coming year will be pretty busy. Even so, it would be better to conduct case studies if possible. To be honest, Prof. Ichihashi, Prof. Suetsugu, and Prof. Yamanishi, the researchers who participated in the past case studies, would agree that their involvement was beneficial, although they might have thought that these tasks were challenging and time-consuming from time to time. The significance of the Forum on Genome Ethics lies in the creation of better research projects for citizens by promoting collaboration between the CREST/PRESTO researchers and the researchers in humanities and sociology involved in genome ELSI issues. In this sense, case studies are considered a convenient tool to help implement collaboration with researchers. Another significant point is that Prof. Siomi, Program Supervisor, has been involved in this program through case studies.
  - We have conducted case studies inviting three researchers so far. As a result, all three have recognized the importance of researching ELSI even in their research and development. Accumulating these case studies is needed to disseminate this understanding further and share it with general researchers. Therefore, we should conduct case studies in FY2025.
  - We should continue case studies because they were so significant.
  - The case studies are important activities. However, because researchers can hardly generate spontaneous momentum, we will need support for where the planning and the associated issues and questions should be clarified and where the opinions obtained should be consolidated (we look forward to continued support).

- We agree that case studies should be conducted. It may be necessary to get the support of RISTEX to devise an effective method for conducting case studies in the shortest time possible.

[6] Activities of the Forum on Genome Ethics in FY2025 and later: [Ideas other than case studies]

- A plan to publish a book summarizing the activities of the Forum on Genome Ethics is currently underway. Also, it might be intriguing to plan an exhibit at the Science Agora, which we had to abandon in FY2024.
- The “Tour of Mori Art Museum plus Workshop” held immediately after the launch of the Forum on Genome Ethics was a pretty innovative idea. We wonder if we can plan a similar concept to encourage citizens to consider the very nature of genome ethics. This should be an idea worth pursuing.
- We may want more time for writing a book as representation of our activities. We want to hold sessions everywhere to introduce this book and listen to citizens’ opinions.
- At the Citizen WS, we thought the process flow should start with providing an opportunity to carefully introduce the research content in a somewhat unilateral manner, followed by opinion consolidation and subsequent discussions.
- How about holding a roundtable talk about the significance of conducting case studies by gathering several researchers who have participated in case studies and those who have not?
- A molecular robot researcher conducted his own ELSI studies and published the results. As a result, investor confidence in his research increased, and so did the amount of investment. How about inviting a researcher like this to discuss the relationship between ELSI research and investment?
- We want to see the efforts to expand citizens' image of ELSI research by outsourcing related novels and animation continue to grow in the future. Combining this with other events, such as the Science Agora, might also be a good idea.

[7] Others

- Since our research is funded by taxpayers’ money, sharing our research details with citizens and getting them to understand its significance and potential are important activities and duties we must fulfill. If any opposition to the research is raised during the process, it will provide an opportunity to discuss its ethical issues. Therefore, researchers should ask citizens to provide opportunities to present research details in various situations.
- How about actively promoting public relations campaigns to encourage the willingness to conduct case studies by summarizing their significance and actual effects and disseminating them to researchers?

4. Consideration

(1) The Yamanishi PJ's ELSI perspectives

[1] Thoughts of the Forum on Genome Ethics on the Yamanishi PJ's ELSI perspectives

The following table lists the thoughts of the Forum on Genome Ethics on the Yamanishi PJ's ELSI perspectives.

Figure/table 17: Thoughts of the Forum on Genome Ethics on the Yamanishi PJ's ELSI perspectives

a. This technology can be used to treat diseases but changes the very nature of living things
b. What is the range of diseases for which long-chain DNA and chromosome introduction are permitted?
c. Are there inviolable areas that humans must not manipulate? Is it acceptable to retain areas where there is no manipulating technology?
d. Just as a digital divide has emerged in the world of the Internet, a genome divide may also occur
e. Arguments on gene modification need to be reconsidered (how should we consider regulations against genome manipulation?)
f. We should depart from the binary opposition of good versus evil utilization
g. We do not yet know how long-chain DNA is driven. How should we deal with things we don't know or understand?
h. How should we put in order what we are ready for and not prepared for?
i. Creating useful devices and deciding what we use them for are separate things, which must be discussed by the concerned parties
j. We do not want this technology's methods of utilization limited (the direction of development should be decided through discussion)

The above perspectives from a. through e. correspond to the areas of "Understanding and Regenerating Life" and "Advances in Medicine" in the ELSI Perspective Map 2022. These perspectives also appear to correspond to the areas of "Application to Humans" and "Regulations and Rules" of the map concerning the relationship between research activities and society.

The remaining perspectives from f. through j. are not explicitly covered in the existing ELSI maps created by the Forum on Genome Ethics. Therefore, these perspectives can be called new ELSI perspectives, which were obtained through the Yamanishi PJ's case study. The perspectives from f. through j. have diverse meanings and do not appear to be something that should be consolidated into a single category. If someone insists, we would say they might be consolidated into a category, "When should we control what and how?" In other words, like the Yamanishi PJ, this is a point of contention about how we should or should not control technologies whose diverse applications cannot be envisioned at this point in time as research in related fields develops in the future.

Figure/table 18: New ELSI perspectives obtained through the Yamanishi PJ's case study

ELSI perspective	Subdivided perspective	Consolidated framework

f. We should depart from **the binary opposition of good and evil utilization**	We should find a more flexible system without categorizing technology as either good (promotion of utilization) or evil (no utilization).	**When should we control what and how?**
g. We do not yet know how long-chain DNA is driven. **How should we deal with things we don't know or understand?**	Is there any action we must take even when we remain unfamiliar with or ignorant of the research? How can we prepare for that?	
h. How should we organize **what we are and are not prepared for?**		
i. **Creating useful devices and deciding what we use them for are separate things**, which must be discussed by the concerned parties	Is it sufficient to accept a model that allows freedom in creation and applies controls at the point of use? How can we distinguish between creating and using something? Who can define the distinction?	
j. **We do not want this technology's methods of utilization limited** (the direction of development should be decided through discussion)	Who decides how technology is used? Should the pros and cons of technology use be decided for each utilization method? If so, who can manage its utilization method?	

[2] The Yamanishi PJ's ELSI perspectives created through the dialog between the citizen members and the researchers

The following table shows the Yamanishi PJ's ELSI perspectives created through the dialog between the citizen members and the researchers at the 3rd Citizen WS.

Figure/table 19: The Yamanishi PJ's ELSI perspectives created through the dialog between the citizen members and the researchers

k. **The concept of effort might be lost** in the future, where genome manipulation technology enables the acquisition of various functions.
l. Once genome manipulation technology is liberalized, **disparities between people will eventually disappear.** If that happens, **the concept of individuality may be lost or altered.**
m. Genome manipulation technology must be intrinsically controlled by drawing a line between medical treatment and something more than that. However, **the very concept of diseases may be changing** in the first place.
n. Society may be able to control genome manipulation technology only through legislation, but we must remember that **such legislation (as a social technique) also has dangerous aspects.**

The above perspectives k. and l. express anxiety about the concept of "self," which we take for granted in our social lives, changing in a world where the Yamanishi PJ's technology and the like are widespread. Perspective m. is almost the same as "b. What is the range of diseases for which long-chain DNA and chromosome introduction are permitted?" in the thoughts of the Forum on Genome Ethics on the Yamanishi PJ's ELSI perspectives. However,

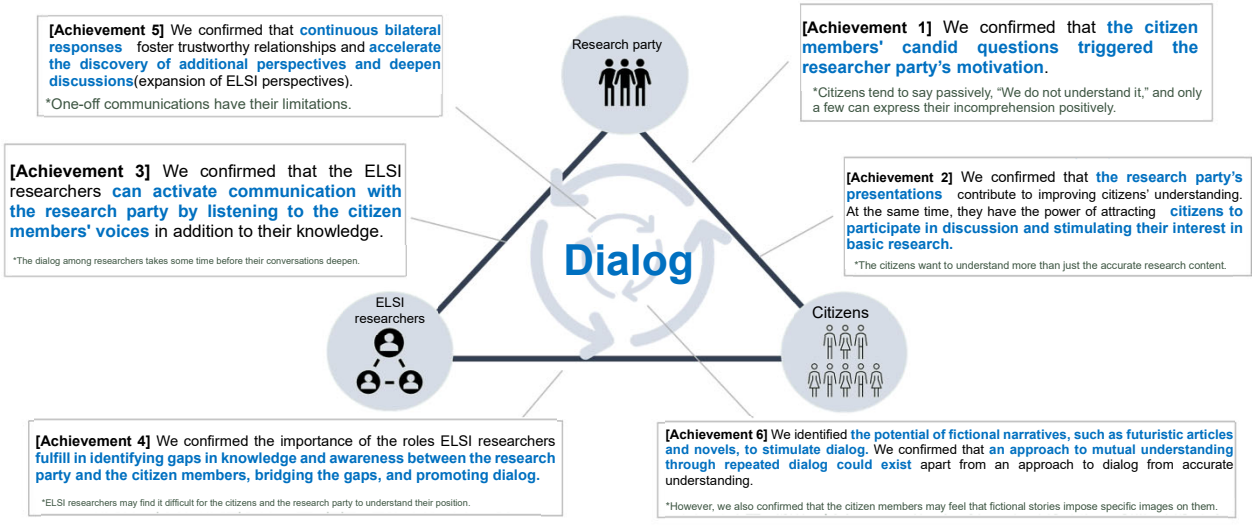
this perspective points out that even if diseases can be used as criteria for drawing lines to control genome manipulation technologies, the very criteria for diseases will alter in the long run. Put differently, the perspective asks based on what kinds of standards such technologies should be controlled, with the very criteria changing. Perspective n. is almost the same as m, saying the legislation for the social control of genome manipulation technologies sometimes shows dangerous aspects.

We can say that m. and n. are the same as the new ELSI perspectives obtained through the Yamanishi PJ's case study, which we described earlier. Perspectives k. and l. were not included in the new ELSI perspectives obtained through the Yamanishi PJ's case study, so they can be said to be unique perspectives that arose from the citizen members' participation. These perspectives might be roughly classified into a framework like "loss of individuality."

(2) Achievements from the trialogue (three-way dialog) between the research party, ELSI researchers, and citizen members

Case Study 2024 aimed to explore "(ELSI) perspectives to be discussed together" through a trialogue among the three parties: the research party, ELSI researchers, and citizen members, while understanding the differences in their positions and knowledge. What we could confirm during the trialogue discussion is described below.

Figure/table 20: The effects generated through the dialog with citizens exploring ELSI perspectives



[1] Citizens' candid questions can trigger the research party's motivation

At this Citizen WS, Ichinoseki Kosen's students, teachers, and members of society expressed their candid opinions and questions as citizens. The research party shared such comments, albeit indirectly, enhancing its awareness and ingenuity about how to explain its research, step by step as it experienced more rounds of workshops. The effort eventually led to Prof. Yamanishi speaking directly to the citizen members about the Yamanishi PJ's research at the 3rd Citizen WS. As a result, Prof. Yamanishi's presentation received remarkably high praise from the citizen members for its clarity and passion for the research.

We believe what brought them to such interaction was that Ichinoseki Kosen's students

did not say passively, “We do not understand it,” but expressed their incomprehension positively by saying, “We try to understand it but cannot understand this particular part,” or “We might be able to understand it if you could explain this way.” This achievement may attributable to the uniqueness of the citizen members as Kosen students. It might not be the attitude we could expect from most citizens, but we confirmed that at least some citizens have the potential to co-create such an effect.

[2] Presentations by the research party encourage citizens to participate in discussion

In contrast with [1] above, we confirmed that the research party’s face-to-face presentations had the overwhelming power to encourage citizens to understand research and stimulate their interest. The citizen members’ reaction to the face-to-face presentation differed significantly from the video presentation by the research party at the 1st Citizen WS.

Again, this may not be the case with all citizens, but we are sure many felt the research party’s passion to explain the research content better. At least, it triggered their motivation for the research.

[3] Citizens' voices boost the dialog between the ELSI researchers and the research party

The ELSI researchers seemed able to activate communication with the research party by adding citizen members' reactions to the research to their knowledge as material for discussion. In other words, deepening the dialog between the ELSI researchers and the research party might take a considerable amount of time. Unless both sides have clarified and agreed to the preconditions for their dialog in the future, they can hardly come closer to each other. In this sense, the trialogue in the Citizen WS suggested that communication between the ELSI researchers and the research party could develop with citizens' voices as a catalyst.

[4] ELSI researchers as mediators and problem-setters

We confirmed the importance of the roles ELSI researchers fulfill in identifying gaps in knowledge and awareness between the research party and the citizen members, bridging the gaps, and promoting dialog. While the citizen members’ candid opinions and the research party’s presentations are important, they will not be accomplished without the presence of someone who understands and edits them. Without ELSI researchers who understand both perspectives to some extent as mediators, an opportunity for discussion will not be created to bring out the potential of the citizen members and the research party.

However, the ELSI researchers are not just expected to act as mediators or coordinators. Through these activities, we confirmed the importance of ELSI researchers as problem-setters in getting the citizens and the research party to recognize the significance of discussing ELSI issues now.

[5] Dialog continuation

We confirmed that repeated bilateral responses can foster a measure of trustworthy relationships and accelerate new perspectives and deeper discussions (expansion of ELSI perspectives). One-off communications have their limitations. We could continue our dialog this time, particularly because Ichinoseki Kosen was a collaborating partner. However, we must say the likelihood of general citizens continually being involved in dialog of this kind would be low. Through this attempt, we learned the importance of dialog continuation to some extent. Because we also found the cost to be considerable, we must further study what kinds of dialog continuation methods are possible in the future.

[6] Products that stimulate dialog (such as futuristic articles and novels)

At the 3rd Citizen WS, we showed a video of a futuristic novel created using an SF prototyping technique, which seemed to free up the citizen members' thoughts. After viewing a story depicting a society 40 years away where genome editing therapies are widespread, citizens considered how they would accept such a society and finally became conscious of their choices in the near future (how to create their future). We confirmed the possibility of the video being used as a device for such an approach. This approach discusses the very nature of controlling today’s cutting-edge research by backcasting the world 40 years from now, which differs from the pattern that considers how technologies currently under development will affect society in the future. Therefore, this approach might be used to explore with citizens ELSI issues that cannot be seen only from today’s perspectives.

However, how this approach can be utilized in case study activities remains to be studied. To envision a fictional future society, we will temporarily put research that requires case studies on the back burner and depict a society that implements far more research and technologies. Even if we eventually link subsequent discussion to research and technology that require case studies, there may be limitations to how specific we can be. This requires further studies.

In addition, some citizens pointed out that they might feel this type of fictional story imposes a preset image on them. We confirmed the need to pay appropriate consideration to this concern.

5. Toward the future

This case study was the second attempt following the previous one in FY2023. We found several issues, such as how to proceed with the case study, aligning the understanding among the concerned parties, and the heavy workload on the forum core members responding to the citizen members' side. Despite that, the Yamanishi team, the forum group members, and the citizen members who participated in the three workshops positively evaluated the case study. We therefore believe this initiative by the Forum on Genome Ethics had a measure of significance.

First, Prof. Yamanishi and the Yamanishi PJ researchers came to recognize the importance of case studies as they experienced rounds of meetings. In the latter half, they became quite actively involved in both the workshops and the preliminary planning meetings. This point of improvement was precisely the benefit obtained from the case study methodology.

On the other hand, the significance of the Forum on Genome Ethics lies in the creation of better research projects for citizens by promoting collaboration between the CREST/PRESTO researchers and the researchers in humanities and sociology involved in genome ELSI issues. We reconfirmed that raising specific cases helped to bring out diverse viewpoints from the humanities and sociology researchers. In addition, intensive discussions among the forum core members focusing on the Yamanishi PJ resulted in the emergence of some ELSI perspectives that are slightly different from those previously identified. Furthermore, we obtained exceptional cooperation from Ichinoseki Kosen in demonstrating the significance of considering ELSI issues with the citizen members. This was one of the most important achievements this time. Because of this achievement, we gained an insight into how information should be provided to citizens. We also confirmed that citizen members' candid opinions stimulated CREST researchers and genome ELSI researchers (in a good sense). Prof. Siomi, Program Supervisor, commented, "By interacting with citizens, researchers can learn what they do not know. Getting the citizen members to tell how they can better understand something unclear is essential, and accumulating such interactions may change society." As a result, the CREST/PRESTO researchers and the researchers in humanities and sociology involved in genome ELSI issues shared the importance of continuing such initiatives.

Regarding our future activities, we can think of many possible directions. Conducting additional case studies by inviting new CREST researchers might provide opportunities to discover new ELSI perspectives. Another direction could be discovering new ELSI perspectives through dialog with citizens or delving further into existing programs. Someone said it might be intriguing to plan an exhibit at the Science Agora, which we had to abandon in FY2024, to widely disseminate the activities of the Forum on Genome Ethics. Some expressed an idea, by reference to the "Tour of Mori Art Museum plus Workshop," an innovative event held immediately after the Forum on Genome Ethics was launched, to create a mechanism for considering the very nature of genome ethics based on a new concept. Furthermore, many other events are also possible, including an attempt to gather several researchers who have participated in case studies and those who have not to hold roundtable talks and discuss the significance of conducting case studies more deeply, and a trial to create a forum for discussion on the relationship between ELSI research and investment opportunities.

Because it has made a measure of accomplishments so far, the Forum on Genome Ethics can gradually undertake diverse projects in the future. We think we must continue to drive the challenge to utilize the potential of the valuable social system called the Forum on Genome Ethics by questioning again, through a series of discussions, what it should aim for next within the limited resources and time available, and what the significance of its existence should be.

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Explanatory materials: Citizen members' opinions on the Yamanishi PJ's initial explanatory materials at the 1st Citizens WS

(1) Overall impressions (after reading and viewing the Yamanishi PJ's press releases, PPT slides, and videos)

[1] Opinions from students in the chemistry and biotechnology courses

[Specific uses and applications (more information is needed)]

- This research sounds great, but I cannot picture its clear image. It is the world of Doraemon. This technology falls under biology, and I cannot understand it because I major in applied chemistry.
- The technology of introducing long-chain DNA sounds great, but I do not know what is in it for us. I understand this research is more advanced than what we learned in textbooks, but I sense a long distance between research and practical use.
- It would be easier to understand this technology if it was explained using a picture like the one on the first page.
- It would be easier to understand if this technology was explained like a picture-story show.
- I did not fully understand the principles of this research. When getting citizens involved, they must start with understanding the research. This comment may be somewhat technical because I routinely handle cells, but I wanted to know how strong the cells would be after introducing long-chain DNA.
- How exactly is this technology used? I wanted to know the more specific advantages of this technology in an easier-to-understand manner. There were some understandable descriptions on P11 of the video presentation, but I wanted to have still more specific explanation. I wanted to know more about what advantages this technology might bring to us in the future.
- I want to know what is the most promising application (although Prof. Yamanishi might say it could be used for anything). I can hardly picture the image that it can be used for anything. It would be easier to picture the image of "this technology can do such and such."
- Saying this technology can be used for anything might hinder the generation of dialog with citizens.

[Issue with technical terms]

- When considering how citizens should get involved in the social implementation of a technology, I realized that we must first understand the technical terms involved before arguing about the technology's impact on society. I listed below technical terms that caught my attention and those that I felt would be better explained in more detail. I understood their meanings a little better after viewing the video.
- DNA nanoparticles, environmental impact, intracellular delivery, delivery technology, creation of new devices, cell massage
- I did not understand the meaning of the words "controlled release." What does this technical term mean? The video explained that this term means enzyme-based decomposition.

[Flow and story of explanation]

- The explanation's flow was obscure, and I found it difficult to understand. The technology appeared great, but the story did not make sense.

[Variations in understanding and interest among individuals]

- Some researchers and Kosen students in the science course might find it interesting, but general citizens would probably not be interested. The difference in interest levels might depend on the individual's position.

[2] Students from the machinery and intelligence courses and the information and software courses

[Issue with technical terms]

- I was told the video was made for citizens, but it was difficult. I did not even understand the technical terms.

[Clarity and difficulty of explanations]

- I could not understand anything even after reading the PPT slides.
- I could not understand anything, even the title, so I was stuck on the start line.
- I did not even know what long-chain DNA was in the first place. I wanted visual images for better understanding.
- I think the presentation's point was long-chain DNA, but I could not understand how electric field-induced microbubbles are related to the long-chain DNA. This kept bothering me through the video presentation.
- While I did not understand the content of the PPT slides, I later understood some parts that were covered by the video presentation.
- The red ginger illustrated on the first page was easily understood.
- It was not until I viewed the video that I understood that the red ginger represented cells.
- The illustration on the front cover was everything!

[Story consistency in explanation]

- This does not explain what happens when it enters the cell (when the ship enters the gate).
- The story of the gate improved my understanding, so I wanted that story to continue through the latter half.

[Specific uses and applications]

- I wanted to ask what happens when long-chain DNA is introduced.
- The technology's applications are described on P11. It listed a, b, ... f, but I wanted to know more information about a, for example, such as it will become this kind of medicine. General citizens cannot understand what is explained without a minimum amount of information. However, it is not necessary to show specific examples for each of a,b・・・f.
- The expression "It impacts the medical, dental, and pharmaceutical areas" at the bottom of P12 is easy to understand. That expression was more specific than the above explanation: "Various areas are involved." Did you mistake it for "dental" medicine area?

[Novelty and originality of technology]

- The explanatory materials explained that while gate technology has been around for a long time, the new technology can make a hole in an osteoblastic cell. This was my understanding but I wondered why.
- I have heard that protein crystallization has been a difficult process for years, so I

wanted to learn more about it.

[How to prepare and present explanatory materials]

- I was overwhelmed by the flurry of articles (press releases and other materials to read first).
- I did not even know where to start reading the PPT slides.
- From the standpoint of how explanatory materials should be prepared and presented, I wanted to know first specifically what the introduction of long-chain DNA into cells would change. In short, it would be difficult to understand the main parts of this technology if I could not first imagine what it is used for. I wanted to know first what ultimate goal motivated Prof. Yamanishi and her team to devise and develop this technology, and why existing technologies could not do the job. (I could not get the answer.)

[3] Members of society

[Clarity of explanatory materials]

- I could not picture any image when reading the articles (press releases and other materials to read first).
- The PPT slides were a bit easier to read, but the technical terms were so mysterious that I had to look up those terms one after another. Still, I could not understand them well.
- I probably understood them a little better after viewing the video presentation. The use of cartoons and scales was good.
- I focused on the research background. I did not understand why molecules are inserted into cells. Partly because of my experience with COVID-19, I felt familiar with inserting something into the body, which helped me picture the image of this technology.(I thought relating this technology to such a social background helped improve my understanding.)

[Expectation and interest]

- When I read the Prof. Yamanishi's home page and first encountered the term genome, I thought of medical care. I had high expectations for this technology, which is a dream technology today but may become commonplace in a few decades.
- I was curious about what made such an interdisciplinary approach possible, which many researchers had attempted until now. I wanted to know whether it depended on her personal qualifications or had some specific background.
- The illustration on the first page was easy to understand, but the figures on P9 were incomprehensible for beginners. I did not understand how difficult installing the machine is and the level of the machine’s reproducibility. I wanted the figures on P9 explained using simple analogies so even beginners could understand them easily.

[Research background and objectives]

- I wanted to know why the Yamanishi PJ was needed in the first place.
- I wanted to know more about what brought the Yamanishi PJ to challenge a long-chain DNA delivery device. With that information, I would be able to imagine a little more about the impact this technology will have on society. As CREST sets the internal division of research roles, I could guess that the long-chain DNA delivery device falls under Prof. Yamanishi’s roles. However, I could not understand what CREST wants to accomplish in this research without knowing its overall picture, including the division of roles for other studies.
- The explanation centered around good news. However, I wanted to hear the bad news about this technology as well.

(2) Thoughts of citizens on what society as a whole should discuss (such as ELSI issues)

[1] Opinions from students in the chemistry and biotechnology courses

[Clarification of research objectives]

- I want the research's objectives clarified. For example, whether the target cells are human cells or not would change the outcome significantly.

[Consider the technology's ELSI issues after we have identified its applications in society]

- Once we have completed this process, we should embody social application plans and discuss ethical acceptance standards.
- We must discuss specific applications (as a precondition for considering ELSI issues). Once we have completed this process, we must make the research content transparent and clarify the ELSI standards.
- There is an explanation of application of the research on P11, but it was insufficient. I wanted an explanation like, "this biopharmaceutical is used for cancer treatment this way."
- Such an example helps improve citizens' understanding.
- We need something specific that we can imagine, even if it is just Prof. Yamanishi's dream. That does not need supporting evidence.
- Having an image is the first step toward considering ELSI as something familiar to you. As a result, we might see citizens make their proposals.

[Explain it to citizens before applying a new technology]

- Researchers must explain to citizens who may gain benefits or suffer losses about the new technology before it is applied in society.

[Draw the line between good and evil utilization]

- It is also important to clarify the standard.
- Is it up to the country to implement the new technology? Should the organizations implementing the technology in society be accountable for explaining it? It is unreasonable to place all the accountability on Prof. Yamanishi.
- This is considered a future technology, so we must create appropriate guidelines.
- It would be best if all concerned parties could create the guidelines together. It would be more interesting if students created the guidelines. I want various people to get involved. It is essential to ensure diversity, and it must include young children. It is not that only those creating the guidelines use the technology or are subject to its influence. Many other people are also affected by the technology. We need imagination to control this complex situation.
- It is important that citizens understand the technology appropriately and that they can understand it correctly. Once citizens have understood the technology, they must consider its applications from various perspectives.
- What does understanding mean? If citizens can learn something from the essence illustrated on the cover page, they may have understood the technology. If citizens can colloquially explain the technology, they may have understood it.
- The level of understanding should vary from person to person, so it would be good to have something that could define understanding, like shared awareness (with a certain degree of flexibility allowed).
- I want a unified image. If everyone has a common image, we can communicate various matters based on that platform. While variations in methods for the social implementation of technologies are acceptable, it would be better to have a unified understanding of the technology's principles.
- Sketches are essential in research proposals and similar documents, and a new

business emerged recently to help make research more understandable using effective sketches.

- Someone earlier talked about levels of understanding, but I want to understand everything. It would be better to understand every technical term one by one.
- It is also essential to output what I thought I had understood. Creating a manual that explains what I understand to others would improve their understanding. Although such understanding may vary depending on the individual, I thought everyone would learn about the technology enjoyably.
- Such a workshop must be enjoyable. In that environment, I can consider how the technology relates to my life. It looks like a newspaper. What is interesting depends on the individual.
- The need to shave off the unnecessary parts may make the story interesting.
- It would be good to try it at the 2nd Citizen WS. If you summarize something yourself, you take it as your personal issue.
- This process also plays the role of a mechanism or mediator that promotes understanding. For example, it might be interesting to create a system in which young children learn something at school and then pass them on to their parents. It would be ideal to create a cycle where even those unfamiliar with the latest research can learn about it. When children take the lead, the rest of the family will listen. Children might be appropriate as new information mediators. It might be better to spread the awareness of new technologies by getting researchers to hold workshops at schools to educate children.

[Who should be accountable for explaining the risks that may arise from research?]

- First, regardless of who explains it, identifying who is accountable or responsible for the research is difficult unless the research's applications are envisioned to some extent.
- It is necessary to take some actions in advance, assuming the technology will be used to some extent (even if it is still uncertain).
- Whether good or bad, technology is all about how it will be utilized. The technology's risks are a problem the user and application side must solve (not the researchers who developed the technology), and the user side has its responsibility.
- In the first place, can the researchers who developed the technology stop its use?
- As a leading researcher in this field, I want Prof. Yamanishi to explain the risks of her research.
- The researchers should know the risks involved in their research better than anyone else.
- In a practical sense, the ability to respond to research-related risks varies depending on whether the researcher is ready for them.
- Although establishing clearly stated standards is difficult, we would feel at ease if the standards were implemented partly.
- It would be good to create a system in which we can entrust our new technologies to an institution that issues use permits. In this case, the institution entrusted with our new technologies is expected to take all responsibilities.
- If we include students from the liberal arts in this discussion, we may be able to generate a broader range of perspectives. (We are students in a field related to this research.)

[2] Students from the machinery and intelligence courses and the information and software courses

[Disseminate specific application examples to stimulate social discussion]

- In the first place, I did not know how this research would be utilized in society. Not knowing the specific research details, I found it difficult to imagine how I should discuss ethical issues related to this research. This point is essential if citizens are involved in the discussion.
- If I had been told differently, for example, “this technology can kill cancer cells when used this way,” I would have understood it immediately.
- Specific examples play the role of research goals, so they should be written in a way that catches the eye first.
- We should disseminate specifically how it can be utilized in society. Information like this should be disseminated as if a doctor tells a patient how they will cure their disease. Transparency would increase if specific methods of technology utilization were recognized. By doing so (disseminating specific technology utilization), we can deepen the level of social discussion.
- However, I am not saying Prof. Yamanishi should disseminate her views on ethical issues. Ethical issues should be disseminated to citizens through JST and other relevant institutions.
- I believe Prof. Yamanishi had a motivation, such as “I started this research to accomplish this. ”I would never think she set no goal (in her mind) at the outset of her research. Although I am unfamiliar with the world of cutting-edge research, would it be possible for someone to start research just by saying: “It seems something good may happen if I put something long into cells?” If this is the case, I wonder if the research could end up completely useless.
- For citizens, it does not matter whether Prof. Yamanishi will also lead the application side of this research or whether other researchers/companies will do the job. In any case, I want this point explained more specifically.

[Draw the line between good and evil utilization]

- We must draw the line between the good and evil utilization of technologies.
- For example, the ethical issues of evil utilization included preventing the technology from being used for crimes, but it was too abstract to imagine.
- Furthermore, we must also consider the possibility of this technology being combined with another new technology and used for evil applications. So we need long-term monitoring to avoid such unwanted consequences.

[Citizens must have an appropriate level of technical understanding before starting the discussion]

- The citizens must have appropriate knowledge about the technology. The citizens must be provided with appropriate knowledge before the discussion. Example: What is long-chain DNA?
- Once the citizens have a shared understanding of the basics, they might be able to discuss possible applications for this technology.
- Even if all keywords are explained, a question remains whether the explanatory materials will become easier to understand. However, the discussion method can be improved by adequately setting the discussion’s objective. If the citizens are asked to discuss the technology based on this limited knowledge, they need no more information ... We wondered what was expected from the citizens.
- The citizens do not need to know the details of long-chain DNA, but they should understand how it is used. The citizens do not need to understand how to make long-chain DNA (although it is Prof. Yamanishi’s research).
- We all should recognize the possibility of citizens feeling scared because they do not understand technology or have the necessary knowledge.

[We want relevant experts to collaborate]

- I first assumed this research intended to administer a drug to cells. If my assumption is correct, the research requires animal testing. In this case, it would be good to judge

whether such an experiment was ethically possible and proceed with the research in collaboration with experts in the field of genetics. In other words, ethical standards are required at the experimental research stage. In this sense, ethical issues still need to be addressed even when the final implementation is not identified.(I am not sure whether citizens must be involved in this process.)

- I thought this research would be used for humans. If so, the users of this research should be in the medical field. In this sense, I first thought collaboration with the medical field (discussing the ethical issue) would be necessary.

[Ethics from the citizens' perspective: Law, favorite fields, and existing knowledge]

- I could not understand the research at all. I could not understand what was expected from the research and how it relates to social issues. If we are given one specific example that seems helpful in our daily lives, we can consider possible ethical issues. We wanted some specific examples explained to understand the ethical aspects of this research.
- I am not interested in any topic that has nothing to do with me. The most important thing is whether it has something to do with me.
- (When I research something...) I care no more than whether it could be a crime or not. As exemplified by “you must not ask AI about how to make bombs,” what is important is whether your conduct may violate the law.
- I want to participate in discussions about what I like and the knowledge I already have. For example, as I am a great fan of robots, I would actively engage in various robot-related discussions. One such example is “robots must not harm humans.”
- Ethical issues with machines are relatively easy to understand, such as “machines must not harm humans.” However, I cannot picture the image of ethical issues with chemistry.
- Although people tend to highlight the advantages of new research, we must also discuss its drawbacks.

[3] Members of society

[Build the bases for discussion]

- I heard the term genetic modification for the first time. The technology may improve the efficiency of human bodies, but it should also have drawbacks. I first thought the need to build the bases for the discussion by organizing the advantages and disadvantages.
- In doing so, the research party should communicate to citizens in an easy-to-understand way.
- It is important to draw sketches to improve the citizens’ understanding. When it comes to finance, we must explain financial matters depending on each client’s level of understanding. In this cutting-edge research field, it should be appropriate to disclose information depending on each participant’s level of understanding.
- For example, if people interested in science, or the mass media, explain the research in an easy-to-understand way so that general citizens can understand it, we will know the differences in the level of understanding among the participants.
- It is difficult to compare the advantages and disadvantages of doing or not doing the research. We may feel most convinced when comparing the disadvantages of doing the research with the disadvantages of not doing it.

[Risk and technology governance]

- This research will find its way toward a bright future in the medical, dental, and pharmaceutical areas. On the other hand, this research is expected to create novel living organisms, which makes it essential to regulate the risks of bioterrorism and pandemics.

- Once this technology is made public, it will spread globally at a stroke. The question is how to regulate the development of better technology and genes overseas based on this technology. Once a nation intends to do so, we cannot stop it. So I feel uneasy about this, but I do not think we can stop such a movement.
- However, as exemplified by the case of ChatGPT, rule-making has been implemented after the need arose in most cases. Regenerative medicine is an example of rule-making being implemented early on. I wonder if this may be the way we should follow. However, if a malicious country or organization attempts this, it would be impossible to prevent it.
- As a parent, I feel long-term anxiety. Even if my health and safety are ensured, I am concerned about how this technology will affect the next generation, including my children and grandchildren. However, I would choose this technology no doubt if there were no other options (treatments). This is not just how to deal with an independent issue. The real problem lies in what to choose from the limited options available and what to trust.
- These explanatory materials, for example, provide a sense of anxiety about gene modification. While genome editing seems relatively safe, we do not know its impact yet.
- The case of mRNA in the COVID-19 pandemic falls under this situation. Because its long-term effects could not be measured clinically, the vaccine injection almost everyone received was a human experiment. Once the vaccination was established as a treatment, general citizens had no choice but to accept it. I received the vaccination five times, but I still feel uneasy. However, if the vaccination is the only option available, I must continue to receive it while understanding its risks.
- I had a sense of resistance to the vaccination being used on healthy people.
- While I thought excessive vaccination was not good, there was no option of not receiving it. Japan could not produce coronavirus vaccines due to the government's strict regulations. The victims of the vaccination who sued the government lost the court case. Japanese pharmaceutical companies were powerless.
- When watching the issue of genetically edited babies on TV, I wondered why that technology was not allowed. If modifying fertilized eggs, instead of human bodies, were ethically acceptable, parents would tend to have higher expectations of their babies, such as smarter or cuter children. I understand that is why genetically edited babies are restricted worldwide.
- The media's influence on citizens is tremendous, although it depends on how it is utilized. I was working at a medical institution during the COVID-19 pandemic. Since we could not accept any requests for vaccination, the medical institution received too many phone calls, which troubled me a lot. At that moment, I felt the power of the media. I think involving the media has both good and bad aspects.

  (Reference: the discussions that arose at the time)

  Q: Why are designer babies a bad idea?

  A: It is an option available only for wealthy people. The long-term effects are unknown.

  Q: Genetically edited babies can be created relatively easily if everyone wants them. How do you think about it?

  A: This is not good.

  Q: It should be okay if the parent takes care of all the responsibilities. How do you think?

  A: It is up to each parent's call. It depends on common sense. It is like the world of gene-edited Gundam. It may end up with human selection. This must be a nation-level discussion. The law must prohibit creating gene-edited stronger soldiers.

  Q: Where should we draw a line between treatment and non-treatment? If I continue

treatment, I might become a cyborg in the end.
A: Curing diseases is a good thing. It is not a problem to deviate from our original DNA. However, genome editing to make our brains smarter is unacceptable.

- There is a risk of such discussions gradually drifting toward a more lenient direction (unconsciously). For example, some businesses may lead the discussions in that direction for profit-making purposes. On the other hand, we want researchers who stand in the same position as Prof. Yamanishi to refuse such a movement. Under normal conditions, we must create a system where they do not have to care about such a thing. Democratic countries are expected to regulate those unwelcome acts. We are not so worried about it within Japan, but we seriously wonder what would happen if our technologies leak to overseas or authoritarian regimes. We must continue discussing this issue in connection with national security.
- The definitions of diseases might be changing in the future. For example, cosmetic surgery might be defined as therapy someday. In this case, both technology and legal discussions may be shifting to different levels.
- If biological information leaks out of control, it might lead to more dangerous situations than smartphones could, such as the creation of clones. The images of gene modifications we see in movies. They generally bear negative images.
- We are not interested in new technologies without understanding what specific benefits we can get from them. We do not know the impact of new technologies on us because we have no idea what services will be available as derivatives of those technologies. Are there any specific examples of cosmetic surgery in the future? We tend to picture the images we usually see in movies.

(3) Significance of citizens participating in ongoing cutting-edge research (Significance and challenges of participation from the perspective of citizens)

[1] Opinions from students in the chemistry and biotechnology courses

[Necessity and significance of citizens' involvement]

- Citizens should be involved in ongoing cutting-edge research.
- Citizens' involvement might allow researchers to realize the hurdles (requirements) the social implementation of their research must overcome.
- Researchers can perceive those hurdles by talking to citizens about how this technology could be used and receiving their feedback, such as acceptance or criticism.
- The citizens' side has the advantage of being aware of the emergence of such research earlier due to their involvement. The citizens' involvement also benefits the researchers because they can get helpful feedback. In addition, the citizens' involvement allows the researchers to shift their research in the direction the citizens want.
- We have never heard of this type of research before. However, according to its application examples, this research could contribute to our business in the future. This research might become more relevant to society by reflecting opinions from citizens.

[Citizens' involvement in ongoing research carries greater significance]

- Citizens' involvement in ongoing research is essential, and it should lower the hurdles the researchers must overcome in the social implementation process (which means we can avoid setting the bar too high).
- It would take a lot of time to incorporate citizens' opinions after the completion of the

research, making their involvement in ongoing research particularly important. Improving ongoing research while reflecting feedback from citizens would help shorten the cycle time.

- In the case of completed research, citizens have no other option but to appreciate the research outcomes. Ongoing research involving citizens might offer an opportunity to change its direction, rather than evaluating the research. Citizens should feel a sense of responsibility because they were involved in the research. Citizens also have the advantage of becoming a research party.

[Citizens involved in ongoing research]

- Some researchers and Kosen students in the science course might find it interesting, but general citizens would probably not be interested. The difference in interest levels might depend on the individual's position.
- When determining the types of citizens who should be involved, considering the diversity of citizens, such as in the breadth of knowledge and age demographics, would help the ongoing research shift in a more effective direction.
- It would be good to hold workshops where citizens can share their opinions. However, we do not believe many citizens are eager to participate in workshops.
- This is the reason for the particular layers of those citizens being selected.
- It is meaningful (for citizens) to disseminate information in public spaces. There is a possibility that the research party's comments are understood only through critical eyes. It might be better if some citizens understand the research party's comments first and then pass them on to many other citizens.

[Discussion of specific application fields inviting experts from those fields]

- When we want to discuss with citizens, exactly with whom should we discuss? It is a difficult decision. We may think of doctors first. They can play the role of the users of Prof. Yamanishi's technology.
- Although politicians are more influential, doctors seem appropriate when it comes to using the technology.
- It would be better to narrow down the application fields for meaningful discussion. If the discussion concerns the environment, we need to narrow down the application fields to the electrical or environmental fields.
- If the application fields are too broad, we may struggle to control the discussion. As a result, the discussion may go nowhere.

[2] Students from the machinery and intelligence courses and the information and software courses

[There is significance in citizens participating in ongoing research]

- The significance of citizens' involvement in ongoing research lies in the smooth acceptance of its social implementation. However, the citizen members could not imagine the significance of this research.

[Is it necessary for the citizen members to discuss this research at this stage (specific applications are unknown)?]

- We do not know the answer based on the research details we have heard so far. Although the citizen members were asked for their opinions, the discussion did not make any progress today. Today, we only criticized the content of the explanatory materials. It was not necessary to explain the research details to the citizen members at this stage. The citizen members would have become interested in this research if the explanation had provided specific application examples and outlined possible advantages for them.
- We wondered if the only way the citizen members could be involved in this research

was as test subjects. Of course, we intended to engage in the discussion on the research.

- We received the materials without prior notice, and we were unable to understand the content. If we were supposed to express our opinions on the research, we thought we should have received a preliminary explanation.
- The citizen members' involvement in the research would not begin until they are informed more about the research. Doing so would require making the research high-profile. The awareness of the research would spread by informing people about it through advertisements, social media, and animations, as well as by explaining it to those who are interested.
- With no prior knowledge of this research, we wondered if there was a low-key workshop where we could learn the basics of biotechnology.

[Creating an environment that motivates citizens to participate in research]

- Citizens lack an understanding of the technology in the first place. It might be important for citizens to gain more hands-on experiences, such as lab tours and workshops. It is necessary to get citizens to feel interested in participation. Doing so would require creating the atmosphere and research content that motivates them to get involved.
- In this case, citizens would feel more interested in being involved in something that has a direct connection to them.

[Roles of intermediaries: Function to explain in simpler terms]

- Should researchers engage in direct dialog with citizens, or should they have someone who explains the research in simpler terms in between?
- If a researcher abruptly asked a citizen to give their ethical views on the technology, the citizen would say they cannot, and the dialog would stop there. Citizens would feel more comfortable expressing their opinions after hearing the views of experts.
- Should the intermediary explain only information in simpler terms, or should they ask citizens ethical questions? The purpose of the intermediary asking citizens is to identify points that experts may overlook. If the intermediary (a knowledgeable person) inappropriately explains the research in simpler terms, the opinions of the intermediary or knowledgeable person might influence citizens. We must pay attention to this point. Knowledgeable persons would not need to explain products in simpler terms, but they should do so when it comes to research.
- Researchers sometimes use specialized knowledge as if it were generally accepted knowledge. In this sense, intermediaries need to explain such seemingly common knowledge in simpler terms.
- Intermediaries may need to refine the method of preparing reference materials to facilitate the citizens' understanding. For example, we found it challenging to understand materials that presented both abstract perspectives and specific details simultaneously. For example, we wondered why details such as the size of the molecules needed to be described in this material. We found the slides difficult to read because they were out of order. No conclusion was written either. If these materials were intended for use by citizens, we would have liked to see more concise messages. Even the title of this research did not make sense. This title would not motivate citizens to read the research details. These materials would make citizens feel, "I do not want to get involved in this." We do not want reference materials like this. If these materials were interesting, some citizens might want to learn more. We want reference materials that are interesting enough to evoke such behavior.
- We want such an approach to be taken for citizens, particularly for research related to life-or-death matters, substances introduced into the human body, and those

affecting a large number of people.

[3] Members of society

[Research party's accountability]

- (In response to a question about whether Prof. Yamanishi sees no practical applications for the technology she developed) I would be shocked as a citizen if that is the case. However, Prof. Yamanishi is working on her research understanding it's potential applications. Since the government allocated its budget as part of CREST and Impact, I believe as a citizen that the researcher must consider this point.
- We expect to see more simply explained information about practical applications and benefits. For example, how will this research lead to business opportunities for small and medium-sized enterprises? This way, everyone's discussions would deepen.
- The explanation was too vague. While the explanatory materials referred to interdisciplinary areas on P12, we wanted to see more specific descriptions, for example, how stage 3 cancer will be treated. We wanted to hear a more straightforward explanation, instead of referencing the movie Fantastic Voyage.
- It would be more understandable if someone told me that I would become like this in the future. This makes me feel that the issues to be addressed are my personal issues. It would be good if this research were disclosed at events such as open campuses, where many people can interact. It would surprise me a bit if these materials used today are the same as those made public in the press release.

[Timing for citizen involvement]

- On the other hand, amid concerns that Japan's basic research capabilities are weak, citizens' involvement in basic research might pose a risk of losing the freedom of research. We should also carefully consider at which stage of research the citizens' point of view should be incorporated.
- It seems acceptable if the timing for citizen involvement goes a little downstream. It is essential to have citizens review the research before it is put into practical use.

[How citizens should be involved: Involving citizens through policy changes]

- The most important thing is specifically what should be done with citizens. The candidates include joint projects with citizens and workshops, such as science cafés, which help foster a problem consciousness among people across generations. We must involve citizens in such activities while developing the necessary human resources simultaneously.
- We need to implement these activities in a way that can attract the interest of citizens. In this sense, we need to allocate more money to science education. The two parties must work together while paying attention to preventing unilateral communication. We must first have citizens understand why participating in town meetings is essential. This requires policy changes at the national level. Japan lacks innovation power. As the number of young people engaging in science increases, Japan will see its innovation become more powerful. Town meetings may provide opportunities for young people like these to grow. We must steadily proceed with such a bold initiative. We must not be satisfied just with superficial discussions with citizens.
- We must create a system in which research can be used as children's homework or college credits. Since countries that deepen their knowledge of natural sciences are said to prosper, we need to put in place appropriate policy guidance. Researchers are busy, so giving them some incentives is necessary. There is still a significant shortage of research funding. If we lack innovation, we must increase our research funding.

- If we want to disseminate research-related activities to the general public, we must consider implementing appropriate reward systems.
- The viewpoint emphasizing the trust relationship between science and citizens is important. This includes encouraging citizens to become interested in research. When hosting exchange events on YouTube, we often notice discrepancies between our intended actions and the feedback we receive. It is beneficial to establish trust relationships with individuals from diverse fields. When I first saw the explanatory materials, I wondered what they were used for. However, I noticed that those materials were written with confidence in the research's merit. The same was true for YouTube. We can attract the user's interest by informing them of the benefits we provide. After they have shown their interest, we start explaining the details of our technology.
- We can perceive the citizen’s zeal through direct interactions, in addition to research content. The researchers would no doubt be motivated by the citizens’ reaction. They also feel motivated when meeting their supporters.
- First, we must know the presence of excellent technologies. Taking the level of “knowing” positively would improve your understanding, which in turn would increase the number of individuals who invest in the industry and those who aspire to become researchers. For example, it might be interesting to let the president and ordinary employees discuss diverse topics at company workshops. It would also be possible to incorporate technical information into the teaching materials for internal training.

[Methodology for future citizen involvement]

- Future town meetings may differ from the traditional ones. One thing is the use of social media. The communication tool enables the dissemination and collection of diverse opinions. Such communication has become easier than it used to be. ChatGPT can be used to invite many people effectively. This new tool also carries a risk of causing misunderstandings, but it works well if we strive to generate fair data.

Reference material: A futuristic novel created using an SF prototyping technique

(Showing a 12-minute-long video created using SF prototyping)

「Kind Dreams of Un-Kind」

It is said that people began to call their desire for the future “dreams” after the English word dream was introduced into our language. Seth remembered it while standing in the corner of the classroom with Lumina and watching the children's backs.

The word “Future Dreams” is dancing around the center of the classroom, surrounded by the children’s writings and videos. In the whirlwind of ideas, popular occupations such as genome traders and urban conductors are seen lined up.

“You all have come up with lots of dreams, haven’t you? Let's start shaping them more specific little by little for the Tanabata Festival a month from now. What inspired you to become that professional? Please discuss it with your “kinds” who came to see this class at work.”

The teacher said the above and wrapped up her class. Elijah rushed straight to Seth and Lumina. The two left the classroom together, walking toward the commune’s urbanized area.

Now that the population has declined significantly, the basis of people’s lives in some areas is shifting from countries and prefectures to medium-sized communities called communes. In communes operated by residents, it is not uncommon to see their mutual-aid relationships tighter than blood ties. The traditional family structure has gradually eroded, and the expanded network of people is called “kinds.” Seth and Elijah were not related by blood, but they shared more time together than real brothers.

“By the way, what was Elijah’s dream?”

Elijah smiled shyly at Seth's question.

Speaking about one’s dreams for the future holds significant meaning these days. For Elijah and others in the same generation, “what they want to become” is directly linked to the decision of “which genes they should express.”

Human gene editing, previously permitted only for treating serious diseases, has gradually evolved in terms of accuracy and flexibility. Today, even voluntary human gene editing not for medical purposes is also becoming permitted. Seth, a college student, falls under the first generation of applicants, and Elijah, an elementary school student, falls under the second generation.

Particularly, the second generation of applicants, including Elijah, had a “library” introduced into their cells. A library is an intracellular organelle, a collection of genes related to diverse abilities, which can selectively express specific genes in response to acquired stimuli. It is fair to say that Elijah and others are allowed to adjust themselves to transform into “what they want to become.” With the help of the libraries, gene editing is now regarded as the “extension of the right to self-determination,” not something “imposed by parents.” We should determine how we use our bodies and time. This is a taken-for-granted right in this era, and many now regard it even as a responsibility.

“This is it!”

Elijah showed Seth a drawing paper with “Product Breeder” written on it.

A product breeder is a professional who nurtures bioproducts. Now that gene editing for animals, plants, and microorganisms has become commonplace, bioproducts made from cells with various added functions are being distributed into the market. Lumina, which is scampering around Elijah’s head, is one such example.

Lumina is a representative personal bio-product called MC, a product that combines the features of an old-fashioned smartphone and a pet.

Lumina slipped into Seth’s breast pocket and vibrated. It was a message from Seth's grandfather, Takeru. Lumina is a mouse-based MC, currently integrated into a handheld game console that Seth’s grandmother had been using. Lumina’s round plastic enclosure, fur, and a long, slender tail wriggled in Seth's palm.

“Elijah, will you come with me to see Grandpa?”

As soon as Seth said so, Lumina started to run. Seth followed it with his gaze. Seth saw the road in front of him smoothly connecting to buildings in the distance. The commune’s basic structure consists of web-like architectural buildings that envelop the ruins of abandoned concrete buildings. Porous components akin to insect cocoons and coral skeletons shape the roads, roofs, and walls. All of these were also generated by gene-edited animals and plants. Fast-growing wood constructs the commune’s main facilities, with the infrastructure based on “living” trees that have self-healing and immune functions.

Suddenly, Seth heard “miners” flapping their wings in the sky. A miner is an insect-based bio-product that extracts sap from living building components and refines it inside the body to produce industrial resins. The commune was in the process of developing an ecosystem that fosters the coexistence of cities and products.

The nursing home where Takeru lived was a little away from the center of the commune. Other communes could be seen in the hazy distance through a scenic window.

“Sorry for bothering you again today.”

Takeru talked to Seth while taking care of Elijah.

Takeru is turning 80 this year. Many years ago, his doctor told him he would not live up to the age of 30. The diagnosis was made based on his congenital genetic disorder. However, he was saved by experimental genomic medicine that was just starting at the time. Of course, that happening was something Takeru should be happy about. However, as he lived through the years, he began to feel fear that the person once destined for death had survived this long. He also felt horrified by the fact that he had a son and grandson, who should not have been there under normal conditions. Takeru grew up with a pain that would never leave him. When he was a teenager, he desperately tried to swallow his despair and accept his fate. Those memories have been completely detached from him by now, as if they had happened in a parallel universe. That is what makes him feel so eerie from time to time. Takeru now thinks, “I probably have formed my self-identity with my illness as part of it.” Therefore, he wondered where he came from after losing his illness. Every time he thought about it, he felt a chill run down his spine as if the ground beneath him gave way. That feeling popped up in his mind particularly vividly every time he looked at “somebody else who bears some resemblance to him,” that is, his son or grandson.

Perhaps because of this, Takeru did not allow any intervention in Seth's congenital genomes. Takeru still appeared to be wondering whether that decision was the right one.

Despite that, Seth has neither had any particular problems nor felt a strong sense of inferiority. Nowadays, few people stick to self-realization as individuals. Seth, Elijah, and others in their generations have been touching gene editing from birth, growing up among living organisms and products, nature and artificiality, and destiny and design. Therefore, they are aware of the ambiguity of boundaries, such as species and individuals. Humans have become capable of rewriting their genes. Seth believes that this is akin to the system of various bacteria exchanging their genes with each other to survive through gradual mutations. As such, the fact that someone else can do something he cannot do is what he should be happy about.

However, it was also true that there was an indescribable sense of anxiety. It is the feeling that everything is suspended in the light of diversity. Whether to take it as ecstasy or fear is ultimately

a matter of personal interpretation, Seth believes.
“The Tanabata Festival will be held at Elijah’s school next month. Why don’t you come, Grandpa?”,

said Seth to Takeru. The Tanabata Festival holds special meaning for the generations of Seth and Elijah. Children must think about their future with a high level of resolution to make their choices about gene editing. The concept of the Tanabata Festival is that such choices require the cooperation of not only individuals but also the entire commune. On that day, the commune temporarily becomes a place to simulate the future. Children act out their dreams for the future, and the people in the commune respond to them accordingly. The festival is like a huge occupational experience center or a street theater. Children dressed in uniforms representing various occupations abound in the streets, where they attempt to create part of the commune's daily life together with the adults. Seth remembered such scenes.
“Oh! I will think about it.”

Takeru said and returned to his room. Lumina rushed out to chase Takeru, but Seth hurriedly caught it.

When Tanabata Festival day comes, people are animated in every corner of the commune. There are voices of people selling lunch, directing traffic, and working on construction. Children's voices bubble up and fade away from all over the town like carbonated water. A young boy aspiring to be an urban conductor cautiously inspects the edges of roads that are still under construction to develop a commune development plan. In front of the boy, a girl who aspires to be a police officer was running while maneuvering a drone, chasing an escaped bioproduct shaped like a bird. On the device in his hand, Seth saw a live advertisement flow, showing five kids dancing a faltering dance. The entire commune was becoming filled with the warm glow of a bright future. In such scenes, only Seth remained frozen.

Lumina died yesterday. Lumina died due to an electric leak from its aged enclosure. It seemed to Seth that the cracked plastic enclosure and cold fur denied Lumina's seemingly eternal industrial life and redrew the blurred boundary line between a product and a living organism. Should he repair Lumina and reactivate it? Whenever Seth thinks about such a thing, he feels as if the song of praise for the future that envelops the commune sounds farther in the distance. Seth thought he could understand a little bit of the fear Takeru was feeling.
“Look at me, Seth.”

Elijah, dressed in a breeder's uniform, said to Seth. Behind him, Seth saw Takeru in a wheelchair.
“Lumina, come here.”

Elijah picked up Lumina from Seth's hand. Taking care of the whole life of bio-products is the responsibility of breeders (producers). That meant “how they should mourn products at the end of their lives.”

Elijah carefully reshaped the broken area of Lumina. It seemed to be something like embalming. A little time passed, and Lumina reappeared, with its former appearance regained. Seth gazed at the figure once again. A long, long time ago, it was said to be popular among people to keep a digital pet on a mobile game console like this. As life flows through particles of electrons, fragments of resin, and clumps of protein, people cannot catch it.

People are still unable to handle life that has been freed from the constraints of species, individuals, and nature. Even so, people can feel that they and the life of a product definitely coexisted at that moment. Seth wanted to show the prosperity of this commune (the changing, intertwining, and mingling web of life) to Lumina for a little while longer.
“I wish I would be cleaned up like this when I die,”

Takeru murmured.

“Grandpa is not a product, so you will not be cleaned up like Lumina.”

Elijah said so seriously that the two burst into laughter.

Seth placed Lumina on his palm. Elijah and Takeru walked behind him. A short funeral procession of only three people quietly made its way through the hustle and bustle of the Tanabata Festival.

End