Mini Horizon Scanning Round-Table Discussion by GteX Members: Report

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* Original Japanese report can be accessed below
https://www.gtex-microbe.jp/wp-content/uploads/2024/09/20240901-1.pdf

1. Introduction

Amid rapid technological advances, “anticipatory governance” is called for. It aims to anticipate what kind of research and technological developments will progress and what social impacts they may have in the future. Based on the anticipated future, backcasting is conducted for discussions among the people concerned to formulate the responses in advance. “Horizon scanning” is an activity to identify future trends in technologies – searching signs of future technological development in a timeline to study various opportunities and challenges that may be brought about by those technologies.

The Organisation for Economic Co-operation and Development (OECD) has set up an expert meeting to discuss synthetic biology[2]. As part of its activities, a survey by questionnaire on horizon scanning was conducted among the members of the expert meeting. With this background, a similar survey was conducted among the GteX[3] members in May 2024 using the same questionnaire as the OECD’s with a view to provide the OECD with the ideas held by GteX researchers engaged in biomanufacturing and also to study the future of the biomanufacturing research community in Japan. Consequently, various information was obtained in a limited time, and interested GteX members organized a mini horizon scanning round-table discussion (hereinafter the “Round-Table Discussion”) to review and discuss the results in July 2024. This report provides a summary of the discussion.

2. Outline of Round-Table Discussion

(1) OECD’s horizon scanning questionnaire and the Round-Table Discussion procedure

[1] We gained cooperation from Mr. Katsumi Hagino (The University of Tokyo), a research assistant, in summarizing this round-table discussion.
[2] OECD Website, Synthetic Biology Briefing Document, 3 April 2024, Global Forum on Technology (GFTech) https://www.oecd.org/content/dam/oecd/en/networks/global-forum-on-technology/global-forum-on-technology-synthetic-biology-brief-2024.pdf
[3] JST Green Technologies for Excellence (GteX)/Biomanufacturing Area (PO: Akihiko Kondo (Kobe University)) “Development of DBTL Technologies for Bioengineering to Pioneer Diverse Microbial Functions” (Project Leader: Kohsuke Honda)

A survey was conducted among the 37 GteX members using the OECD's horizon scanning questionnaire (period: May 21–24, 2024). The answers were obtained from 16 members.

The OECD questionnaire has the following four questions:

i) What new scientific knowledge and research fields are needed to drive synthetic biology forward?

ii) What technological developments are on the horizon that you expect to revolutionize synthetic biology?

iii) What synthetic biology derived products and innovations do you foresee having a major impact and in which sectors?

iv) What are the challenges and opportunities for scaling synthetic biology innovations?

(Provide their respective reasons and timelines: 1–5 years, 5–10 years, 10 + years)

Based on the diagrams summarizing the survey answers (Appendix 1), the Round-Table Discussion was held in a hybrid setting on July 18, 2024 to discuss two subjects: the review of trends in science and technology (corresponding to i) and ii) above), and the review of social impacts and challenges (corresponding to iii) and iv) above)[4].

(2) Summary of the discussion

Concerning the first subject, i.e., the review of trends in science and technology, the first argument was that the technologies covered are limited and that discussion from a holistic perspective is needed, demonstrating the fact that the survey was conducted among GteX members and the results clearly reflected GteX members' interests. A suggestion was made that more items should be added to expand the diagrams, such as technical development in the field of process engineering, artificial photosynthesis, protein sequencing, fermentative production, and optimization of culture media compositions.

After that, a discussion was held to primarily cover data, laboratory automation, and AI. Regarding data, the importance of databases and the challenges related to a repository

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[4] It was expected that opinions and how they are expressed would vary depending on what standpoint/perspective each researcher/expert takes. Therefore, in the Round-Table Discussion, participants were requested to discuss things from a holistic perspective to the extent possible what they expect of policymakers and they think are necessary to improve the entire synthetic biology research community in Japan.

for storing research results were discussed, including the following: Storing data in a common format is ideal; such standardization has various challenges (e.g., obsolescence due to rapid technological advances in analytic methods and instruments); there is no uniform format at present because research contents are diverse; and if data are to be standardized, it is important to do it in a way that benefits researchers. Concerning the collection of experimental data: it is technologically possible despite costs that are involved; there are many challenges in processing raw data and linking them to a database; and we need to learn from other cases, including overseas successful cases. As to laboratory automation and the use of AI: we are only beginning to understand their characteristics and areas in which they can contribute to research (increasing data accuracy and speed, image processing) and those in which they cannot (areas where peculiarity of living things is dominant, areas requiring the skill of a craftsman) and it is necessary to clarify them further and consider where to focus (note that the latter may also be resolved by technological advances in the long run); AI-assisted rational engineering is becoming technologically possible at enzyme level but those at genome-level is difficult and phenotype-level has a long way to go; and advances in AI and laboratory automation may lead to a technology capable of exploring the optimal genome sequence with a desired phenotype in the future. There was another comment on the need for robust data security, as well as the changes in the modality of education that would be caused by advances in AI and laboratory automation. Data, laboratory automation, and AI are interlinked, and considered as important subjects to be delved into.

Regarding the second subject, social impacts and challenges, the discussion started with areas subject to significant impact. Firstly, as demonstrated in the survey results, medical service was identified as an area that would be significantly impacted. At the same time, the need to discuss the impact of application to food and other areas was indicated. Moreover, importance for the GteX to focus on environmental and energy issues was argued. Specifically, it should focus on research and development aimed at creating a system that can continuously produce useful substances from raw materials found in Japan using sunlight, instead of aiming for an industrial structure that can exist only by continuing to procure raw materials from overseas, and the existing technological gap needs to be studied using simulation and other techniques. In that regard, it is necessary to consider utilizing unused resources including waste and sewage sludge/water treatment sludge, although this point was not included in the diagrams. There was additional comment that in taking these things into account, we should not only identify the domestic availability of bioresources in the downstream of the value chain but also consider their procurement costs and practical limitations in terms of social implementation. Secondly, the topics of standardization and human resource development were discussed. In regard to standardization, various opinions were expressed: commitment is required to establish international standardization rules from an early stage, particularly for data and AI, on the basis of successful cases in laboratories and other instances; a bottom-up approach initiated by researchers who spend time and effort to achieve standardization through, for example, international projects, is needed, instead of a top-down approach led by the government or other organizations; if a good thing is created and there is demand for that, it will spread automatically; and the need for science-based approaches (for the standardization of LCA and other matters). Concerning human resource development and education, they were viewed as a matter requiring immediate attention, and the discussion covered divers areas: the necessity for the development of personnel leaning towards engineering; a need for multi-skill education, including the ability to see the entire value chain comprehensively, entrepreneurship, and ELSI/RRI; the importance of producing more Ph.D. and challenges related to career paths in Japan; and the importance of long-term continuous efforts in human resource development and education because they cannot be achieved in a short time. The discussion covered other topics, including regulations, challenges in academia-industry cooperation (difference of perception in publishing papers, intellectual property/patent, etc.), and how university-initiated startups should be supported.

3. Conclusion

Information obtained through horizon scanning provides a basis for considering many things. It is useful for policymaking. It is also useful as evidence that enhances persuasiveness in studying the direction of research activities by scientists/engineers and in developing technologies/acquiring a budget or investment, and as source of topics for ELSI discussions.

This horizon scanning was conducted by the interested GteX members by taking the opportunity of the OECD's horizon scanning questionnaire, and although it was conducted in a short period of time, various information was obtained about trends in science and technology as well as social impacts and challenges. Regarding trends in science and technology, data, laboratory automation, and AI were identified as important subjects that need to be discussed from various viewpoints. As to social impacts and challenges, standardization and human resource development generated a lot of discussions. There was also an important comment that we should aim for research activities with the understanding of environmental and social contexts (soft science) such as the availability of bioresources in Japan.

We understand now that these findings will serve as useful information when we in the research community carry out various activities for research and development for Japan's biomanufacturing in the future. This suggests that, in the long run, it will be beneficial for GteX to design horizon scanning to have more specific objectives and conduct it on its own.

Appendix 1

※ The red letters represent the points added on the basis of the Round-Table Discussion.

1)What new scientific knowledge and research fields are needed to drive synthetic biology forward?

	1 year →	5 years →	10 + years →
Gene synthesis technology	Design of long-chain DNA and synthesis technology →	Genome synthesis technology for smart cells	
Cell regulation technology	・Control of cellular activity ・Control of transcription and translation factors →	・Comprehensive control of the entire transcription and translation system	
Monitoring	*In vivo* assays for metabolic flux →	・Monitoring with biosensors ・Real-time monitoring of large-scale bioreactors →	
Utilizing AI	Computational biology and bioinformatics →	・Various data collection ・AI for material production ・AI analysis of omics data ・Design and manipulation of organisms by AI →	Construction of the database
Production efficiency	Elucidation and librarying of membrane transport mechanisms →	・Library expansion ・Development of high production efficiency devices	
Bioprocess	・Fermentative production ・Optimization of culture medium	Technical development in process engineering	
Others		・Artificial cells that convert CO_2 to fuels and foods ・Protein sequencing ・Artificial photosynthesis	

Diagram.1 Summary of answers to question 1

2) What technological developments are on the horizon that you expect to revolutionise synthetic biology?

	1 year →	5 years →	10 + years →
Metabolic design	· Metabolic design with mathematical model · *in vivo* assay technology for metabolic pathways	Developing AI for rational design of metabolic pathways	· Increasing efficiency with AI · Maximize yield · Sustainable and energy-efficient production
Genome design	· AI-assisted rational design of genome sequence · Accurate and highly efficient genome editing (CRISPR-based)	Rapid whole genome sequencing for evaluation of genome-edited strains	Automated genetic engineering
Artificial cell	· Artificial cells capable of efficiently producing high-value chemicals		Artificial cell design by AI
Comprehensive engineering of the ribosome	Translation factor engineering (aaRS, EF-Tu)	Comprehensive engineering of translation systems(+ Ribosome, tRNA)	
Others		Formation of on-demand microbiota through calculation and automation	Acceleration DBTL cycle by automating experiments

Diagram.2. Summary of answers to question 2

3)What synthetic biology derived products and innovations do you foresee having a major impact and in which sectors?

	1 year →	5 years →	10 + years →
Environmental problem	· Development of biopolymers alternative fossil fuel-derived materials · Sustainable biomanufacturing	· Chemical production from C1 substrates or CO_2 using an artificial cell factory · Bio-production to reduce CO_2 emissions · Waste, sludge, and water treatment	
Energy problems	· Production of biofuels (SAF) by synthetic biology · Carbon-neutral production of key Materials for Industry · Utilization of marine biomass resources	Systems that continue to produce useful substances by sunlight.	Using synthetic biology to solve the energy crisis
Medical related	· *In vivo* synthesis of N-alkyl peptides/proteins · Enzyme-based therapy	· Protein synthesis with D-amino acids · Protein/mRNA-based therapy	
Other technologies	· *De novo* design of artificial enzymes · Innovation for Agriculture and foods		

Diagram.3. Summary of answers to question 3

4) What are the challenges and opportunities for scaling synthetic biology innovations?

	1 year	5 years	10 + years
Research efficiency		Automating wet labs to obtain data needed to train generative AI	Automation of complex experimental flows
Technological innovation	・Long-chain DNA synthesis technology ・Directed evolution with bioinformatics and structural biology	・Flexible *in silico* protein design ・Design of precise biological functions using deep learning	・Maximize yield ・Sustainable and energy-efficient production
Improvement of the research environment	・Expansion of research funding ・Proposing cutting-edge ideas, and Fostering Excellence ・Sharing of problems and directions in the field	・Bridging research and industry ・Improvement in the number and quality of researchers (~10 years)	
Social conditions and regulations	・Regulations based on ethics ・Regulation of recombinant organisms ・Expansion of GM microorganisms (without exogenous genes) in open systems ・Inspection methods to achieve this expansion	Resolving economic issues	

Diagram.4. Summary of answers to question 4

Appendix 2

Mini Horizon Scanning Roundtable Discussion Outline

Date: July 18, 9:30 - 11:30 a.m.

Place: Seminar Room, 5th floor, International Center for Biotechnology, Osaka University

Participants:

Kohsuke Honda (International Center for Biotechnology, Osaka University)

Tomohisa Hasunuma（Engineering Biology Research Center, Kobe University）

Fumio Matsuda (Graduate School of Information Science and Technology, Osaka University)

Isao Yumoto (Institute for Open and Transdisciplinary Research Initiatives, Osaka University)

Yoshihiro Toya (Graduate School of Information Science and Technology, Osaka University)

Kenya Tanaka（Engineering Biology Research Center, Kobe University）

Wataru Aoki (Graduate School of Engineering, Osaka University)

Makiko Matsuo (Graduate School of Public Policy, The University of Tokyo）

Katsumi Hagino (Graduate School of Arts and Science, The University of Tokyo)

Observer: Wataru Mizunashi (New Energy and Industrial Technology Development Organization)

Schedule for the day

9:30～ Introduction (Dr. Kohsuke Honda, Osaka University) 5 minutes

9:35～ “What is horizon scanning and why researchers need to think about it”
(Dr. Makiko Matsuo, The University of Tokyo) 20 minutes

9:55～ (45 minutes) “Science and Technology Trends Revisit

10:40～ (45 minutes) “Social Impact/Issues Revisit