Acquisition of New Large National Projects and Future Research and Development Prospects

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1. Introduction

Biomanufacturing is expected to contribute to carbon neutrality for the realization of a sustainable society. This technology uses biological processes to produce products independent of fossil fuels. An example is carbon recycling that uses CO_2 to directly feed microorganisms and will convert atmospheric CO_2 into useful compounds and contribute to the reduction of greenhouse gases. Products such as bio-plastics and biofuels made from renewable resources such as biomass resources have a lower environmental impact than conventional petroleum-based products. The widespread use of these products is expected to reduce the carbon footprint of the entire industry.

The Research Institute of Innovative Technology for the Earth (RITE) has been working on producing biofuels and green chemicals through research and development of smart cell and biorefinery technologies. In FY2023, RITE was entrusted with the Green Innovation Fund (GI) Project and Research and Development of Technologies to Promote Biomanufacturing, taking a new step toward realizing a sustainable society. These projects will develop carbon-recycling technologies to produce chemicals and fuels from CO_2 and biomass resources. In the future, RITE aims to contribute to realizing a carbon-neutral society by building an innovative manufacturing method to produce high-value–added chemicals from diverse biomass resources and CO_2, with biomanufacturing technology at its core. This initiative can be expected to become the industrial foundation for the next generation as a sustainable manufacturing process that replaces the conventional manufacturing process that use fossil resources as raw materials.

In this special issue, the efforts of RITE in the GI Fund Project and Research and Development of Technologies to Promote Biomanufacturing will be introduced after an overview of the current trends in biomanufacturing.

2. Global trends in biomanufacturing

Biomanufacturing is gaining worldwide attention as a sustainable manufacturing method and is experiencing intensifying competition, especially in Europe and the United States.

In the U.S., a presidential decree on the promotion of biotechnology and biomanufacturing has been signed, stating that biomanufacturing will replace one-third of the manufacturing industry within the next 10 years, with the market size estimated to reach approximately $30 trillion[1)]. These policies indicate a policy of expansion and intensive investment in biomanufacturing.

In Europe, emphasis is being placed on the formation of international rules for creating a recycling-oriented society, and environmental regulatory strategies such as the adoption of the "Draft New Regulation on Packaging and Packaging Waste"[2)] and the revision of the European Renewable Energy Directive (RED III)[3)] are being used to provide direction for biomanufacturing and to promote the bioeconomy.

In Japan, to secure competitiveness in this field, the

New Energy and Industrial Technology Development Organization (NEDO), a national research and development corporation, has been implementing the "Development of Highly Functional Materials Production Technologies Using Plants and Other Organisms (Smartcell Project, FY2016–2020)"[4] to build unique and efficient gene design and recombination technologies by combining biotechnology and digital technology, and has produced many results[5]. This concept and its results have been carried over to the current "Development of Production Technology for Biobased Products to Accelerate the Realization of Carbon Recycling (Biomanufacturing Project, FY2020–FY2026)"[6] and other projects. RITE has participated in these projects and developed several core technologies that are now being used to develop current technologies (see Research and Development Activities of the Molecular Microbiology and Biotechnology Group, RITE).

In October 2020, then Prime Minister Suga declared the goal of carbon neutrality (zero overall greenhouse gas emissions) by 2050. In June 2021, the government formulated a "Green Growth Strategy"[7] and created a 2 trillion yen GI Fund[8] at NEDO as a budget for addressing global warming as an opportunity for growth.

Furthermore, in June 2022, Prime Minister Kishida announced the "Grand Design and Implementation Plan for New Capitalism."[9] This states that bold and focused investment will be made in biomanufacturing, a research field that can pursue both economic growth and solutions to social issues on a global scale.

Based on these policies, in 2023, NEDO launched the "Green Innovation Fund Project/Development of Production Technology for Biobased Products to Accelerate the Realization of Carbon Recycling" and the "Research and Development of Technologies to Promote Biomanufacturing" to support the diversification of raw materials and products for biomanufacturing and the advancement of production technology, as well as the development of domestic platforms to design and develop efficient material production microorganisms based on the outlook for future industrial structure[10].

RITE has proposed and been adopted for these two projects in collaboration with companies, and is carrying out the projects. The following is an introduction of the contribution of RITE to these projects.

3. GI Fund Projects*

3.1. Project overview

The Green Growth Strategy was formulated to meet the Japanese Government's 2020 target of achieving carbon neutrality (zero greenhouse gas emissions overall) by 2050, and the GI Fund was established at NEDO in 2020 as one of the initiatives to achieve this target. In 2023, as part of the GI Fund project, NEDO announced that this would launch the "Promotion of carbon recycling using CO_2 as a direct raw material through biomanufacturing technology" (total budget: 176.7 billion yen), and six themes were selected. The main feature of the GI Fund project is that this uses "CO_2 carbon as a direct raw material," rather than the conventional biomanufacturing by microorganisms from "biomass resources."

Therefore, the aim is to contribute to achieving carbon neutrality through the development and social implementation of new biomanufacturing products using CO_2 as a raw material and to change the industrial structure through the conversion of CO_2 into resources.

RITE, in collaboration with Sekisui Chemical Co., Ltd. is currently implementing the "Green Innovation Fund Project: Promotion of Carbon Recycling Using CO_2 as a Direct Raw Material through Biomanufacturing Technology, Development and Improvement of Microorganisms Capable of Producing Materials from CO_2, Development and Verification of Manufacturing Technology Using Microorganisms Capable of Producing Materials from CO_2, Development and Demonstration of

Microorganisms that can Produce Materials from CO_2, Development and Commercialization of High-value–added Chemicals using CO_2 as a Raw Material through Biomanufacturing Technology" (project period: 8 years from FY2023 to FY2030).

3.2. Challenges in biomanufacturing from CO_2 by microorganisms

The acetate-producing bacteria (e.g., CO-assimilating bacteria) used in this project by RITE/Sekisui Chemical Co., Ltd. can efficiently fix gases with the lowest ATP energy consumption among the seven previously reported metabolic pathways that enable gas fixation, including CO_2. Therefore, useful substances can be efficiently produced using gas as a raw material. The disadvantages are that most acetic acid-producing bacteria are anaerobic, requiring dedicated anaerobic culture facilities and culture knowledge, as well as the development of genetic modification tools and technology to construct smart cells from acetic acid-producing bacteria. These aspects will be addressed through research and development by RITE under the GI Fund project.

For many years, RITE has enabled the production of various useful chemicals and biofuels from sugar feedstock derived from various biomass resources using Coryneform bacteria.

3.3. Themes contributed by RITE

Figure 1 shows the research and development image of this project conducted by RITE and Sekisui Chemical Co., Ltd. Sekisui Chemical Co., Ltd. converts CO_2 to CO with high efficiency by using a chemical catalyst, which has a high energy level (easily used by living organisms). RITE converts CO to polymer raw materials for epoxy resin in a bioprocess using acetate-producing bacteria (e.g., CO-assimilating bacteria, etc.). The resulting polymer raw materials are photodimerized and epoxidized by Sekisui Chemical Co., Ltd. to produce heat-resistant adhesives. This high-value–added heat-resistant adhesive is used for specialized bonding of components that require heat resistance, such as smartphones, aircraft, and automobiles. After use, the adhesive can be combusted into CO_2, and the same scheme can be used for resource recycling. The production cost of the adhesive is expected to be 1.2-fold less than that of the current product.

RITE will use the smart cell technology and bioproduction technology it has developed to date to develop strains that can convert CO to polymer raw materials (by developing genetic recombination tools for CO-assimilating bacteria and constructing production strains for intermediate and polymer raw materials from CO), which are the most important issues, using CO-assimilating bacteria, which are acetic acid-producing bacteria,

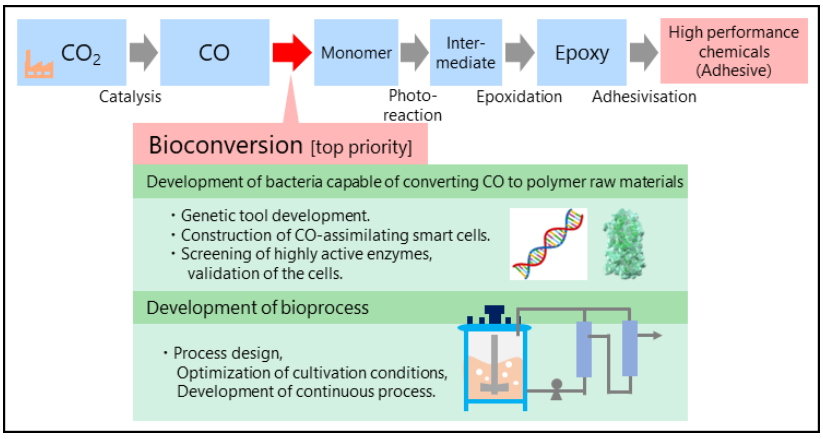

Fig. 1 Image of commercialization of high value–added chemical products from CO_2 by biomanufacturing technology

and developing bioproduction processes for polymer feedstock (process design, optimization of culture conditions, and developing continuous processes), mainly on a laboratory scale.

3.4. Future perspectives

Many refuse combustion facilities in Japan are of the "complete combustion type," and if NOx and SOx are removed according to established methods, exhaust gas mainly comprising CO_2 can be obtained. Since there are approximately 10,000 such facilities in Japan, the technology developed in this project could be applied to waste treatment facilities nationwide. In addition to these facilities, if CO_2 emitted from steel mills, thermal power plants, factories, and other facilities can be efficiently used for biomanufacturing, this would contribute to promoting carbon recycling and to the domestic carbon fixation and transporting biomass resources, rather than using sugar and other materials derived from biomass resources. This could also contribute to reducing CO_2 emissions. In Japan, where edible and non-food biomass resources are not abundant, the ability to use atmospheric CO_2 as a resource is advantageous from the perspective of securing future raw materials.

In the future, new developments are expected to include the development of technology for continuous bioproduction of various high-value–added compounds from CO_2 at high concentrations and yields, and the selective bioproduction of highly functional and high-value–added compounds from CO_2 that are difficult to produce using chemical methods because of isomer by-products.

4. Research and Development of Technologies to Promote Biomanufacturing*

4.1. Project overview

The "Research and Development of Technologies to Promote Biomanufacturing" project launched in 2023 conducts development of technologies necessary to build a biomanufacturing value chain that uses diverse raw materials as input and diverse products as output. The project aims for both economic growth and solving social issues such as environmental problems by converting the manufacturing process to biomanufacturing and promoting the social implementation of biobased products. The project conducts the following: Developing technology for procuring raw materials for biomanufacturing, developing microbial-modification platformers that can promote social implementation of biobased products, developing improvement technology for microorganisms, and developing and demonstrating manufacturing technology for mass production.

Together with TAKASAGO INTERNATIONAL CORPORATION and TEIJIN LIMITED, RITE drafted and proposed a development plan to strongly promote the social implementation of biobased products, and the project was adopted.

4.2. Our theme

In our proposal, "Development of bio-upcycling technology to produce useful chemicals from unused raw materials," RITE develops strain-breeding technologies and establishes a strain-development base. The coproposers, TAKASAGO INTERNATIONAL CORPORATION and TEIJIN LIMITED, conduct practical development of bio-aroma ingredients and high-performance bio-fiber in their respective industrial fields of expertise.

More specifically, to produce results that are unique and industrially competitive compared with research and development in biomanufacturing in Japan and around the world, we will conduct research and development focusing on the following items.

i. Food waste and surplus biomass currently being discarded will be positioned as unused domestic resources, and technology will be developed to process them into raw materials for fermentation.

ii. We will also develop breeding techniques and establish a base for developing microorganisms that can utilize raw materials derived from unused resources and produce even chemicals that are toxic to living microorganisms.

iii. By establishing large-scale production technology and purification technology, we will develop manufacturing technology for useful chemicals.

iv. We will conduct Life Cycle Assessment (LCA) on the manufacturing process of biobased products from unused resources to clarify the environmental performance, such as the CO_2 reduction effect, of converting from conventional petrochemical methods to biobased methods (Fig. 2).

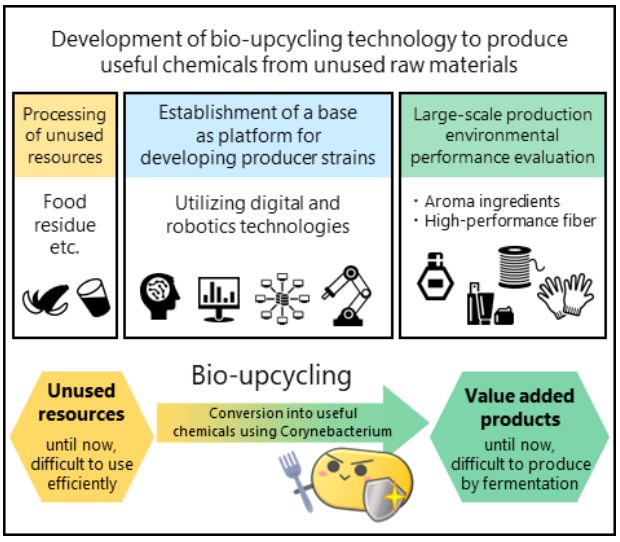

Fig. 2 Overview of RITE's theme

4.3. RITE's challenge to become a strain-development platform

A platform operator (platformer) is a company or organization that provides the foundation for users, such as individuals or companies, to develop their businesses. As the number of users increases, the amount of information stored on the platform increases and can be analyzed and used to expand business. Amazon, Google, and Apple are representative examples of platform operators that have a huge impact on their respective markets. The strain-development platformer referred to here is an organization that provides a service for developing high-performance producing strains. This service is the core of commercializing chemical production technology using microbial fermentation.

RITE has developed various producing strains through national projects and corporate joint researches. Since developing these strains requires advanced biotechnology, companies without experience face extremely high hurdles, including initial investment, training of engineers, and acquiring knowledge. For this reason, many companies hesitate to enter the biomanufacturing industry. Strain-development platformers are commissioned to develop and provide strains that can produce chemical products desired by these companies. These strain-development platformers strongly promote the conversion of manufacturing processes to biomanufacturing and the social implementation of biobased products. However, very few organizations that currently operate in Japan that can do this. RITE aims to become an organization that revitalizes the entire bioindustry as a bacterial strain-development platformer by fully using the microbial fermentation production technology we have accumulated over the years.

4.4. Future perspectives

The use of biotechnology has extremely high expectations for supporting a shift toward biomanufacturing using unused resources that can simultaneously solve the dual challenges of environmental problems and domestic economic growth. Strain-development platformers play an important role in achieving these changes, and the role of RITE as such a platformer is expected to make the following contributions.

1. Discovering and improving new microbial functions: The RITE platformer can explore new microorganisms and microbial functions and discover strains with useful properties. This is expected to improve existing

microorganisms and create more efficient and environmentally friendly bioprocesses.

2. Use of sustainable resources: The RITE platformer can develop microorganisms to utilize renewable raw materials. Technologies that generate energy, such as bio-fuel, using non-food or discarded biomass as raw materials are attracting attention as a sustainable energy source.

3. Collaboration with industry: The RITE platformer is expected to collaborate with industry to provide practical solutions through promoting applied research and commercializing production using newly developed production microorganisms.

4. Human resource development: The RITE platformer has a role in nurturing the next generation of researchers and engineers. This includes spreading knowledge and developing biotechnology by sharing research results to the extent possible.

The RITE platformer takes advantage of its characteristics as a Public Interest Incorporated Foundation, allowing the conduct of research and development and human resource development without conflicts of interest. RITE will solicit joint research not only from specific companies but also from a wide range of industries and contribute to create a sustainable society by bringing to the world many bioproducts derived from unused and renewable resources (Fig. 3).

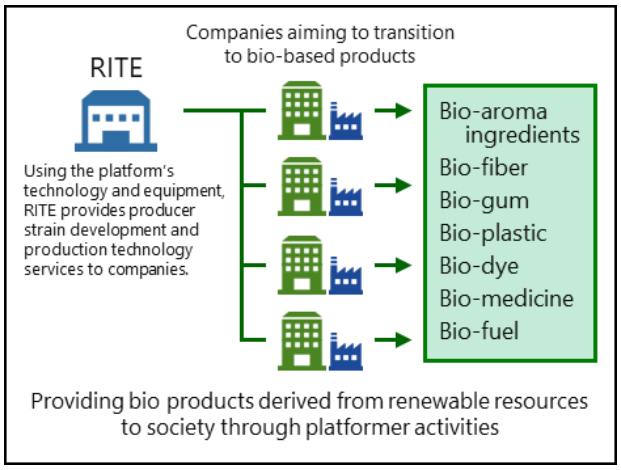

Fig. 3 Social contribution through RITE platformer activities

5. Closing remarks

Innovation in biomanufacturing technology is an essential element in building a new industrial structure and accelerating sustainable economic development. RITE will not only develop these technologies but will also focus on addressing the challenges faced in social implementation and promote the spread of biomanufacturing. Therefore, RITE plans to construct two new research facilities that will integrate technology and equipment. Each corresponds to the two new projects described in this feature.

The research building to be developed under the GI Fund project will be equipped with facilities specializing in fermenting polymer feedstock from CO and developing associated bioprocesses. This research building is scheduled for completion this year (FY2024) and will considerably accelerate the development of technology for the fermentation production of high-value–added compounds from CO.

The Research and Development of Technologies to Promote Biomanufacturing is also moving forward with plans to construct a dedicated experimental building that will integrate platform functions. Incorporating digital robotics technology to enable the breeding of ultraefficient high-producing strains of bacteria. Since

multiple strain development requested by companies will be conducted simultaneously, the structure will be designed with sufficient consideration for information security. Construction on this site is expected to begin this year.

By promoting the GI Fund Project and the Research and Development of Technologies to Promote Biomanufacturing in this special feature and by progressing the activities in the respective dedicated research buildings on track, RITE aims to explore the feasibility of manufacturing processes that do not depend on fossil fuels and contribute to environmental conservation by reducing CO_2 emissions.

These activities are important steps toward building a recycling-oriented society and achieving carbon neutrality by 2050. RITE will continue to pursue the further evolution of biomanufacturing, and the realization of a sustainable society brought about by this. We sincerely hope that RITE's efforts will serve as a foundation for building a better environment for future generations.

We hope that this special issue of RITE will help spread awareness of our activities and inspire people to work together to create a sustainable future.

References

1) Ministry of Economy, Trade and Industry, Realization of Biomanufacturing Revolution, April 19, 2023, (In Japanese), https://www.meti.go.jp/shingikai/sankoshin/shin_kijiku/pdf/014_05_00.pdf
2) Ministry of the Environment, Commissioned Research and Study for Promotion of Bioplastic and Recycled Materials Utilization, Report, March 24, 2023, (In Japanese), https://www.env.go.jp/content/000136496.pdf
3) Renewable Energy Directive (RED III) to be Revised, (in Japanese), https://baumconsult.co.jp/2022/10/07/%E5%86%8D%E7%94%9F%E5%8F%AF%E8%83%BD%E3%82%A8%E3%83%8D%E3%83%AB%E3%82%AE%E3%83%BC%E6%8C%87%E4%BB%A4renewable-energy-directive%EF%BC%9Ared%E2%85%B2%E3%81%8C%E6%94%B9%E6%AD%A3%E3%81%B8%EF%BD%9E/
4) NEDO Smartcell Project, https://www.jba.or.jp/nedo_smartcell/en/
5) NEDO "Smartcell Project Results", (In Japanese), https://www.nedo.go.jp/content/100923930.pdf
6) NEDO Bio-manufacturing Project, (In Japanese), https://www.jba.or.jp/b-production/
7) Green Growth Strategy with Carbon Neutrality in 2050, Cabinet Secretariat Ministry of Economy, Trade and Industry Cabinet Office Financial Services Agency Ministry of Internal Affairs and Communications Ministry of Foreign Affairs Ministry of Education, Culture, Sports, Science and Technology Ministry of Agriculture, Forestry and Fisheries Ministry of Land, Infrastructure and Transport Ministry of the Environment, June 18, 2021. (In Japanese), https://www.meti.go.jp/policy/energy_environment/global_warming/ggs/pdf/green_honbun.pdf
8) NEDO Green Innovation Fund, https://green-innovation.nedo.go.jp/en/
9) Grand Design and Implementation Plan of the New Capitalism, June 7, 2022, (In Japanese), https://www.cas.go.jp/jp/seisaku/atarashii_sihonsyugi/pdf/ap2022.pdf
10) Ministry of Economy, Trade and Industry, "Progress and Future Issues of Biotechnology Policy," May 12, 2023, (In Japanese), https://www.meti.go.jp/shingikai/sankoshin/shomu_ryutsu/bio/pdf/016_04_00.pdf

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