Molecular Microbiology and Biotechnology Group

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Development of Bio-manufacturing Technologies that Contribute to Carbon Neutrality

1. Introduction

Bio-manufacturing technology is a key field that utilizes advanced genetic modification techniques to enhance microorganisms' fermentation capabilities or to confer the ability to produce desired substances on them. It also includes ways to effectively obtain target breakdown products from raw materials by enhancing microbial enzyme functions. Bio-manufacturing uses these approaches to replicate biological mechanisms in nature and apply them to industrial manufacturing processes. Its features and advantages are as detailed below.

Bio-manufacturing utilizes microbial cells' inherent bio-processes and enzymes in production. This allows the synthesis of compounds that are difficult to produce through chemical processes, using highly precise bio-processes involving microbial enzymes, resulting in high yields with few by-products. Various enzymes in microbial cells collaborate to facilitate multi-step synthesis reactions, making them ideal for synthesizing substances with complex structures and high carbon numbers. Bio-manufacturing has been primarily used in the biopharmaceuticals and food industries. However, as biotechnology advances rapidly, its application in a variety of industrial fields, including fuels, chemicals, and textile materials, in on the rise.

The greatest advantage of bio-manufacturing is its ability to drive innovation in industrial activities, such as new product development and manufacturing process transformation. It also addresses social issues such as reducing environmental impact and utilizing sustainable resources. For example, conventional chemical-based manufacturing processes are often high-temperature and high-pressure reactions. In contrast, bio-manufacturing can carry out reactions at room temperature and pressure, which is expected to reduce CO_2 emissions compared to chemical processes. Bio-manufacturing can also utilize bio-based resources as raw materials, such as biomass, which absorb CO_2 during its growth process. Unlike chemical processes that depend on fossil resources like petroleum, this method considerably reduces the emission of new CO_2 that affects climate change. Meanwhile, advanced bio-manufacturing technologies are making it possible to recycle waste derived from chemical products. While previously such waste could only be disposed of by landfill or incineration, now it can be converted into fuels (biofuels) and new chemicals (green chemicals) or their starting materials necessary for industrial activities.

In short, bio-manufacturing is vital to achieving carbon neutrality. Sustainable bio-manufacturing also provides a competitive edge in various industrial sectors, laying the groundwork for a resource-circulating next-generation industry. Recognizing its potential early on, RITE has been actively focused on developing core technologies for industrial applications.

This overview will first introduce RITE's core technologies, including the "RITE Bioprocess"[*1] and "Smart Cell Creation Technology." Next, it will highlight the progress in developing fundamental technology in the fast-evolving "Bio × Digital" field through Japan's national projects involving RITE. Finally, it will discuss efforts towards commercialization and future prospects.

2. The Core Technologies of RITE

2.1. "RITE Bioprocess"

RITE has focused on developing core technologies for the industrial use of Corynebacterium, which possesses unparalleled substance production capabilities among microorganisms. As part of RITE's research, it was discovered that while its growth is suppressed under anaerobic conditions, Corynebacterium is able to maintain metabolic functions necessary for substance production, efficiently converting sugars into organic acids. Based on this phenomenon, RITE established the growth-independent bioprocess known as the "RITE Bioprocess." This highly productive method is unique to RITE and is considered as one of the most important core technologies for promoting the social implementation of bio-manufacturing (Fig. 1). Below are its three main features.

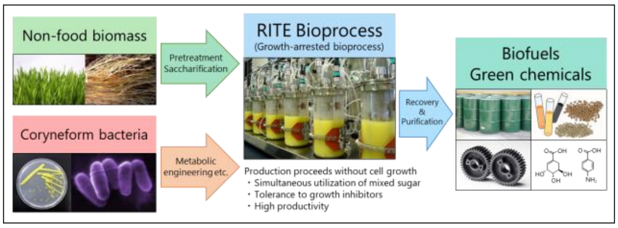

Fig. 1 Bio-manufacturing using the "RITE Bioprocess"

Feature 1: Growth-arrested bioprocess

In nature, fermentation typically requires microorganisms to grow while producing substances. However, RITE has established a bioprocess in which cell growth is inhibited under certain anaerobic conditions or by removing key growth factors under aerobic conditions suited for growth, yet target substance production continues (Fig. 2). In the "RITE Bioprocess," nutrients and energy that would normally be consumed for microbial growth are instead used solely for the production of the target substance, achieving productivity equal to or greater than chemical processes.

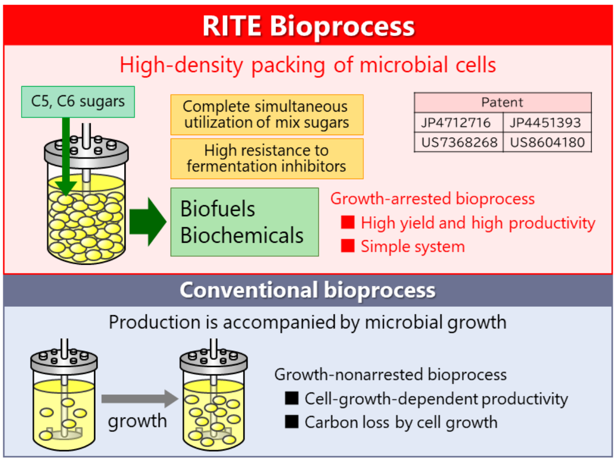

Fig. 2 Feature 1 of the "RITE Bioprocess"
(Growth-arrested bioprocess)

Feature 2: High tolerance to fermentation inhibitors

In bio-manufacturing, raw materials such as biomass or waste-derived unused resources often contain chemicals that inhibit microbial growth. Also, the target substances produced by microorganisms can themselves inhibit growth or damage the microorganisms. It limits the types of substances that can be produced through fermentation. Since "RITE Bioprocess," is a production system that does not involve microbial growth, it is highly resistant to various fermentation inhibitors (Fig. 3). This allows high productivity even with previously unusable raw materials and for various substances that were difficult to produce through fermentation.

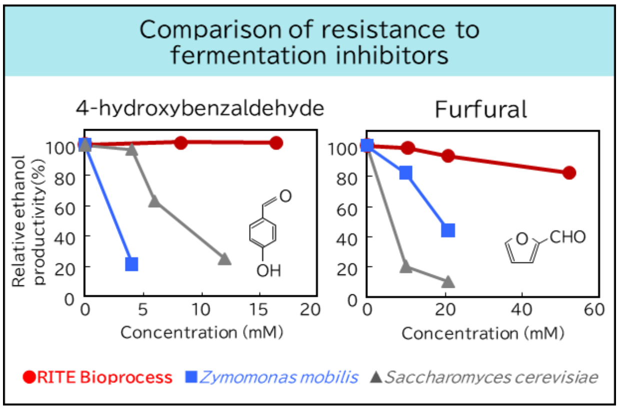

Fig. 3 Feature 2 of the "RITE Bioprocess"[*1]
(High tolerance to fermentation inhibitors)

Feature 3: Complete simultaneous use of mixed C5 and C6 sugars

Non-edible cellulose-based biomass is a common raw material in the bio-manufacturing sector. This biomass contains a mixture of C6 sugars, such as glucose, and C5 sugars, such as xylose and arabinose. Microorganisms typically favor C6 sugars utilization for substance production, which reduces C5 sugar utilization efficiency. At RITE, new C5 sugar metabolic and transporter genes were introduced into microorganisms to increase the utilization rate of C5 sugars to the same level as C6 sugars (Fig. 4). The complete simultaneous utilization technology of C5 and C6 sugars is an essential core technology in bio-manufacturing, enabling maximum production efficiency while minimizing waste of non-edible biomass raw materials.

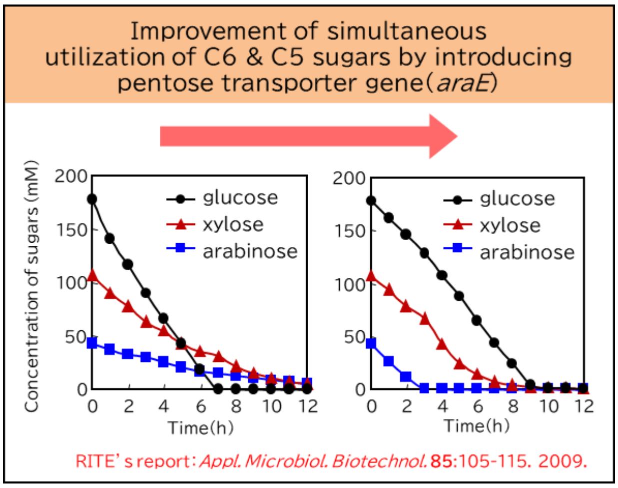

Fig. 4 Feature 3 of the “RITE Bioprocess” (Simultaneous usage of mixed sugars)

2.2. Smart Cell Creation Technologies

RITE has participated in the Smart Cell Project (NEDO "Project for Development of Production Techniques for Highly Functional Biomaterials Using Smart Cells of Plants and Other Organisms", 2016-2020) and has been involved in the development of technology sets to create smart cells. Smart cells are biological cells whose functions have been highly designed and whose gene expression has been controlled through genetic modification. More specifically, they are cells that combine cutting-edge biotechnology and digital technology to maximize the biological cells capacities and optimize its chemical production. This enables us to set specific a target compound and fine-tune its smart producer strains efficiently by developing and incorporating metabolic pathway design technology, breeding technology, and fermentation production technology (Fig. 5). This method can also be applied to develop producer strains for various other biofuels and bio-based chemicals. We will continue to brush up on these technologies and aim to make effective use of smart cell creation technologies.

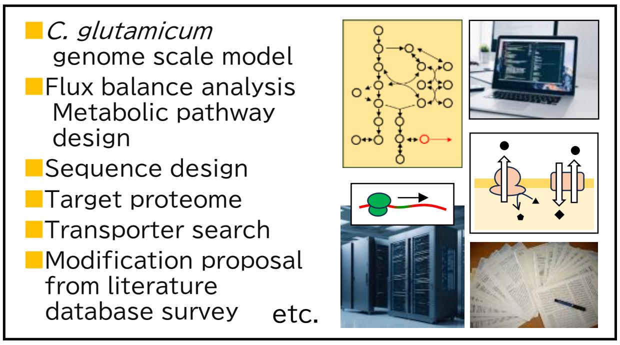

Fig. 5 Smart Cell Creation Technologies

2.3. Cytotoxicity Control Production System

RITE has developed biotechnological processes to produce various compounds. In this development activity, we have faced the problem that several target compounds exhibited profound antibacterial properties that halted production due to their accumulation during the process. For example, the production of catechol, a type of aromatic compound, has been limited to a certain concentration in the conventional batch method. To avoid cytotoxicity and achieve high production, we constructed a cytotoxicity control production system that selectively removes the target compound from the reaction solution and recovers it altogether. Fig. 6 illustrates our catechol continuous reaction method that combines membrane separation and resin adsorption. The catechol produced in the reaction solution is continuously collected in the adsorption resin, allowing production while maintaining a low concentration of catechol in the reaction solution. This enables exceptionally efficient catechol production compared to the conventional batch method. In other words, by avoiding the strong catechol cytotoxicity, the producer strain’s true productivity was demonstrated, resulting in enormously higher catechol production.

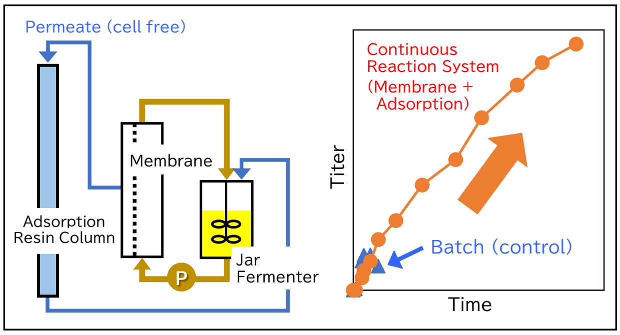

Fig. 6 A continuous reaction system using membrane separation and resin adsorption

2.4. Substances Produced by the "RITE Bioprocess"

RITE has achieved high production levels for various substances, as shown in Fig. 7. Many of these compounds have reached exceptional productivity levels. In the biofuel domain, RITE has expanded its lineup to include not only ethanol and biohydrogen but also butanol and high-performance bio-jet fuels. Meanwhile, our green chemicals focus has broadened to include *L*-lactic acid, *D*-lactic acid, amino acids, and high-functional chemicals such as aromatic compounds.

Biofuels	Green chemicals
■ Gasoline additives ・Ethanol * ■ Bio-jet fuels ・Isobutanol * ・n-butanol * ・C9-C15 Saturated hydrocarbon + Aromatics ■ Biohydrogen * : Polymer raw materials Red character: World's highest productivity achieved	■ Aromatics ・Shikimic acid (Anti-influenza drug; Tamiflu raw materials) ・Phenol * (Phenolic resins, Polycarbonates) ・4-hydroxybenzoic acid * (Polymer raw materials) ・Aniline * (Natural resource tire (Age resistor)) ・4-aminobenzoic acid * (Pharmaceutical raw materials) ・Protocatechuic acid * (Cosmetic raw materials) ■ Organic acids ・D-lactate *, L-lactate * (Stereo-complex PLA) ・Succinate * ■ Amino acids ・Alanine (Chelators) ・Valine (Next-generation feed-use amino acids) ・Tryptophan (Next-generation feed-use amino acids) ■ Alcohols ・Isopropanol (Propylene raw materials) ・Xylitol (Sweetener)

Fig. 7 Substances produced using the "RITE Bioprocess"

Aromatic compounds, in particular, are essential basic industrial chemicals that serve as raw materials for polymers and other products. Among these are numerous high-value compounds that are used as ingredients in pharmaceuticals, functional dietary supplements, fragrances, and cosmetic products. Currently, aromatic compounds are primarily manufactured from petroleum, with only a small fraction derived from natural plants. However, from reducing petroleum dependency, environmental conservation, and ensuring productivity perspectives, bio-manufacturing is eagerly anticipated. Microbes biosynthesize a variety of aromatic compounds, such as phenylalanine, tyrosine, tryptophan, folic acid (vitamin B9), and coenzyme Q. All these compounds are derived from a metabolic pathway known as the shikimate pathway. By utilizing advanced bio-manufacturing technologies, RITE has successfully established non-edible biomass-based high-production bioprocesses for shikimic acid (a raw material for the influenza drug Tamiflu), 4-aminobenzoic acid (a promising raw material for functional polymers), and aromatic hydroxy acids, which are favorable raw materials for polymers, pharmaceuticals, cosmetics, adhesives, and fragrances (vanillin).

3. Fundamental Technology Development (National Projects)

The Japanese government is currently providing substantial support for bio-manufacturing as an innovation that simultaneously pursues economic growth and address social issues. Fig. 8 summarizes the national projects in which RITE participates, as well as the bio-manufacturing technologies that RITE is responsible for developing. We are involved in the NEDO Green Innovation Fund Project and the NEDO Bio-manufacturing Revolution Promotion Fund Project, which is to develop bio- manufacturing technologies for high-performance adhesive raw materials from CO_2 and bio-upcycling technologies to produce useful chemicals from unused resources (Sections 3.1 and 3.2). RITE also participates in the NEDO "Moonshot" Project, where we conduct research and development on multi-

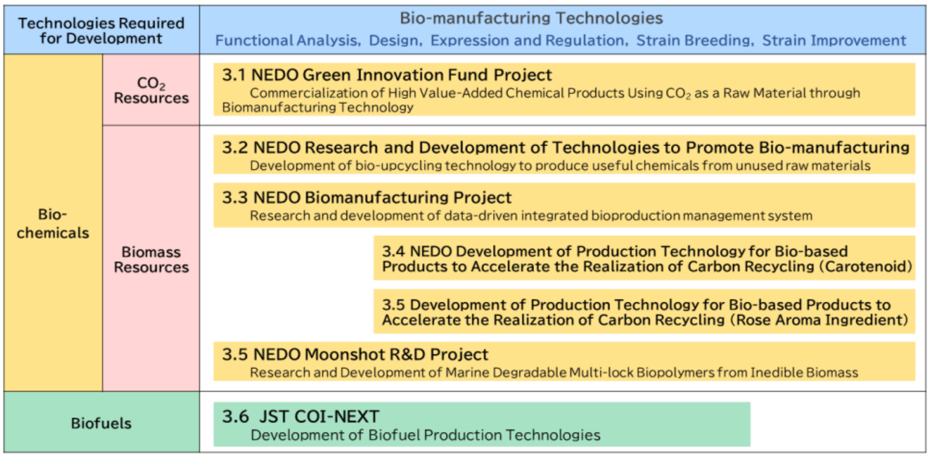

Fig. 8 Overview of participating national projects and new technologies required for development

lock type biodegradable biopolymers made from non-edible biomass (Section 3.6).

Furthermore, RITE is involved in the NEDO "Bio-manufacturing Demonstration" Project, in which we collaborate with private companies to commercialize the bio-production of carotenoids and fragrance compounds (Sections 3.4 and 3.5). RITE also promotes the transformation of manufacturing processes and the social implementation of products by developing and demonstrating the necessary technologies to build a bio-manufacturing value chain with diverse raw materials and products. Below are the details of RITE's initiatives.

3.1. NEDO Green Innovation Fund Project: “Commercialization of High Value-Added Chemical Products Using CO_2 as a Raw Material through Biomanufacturing Technology”[*2]

This project aims to contribute to “carbon neutrality realization by 2050” by developing and implementing novel biomanufacturing products that use CO_2 as a raw material. This breakthrough also seeks to reform the industrial structure by embracing CO_2 as a resource.

In this respect, RITE, together with Sekisui Chemical Co., Ltd., started this project in FY2023 and is currently implementing it (project period: 8 years from FY2023 to FY2030). For more details, see the “Special Feature” on the recently constructed “Biomanufacturing Experimental Facility.”

Fig. 9 displays the research and development conducted in this collaboration. In this project, Sekisui Chemical utilized chemical catalysts to convert CO_2 efficiently into CO with high energy levels, making it easier to use by organisms. RITE then converts CO into polymer raw materials for epoxy resin by using a bioprocess using CO-utilizing bacteria. The resulting polymer raw materials are dimerized and epoxidized by Sekisui Chemical to produce high-value-added heat-resistant adhesives, which are used to bind special components that require heat resistance, such as smartphones, aircraft, and automobiles. After use, these adhesives can be combusted into CO_2, thus closing the resource recycling loop.

RITE is harnessing the smart cell technology and bioproduction technology it has cultivated to date to address the most important issues: (1) development of bacteria strains able to convert CO to polymer raw materials (such as developing genetic recombination tools for CO-utilizing bacteria and constructing producer strains of the intermediates and the polymer raw materials from CO), and (2) developing bioprocesses for the target polymer (including process design, optimization of culture conditions, and continuous process development) on a laboratory scale in general.

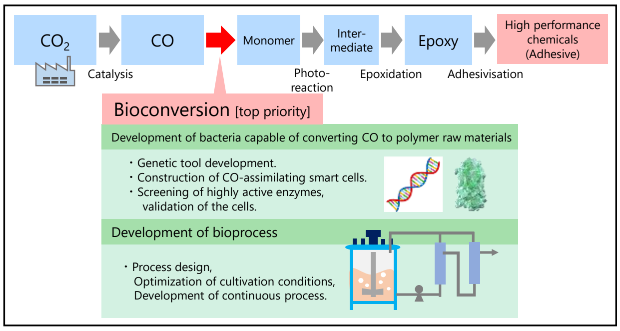

Fig. 9 High-value-added chemical products made from CO_2 by bio-manufacturing technology

3.2. NEDO Research and Development of Technologies to Promote Bio-manufacturing: "Development of bio-upcycling technology to produce useful chemicals from unused raw materials"[*2]

The shift to sustainable manufacturing and the promotion of social implementation of bio-based products are important issues that must be addressed in order to foster the next generation of industrial infrastructure. In addition, there is a need to develop biomanufacturing technologies that use domestic unused resources as raw materials rather than relying on imported biomass. In response to these circumstances, NEDO launched a project "Research and Development of Technologies to Promote Biomanufacturing" in 2023. This project aims to strengthen Japan's industrial competitiveness and solve social issues by aiming to build a value chain for biomanufacturing that uses a variety of raw materials and produces a variety of products. In this project, RITE raised issues with Takasago International Corporation and Teijin Limited and began research and development to solve them (more information here in our Japanese press release). We are developing new high-efficiency production strain breeding technologies from both the Dry (computer-based information analysis) and Wet (biological experiments) perspectives. As an example of the development technology, we are building a database to improve the efficiency of metabolic design and production condition determination. We will store the vast amount of production strain information we have accumulated, as well as newly acquired information on unused resources and production inhibition effects (cytotoxicity by compounds) of products in our own database, thereby strengthen our breeding competitiveness (Fig. 10).

Based on RITE experience in developing various production strains so far, such strain development requires advanced biotechnology. Consequently, companies without prior experience might face substantial hurdles in terms of initial investment, specialists' training, and know-how acquisition. These factors reasonably wary many companies that want to enter the biomanufacturing industry. We aim to fulfill the role of a "microbial development platform" that undertakes the development of producing strains that these companies need and provides production technology. For this purpose, we develop research facilities that bring together bio-specialized personnel, research equipment, technology, information, etc. named the "RITE Biomanufacturing Center" (Fig. 10). The construction began in December 2024 and is scheduled to be completed in November 2025, with preparations underway to start operations in fiscal year 2025.

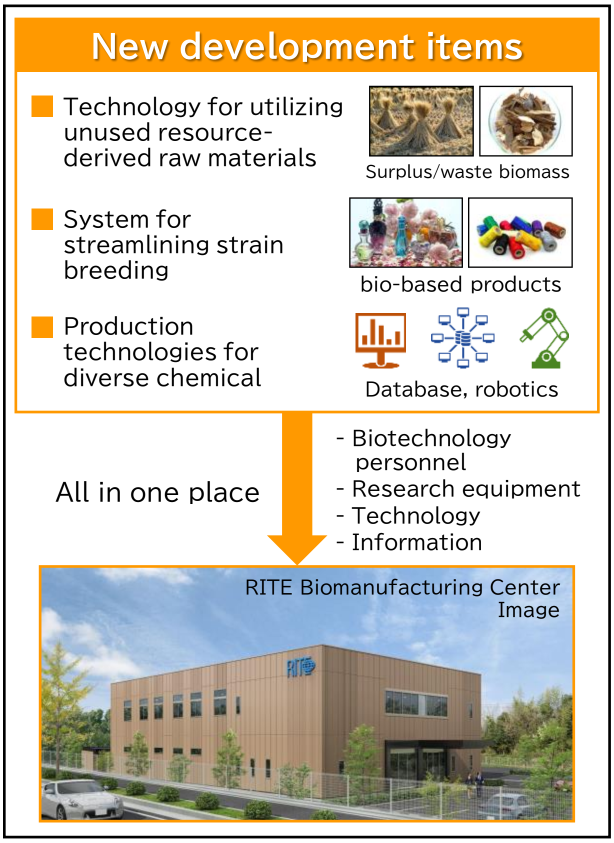

Fig. 10 RITE Biomanufacturing Center

3.3. NEDO Biomanufacturing Project "Research and development of data-driven integrated bioproduction management system"[*2]

"Development of Production Technology for Bio-based Products to Accelerate the Realization of Carbon Recycling" was launched in FY2020. This initiative, which is commonly known as the NEDO Biomanufacturing Project, is creating technology to address practical application challenges so that laboratory-optimized smart cells can demonstrate their capabilities in industrial processes. RITE has been involved right from the start, where we developed a group of new technologies to resolve issues associated with the practical application of biomanufacturing technology, including product inhibitory properties and scale-up issues (Fig. 11).

Our research has shown that there are several cases in which the target chemical itself is responsible for limiting the activity of enzymes necessary for production. To resolve this issue, we developed new technology with collaborating research institutions in FY2024. The resulting experimental data has identified the mechanism behind the reduction in activity. In addition, we discovered that the decrease in enzyme activity could be avoided by estimating the mechanism and substituting appropriate amino acids.

On the other hand, we observed that various parameters, including the temperature, pH, nutrients, and dissolved oxygen, are likely to become spatially biased and uneven in the larger-scale bioproduction. Research and development were conducted with collaborating research institutes with the aim of developing design technology for robust producer strains that can maintain high productivity even in such circumstances. In 2024, RITE identified conditions that reproduced the environmental fluctuations. The detailed gene expression and metabolite data we obtained contributed to constructing and verifying a simulation model for the fermentation production.

By researching and delivering solutions to problems that may arise during actual production, we aim to eliminate the need for rework in the producer strains' development, thus accelerating the social implementation of bio-derived products.

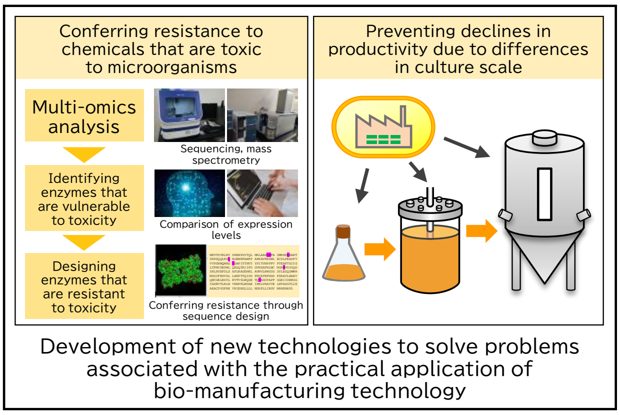

Fig. 11 Technology development in the Biomanufacturing project

3.4. NEDO Development of Production Technology for Bio-based Products to Accelerate the Realization of Carbon Recycling (Carotenoid)[*2]

Carotenoids are functional ingredients with high antioxidant activity. However, the bioavailability of most carotenoids on the market is notably poor due to their all-*trans* chemical configuration.

Since 2022, RITE has worked with Harima Chemicals, Inc., on the NEDO “Industrial Material Production System Demonstration” project, which aims to socially implement a biobased mass production system for highly bioavailable carotenoids (Fig. 12). In 2024, we have developed genetically modified enzymes that synthesize *cis*-configured carotenoids more efficiently and established a novel cultivation condition that uses saccharification liquor as a carbon source. We are currently expanding our cultivation scale for social implementation of bio-based functional ingredients.

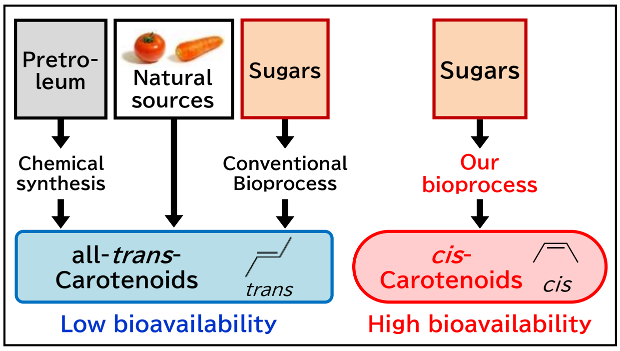

Fig. 12 Outline of our project for bio-based production of highly bioavailable carotenoids

3.5. Development of Production Technology for Bio-based Products to Accelerate the Realization of Carbon Recycling (Rose Aroma Ingredient)[*2]

Since 2022, RITE has been participating in the NEDO Demonstration Project for Industrial Substance Production Systems, titled "Demonstration of a Rose Fragrance Production System Using a Flow-Continuous Isolation Method and a Growth-Independent Bioprocess" (representative organization: Takasago International Corporation). In addition to developing industrial smart cells, RITE is advancing the development of a bioproduction system that avoids microbial fermentation inhibition caused by fragrance materials (Fig. 13). In FY2024, we increased productivity using the aforementioned production system by establishing production strains and improving production conditions, obtaining the productivity required for practical application in the laboratory. We also successfully scaled up the aroma ingredients bioproduction to a 90 L fermenter. Moving forward, we will continue to study and expand the scale-up production for practical application, aiming for the social implementation of the first domestically produced fragrance material manufactured through synthetic biology.

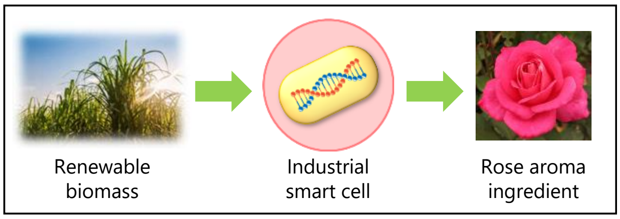

Fig. 13 Production of a rose aroma ingredient

3.6. NEDO Moonshot R&D Project: “Research and Development of Marine Degradable Multi-lock Biopolymers from Inedible Biomass”[*2]

This project focuses on research and development to introduce a “multi-lock mechanism” for plastic degradation (Fig. 14). The degradation in this mechanism specifically requires simultaneous multiple stimuli, including light, heat, oxygen, water, enzymes, microorganisms, and catalysts. As a result, the plastic would not degrade throughout typical use, ensuring its durability and toughness. However, unintentional dispersal of our target plastic in the marine environment will trigger the multi-lock mechanism, resulting in high-speed on-demand degradation.

There have been strong concerns that various plastic-based products discharge into the oceans expose adverse effects on marine organisms and its environment. Accordingly, various practical products are targeted in this project, including tires, that generate secondary fine plastic particles when used; agricultural equipment; also fishing nets and fishing gear which waste continue to harm marine life.

By FY2024, RITE developed technology that enables artificially control the timing of multi-locked plastics degradation initiation. This includes development of new technology utilizing degradative enzymes. First, electrostatically binding the thermostable plastic-degrading enzyme to a biodegradable carrier notably improved its thermostability. We added the enzyme into plastic and thermally melt the mixture resulting in a test plastic film. Using the film, we were able to confirm that rapid enzymatic degradation (degradation on demand) occurs only when exposed to seawater, both on laboratory test and marine field tests. In the future, we aim to increase degradation speed by improving the plastic-degrading enzyme functionality, reducing the carrier size, and optimizing the plastic manufacturing process.

On the other hand, we started a new international joint research project with the U.S. Department of Energy's ARPA-E to develop biomanufacturing from marine-derived inedible resources, thereby closing the plastic cycle in the marine environment.

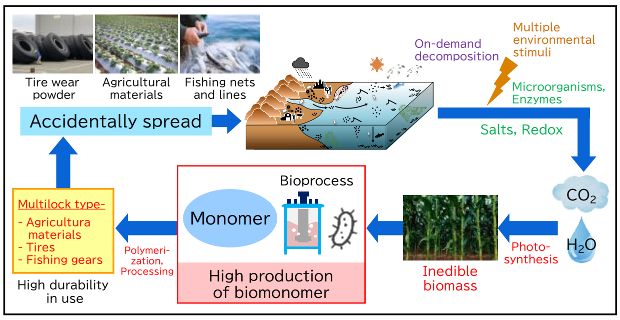

Fig. 14 Development of multi-lock biodegradable plastic and realization of resource recycling

3.7. Japan Science and Technology Agency (JST) the Program on Open Innovation Platforms for Industry-academia Co-creation (COI-NEXT): "Development of Biofuel Production Technologies"

RITE took part in the Japan Science and Technology Agency (JST)-commissioned program on open innovation platforms (COI-NEXT) themed "Carbon Cultivation Hub Challenging the Limits of Carbon Negativity." Started in 2023, we are working on developing biohydrogen production and liquid biofuel production technologies for establishing carbon-cultivation–based fuel-production technology. RITE develops biological conversion technologies for efficient fuel (hydrogen/liquid fuel) production based on various biomass feedstocks. Meanwhile, we collaborate with the participant organizations specialized in biomass cultivation technologies, thus enabling an increase in CO_2 fixation by photosynthesis (Fig. 15). Using these technologies, we target liquid-fuel production for our short- to medium-term goal. Yet since hydrogen is expected to be the ultimate clean energy and is key in realizing carbon neutrality/negativity, our medium- to long-term aim is to develop CO_2-free hydrogen production processes.

One of the key challenges for the social implementation of biomass fuel-production technology is lowering production costs. In addition, the components of biomass feedstock are diverse, and their composition considerably varies depending on the feedstock type. It is challenging to funnel this wide range of demands into a uniform technology. To solve these issues, this project will promote technology development in different fields, including various thermochemical and biological conversion technologies in an integrated manner to enable the construction and expansion of a flexible biomass-based fuel supply system tailored to each regional and feedstock needs.

Based on RITE success in developing a biohydrogen production process with high production rate, we are currently developing producer strain with improved hydrogen yield based on biomass-derived sugars. In order to construct a genetically engineered microorganism with a novel hydrogen production pathway, we examine two different hydrogen-producing enzyme recombinants, each with its reaction mechanisms and hydrogen productivity.

In liquid fuel, previously RITE has also established a bioprocess that efficiently converts C6 and C5 sugars mixture derived from non-edible biomass to ethanol. We applied the RITE bioprocess in this project and demonstrated ethanol production from various non-edible biomass-based sugar, with comparable high titer and yield to reagent sugar mixture-based production. Using this technology, we aim to develop an alcohol to jet (ATJ) process to produce a sustainable aviation fuel using various biomass feedstocks, such as energy crops, rice with high CO_2 fixation capability, and microalgae with high sugar content.

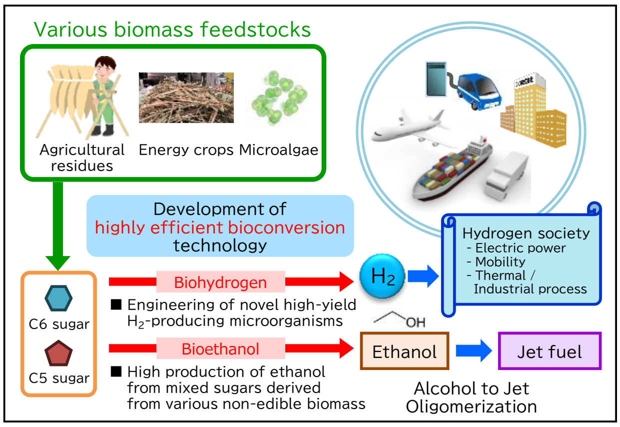

Fig. 15 Development of biohydrogen/bioethanol production technologies

4. Future Industrialization of Our Technologies

4.1. Green Chemicals Co., Ltd. (GCC)

(Head Office・Laboratory: in Kyoto headquarters, RITE; Shizuoka Laboratory: in Shizuoka plant, Sumitomo Bakelite Co., Ltd.) (Here's a link for GCC website)

In February 2010, RITE established the "Green Phenol and High-Performance Phenolic Resin Production Technology Research Association" (GP Association) with Sumitomo Bakelite Co., Ltd. to develop fundamental technologies related to phenol production and phenolic resin production through the application of bioprocesses that use cellulosic raw materials (non-food biomass).

The GP Association was reorganized in May 2014 as "Green Phenol Development Co., Ltd." (GPD), which became the first example of demutualization of a technology research association.

Green Phenol Development Corporation's trade name was changed to Green Chemicals Co., Ltd. (GCC) in April 2018, in recognition of the fact that GPD technology is able to develop valuable compounds alongside phenol bioproduction.

Leveraging the mass production technology and know-how cultivated for green phenol manufacturing, GCC has established mass production technologies for green chemicals such as aromatic compounds, which were previously considered difficult to produce in large quantities. We have pioneered mass production technologies for high-value-added 4-hydroxybenzoic acid (4-HBA), protocatechuic acid, and shikimic acid (Fig. 16). Furthermore, regarding the secondary use of genetically modified organisms, etc., for the industrial application of their production strains, we have obtained confirmation from the Minister of Economy, Trade and Industry (Ministerial Confirmation) for all of these substances and are promoting the commercialization and business development of these green compounds.

We are currently receiving numerous inquiries from companies both domestically and internationally, and commercialization negotiations are underway. To meet various needs, we will further accelerate our efforts toward the practical application of bio-manufacturing, including further reducing production costs and improving product quality.

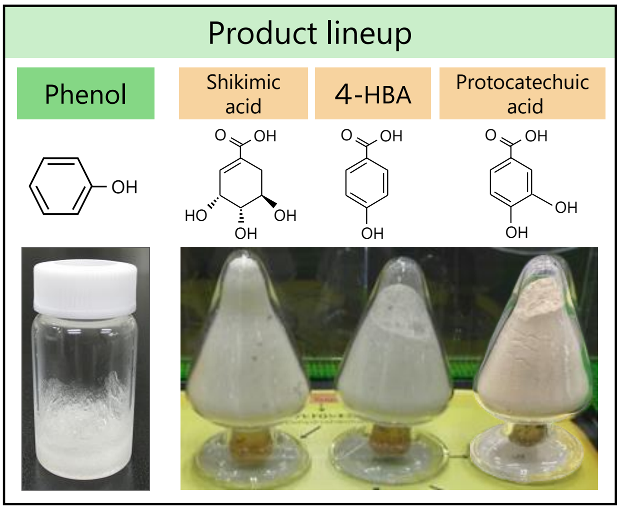

Fig. 16 Major product lineup of Green Chemicals Co., Ltd.

4.2. Green Earth Institute Co., Ltd.

(Head office: 6F Q Plaza Shinjuku 3-chome, 3-5-6 Shinjuku, Shinjuku-ku, Tokyo, Laboratory: 2-5-9 Kazusa-kamatari, Kisarazu-shi, Chiba)

(Click here for the Green Earth Institute Inc. website)

In September 2011, RITE established the Green Earth Institute Inc. to commercialize "RITE Bioprocess"[*1]. Due to successful business results, the company was listed on the Tokyo Stock Exchange (Mothers) in December 2021. By the following April, it moved to the Tokyo Growth Market due to market reorganization.

In February 2025, the company announced that it would establish a joint venture for the production and sale of "Bioethanol" and other products from "Wood Biomass".

Currently, the company is promoting research and development with domestic and overseas partner companies, including "Biofoundry Base" (based on the government's "Biostrategy 2020), NEDO’s "Green Innovation Fund Project," and NEDO's "Bio-manufacturing Revolution Promotion Project."

4.3. Joint Research with Companies

In addition to Harima Chemicals, Inc. and Takasago International Corporation, which are part of the NEDO Bio-manufacturing Demonstration Project, RITE is conducting collaborative research in response to requests from many other companies. Besides the main compound products introduced in this overview (Section 2.4), bio-manufacturing is possible for numerous other substances, and RITE is developing collaborative research tailored to the needs of each individual companies. The requests vary, ranging from the desire to quickly convert fossil resource-derived products to bio-based production, to the goal of transitioning main products and key raw materials from fossil resources to bio-based sources over the mid- to long term. Leveraging its advanced expertise and extensive experience, RITE offers bio-manufacturing solutions that are closely tailored to the specific needs of each company.

5. Closing remarks

RITE will continue to advance bio-manufacturing technologies, including smart cell creation technology, by leveraging the national projects introduced in Chapter 3. Technological innovations in the "Bio × Digital" field are progressing rapidly, with smart cell development expected to make significant strides in the future. However, the creation of industrial smart cells, which require advanced bio-manufacturing technologies, is becoming increasingly difficult for individual companies to undertake on their own due to factors such as technical complexity, cutting-edge research facilities, cost performance, and maintaining competitiveness. Additionally, process development requires a certain level of production as well as a specialized platform, which demands capital investment and securing specialists experienced with bioprocesses. In the near future, the promotion of the smart cell industry by bio-platformers is expected to lead to the bio-manufacturing establishment in the energy and chemical industries (Fig. 17).

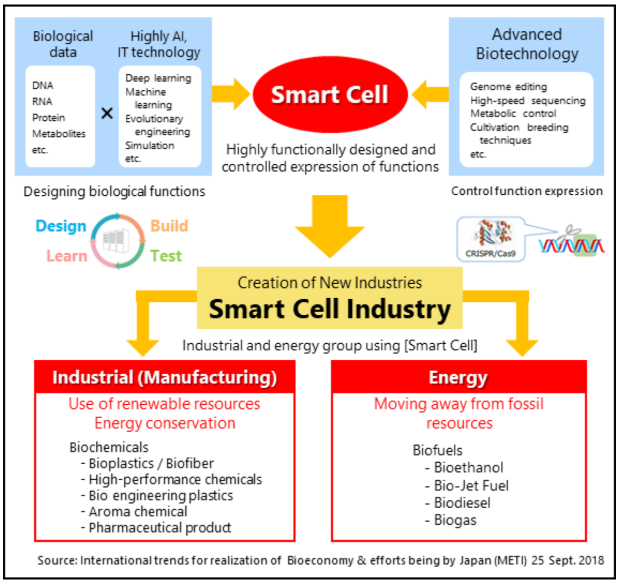

Fig. 17 Fusion of industrial / energy fields impacted by new bio and digital technologies

RITE will continue to develop the RITE Bio-platform, which provides optimal bio-manufacturing technology development services for each product, based on "RITE Bioprocess" and "Smart Cell Creation Technology." We encourage you to actively utilize these services. Since Japan's "2050 Carbon Neutral" declaration in October 2020, inquiries and requests from companies have surged, and the number of collaborative research projects with companies has increased.

We are also recruiting personnel to develop bio-manufacturing technologies together. We are looking for individuals who are interested in designing and developing bioprocesses using microorganisms and enzymes along those who are eager to create new products and processes using the latest biotechnology and digital technologies.

Compounds that were previously difficult to produce with microorganisms may now achieve high production with RITE's latest technologies. If you have compounds you would like to make with bioconversion, or if you are attracted to RITE's bio-manufacturing, please contact us. We look forward to collaborating with you to drive innovation and sustainability in the bio-manufacturing industry.

*1 "RITE Bioprocess" is a registered trademark of RITE.

*2 This article is based on results obtained from a project commissioned or subsidized by the New Energy and Industrial Technology Development Organization (NEDO).