NEDO

focus NEDO

2024
No.92

Reporting on Today and Tomorrow's Energy, Environmental and Industrial Technologies

Special Report

Biomanufacturing Bases

Hubs That Ease the Transition to Commercialization

New Energy and Industrial Technology Development Organization

NEDO Hosts Booth at ENEX2024, Showcases Achievements in Development of Energy Conservation Technologies; Grants Energy Conservation Technology Development Award

ENEX2024, an energy innovation trade fair showcasing the latest products, technologies, and services related to decarbonization and energy conservation, took place at Tokyo Big Sight for three days between January 31 and February 2, 2024. NEDO's team performed demonstrations in the booth, which displayed graphics and prototypes of the latest research and development and international demonstration projects focusing on 27 themes in the field of energy conservation.

Seminars were held by the project participants, and NEDO publicized achievements in its research and development projects, attracting the attention of attendees. Some project participants found companies and other organizations that they could work with on their developments or consult with to introduce their technologies, increasing anticipation for accelerated real-world social implementation.

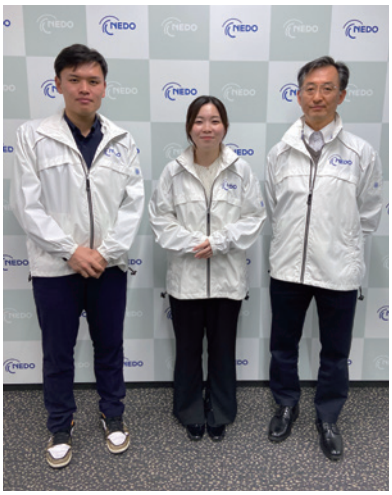
On February 1, NEDO granted the NEDO Energy Conservation Technology Development Award on 18 themes to 29 project participants who had achieved outstanding results in the Strategic Innovation Program for Energy Conservation Technologies and the Program to Develop and Promote the Commercialization of Energy Conservation Technologies to Realize a Decarbonized Society.

The NEDO Chairman's Award was won by the research group comprising Takasago Chemical Corporation, Mitsubishi Tanabe Pharma Corporation, and Konica Minolta Chemical Co., Ltd., which developed iFactory® for pharmaceutical production. The idea behind iFactory® is to reduce waste and CO_2 emissions and achieve energy conservation with enhanced production efficiency for pharmaceuticals. Saito Takao from Takasago Chemical Corporation stated: "More than 140 people were involved in research and development to achieve this result. By focusing on the continued promotion and development of iFactory®, we will work toward a 'great reset' from batch production to continuous production through the advancement of the system and engineer training."

The newly established Small- and Medium-Sized Business or Startup Award was won by Mabuchi Engineering Co., Ltd. for their development of a stand-alone ORC* power generation system. This waste heat system provides both top-of-the-line power output and has achieved Japan's highest level of energy conservation. Ono Toshimitsu from Mabuchi Engineering said of the recognition: "As a startup, receiving this award is a great honor. As we focus on research and development to effectively utilize waste heat in rural areas, this is a great encouragement to everyone on the development team."

* ORC: Organic Rankine cycle
The process of generating electricity by using a low-boiling-point fluid instead of water as a working fluid in the steam cycle.

NEDO's booth



ENEX2024 staff from NEDO's Energy Conservation Technology Department
KASHU Daisuke (left), HIROTA Yuna (middle), and YAMADA Junji (right)

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Winners of the NEDO Chairman's Award

From left: Representative of Konica Minolta Chemical Co., Ltd., representative of Takasago Chemical Corporation, SAITO Tamotsu, Chairman of NEDO, representative of Takasago Chemical Corporation, and representative of Mitsubishi Tanabe Pharma Corporation

Scan here to view the NEDO News Release on their achievements (Only available in Japanese)
https://www.nedo.go.jp/news/press/AA5_101710.html

Winner of the Small- and Medium-Sized Business or Startup Award

From left: HAYASHI Shigekazu, Executive Director of NEDO and a representative of Mabuchi Engineering Co., Ltd.

Scan here to view the NEDO News Release on their achievements (Only available in Japanese)
https://www.nedo.go.jp/news/press/AA5_101610.html

Scan here to view the NEDO News Release on the NEDO Energy Conservation Technology Development Award (Only available in Japanese)
https://www.nedo.go.jp/news/press/AA5_101722.html

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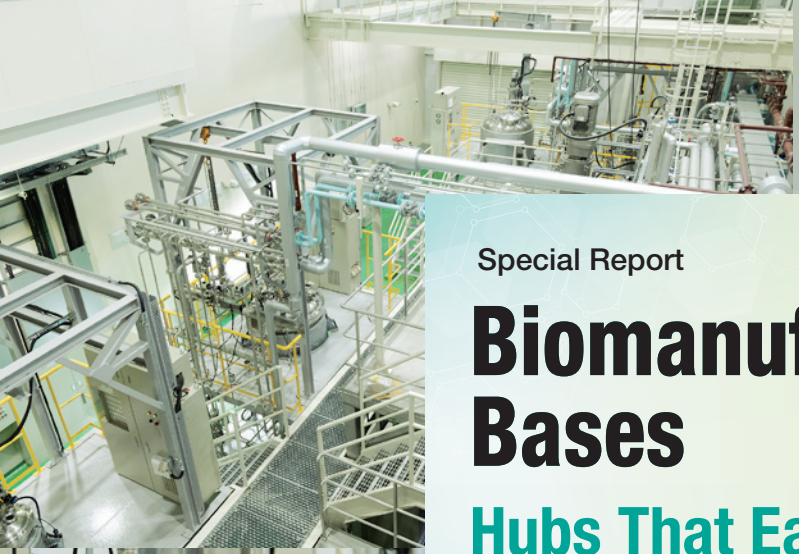
A WORD FROM THE EDITOR

No. 92

Craftsmanship has been long fostered by breweries and manufacturers of fermented foods. But how should we take this craftsmanship into the future? There is an urgent need for advancements in biomanufacturing to address social challenges such as climate change and food and resource depletion, as well as to achieve economic growth. Today, there is fierce global competition in this area, with the hope that biofoundries will be venues for businesses to develop technologies that transcend even the old artisans.



Special Report

Biomanufacturing Bases

Hubs That Ease the Transition to Commercialization

Development of
Bio-Based Production Technology
to Accelerate Carbon Recycling

"Our goal is sustainable, circular manufacturing that isn't dependent on fossil fuels."

"I think more and more companies are looking to transition to biomanufacturing."

HAYASHI Chikako

Project Manager
HAYASHI Chikako
Director, NEDO
Materials Technology and Nanotechnology Department
Bioeconomy Promotion Division
Ph.D. (Doctor of Science)

MINEGISHI Fuko

Sub-Project Manager
MINEGISHI Fuko
Chief Officer, NEDO
Materials Technology and Nanotechnology Department
Bioeconomy Promotion Division

What is biomanufacturing?

Biomanufacturing is a method of producing materials by harnessing the power of living organisms. Traditional examples include fermented foods such as soy sauce and miso. By combining conventional methods and cutting-edge technologies, modern biomanufacturing employs techniques such as genetic engineering and genome editing to design microorganisms that can produce materials useful to humans.

Biomanufacturing will enable a transition from petroleum-based raw materials to bio-based raw materials. It also allows a switch from high-temperature, high-pressure chemical synthesis processes to ordinary temperatures and pressures. These benefits can help to ease the adoption of society-wide carbon recycling.

Director and Project Manager Hayashi Chikako says, “Manufacturers are working to achieve carbon neutrality by 2050, and the need for manufacturing that leads to reduced environmental impact is increasing. Meeting this need and creating a bioeconomic society is a major goal of this project.”

Development of biofoundries is well underway

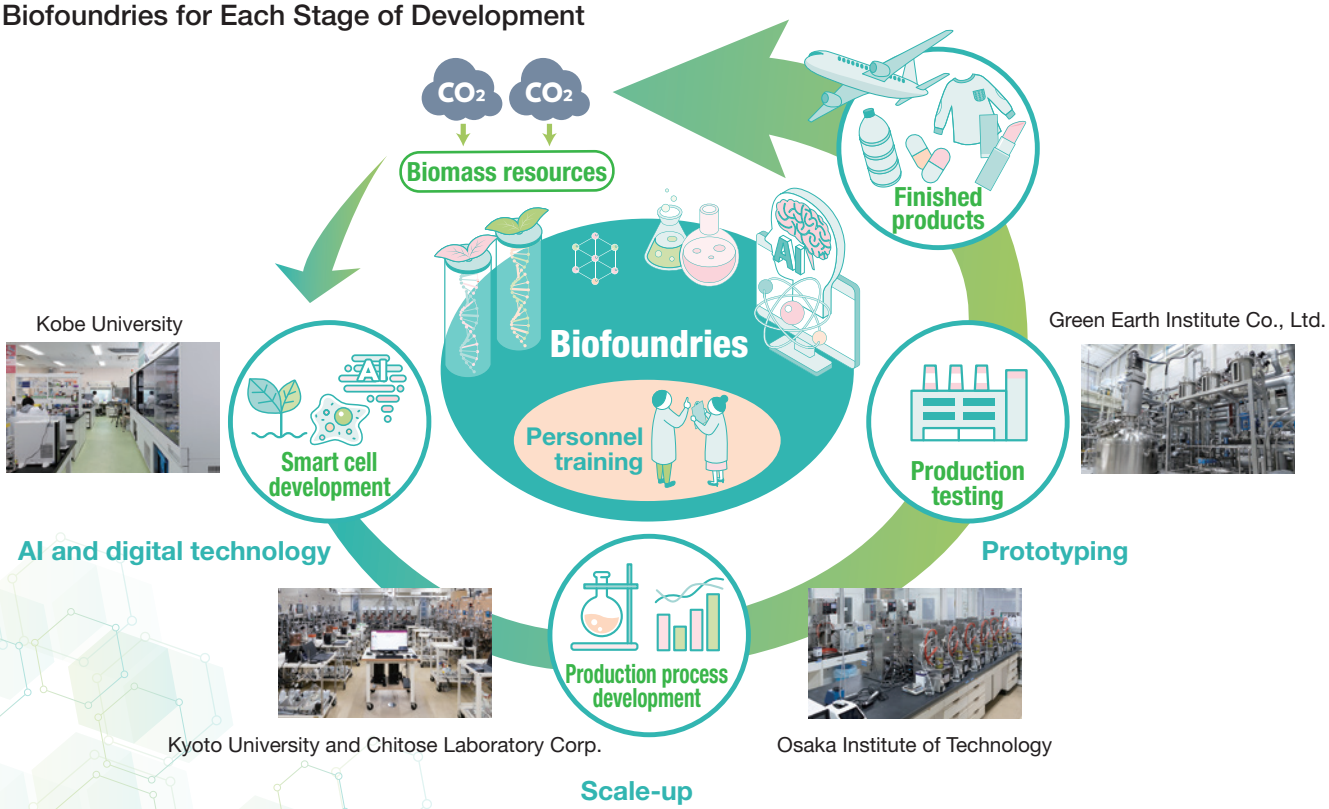
NEDO’s project for the Development of Production Techniques for Highly Functional Biomaterials Using Smart Cells of Plants and Other Organisms, carried out over five periods from FY2016 to FY2020, aimed to develop technology to create smart cells with enhanced capability to efficiently produce a desired material. For example, a smart cell was developed that increased the production and secretion of cholesterol esterase by over 30 times compared to natural strains, and this was successfully commercialized as a raw material for *in-vitro* diagnostics.

However, further expansion of manufacturing with smart cells requires scaling up results from experimental to industrial levels, and many hurdles must still be overcome. It is essential to offer training at the same time as establishing next-generation production processes, carrying on a tradition of manufacturing craftsmanship using digital technology. NEDO is also working to overcome these challenges to accelerate progress in biomanufacturing.

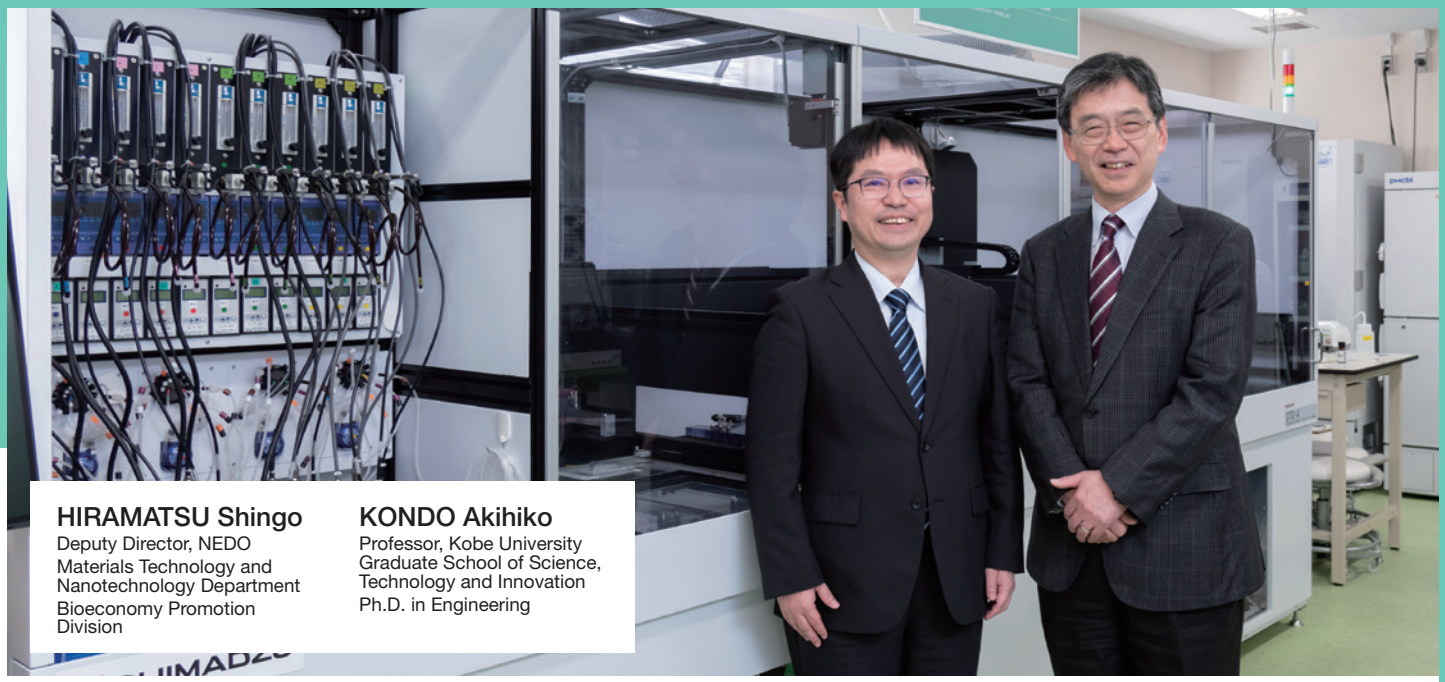
Biofoundries are an essential part of this process. They allow for prototyping and scale-up to ease the transition to commercialization. Biofoundries are also expected to become training centers that foster the skills needed for biomanufacturing. “Manufacturing companies encounter challenges when shifting from fossil fuel-based manufacturing to bioprocesses. However, the establishment of biofoundries with equipment necessary to solve these challenges is well underway, so we encourage many companies to take advantage of these biofoundries,” Chief Officer and Sub-Project Manager Minegishi Fuko expresses hopefully.

The following pages explore the activities and roles of the biofoundries established at different locations in this project.

Biofoundries for Each Stage of Development



The development of smart cells, production processes, and testing happen simultaneously, while personnel training speeds up commercialization.



HIRAMATSU Shingo
Deputy Director, NEDO
Materials Technology and Nanotechnology Department
Bioeconomy Promotion Division

KONDO Akihiko
Professor, Kobe University
Graduate School of Science, Technology and Innovation
Ph.D. in Engineering

Bio + Digital Makes for Rapid Advancement in Smart Cells

Biofoundry

Kobe University

Development at 10 times the speed with "Design, Build, Test, and Learn"

NEDO has teamed up with Prof. Kondo Akihiko of Kobe University to work on accelerating production of useful materials such as pharmaceuticals and biofuels. By combining biotechnology and computer science to the Design, Build, Test, and Learn Cycle (DBTL), the hope is to make progress rapidly.

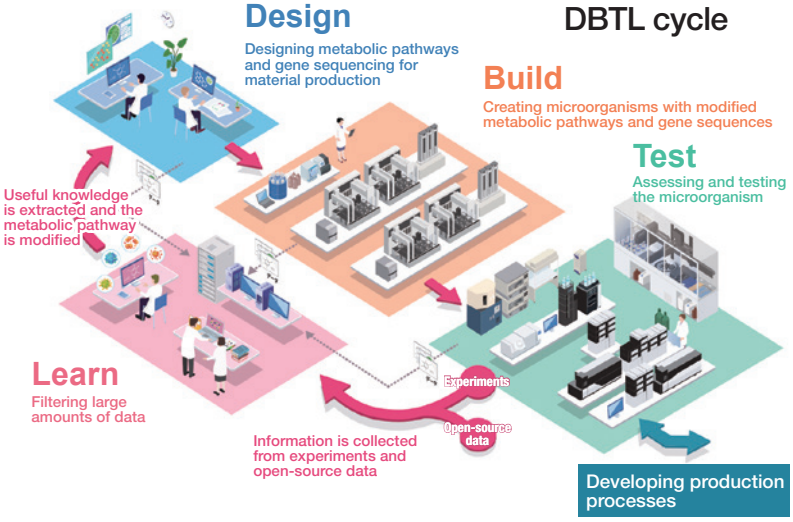
Prof. Kondo explains, "In order to create a smart cell that produces a useful material, we need tens of thousands of hypotheses, and they must be tested one by one. We can speed up development by leaving these tasks to artificial intelligence and robots instead of humans."

The Kobe DBTL Biofoundry, a center for biomanufacturing, develops smart cells that can produce high-yield, high-concentration materials 10 times faster than previously using combinations of its own developed technologies. The aim is to support companies that want to manufacture raw materials for chemicals and pharmaceuticals through extensive use of this biofoundry as a venue for smart cell development. Prof. Kondo considers real-world social implementation of biomanufacturing important not only for human health but also for the health of planet Earth.

Application: Organizations that want to develop productive smart cells rapidly

Frequent testing is possible thanks to AI and robotic technology, and testing accuracy increases with increased AI training data, leading to reduced testing costs. "One feature of this biofoundry is that researchers specializing in biotech and information technology work together across their specialties," says Hiramatsu Shingo, Deputy Director of NEDO's Materials Technology and Nanotechnology Department.

As the production of functional raw materials for chemicals and pharmaceuticals with biotechnology becomes mainstream worldwide, Kobe University's biofoundry is leading biomanufacturing in Japan as a front-runner in this field.



AI Inherits and Surpasses Human Craftsmanship in the Field of Microbial Cultivation

Biofoundry

Kyoto University and Chitose Laboratory Corporation

Bioproduction Management Using Convolutional Data*

Bioproduction has long relied heavily on the expertise and physical abilities of skilled engineers; in other words, craftsmanship. This means it has been difficult to streamline the process and produce consistent results. Kawai Tetsushi, from Chitose Laboratory Corporation (CHITOSE), explains, "The fundamentals of microbial cultivation technology were formed in the 1940s, but since then, there has been little innovation, and further improvements in productivity were limited. As passing on the craftsmanship of skilled engineers is difficult, we consider it essential to develop technology that enables anyone to carry out stable cultivations."

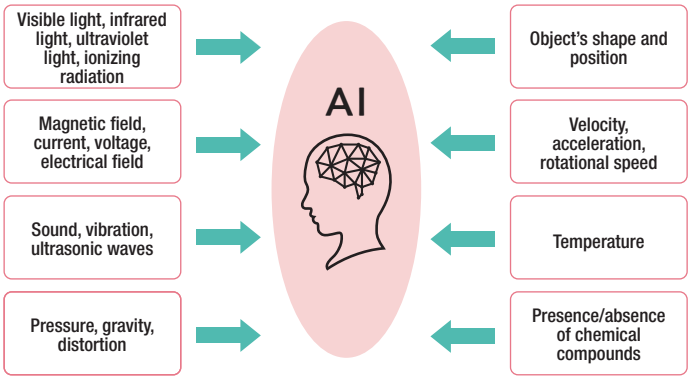
NEDO and CHITOSE have collaborated on developing a variety of sensing devices, some of which are proprietary, to measure data such as temperature, pH, optical systems, and potential change. By aggregating Convolutional Data to train AI, they developed a system that can autonomously optimize culture conditions and assess the dynamics of microorganisms. Kawai explained the significance of working under the support of a NEDO project, saying, "There was a risk that we would not obtain useful data. However, because we were allowed to innovate freely under the NEDO project model, we were able to take on the challenge of sensor development." Remarkably, real-time control of culture conditions lead to approximately 10% higher productivity when compared to skilled engineers during testing conducted by CHITOSE and Kyowa Hakko Bio Co., Ltd.

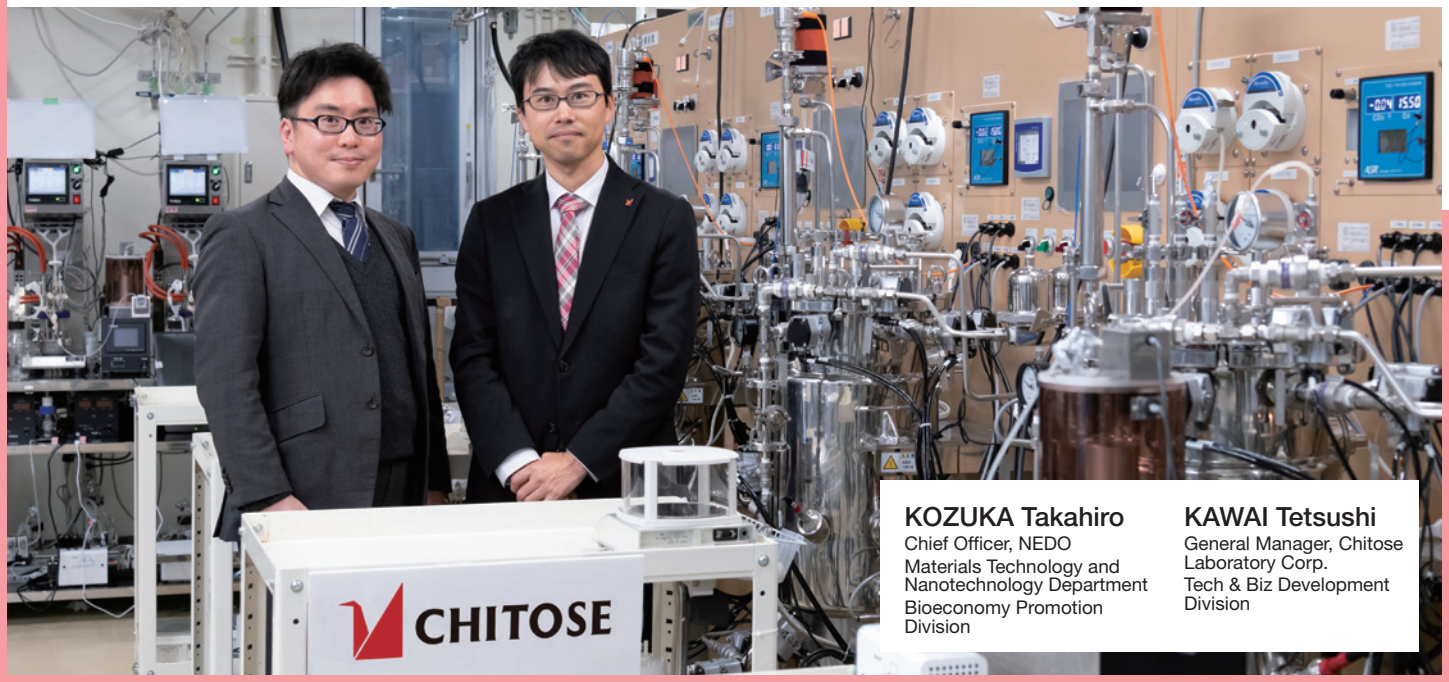
Application Organizations that strive for efficient, consistent bioproduction through optimized culture conditions

The optimizations employed by AI often go against conventional wisdom on the production site. A key feature is its ability to have control that humans cannot achieve. "It's big news for this industry that AI has surpassed humans in terms of productivity," Kozuka Takahiro, Chief Officer of NEDO's Materials Technology and Nanotechnology Department, said of the achievement. CHITOSE's biofoundry will enhance AI's performance in terms of data quality and quantity, and this, combined with the expertise of production staff of fermentation and cultivation, will lead to the establishment of productive, stable cultivation processes, all with the goal of promoting the adoption of biotechnology in industry and realizing a bioeconomic society.

* "Convolutional Data" is a registered trademark of Chitose Laboratory Corporation and is a data set exclusively designed for AI training instead of interpretation or judgment by humans.

Convolutional Data Concept Diagram





KOZUKA Takahiro
Chief Officer, NEDO
Materials Technology and Nanotechnology Department
Bioeconomy Promotion Division

KAWAI Tetsushi
General Manager, Chitose Laboratory Corp.
Tech & Biz Development Division

From Experiment to Implementation at the Biomanufacturing Lab

Biomanufacturing hub nourishes prototyping and personnel training

Bio-based products are attracting attention as the world moves towards carbon neutrality. However, new companies entering the market face numerous hurdles, including high costs, lack of versatility in production, and the availability of facilities for prototyping. NEDO enlisted the help of Professor Nagamori Eiji at Osaka Institute of Technology to establish the Biomanufacturing Lab in 2021, with the aim of solving these problems and supporting the development of production processes. The Biomanufacturing Lab has 32 0.25-liter fermenters, 12 one-liter fermenters, and four five-liter fermenters, and is the only educational facility in Japan that has a 30-liter fermenter. “Using multiple fermenters enables us to verify different sets of conditions simultaneously, reducing the time required for prototyping and evaluation by several years,” Prof. Nagamori says.

Brewing and fermenting rely greatly on the experience and capabilities of skilled workers, and developing the next generation of personnel is crucial. Akiba Yukinori, Technical Researcher in NEDO's Materials Technology and Nanotechnology Department, states, “We are also working on the automation of production processes by developing applications and installing analyzers for self-diagnosis, in order to reduce the workload on engineers and make the industry more competitive.”

Application Businesses that need prototyping and personnel training to enter the biomanufacturing industry

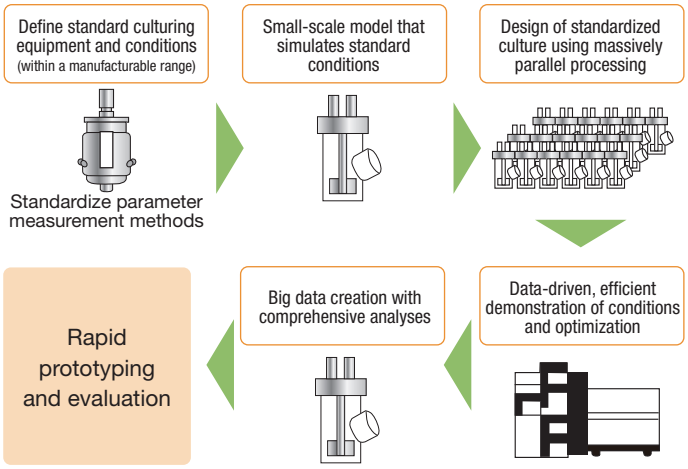
Biofoundry

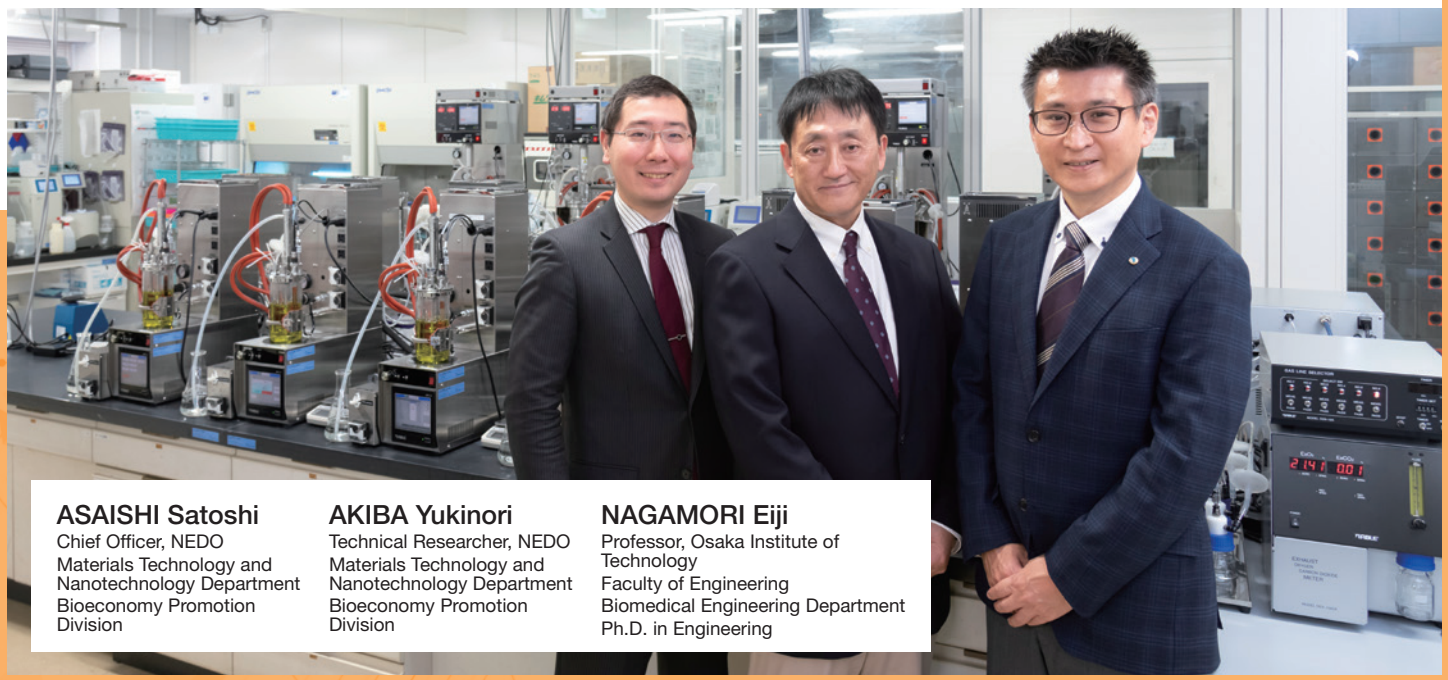
Osaka Institute of Technology

Since engineers need to be able to handle culturing equipment correctly, Osaka Institute of Technology is offering special courses promoted by NEDO that consist of lectures and hands-on practice. Asaishi Satoshi, Chief Officer of NEDO’s Materials Technology and Nanotechnology Department, has been satisfied with the achievements. “The prototyping support and the seminars have been well-received, and offer opportunities for exchange among young engineers,” he says.

As for the next step, Prof. Nagamori explains: “We plan to develop facilities to separate and refine products,” which is expected to speed up advancements in bio-based manufacturing and push society further down the road towards sustainability.

Core mission: data-driven optimization and smooth prototyping through the development of standardized culturing equipment





ASAISHI Satoshi
Chief Officer, NEDO
Materials Technology and Nanotechnology Department
Bioeconomy Promotion Division

AKIBA Yukinori
Technical Researcher, NEDO
Materials Technology and Nanotechnology Department
Bioeconomy Promotion Division

NAGAMORI Eiji
Professor, Osaka Institute of Technology
Faculty of Engineering
Biomedical Engineering Department
Ph.D. in Engineering

OGASAWARA Masato
Technical Researcher, NEDO
Materials Technology and Nanotechnology Department
Bioeconomy Promotion Division

FURUJO Atsushi
Chief Technology Officer and Director, Biofoundry Center at Green Earth Institute Co., Ltd.

Demonstration of Scaling Up With a 3,000-Liter Capacity Fermenter

Biofoundry

Green Earth Institute Co., Ltd.

Developing a production system with a scaled-down model

"The challenges facing the commercialization of biomanufacturing," says Furujo Atsushi, Chief Technology Officer and Director of the Biofoundry Center at the Green Earth Institute, "are achieving scale-up and securing human resources. These are both time-consuming and expensive."

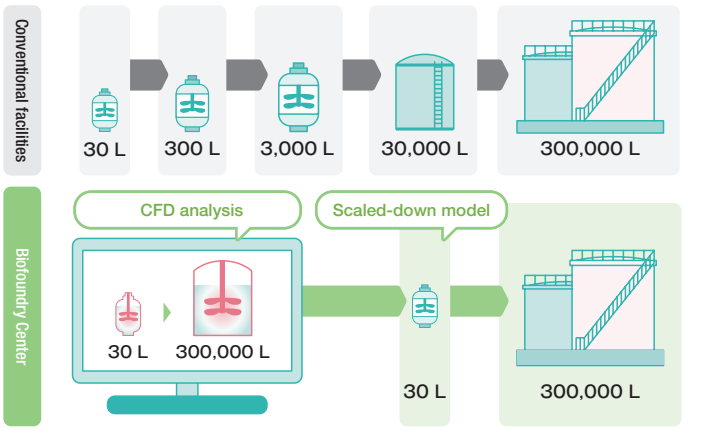
The center began full-scale operation in June 2023 as a base to promote bioproduction. This is the only facility in Japan capable of scale-up testing with 3,000-liter capacity fermenters, where production processes can be optimized to culture useful smart cells developed by companies, universities, and public research institutes who then turn them into market-worthy products. The center plans to install purification equipment in 2024 and will be able to offer a vast array of processing options from biomass pretreatment to purification to sample preparation.

Additionally, they are working on technology to realize a production system with a scaled-down model using computational fluid dynamics (CFD) analysis to simulate the inside of a fermenter, with the goal of significantly reducing the time and cost required for step-by-step scale-up.

According to Furujo, "Developing human resources is a part of bringing these technologies to the real world. Our other mission as an R&D company is to expand the number of companies engaged in biorefinery." Ogasawara Masato, Technical Researcher with NEDO's Materials Technology and Nanotechnology Department, emphasizes that "in biomanufacturing, passing down techniques is important. We hope that people get to experience our technologies first-hand as they are about to be put into practical use."

"Working on new biomanufacturing is rewarding," says Furujo enthusiastically. "Even after the NEDO project ends, we will continue to promote digital transformation and automation to operate as a private business. I hope biomanufacturing flourishes with enterprises from all over Japan."

Scaled-Down Model and CFD Analysis Production System Concept



Application Businesses that aim to implement pilot testing and sample preparation and develop human resources

MESSAGE

Accelerating Development Brings Hope for Real-World Social Implementation

On the need to expand the scope of biomanufacturing by promoting personnel development and exchange

I believe that biomanufacturing holds the potential not only to help us attain a sustainable, recycling-oriented society but also to clarify the underlying foundations of biochemistry. However, there are many challenges to overcome, including securing raw biomass materials, advancing smart cell development, optimizing culturing processes, and developing methods for scaling up. To solve these commercialization challenges, it is important to incorporate information technology, robotics, and other technologies. In addition, to realize a bioeconomic society, expanding the scope of biomanufacturing and including more participants in it is crucial. NEDO projects are intended to set a course toward real-world social implementation by demonstrating success stories, and at the same time develop human talent and establish a common infrastructure for expansion.

When I was involved in national projects as a corporate researcher in my early days, I interacted with many other researchers and obtained a wide range of knowledge and perspectives from them, which was of great use in my studies at university. I look forward to this project promoting exchange among researchers from industry and academia. This way we can develop approaches to real-world social implementation and explore different perspectives on the challenges and future of biomanufacturing in a comprehensive way.

SEKI Minoru
Project Leader
Professor Emeritus, Chiba University
Ph.D. in Engineering

MATSUMURA Takeshi
Sub-Project Leader

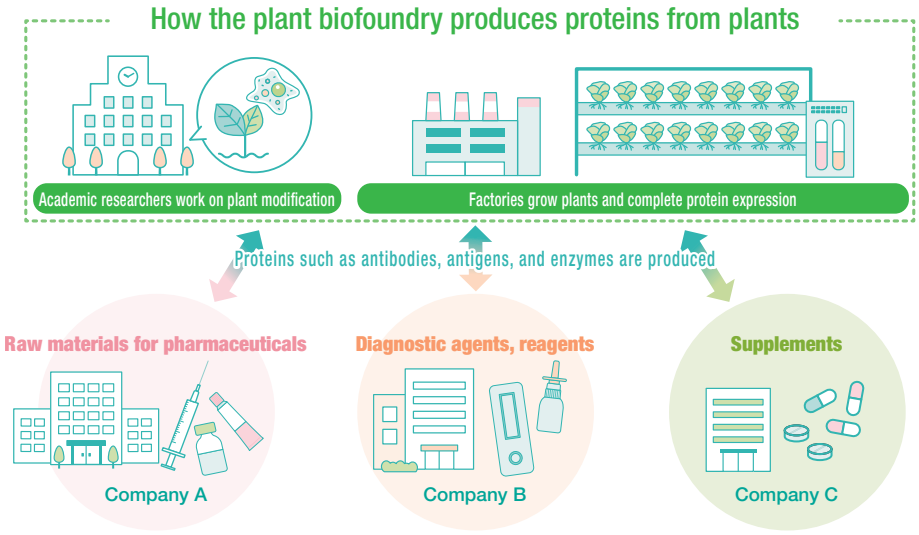
My dream: Japan builds a foundation for plant-based manufacturing and becomes a world leader in the field

Biomanufacturing with plants is an efficient, energy-saving method that produces materials using water, carbon dioxide, and light. However, unlike biomanufacturing with microorganisms, plants have not been used in this way for very long, and we have yet to see practical use, even though research is underway in Japan and internationally. Japan is a world leader in terms of the foundational technology, and it is important to establish Japan as a base, creating an environment where companies can utilize technologies that enable energy-saving and efficient production to take advantage of the beneficial features of plants.

Biomanufacturing with plants requires many kinds of expertise, such as gene manipulation, cultivation, and extraction and purification technology. An advantage of NEDO projects is that companies and academic institutions can integrate people from different fields to work together on everything from the fundamental technology to proof of concept. Thanks to the groundbreaking work from the plant biofoundry introduced on the next page, there has been an increase in the successful commercialization of plant manufacturing. As the technology matures, the needs and challenges will become clearer, leading to even more advances. I hope that, based on the achievements of this project, Japan will become a world leader in the field of biomanufacturing with plants.

Introducing One More Biofoundry

Mass-Production of Valuable Proteins at a Plant Biofoundry



Developing a plant biofoundry for energy-efficient production of valuable proteins

While the development of biomanufacturing using microorganisms is ongoing, biofoundries that can exploit the potentials of plants may become the next big thing. However, there are challenges to overcome in order to produce the proteins that industries value from plants. A lack of standardized cultivation methods, low protein production yield, and lengthy development periods are some of the hurdles holding plant biofoundries back.

NEDO is working to develop plants and growing methods that enable efficient production of valuable proteins by modifying plants' functions. These proteins can be used as raw materials for pharmaceuticals that require advanced post-translational modifications or for diagnostic agents, reagents, or supplements.

Work is also underway to develop technology to extract and purify proteins from large amounts of plant material. Since plants grow with water, carbon dioxide, sunlight, and minimal nutrients, they have the potential to synthesize proteins without using large amounts of energy.

Valuable proteins can be produced only in limited quantities from plants at present. However, if proteins could be produced efficiently and in large volumes, fossil fuel consumption could be reduced, thus achieving environmentally-friendly biomanufacturing. As with microorganism biomanufacturing, NEDO is supporting the development of plant biofoundries as places for research and prototyping to allow logical manipulation of plant genes and cultivation methods that facilitate the synthesis of desired proteins. NEDO hopes that many companies will take advantage of these facilities in the future.

KINOSHITA Riko
Chief Officer, NEDO
Materials Technology and Nanotechnology Department
Bioeconomy Promotion Division

TAKEI Tetsuya
Special Researcher, NEDO
Materials Technology and Nanotechnology Department

Opening the Door to the Future

Demonstration Facility

Recycling plastic waste into raw chemicals

Advancements in Chemical Recycling

MISSION

To save energy and reduce CO_2 emissions through microwave-based chemical

Technology for Plastics

recycling

Oil is decomposed from waste polystyrene using microwave technology (left). Styrene monomer is recovered from the decomposed oil (center). The styrene monomer is then re-polymerized and used to produce recycled polystyrene (right).

It is estimated that Japan generates more than eight million tons of plastic waste each year. Chemical recycling, which decomposes plastic waste into chemical raw materials (monomers) that can be turned into new products, is attracting attention as a way to deal with this problem. However, current chemical recycling technology consumes a significant amount of fossil fuels, as plastics need to be thermally decomposed at high temperatures. Reducing energy consumption, CO_2 emissions, and costs remain significant challenges. Additionally, existing decomposition technology is limited in the types of plastics that can be processed.

In response to these challenges, NEDO and Microwave Chemical Co., Ltd. began developing a new chemical recycling method for plastics using microwave technology, which boasts high energy efficiency. Just like in the microwave in your kitchen, electromagnetic radiation transmits energy directly to the substance being heated. Energy consumption in the thermal decomposition process for plastics is reduced by approximately 50%, and by using microwaves generated with renewable energy sources, plastic waste can be recycled almost entirely without CO_2 emissions.

The Strategic Innovation Program for Energy Conservation Technologies/Commercialization and Development Phase of the joint project began in FY2020. As part of this project, a system was developed to accurately measure the complex dielectric constant[*1] of the microwaves, increasing the types of plastics that can be recycled and enhancing versatility.

Japan's first large, general-purpose demonstration site for chemical recycling technologies using microwaves was completed in 2022. The facility, with a processing capacity of one ton per day, has started tests to monomerize different types of plastic waste in large quantities. Moving forward, there are plans to scale up the processing capacity to 10,000 tons per year and achieve real-world social implementation by 2025. By continuing to refine PlaWave[*2], the plastic decomposition technology developed in this project, NEDO and Microwave Chemical hope to accelerate efforts towards the adoption of this recycling method with the aim of achieving carbon neutrality and a circular economy.

*1 A numeric value indicating a material's ability to absorb microwaves.
*2 Unique plastic decomposition technology platform using microwaves.

Promising NEDO Startups

Taking the Next Step

Innovator File.30

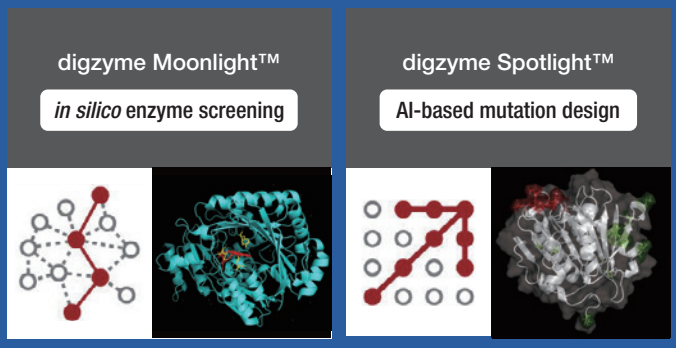
Bioproduction Evolves With AI Enzyme Search and Modification

Enzyme bioinformatics company digzyme Inc. is the pioneer behind digzyme Spotlight, an enzyme function modification platform developed with the support of NEDO. Its mission is to predict the function of enzymes for fast development that meets market demand.

digzyme Inc.

WATARAI Naoki

CEO, digzyme Inc.



Bioinformatics enzyme design platform

Japanese website
https://www.digzyme.com/
English website
https://www.digzyme.com/en/

Q Why did digzyme apply for NEDO's support program?

Innovation in the development of enzymes is essential for many industries, but historically it has relied heavily on trial and error and chance discoveries, making it time-consuming and costly. With the support of NEDO, we hope to develop solutions to overcome these challenges and accelerate the development of enzyme production.

Q How did NEDO's support help you?

In addition to financial support, we gained recognition and credit after we were adopted as a NEDO project. Thanks to NEDO's support, we were able to participate in BioJapan, the Innovation Leaders Summit, and other events, where we could engage in business matchmaking and consultation opportunities, which was a great benefit for us.

Q What is digzyme working on now?

In recent years, industrial enzyme end users have increased the diversity of their needs. Therefore, using our core technology, a bioinformatic enzyme development platform, we hope to rapidly develop and offer an unconventional and unique enzyme library that combines various analyses.

Q What is the future of digzyme?

Our goal is to become a game changer in the enzyme industry. To get there, we will use AI to provide purpose-built, highly functional enzymes rapidly, by searching for them from a wide range of options using open data.

To revitalize the economy, it is important to foster entrepreneurs who have competitive new technologies. NEDO provides startup support from a variety of perspectives. Here, we introduce promising startups that are on a path to keep growing in the future.

digzyme's Projects Adopted by NEDO

February 2022

Technology-Based Startup Support Program, Support for Commercialization of Seed-Stage Technology-Based Startups
- *In silico* bioprocess technology platform development and design

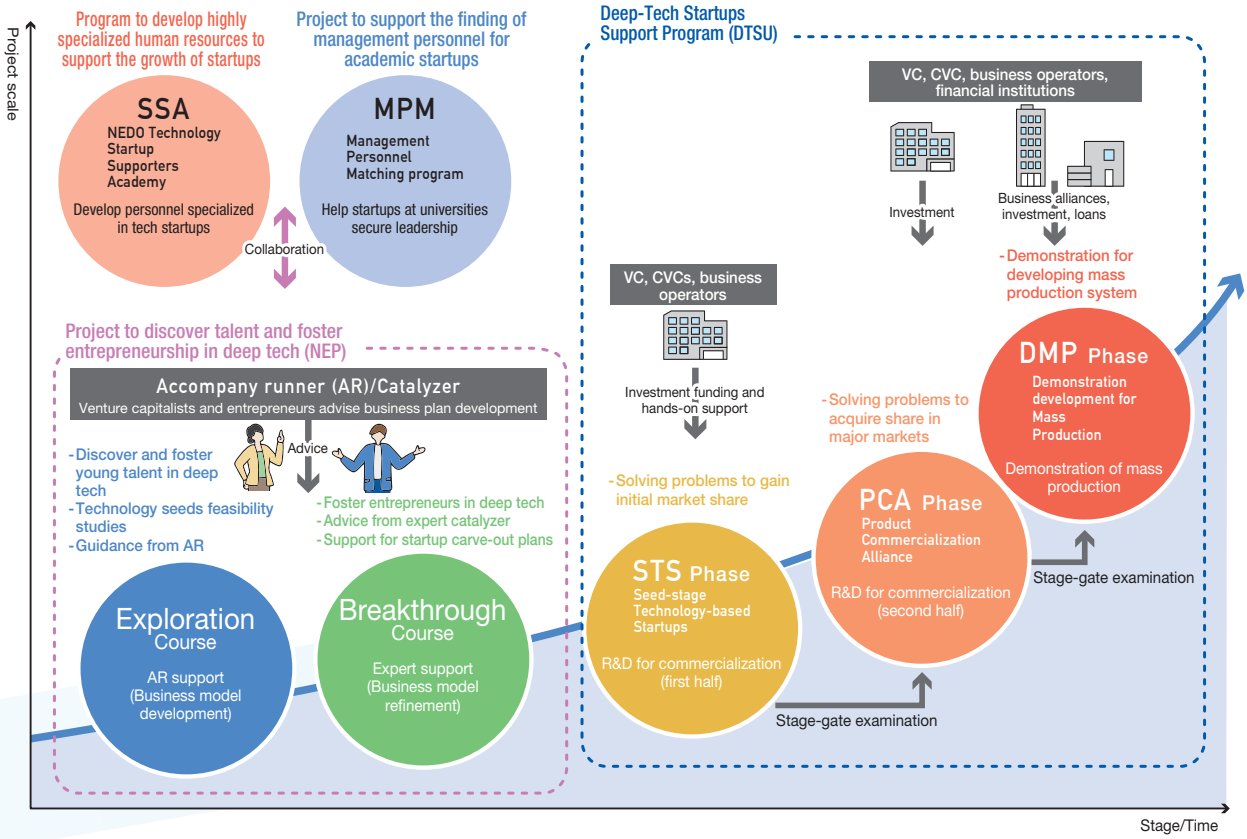
July 2022

Development of Bio-Based Production Technology to Accelerate Carbon Recycling, Industrial Material Production System Demonstration
- Demonstration of cannabinoid compounds production system using actinomyces hosts

Turning Point

"digzyme Inc. was founded as a startup at the Tokyo Institute of Technology in 2019. Through joint research, we keenly felt the need for more efficient bioprocess technologies, so we applied and were selected for NEDO's startup support program. For our two-and-a-half-year-old company, NEDO's backing has helped not only financially but also in terms of our business operations."

NEDO's Startup Support Programs



NEP Exploration Course	NEP Breakthrough Course 500/Carve-Out A	NEP Breakthrough Course 3000/Carve-Out B	STS Phase	PCA Phase	DMP Phase
Budget: 3 million yen 12 months	Budget: 5 million yen Fixed amount or ¾ of the total 12 months	Budget: 30 million yen Fixed amount or ¾ of the total 12 months	Budget: 300 or 500 million yen per project Up to 2/3 of the total 2 to 4 years	Budget: 500 million or 1 billion yen per project Up to 2/3 of the total 2 to 4 years	Budget: 2.5 billion yen per project Up to 2/3 or ½ of the total 2 to 4 years

Domestic Office

Head Office
MUZA Kawasaki Central Tower
1310 Omiya-cho, Saiwai-ku
Kawasaki City, Kanagawa 212-8554 Japan
Tel: +81-44-520-5100
Fax: +81-44-520-5103

Overseas Offices

Washington, D.C
1717 H Street, NW, Suite 815
Washington, D.C. 20006, U.S.A.
Tel: +1-202-822-9298
Fax: +1-202-733-3533

Silicon Valley
3945 Freedom Circle, Suite 790
Santa Clara, CA 95054 U.S.A.
Tel: +1-408-567-8033

Europe
10, rue de la Paix 75002
Paris, France
Tel: +33-1-4450-1828
Fax: +33-1-4450-1829

New Delhi
15th Floor, Hindustan Times House,
18-20 Kasturba Gandhi Marg,
Connaught Place,
New Delhi 110 001, India
Tel: +91-11-4351-0101
Fax: +91-11-4351-0102

Beijing
2001 Chang Fu Gong Office Building
Jia-26, Jian Guo Men Wai Street
Beijing 100022, P.R. China
Tel: +86-10-6526-3510
Fax: +86-10-6526-3513

Bangkok
8th Floor, Sindhorn Building Tower 2
130-132 Wittayu Road, Lumphini
Pathumwan
Bangkok 10330, Thailand
Tel: +66-2-256-6725
Fax: +66-2-256-6727

New Energy and Industrial Technology Development Organization
MUZA Kawasaki Central Tower, 1310 Omiya-cho, Saiwai-ku
Kawasaki City, Kanagawa 212-8554 Japan
Tel: +81-44-520-5100 Fax: +81-44-520-5103
URL: https://www.nedo.go.jp/english/index.html

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