

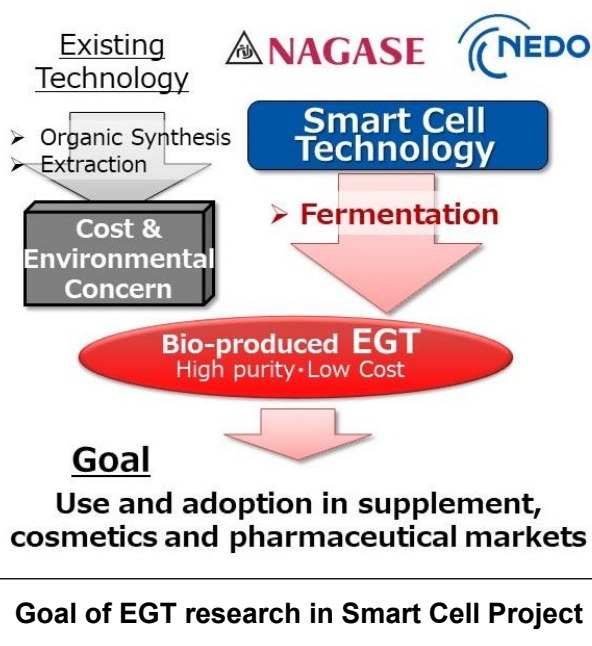
Nagase R&D Center Increases Productivity of Rare Amino Acid Ergothioneine 1000-fold: Highest Production Efficiency reported using Smart Cell Technology

Nagase R&D Center (Kobe), the research and development facility of NAGASE & CO., LTD. (Chuo-ku, Tokyo; Representative Director and President: Kenji Asakura), has been working on the development of fermentative production technology for ergothioneine (EGT)*¹ and researching EGT's functions, with their unique fermentation technology as a core technology. Using revolutionary biotechnology developed as part of the New Energy and Industrial Technology Development Organization (NEDO) Smart Cell Project*², they were able to increase EGT productivity by a factor of approximately one thousand compared to when research first began, achieving one of the highest production efficiency levels using microorganisms in the world*³. The team will now use the strains to work on achieving industrial production as soon as possible.

EGT is a natural amino acid found in trace amounts in mushrooms and other organisms, with excellent antioxidant properties and potential applications in a variety of fields including food products, cosmetics, and medicine. Current EGT production methods include extracting natural EGT and chemical synthesis, but due to the low naturally occurring amounts for extraction and the environmental impact of organic synthesis, Issues such as high cost- and environmental concern forbid the widespread adoption of EGT.

In this situation, the Nagase R&D Center began development of an cost-effective and environmentally-friendly bioproduction process in 2015 that could provide a stable supply of EGT through fermentation using microorganisms. In fiscal 2019, the Center also began the "Development of High-producing Smart Cells for Rare Amino Acid Ergothioneine" research project along with the National Institute of Advanced Industrial Science and Technology (AIST), Nara Institute of Science and Technology (NAIST), Kobe University, and Tohoku University as an issue-targeted industrial technology development grant project, part of NEDO's Smart Cell Project. As a result of using four Smart Cell foundational technologies*⁴ (enzyme design, metabolic pathway design, HTP microorganism construction/evaluation, transporter identification) to attempt to improve the EGT productivity, the production reaction within the microorganism cells was optimized, and an exponential improvement in production became possible.

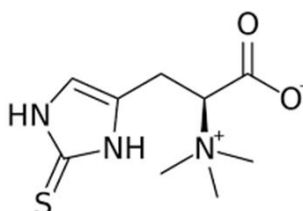
Through research and development using cutting-edge biotechnology, the Nagase R&D Center will provide products with high added value through sustainable processes and contribute to the creation of "a sustainable world where people live with peace of mind." This technology will be exhibited and presented at the NEDO booth at BioJapan 2020, to be held at Pacifico Yokohama from Wednesday, October 14 to Friday, October 16, 2020.



***1: Ergothioneine (EGT):** A natural amino acid (see structural formula below) produced only by some organisms, such as mushrooms. Research in recent years has shown that humans have systems in place to utilize EGT. It has been suggested that EGT ingested through food may help improve brain function and protect cells in the skin, eyes, and various organs from oxidative stress.

(NAGASE article on Nature website URL: <https://www.nature.com/articles/d42473-020-00227-4>)

(NAGASE website URL: https://www.nagase.co.jp/english/enterprise/nagase-r-and-d-center/document/RandD3_Ergothioneine_EN.pdf)



L-ergothioneine

***2: Smart Cell Project:** The common name for NEDO's Project for Development of Production Techniques for Highly Functional Biomaterials Using Smart Cells of Plants and Other Organisms. The goal of this project is to develop a "smart cell industry" by having all of Japan work together to develop next-generation technologies to create "smart cells" which maximize the material production capabilities of the cells of plants and microorganisms, to achieve low-cost, sustainable manufacturing processes for useful materials which are difficult to produce through standard chemical synthesis.

(Articles about this project on Nature website URL: <https://www.nature.com/collections/achfijhibj>)

(Smart Cell Project homepage (Japanese only) URL : https://www.nedo.go.jp/activities/ZZJP_100118.html)



Bringing it all together

***3: According to investigation by the Nagase R&D Center.**

***4: Smart Cell Foundational Technologies:** Foundational technologies developed by the Smart Cell project in order to work towards rapidly increasing the material production capabilities of microorganisms. See the link below for details.

(Introduction of Smart Cell Project technology (Japanese only) URL: https://www.jba.or.jp/nedo_smartcell/theme/)

Overview of NEDO Grant Project

1. Project Name: Development of Production Techniques for Highly Functional Biomaterials Using Smart Cells of Plants and Other Organisms/ Development of Production Techniques for Highly Functional Biomaterials Using Microorganisms/Development of High-production Smart Cells for Rare Amino Acid Ergothioneine
2. Project Period: Fiscal 2019-2020
3. Grantee: NAGASE
4. Joint Research Facilities: National Institute of Advanced Industrial Science and Technology (AIST), Nara Institute of Science and Technology (NAIST), Kobe University, Tohoku University, Kyoto University

News Releases on NEDO's Website

URL: https://www.nedo.go.jp/english/news/archives2020_index.html

■ Inquiries

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