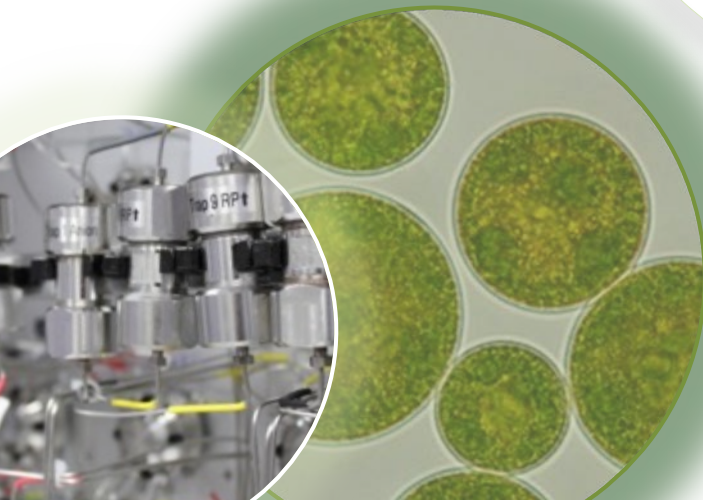
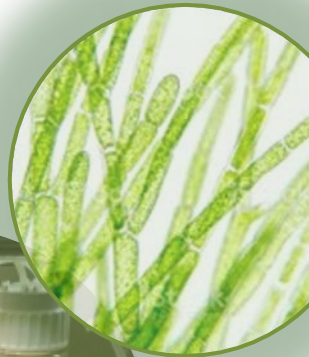




OP Bio Factory Co., Ltd. Company Profile

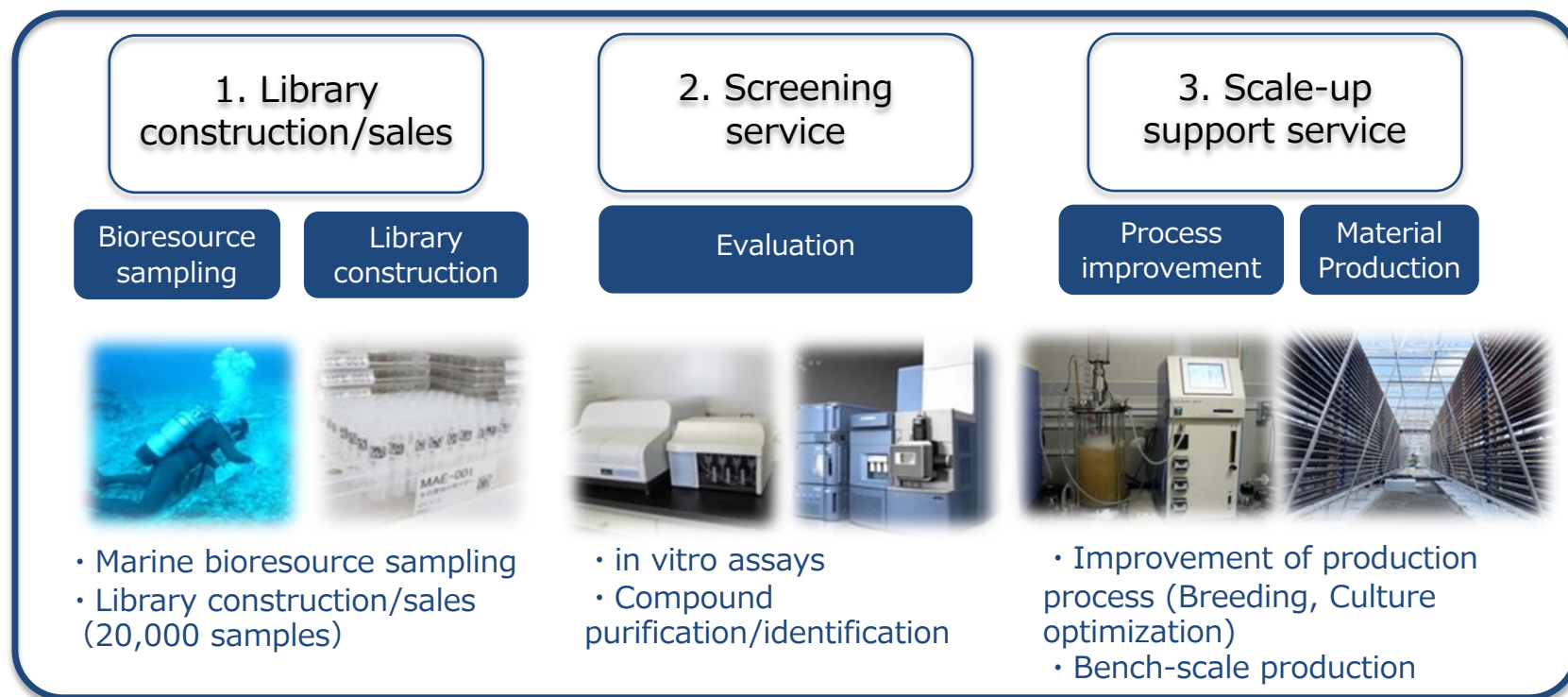
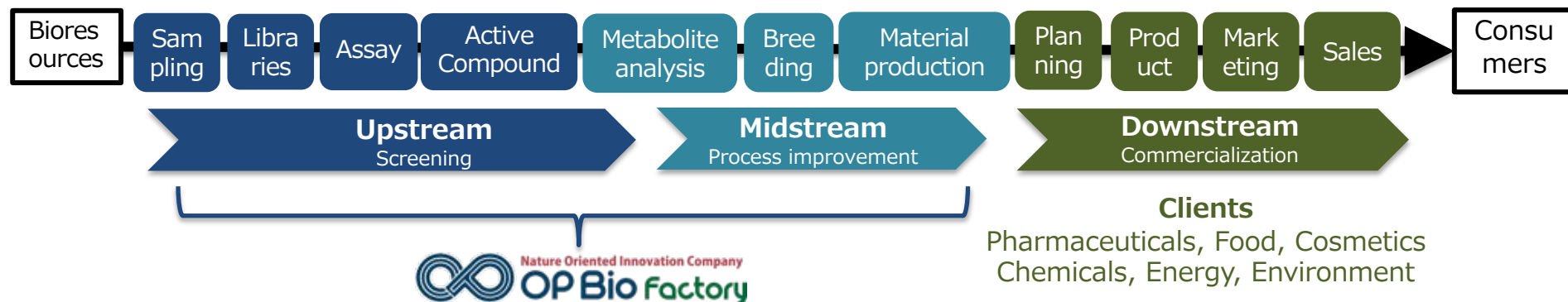


OP Bio Factory Co., Ltd.



Business Model

Value chain of bioresource industry

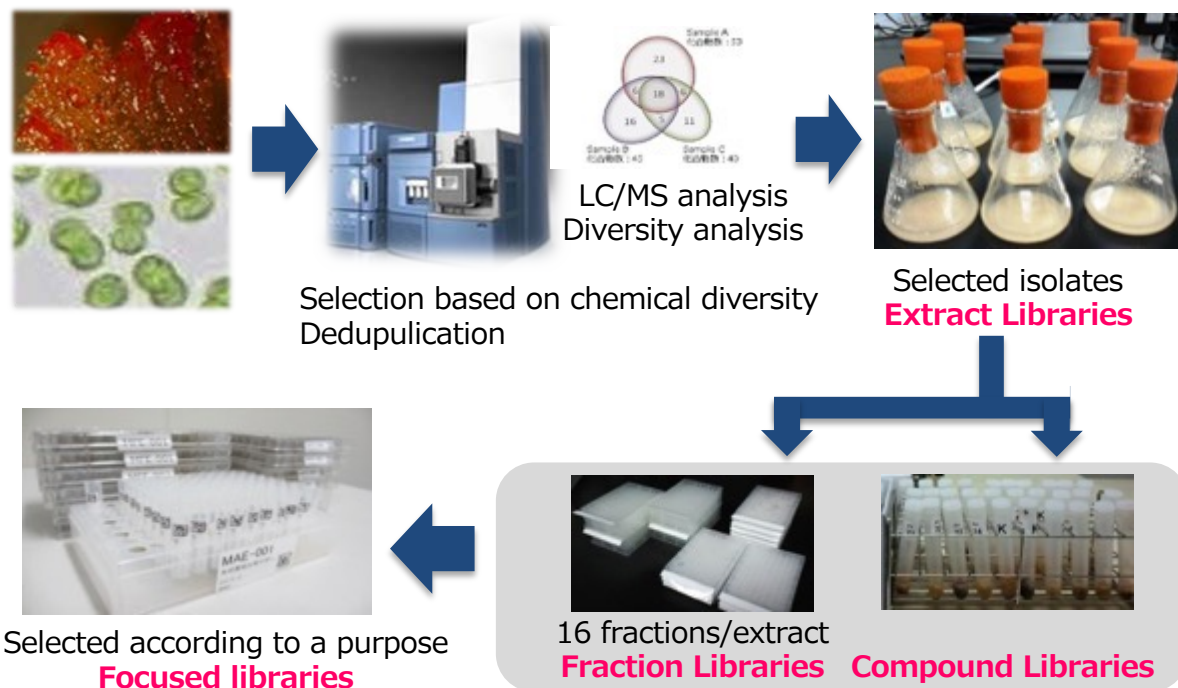


1. Library construction and sales

A Variety of Libraries Fit for Your Purpose

Various Libraries

- Extract Libraries
 - Actinobacteria
 - Filamentous fungi
 - Lactic acid bacteria
 - Yeasts
 - Microalgae
 - Marine invertebrates
 - Plants • Macroalgae
- Fraction Libraries
- Compound Libraries
- Focused Libraries
 - 天然中分子



- Libraries consist of selected **20,000 samples**.
- Because we launched from a marine survey company, one of our strong point is marine bioresource sampling.

■ 2. Screening service (1) Assay

4 Categories of Assays Fit for Your Purposes

For seed exploration, that is, to find active compounds, we undertake commissioned studies categorized as follows:

- (1) In-house assays
- (2) Assay set-up to meet the targets
- (3) Original assays conducted by out partner companies/universities
- (4) Assay transfer from clients to our lab



Assay Services

- Cell morphology observation assays
- Enzyme inhibition/activation assays
- Luciferase tests
- Antioxidant assays
- Various assays associated with gene transfer
- Multi-genes' rapid expression analysis of multi-samples
- Ca influx assays
- ELISA assays

■ 2. Screening service

(2) Compound identification

Purification and Structure Determination of Compounds

Structure determination of complex natural compounds require knowledge and experience. We purify and determine the structure of active compounds using UPLC-MS, GC-MS, and NMR.

Our company has experience in purification and structure elucidation of compounds from a variety of organisms including marine invertebrates, plants, microalgae and microorganisms. For example, Petrosiol A-E, compounds with neurite outgrowth activity, were found from a marine sponge, in a joint research with Nagoya University.

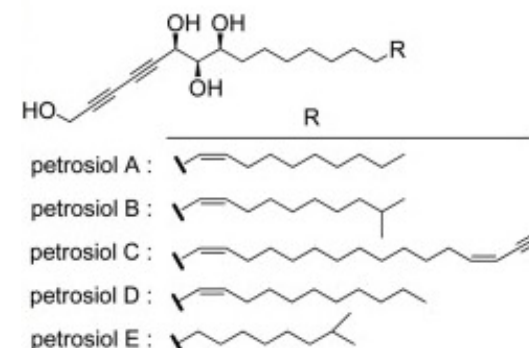
We identify compounds commissioned by our clients, as well as those from our libraries.



Nuclear magnetic
resonance (600MHz NMR)
バイオテクノロジー研究開発センター共通機
器



UPLC-HRMS
WATERS UPLC-G2-S Qtof MS



Petrosiol A-E (Derived from a marine sponge.)
Joint Res. with Nagoya University
Horikawa et al. (2013), Tetrahedron **69** 101-106

■ 3. Support service for scale-up

Support service for commercial scale production

Optimization on fermentation, breeding, extraction, and chemical synthesis for commercial scale production of microorganisms, microalgae, and compounds derived from them.



Support services

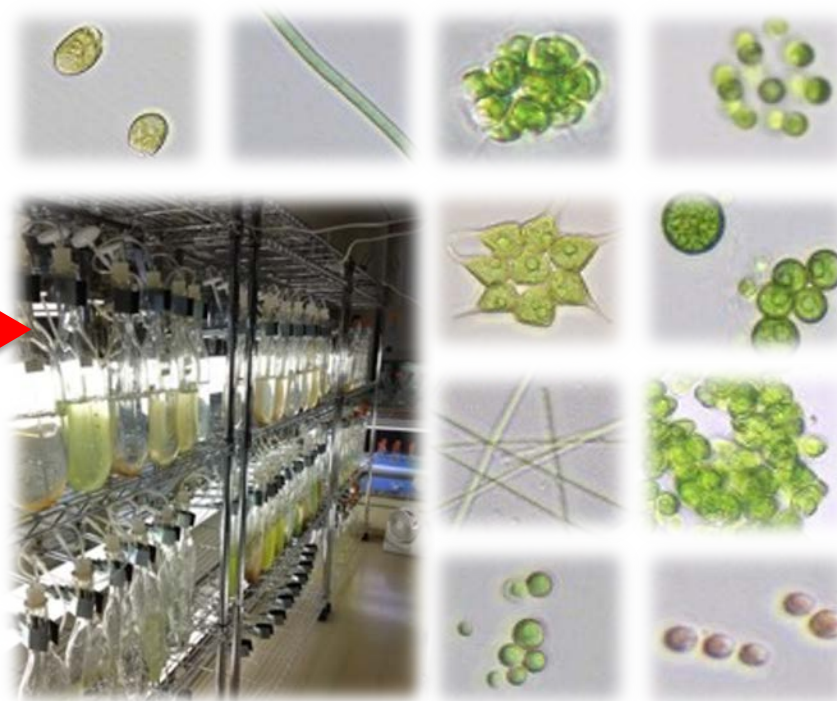
- Various development and management support services by our specialists
- Breeding/culture optimization
- Optimization of extraction/purification methods of compounds
- Chemical synthesis of compounds in case of production by fermentation is very challenging.
- Integrated services can also be provided in collaboration with our partner companies.

Discovery of Pavlova

Our Bioresource Libraries

- Actinobacteria
- Filamentous fungi
- Lactic acid bacteria
- Yeasts
- **Microalgae**
- Macroalgae (Seaweeds)
- Plants

Microalgae collection (1,000 isolates)



Pavlova (OPMS30543) was selected because of high productivity of compounds effective for anti-aging, based on metabolite profiling data.



Screening using our bioresource (Microorganisms)

Case1: Discovery of Kakeromycin by using “Ontime” screening method

**A new antifungal compound
with a new core structure
from a marine actinobacteria.**

Marine sampling × Drug discovery techniques from natural products

“Ontime” screening is the original and innovative screening method for active compound screening.

The method is developed in combination with marine sampling abilities and techniques and ideas of a researcher who developed Micafungin (Mycamine, Fungard). The high selectivity and short evaluation terms of the method make screening in high throughput possible at a low cost. Kakeromycin, a new antifungal compound with a new core structure was found by using this technology.

We undertake screening for antibacterial and antifungal agents using the method. The targets will be expanded to anticancer and antiviral fields in the future.

Common method



Evaluated by extract etc.

Extract/fraction/compound are applied onto test strains for evaluation.

“Ontime” screening



Evaluated with living microbes

Evaluated directly on a specific plate with living cells without making extract/fraction/compound.

Marine samples from various regions of Japan



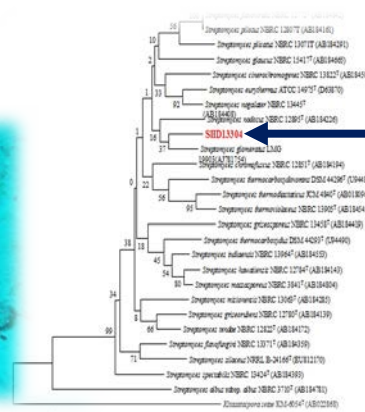
Throughput
1 million isolates/year

The case of Kakeromycin

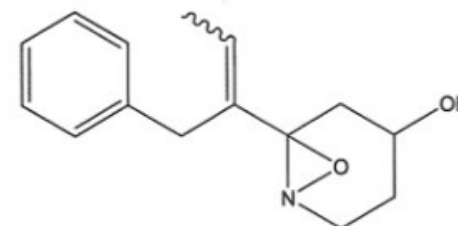
New Antifungal Compound with a New Core Structure

- Kakeromycin (SRI-KH001)

Kakeroma Isl., Amami, South-West
Islands, Kagoshima, Japan
Marine sediment



Producing strain
Streptomyces sp. A84
(undescribed species)



Kakeromycin

- Because Kakeromycin requires sea water for its production, it is regarded as a “true” marine actinobacteria-derived compound.
- Patent application pending in 10 countries.
- Development as an candidate for an athlete's foot medicine is ongoing at a venture company spined out from OP Bio (Stage: L1).



Screening using our bioresource (Microorganisms)

Case2: Discovery of 40551F by using Molecular Networking Technology

**A new active compound
against Mycobacterium avium-intracellulare
complex found in a joint research
with Kitasato University**

Drug discovery using Library data

Plate No.	Position	Total No.	Isolate No.	Identification	MDRP74	EC01	MH01	SA01	SD01	SS01	SU01	Blast
1	1A	K_1	OPMA00015	Streptomyces sp.	x	x	x	O	x	O?	O?	Streptomyces sp. ME02-6979.3a
1	1B	K_2	OPMA00025	Streptomyces sp.	x	x	O	O	O	O	O	Streptomyces olivochromos NBRC 3561
1	1C	K_3	OPMA00026	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces olivochromos NBRC 3561
1	1D	K_4	OPMA00027	Streptomyces sp.	x	x	O	O	O	O	O	Streptomyces fumigaticleroticus strain NRRL B-3856T
1	1E	K_5	OPMA00037	Streptomyces sp.	x	x	O	O	O	O	O	Streptomyces hygrosopicus strain N41-24-1
1	1F	K_6	OPMA00040	Micromonospora sp.	x	x	x	x	x	x	x	Micromonospora matsumotoense
1	1G	K_7	OPMA00042	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces sp. ME04-34E
1	1H	K_8	OPMA00048	Streptomyces rubrogriseus	x	x	x	x	x	x	x	Streptomyces rubrogriseus
1	2A	K_9	OPMA00050	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces phaeochromos strain NRRL B-2031
1	2B	K_10	OPMA00058	Nocardia sp.	x	x	x	O	x	O?	O?	Nocardia beijingensis strain:IFM 732
1	2C	K_11	OPMA00060		x	x	x	x	x	x	x	
1	2D	K_12	OPMA00062	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces sp. ME02-6979.5a
1	2E	K_13	OPMA00063	Nocardia elegans	x	x	x	x	x	x	x	Nocardia elegans type strain IMMIB N-402
1	2F	K_14	OPMA00064	Nocardia elegans	x	x	x	O	O	O	O	Nocardia elegans
1	2G	K_15	OPMA00075	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces sp. VTT E-99-1335 (B323)
1	2H	K_16	OPMA00077	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces lavendulae subsp. lavendulae strain: NBRC 13710
1	3A	K_17	OPMA00102	Streptomyces sp.	x	x	O	O	O	O	O	Streptomyces ambofaciens ATCC 23877
1	3B	K_18	OPMA00105	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces sp. ME02-6979.5a
1	3C	K_19	OPMA00108	Streptomyces sp.	x	x	O	x	x	x	x	Streptomyces sp. VTT E-99-1330 (A83)
1	3D	K_20	OPMA00117	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces sp. 1A01564
1	3E	K_21	OPMA00129	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces sp. ME02-6979.5a
1	3F	K_22	OPMA00134	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces tendae
1	3G	K_23	OPMA00135	Streptomyces sp.	x	x	x	x	x	O?	x	Streptomyces malachitofuscus strain: NBRC 13059
1	3H	K_24	OPMA00142	Streptomyces fradiae	x	x	O	O	O	O	O	Streptomyces fradiae strain: NBRC 12215
1	4A	K_25	OPMA00144	Streptomyces sp.	x	x	O	O	O	O?	O	Streptomyces parvulus
1	4B	K_26	OPMA00147	Streptomyces ghanaensis	x	x	x	x	x	x	x	Streptomyces ghanaensis strain: NBRC 15414
1	4C	K_27	OPMA00148	Streptomyces sp.	x	x	x	x	x	x	x	Streptomyces sp. S240

- OP's microorganism extract libraries are linked with panel screening data.
- By referring to the panel screening data, a screening against *Mycobacterium avium-intracellulare* complex, which causes MAC infection, was conducted in a joint research with Prof. Tomoda (Kitasato Univ.) .

Screening using Molecular Networking

Extract samples of microorganism cultures (About 6600)

↓ Antibacterial activity against 2 MAC species

Hit samples (652)

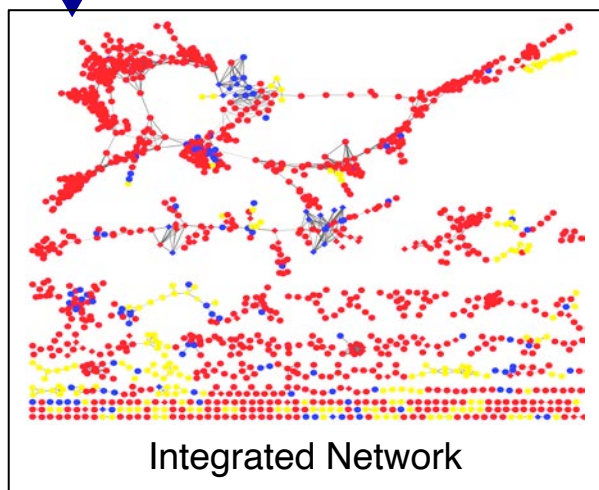
↓ Activities against *Bacillus subtilis* and/or mammal cells

Samples showing high selectivity to MAC (41)

↓ LC/MS/MS analysis

MS spectral data of the 41 samples

MS spectral data of 1,000 marine-derived microorganisms (8,000 metabolites)



- Specificity of strains
- Chemical diversity
- Dereplication

OPMA40551, OPMA00132 were selected as producing strains of highly novel compounds.

→A new compound, 40551F was obtained
PCT/JP2018/032048
[US Patent US 11,407,742 B2](#)

Development ongoing at Kitasato Univ. with support from AMED. In vivo tests are conducted aiming for licensing out.



Screening and product development using our bioresource (Microalgae)

Case3: Pavlova, from it discovery to product sales

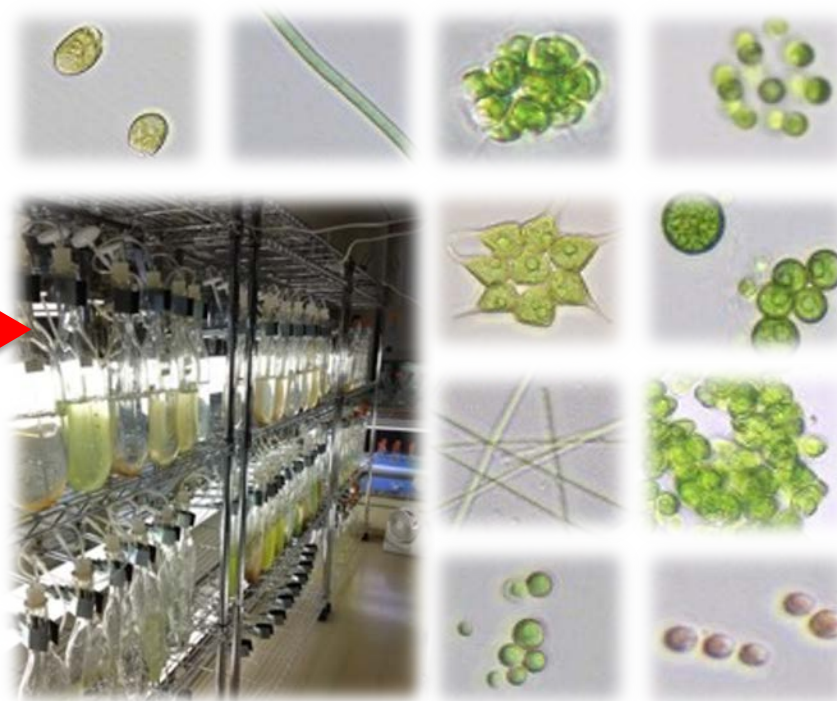
**A new microalgal food and cosmetic
material of Haptophyta.**

Discovery of Pavlova

Our Bioresource Libraries

- Actinobacteria
- Filamentous fungi
- Lactic acid bacteria
- Yeasts
- **Microalgae**
- Macroalgae (Seaweeds)
- Plants

Microalgae collection (1,000 isolates)



Pavlova (OPMS30543) was selected because of high productivity of compounds effective for anti-aging, based on metabolite profiling data.

Supported by Okinawa Prefectural Government (知的クラスター形成に向けた研究拠点構築事業)

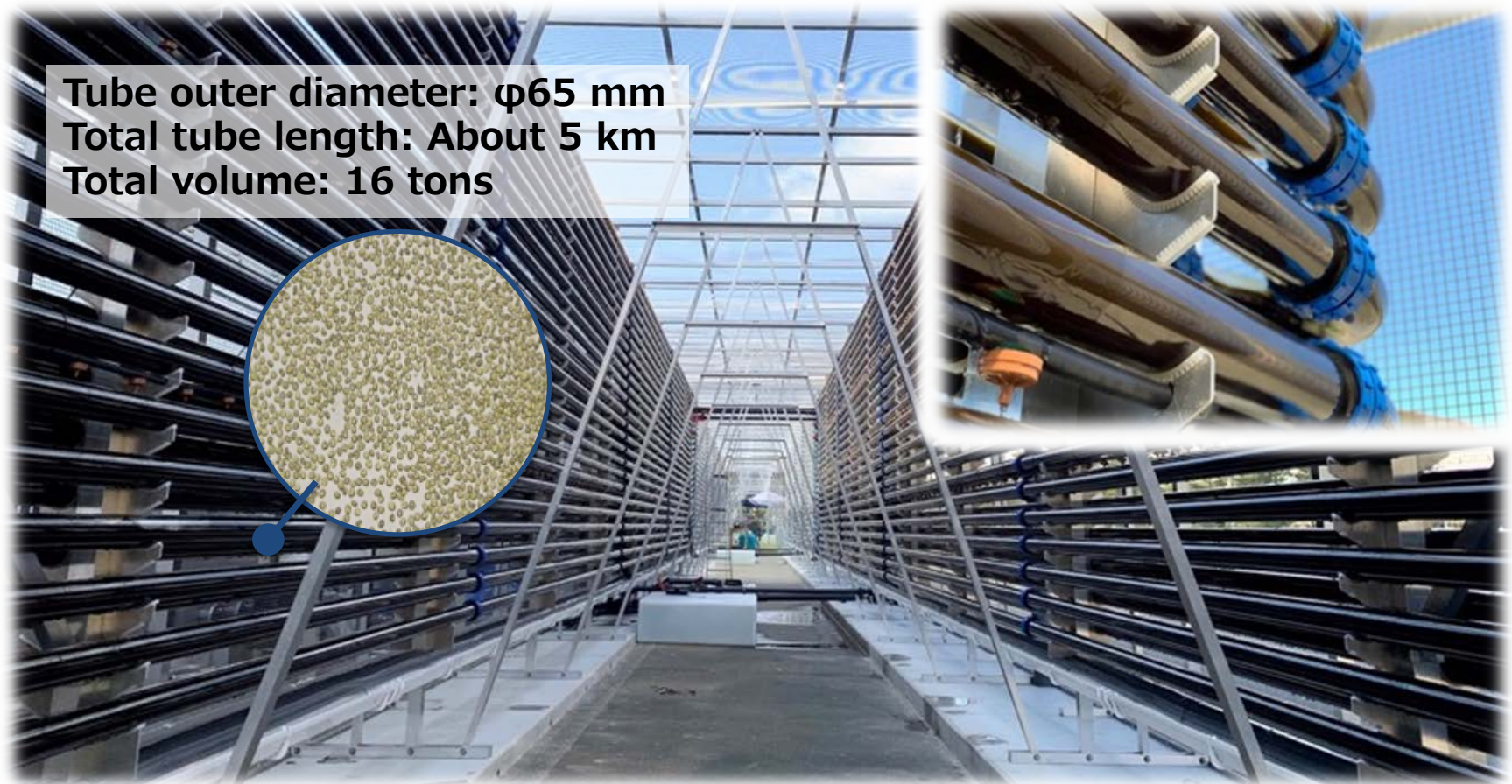
Features of ingredients of Pavlova

	Spirulina*	Chlorella*	Euglena*	Pavlova **
No. of nutrient ingredients	50 and more	59 and more	59	61 and more
Amino acid score	51	54	83	94
Proteins(g/100g)	65.8	58	50.1	46.9
Fat(g/100g)	7.5	8.9	21.3	23.8
DHA(mg/100g)	—	—	100	460
EPA(mg/100g)	—	—	300	3760
Pigments(mg/100g)	Phycocyanin: 6,000 Zeaxanthin: 98 β-Carotene: 185	Carotene: 17	Lutein: + Zeaxanthin: +	Fucoxanthin: 2,000 and more α-Carotene: 24 β-Carotene: 105
Dietary fiber(g/100g)	9.5	11.6	+	7.2
Ca(mg/100g)	379.2	620	532	956
GABA(mg/100g)	—	—	+	357
Hydroxyproline(mg/100g)	—	—	—	170
Product features	✓ Many nutrients ✓ Good nutrient balance ✓ High digestive absorbability ✓ Proteins, Phycocyanin	✓ Many nutrients ✓ Good nutrient balance	✓ Many nutrients ✓ Good nutrient balance ✓ High digestive absorbability ✓ Paramylon	✓ Many nutrients ✓ Good nutrient balance ✓ EPA, DHA, Ca, GABA, Hydroxyproline ✓ ✓ Fucoxanthin

* Cited from data on the web, ** Analyzed by Japan Food Research Laboratories, + : Detected, but no numerical data available

Commercial cultivation of Pavlova

Pavlova is cultured with mineral-rich natural sea water under the bright sunshine of Okinawa. To avoid contamination, it is cultured in outdoor and tube-type photobioreactors, which is first introduced in Japan, under controlled conditions.



Supported by Cabinet Office, the Government of Japan (国際物流拠点構築推進事業)

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Pavlova Products in the Market

Pavlova MCT+ (Supplement)



Pavlova Pasta & Dressing Supervised by BACAR (Italian restaurant)



Online sales at our e-commerce website



Served at Cafes and Restaurants



In-store sales at gourmet/vegan food shops

