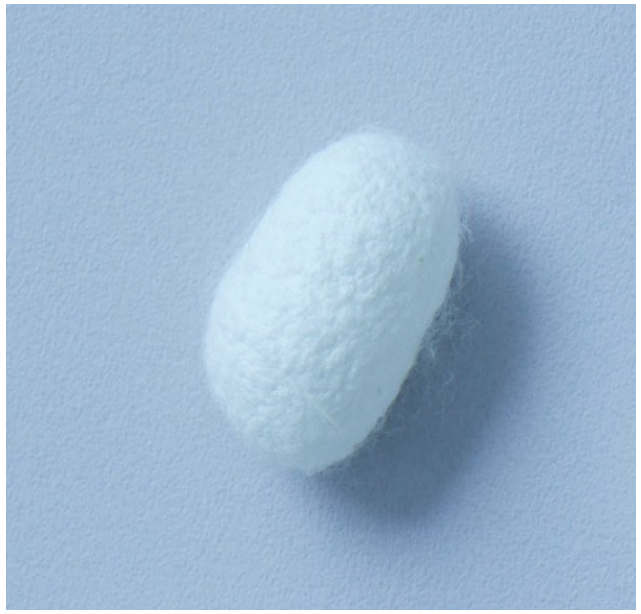
Changing the World with Silkworms

KAICO

Protein Expression Service with “Silkworm-Baculovirus System”

June 2025

KAICO Ltd.



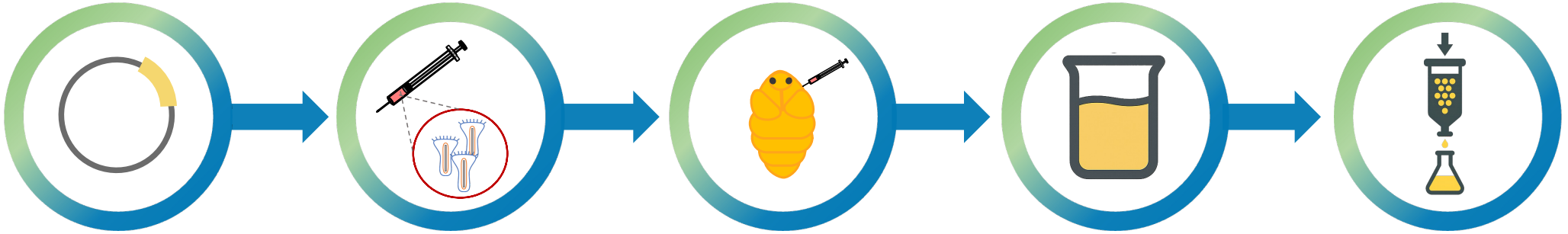
Recombinant protein manufacturing platform

Who We Are

- **Began the journey at Kyushu University in 2018.**
  - ✓ A Japanese national university leading in the entomology field.
- **Brought in novel know-how from Kyushu University.**
  - ✓ Expression of recombinant proteins using silkworms
  - ✓ Modifying natural proteins to additional functions
- **Core tech: "Silkworm-baculovirus* protein expression system"**
- **Vaccines using the core tech are under development.**
  - ✓ Not only injectables but also the oral type
  - ✓ The Japanese government grants both development projects**

* baculovirus: a type of virus that infects silkworms but humans.
** 1). Japan Agency for Medical Research and Development (AMED), 2). Ministry of Economy, Trade and Industry

Overview: KAICO's Expression System



Cloning

Preparation of recombinant baculovirus

Inoculation of the recombinant baculovirus

Milling

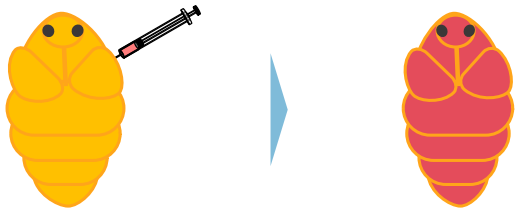
Purification

Our Strength

Fully customizable design

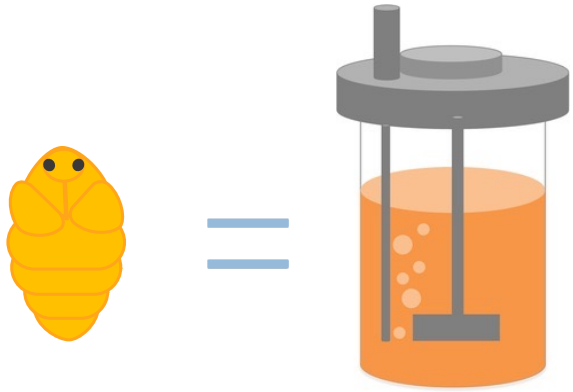
- Codon optimization, tag swapping, secretory signal adjustment.

Difficult Targets Welcome



- Expression rate = 100%
- Complex structures (VLPs), insoluble proteins, membrane, etc.

Flexible scaling



- Scalable production by increasing silkworm pupae.
- Flexible system for low-volume, multi-protein expression.

Six Business Portfolio

Core Technology
Recombinant proteins production platform

- ① CDMO of recombinant proteins
- ② Sales of reagent
- ③ Diagnostics & supplement
- ④ Inj. vaccines for animals
- ⑤ Immune-enhancing feeds for animals
- ⑥ Vaccines for humans

Hard to obtain the target protein in mammalian or insect cells...

I need end-to-end support from design to optimization

Insufficient resources for R&D

I want to produce antibodies but I can't find suitable antigens

Scaling up is a major bottleneck

Introduction of Protein Expression Service

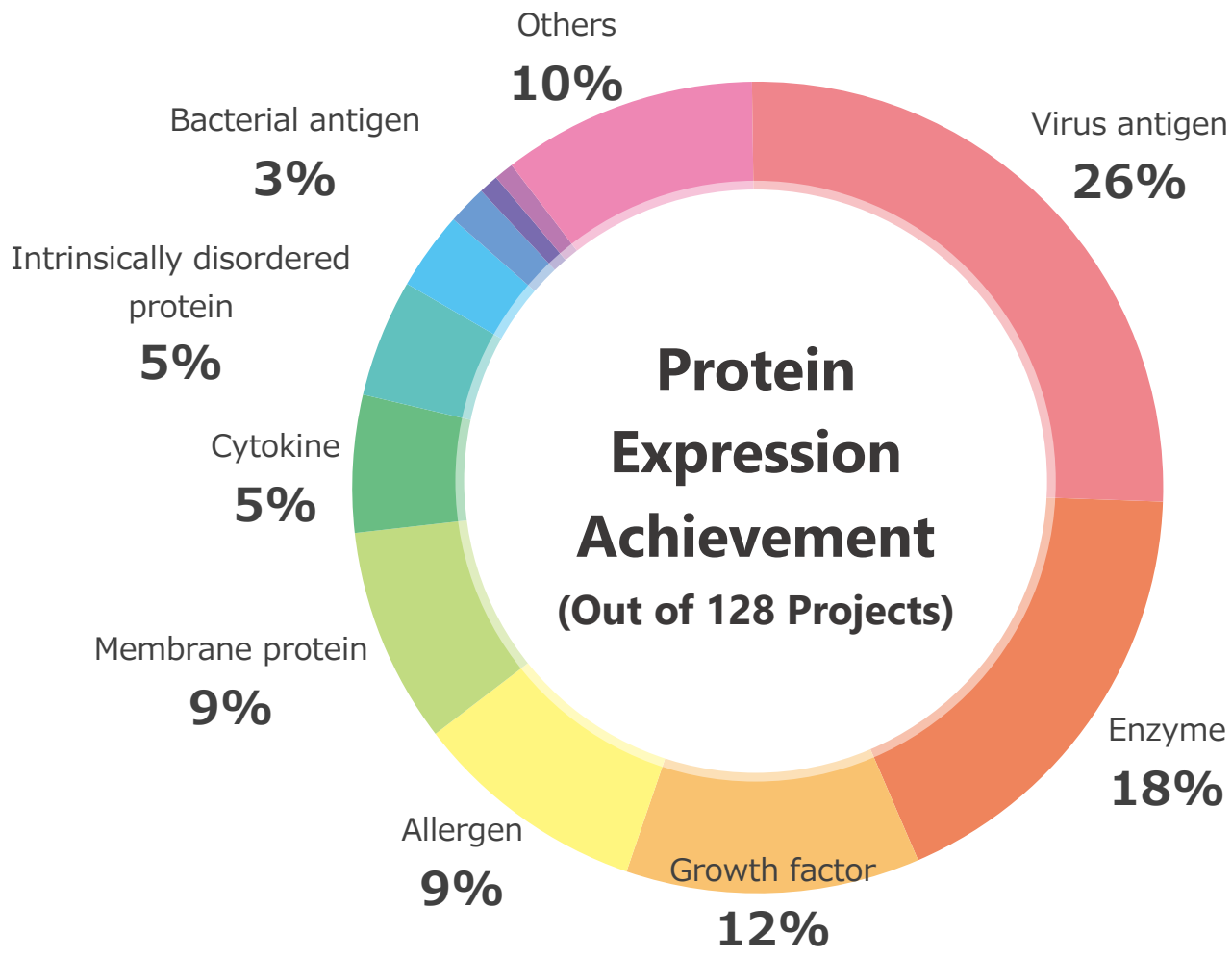
KAICO

Leveraging KAICO's silkworm-baculovirus expression system, we provide tailor-made proteins to meet your specific requirements.

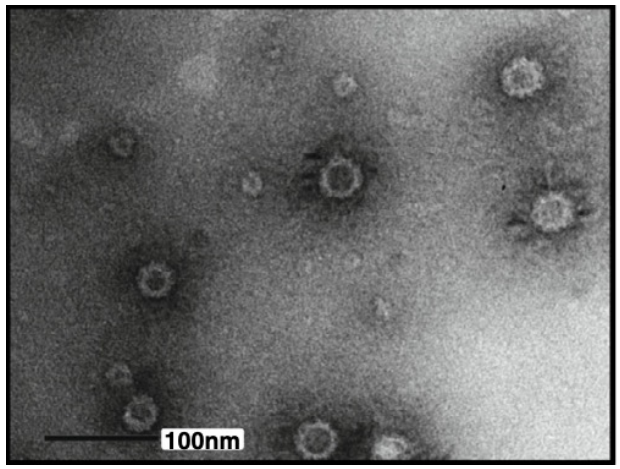
- **In-depth research** on your target protein
- **End-to-end support** – from strategy to delivery
- Capable of expressing proteins **difficult in other systems**
- Future-ready for **GMP-grade production**

Feasible for Any Types of Proteins

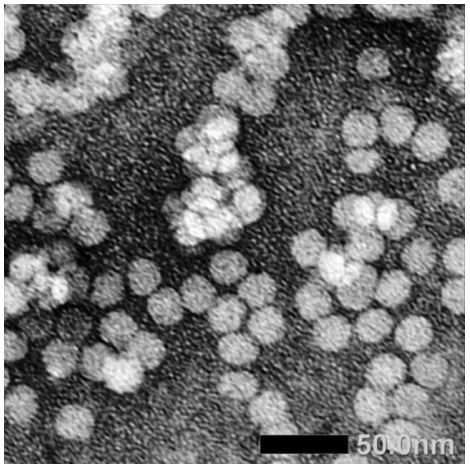
- **Expression rate: 100%**
- **In-house development of full-length recombinant IgG antibodies**
- **Yield: Several dozen µg to several mg per pupa**



Virus-Like-Particles Expressed in Silkworms



VLPs of Human Norovirus



VLPs of PCV2a

*Final yields depend on the target protein

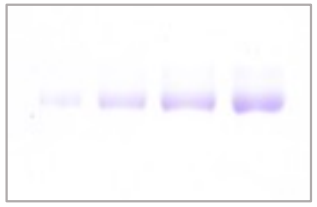
Masuda et al., *Vaccine* 41 (2023)
Masuda et al., *Journal of General Virology* (2018)

Examples of Expressed Protein

< Successful cases of protein expression where other CDMOs failed >

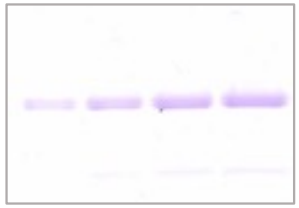
Toxic protein
(Japanese Pharmaceutical company)

Plant-derived, 63kDa

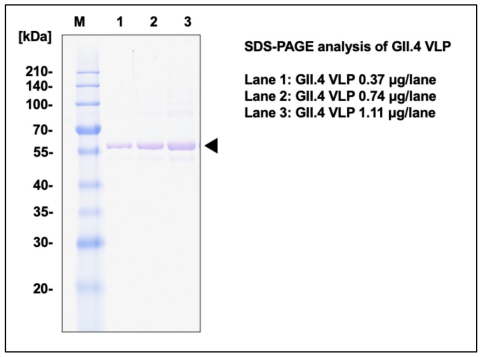


Functional Protein
(Japanese Bio-related company)

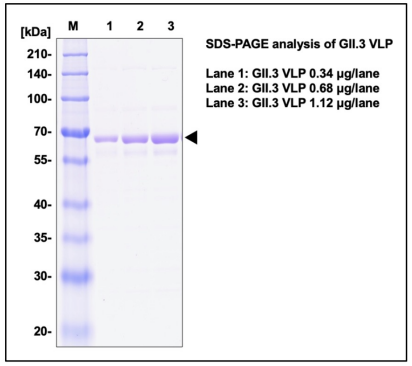
Human-derived, 37kDa



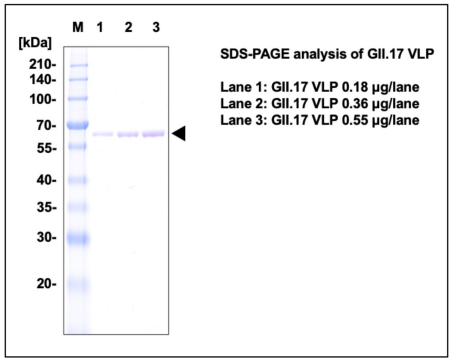
< Norovirus VLPs >



GII.4



GII.3



GII.17

Feedback from Customers

Unlike cell-based systems with costly licensing fees, KAICO's service allows free use of the final product.

Other expression systems kept failing, but when I finally turned to KAICO, they delivered exactly what I needed.

We observed higher activity than a commercially available protein.
(Note: While KAICO does not guarantee activity in its service, this feedback reflects the user's experience.)

KAICO proposed multiple constructs based on deep research and unique expertise – it gave me confidence.

Service Workflow

Briefing of the services.
Discussion on a form of deliverables.

Web meeting

Desk research on the target gene by KAICO.
Proposal of constructs and discussion on the overall strategy.
Quotation and order.

Proposal/ Quotation

The customer prepares the gene material or KAICO synthesizes the DNA

DNA Synthesize

Cloning ~ baculovirus.
Protein expression and purification.

Expression

Submission of the final deliverables using 5 silkworms.

Delivery

References

- Antiobesity-, and glucose metabolism -, and lipid metabolism-improving effects and active components in the mycelia and fruiting bodies of *Cordyceps militaris* (Vuill.) Fr. fermented on pupae of silkworms (*Bombyx mori*). Jxiv. Preprint
- High yield production of norovirus GII.4 virus-like particles using silkworm pupae and evaluation of their protective immunogenicity. Vaccine. 2023;41(3):766-77.
- Active Human and Murine Tumor Necrosis Factor α Cytokines Produced from Silkworm Baculovirus Expression System. Insects. 2021;12(6).
- Stable trimer formation of spike protein from porcine epidemic diarrhea virus improves the efficiency of secretory production in silkworms and induces neutralizing antibodies in mice. Vet Res. 2021;52(1):102.
- Optimization of SARS-CoV-2 Spike Protein Expression in the Silkworm and Induction of Efficient Protective Immunity by Inoculation With Alum Adjuvants. Front Immunol. 2021;12:803647.
- Production of scFv, Fab, and IgG of CR3022 Antibodies Against SARS- CoV-2 Using Silkworm-Baculovirus Expression System. Mol. Biotechnol. Mol Biotechnol. 2021;63(12):1223-34.
- Production of an active Mus musculus IL-3 using updated silkworm-based baculovirus expression vector system. J. Asia-Pacific Entomol. 2021;24(3):544-49
- Efficient production of recombinant SARS-CoV-2 spike protein using the baculovirus-silkworm system. Biochem.Biophys. Res. Commun. 2020;529(2):257-62.
- Expression and activation of horseradish peroxidase-protein A/G fusion protein in silkworm larvae for diagnostic purpose. Biotechnol J. 2018;13(6):e1700624.
- Heme precursor injection is effective for Arthromyces ramosus peroxidase fusion protein production by a silkworm expression system. J Biosci Bioeng. 2015;120(4):384-6.

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