

# Nanoparticle-Based Intracellular Delivery of Arbitrary Proteins to Target Cells

We are looking to out-license the technology for its commercialization.

**Enables efficient encapsulation of diverse proteins into virus-like particles by adding a specific amino acid sequence ("VLP tag").**

## ◆ Background

Virus-like particles (VLPs) are being developed as stable and cell-selective platforms for *in vivo* protein delivery, offering rapid action without the need for transcription or translation. This strategy has attracted attention in antibody therapeutics for delivering antibodies to intracellular targets. However, existing methods are constrained by labor-intensive recombinant protein production and low delivery efficiency, highlighting the need for simpler and more efficient protein encapsulation technologies.

## ◆ Description

Kyoto University researchers have developed a novel amino acid sequence, namely a 'VLP tag', which interacts with lentiviral capsid proteins. Arbitrary proteins fused with VLP tags are self-assembled into and encapsulated within VLPs (Fig. 1). Accordingly, VLPs capable of efficient encapsulation of large quantities of arbitrary proteins can now be produced. This technology is expected to have broad applications, including antibody therapeutics and genome editing.

### ➤ VLP tag facilitates efficient encapsulation of proteins in VLPs.

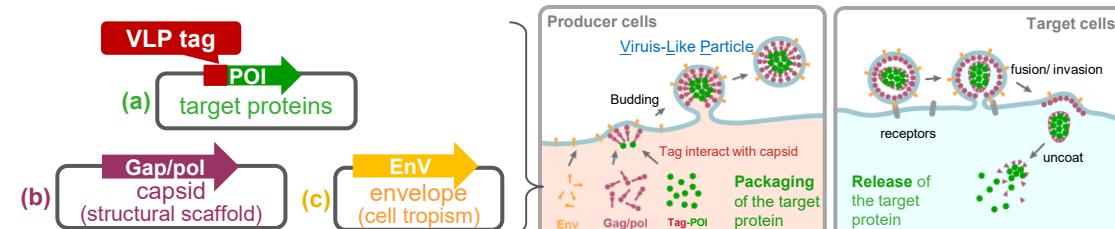
Each particle can package an average of approximately 1,700 nanobody molecules (Fig. 2). Since it does not contain a viral genome, it can be handled in P1-level laboratory facilities.

### ➤ No requirement for protein purification

Production costs are reduced, and large proteins (e.g., Cas9) can be efficiently packaged.

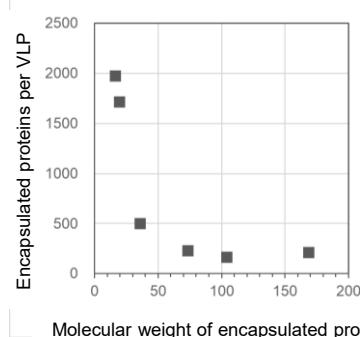
### ➤ Compatible with known envelope proteins (Fig.1)

In combination with envelope proteins, this technology enables cell-specific delivery.



**Fig. 1. Overview of VLP-mediated delivery of target proteins into target cells**

In producer cells, plasmids encoding (a) a VLP-tagged arbitrary protein, (b) a capsid, and (c) an envelope are expressed. Interaction between (a) and (b) drives efficient self-assembly into VLPs, which bind to receptors on target cells, enter via fusion, and uncoat to release the protein intracellularly.



**Fig. 2. Evaluation of encapsulatable protein numbers by molecular weight**

VLPs released into the culture medium were collected and analyzed, showing that each VLP contains approximately 1,700 target protein molecules\* (nanobody).

\*The molecular weights include the target protein, the VLP tag, and detection tags (e.g., luminescent markers).

<Encapsulated proteins in Fig. 2>

From left to right: HIV-1 tat (10 kDa), nanobody (13 kDa), carbonyl anhydride 1 (29 kDa), bovine serum albumin (66 kDa), importin b (97 kDa), Cas9 (158 kDa)

## ◆ Development Status

- Confirmed cytoplasmic delivery profile
- Effective cancer suppression confirmed via nanobody delivery
- Under investigation for vaccine and antibody development

## ◆ Applications

### For pharmaceuticals

- Antibody therapeutics
- Drug delivery systems
- Targeted cell therapy

### For basic Research

- Application for PoC
- Genome editing

## ◆ Offer

- Patent License
- Option for Patent License
- MTA for sample evaluation
- Collaborative Research

## ◆ Contact

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