Biosynthetic Peptide Screening Platform for various Drug Discovery and Delivery

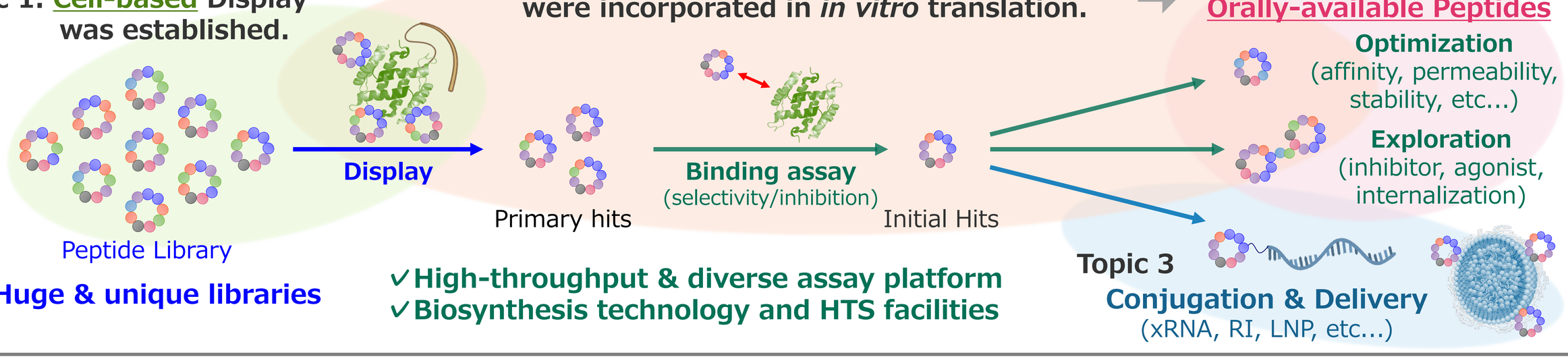
Shin Izuta, Taishi Fuda, Hiroki Takahashi, Koo Suzuki, Nao Yamazaki,
Anri Nishiguchi, Tomoki Ota, Ryo Ukekawa, Yukiko Ishii (FUJIFILM Corporation)

FUJIFILM
Value from Innovation

Partners for *Life*™
collaborated with PURE*frex*® Reconstituted cell-free protein synthesis kit

Peptide screening platform

A representative screening workflow is shown below. Successful examples related to three challenges in peptide discovery; (1) targets that are difficult to isolate, (2) oral abministration, and (3) conjugation for deliverly, were obtained in this report.

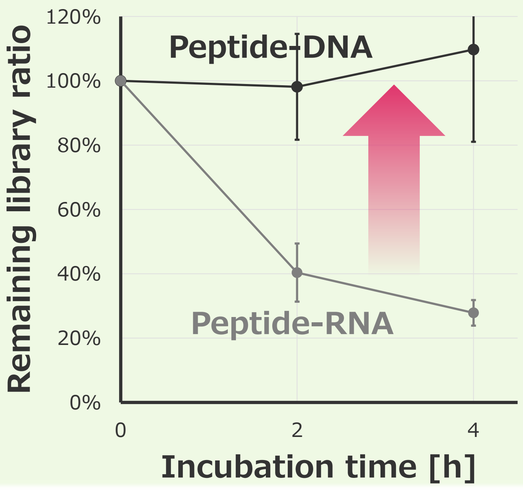


Topic 1. Cell-based Display from Stable Library

The stability of the library has been improved, enabling display screening using cells. Novel peptide binders were successfully identified for FGFR and three GPCR targets; CaSR, FZD5, and GHSR.

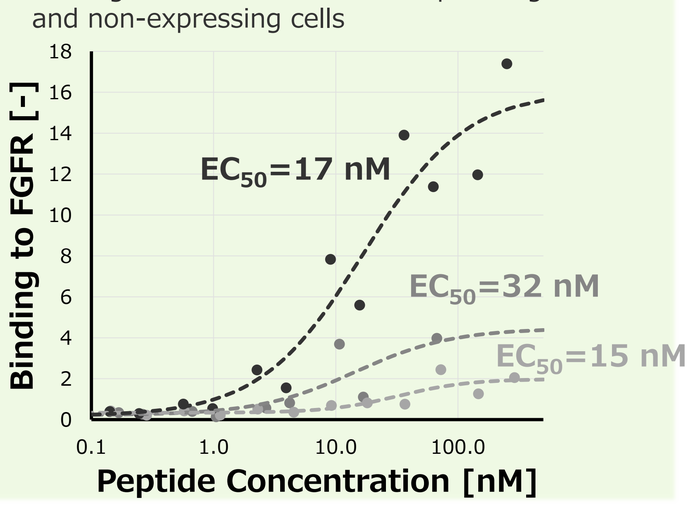
Stability of the Library

···Covalent conjugation of peptides to DNA substantially improved their stability in cell culture supernatants.



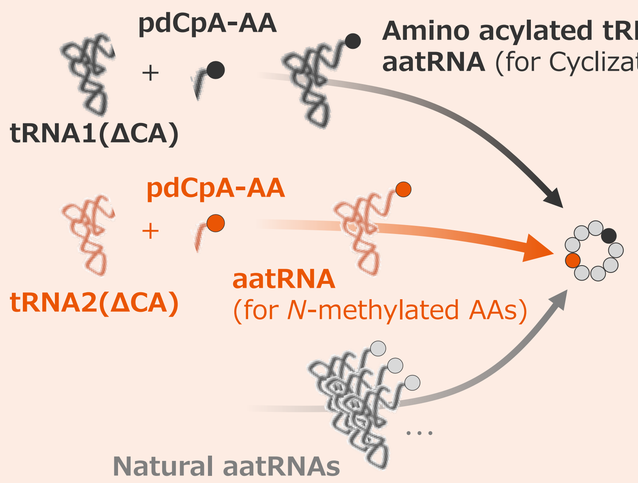
Affinity of the discovered Hits

···A highly target-specific binding signal was observed, as evidenced by the difference in binding levels between FGFR-expressing cells and non-expressing cells

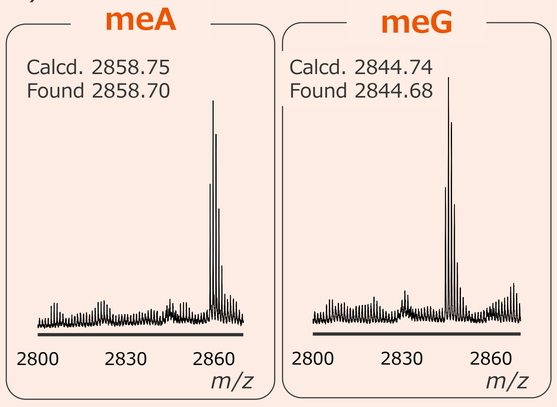


Topic 2a. *N*-methylated AAs in *in vitro* translation system

The combination of the improved pdCpA method and PURE system enabled the efficient incorporation of *N*-methyl alanine (meA) and *N*-methyl glycine(meG) into peptides via *in vitro* translation system.

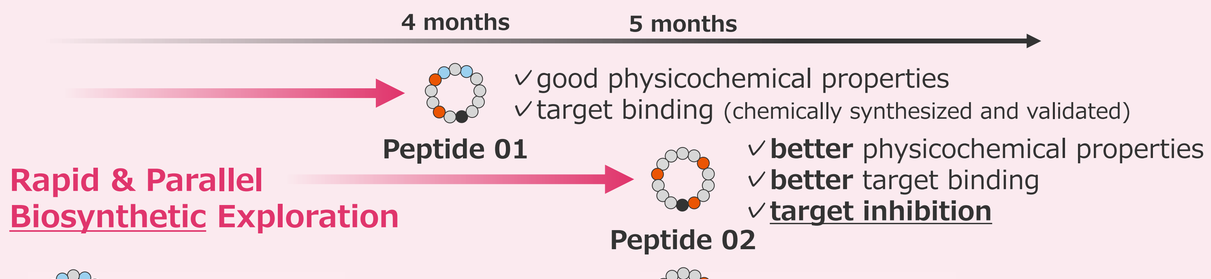


MALDI-MS identification



Topic 2b. Potentially Orally-available Peptides

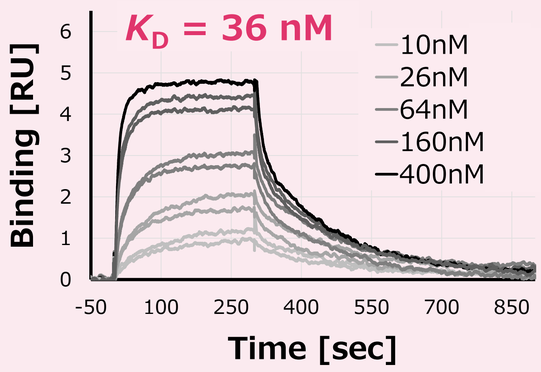
A rapid screening and optimization are being demonstrated with famous IL inhibitor. Within five months, peptides with favorable physicochemical properties, binding, and inhibitory activity were identified, and *in vivo* oral absorption PKs are currently underway.



Peptide 01

- 13 aa ring
- **2 *N*-alkylated residues**
- 2 charged residues

SPR binding validation

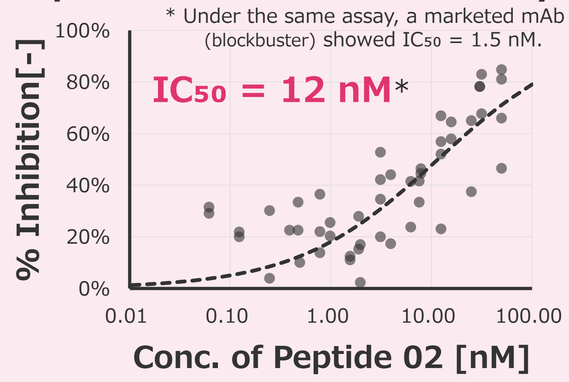


Peptide 02

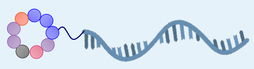
- 14 aa ring
- **3 *N*-alkylated residues**
- **0 charged residues**

Alpha-screen inhibition assay

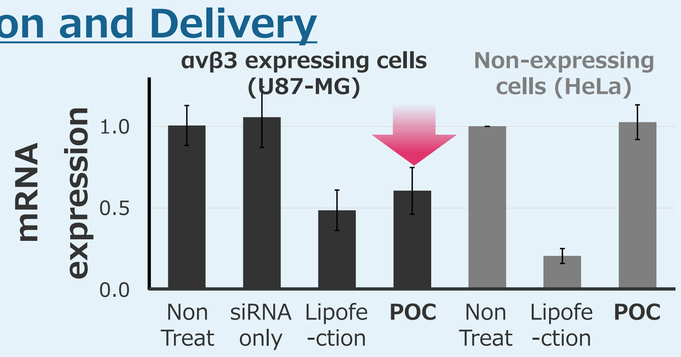
* Under the same assay, a marketed mAb (blockbuster) showed IC50 = 1.5 nM.



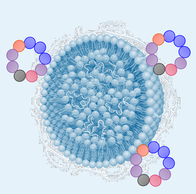
Topic 3. Conjugation and Delivery



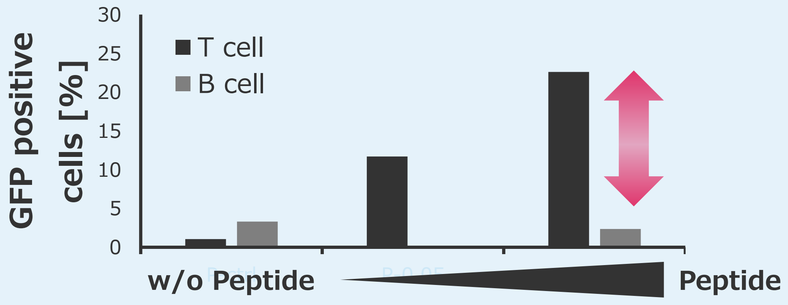
Peptide - siRNA conjugate (POC)



A Integrin-binding peptide was conjugated to a model siRNA. The resulting peptide-siRNA conjugates exhibited selective knockdown activity in cells expressing Integrin at 40 nM.



Peptide – LNP (lipid) conjugate



A CD7-binding peptide was chemically conjugated with a lipid, and peptide-LNP were formed without any additional process. This LNPs enabled T cell-selective mRNA(GFP) delivery in PBMC.

Peptide Discovery Service in FUJIFILM

contact: shin.izuta@fujifilm.com

USEFUL

- **No milestones and no royalty obligations**.
- **No intellectual property claims** on discovered peptides.
- **Rapid discovery** (4Ms for initial hits, +2Ms for SAR).

POWERFUL

- **Huge libraries** (≧10^{13} varieties) with **unique peptides**.
- **High-throughput activity-based screening/optimization** with biosynthetic tech.

→ **High affinity** (K_D: 0.1~50 nM) and **Wide variety** in hits.

Hit peptides have been obtained toward >30 targets with our platform.