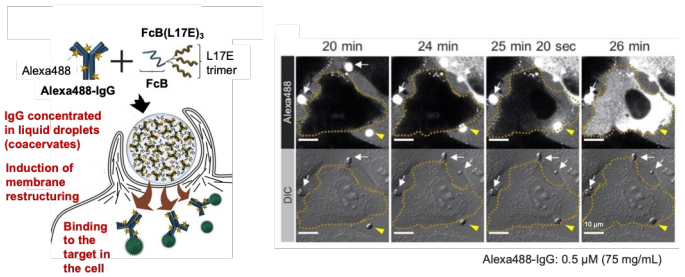
Pullulan-Based Microcondensates with Cationic Peptides for Efficient Cytosolic IgG Delivery

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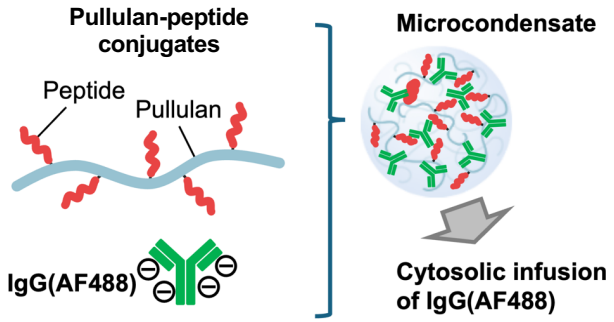
Introduction | Microcondensate-mediated delivery using L17E



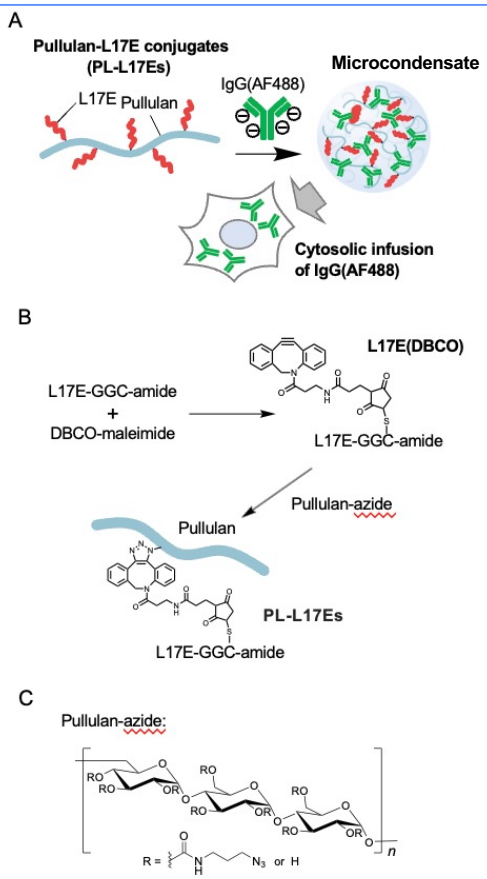
Alexa488-IgG: 0.5 μM (75 mg/mL)

L17E: IWLTALKFLGKHAAKHEAKQQLSKL-amide (Akishiba *et al. Nat. Chem.* **2017**, *9*, 751)
FcB: HWRGWV (Yang *et al. J. Pept. Res.* **2005**, *66*, 120)

Objective | To demonstrate the versatility of the approach

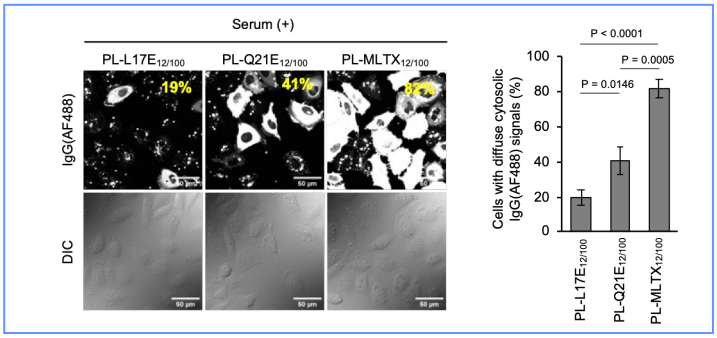


Results 1 | Preparation of the pullulan-peptide conjugates

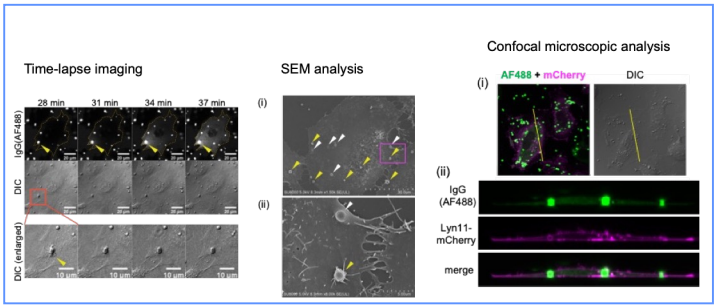


Membrane-permeabilizing peptides:
L17E: IWLTALKFLGKHAAKHEAKQQLSKL-amide
Q21E: IWLTALKFLGKHAAKHLAKQELSKL-amide
MLTX: IWLTALKFLGKHAAKHLAKQQLSKL-amide
MLTXRn: IWLTALKFLGKHAAKHLAKQQLSKL-R_n-amide (n=2~8)

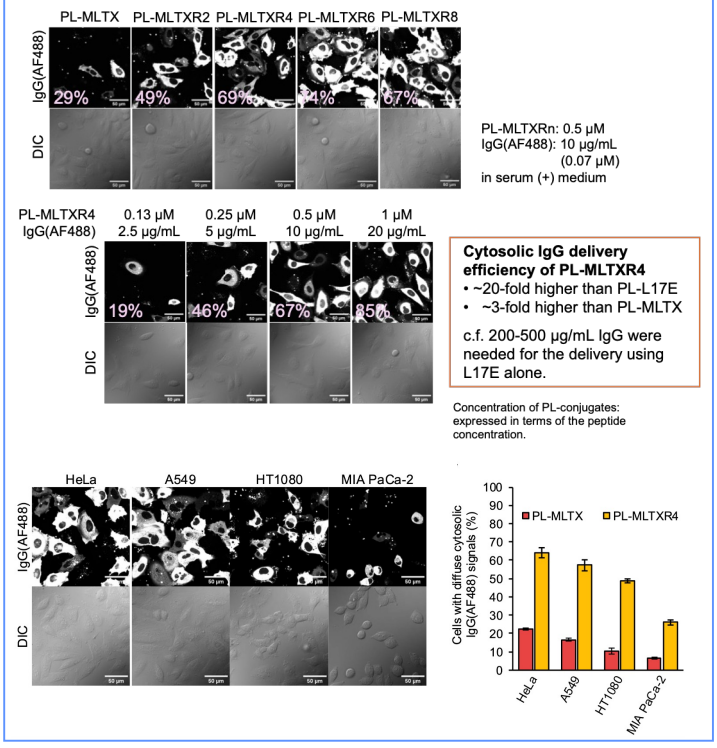
Results 2 | Evaluation of delivery efficiency



Results 3 | Modes of cellular uptake



Results 3 | PL-MLTXR4 exhibits the highest delivery activity



Summary

- Micrometer-sized coacervates (microcondensates) were formed simply by mixing PL-L17E with IgG labeled with IgG(AF488). These microcondensates exhibited efficient cytosolic infusion of IgG.
- Dynamic structural alterations of the cell membrane that entrapped the microcondensates, leading to cytosolic IgG infusion, were captured by confocal and electron microscopy.
- Replacement of L17E with M-lycotoxin (MLTX) or tetra-arginine-tagged MLTX (MLTXR4) further enhanced IgG delivery efficiency, reducing the required amounts of both IgG and the pullulan–peptide conjugate.

1) Michibata et al. *Bioconjug. Chem.* **2024**, *35*, 1888
2) Michibata et al. *Bioconjug. Chem.* **2025**, *36*, 1494
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