

A Functional Peptide Is Delivered into Cells by a CPP via Peptide-peptide Interactions

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It is important to develop methods for delivering peptides and proteins with specific functions into cells because the methods are expected to be drugs to treat certain diseases. In such methods, cell-penetrating peptide (**CPP**) is often used to deliver to peptides and proteins into cells.¹ Functional peptide (**FP**) that does not have cell permeability can be delivered intracellularly by direct bonded with **CPP** (Fig.1 A). However, many **CPPs** are positively charged, so the activity of **FP** may be physically inhibited by nonspecific electrostatic interactions with negatively charged biological substances (DNA and RNA etc.) in the cell. Therefore, **FP** and **CPP** should be separated from each other after delivery into cells so that the activity of **FP** is not inhibited. In this study, we designed “peptide zippering method” to connect **FP** with **CPP** via peptide-peptide interaction for delivering into the cell (Fig. 1 B). In the first approach, we chose to use a leucine zipper (**Lz**) reported by *Bosshard et al.*² In this method, a peptide containing glutamic acid (**LzE**) and a peptide containing lysine(**LzK**) form a heterodimer through electrostatic and hydrophobic interactions. In the second approach, we used a peptide nucleic acid (**PNA**) reported by *P. E. Nielsen et al.* as an alternative to the leucine zipper.³ **PNA** is an artificial nucleic acid, so it has nucleobases on its side chains, like DNA. Therefore, **PNAs** are suitable for use as the peptide zippers because they can form hybrids with each other by nucleobases. In this study, we evaluated the intracellular autophagy activity of **FP**, autophagy-inducing peptides (**AIP**) by delivering it into cells. We also found that the activity of **AIP** depends on the peptide zipper chain length. In our poster presentation, we will describe the effect of its chain length on the activity of **AIP** and demonstrate the utility of these peptide zipping methods.

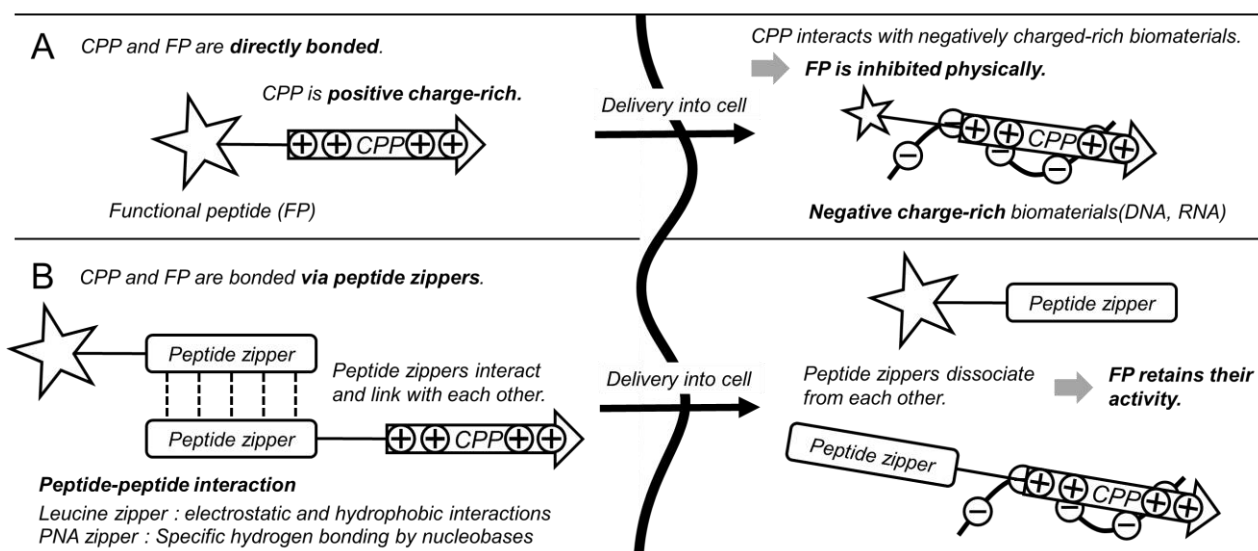


Fig. 1. Schematic illustration of conventional method (A) and peptide zippering method (B) for delivery of the functional peptide via CPP inside cells.

References

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- ² H. R. Bosshard *et al.*, *Biochemistry* **1997**, *36*, 204-213.
- ³ P. E. Nielsen *et al.*, *Nature* **1993**, *365*, 566-568.