# 理学国際教育研究センター 研究セミナー

# Bifunctional peptides altering localization and function of intracellular proteins


## Dr. Ines Neundorf

**（Professor: Institute for Biochemistry, Department of Chemistry, University of Cologne, Germany）**

専門分野：ペプチド科学（膜透過性ペプチド、抗菌ペプチド）


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**中百舌鳥キャンパス A13 棟 323 室**

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会場まで直接お越しください。

Since several years we are interested in the design and application of cell-penetrating peptides (CPPs) [1-3]. CPPs are usually short peptide sequences with an amphipathic or purely cationic nature that supports effective interaction with cell membranes. Notably, CPPs can deliver attached cargoes inside the cell interior including other bioactive peptide sequences. Such chimeric and bifunctional molecules may provide novel cell-permeable peptides with promising new bioactivities and application in various fields.[4]

Recently, we have found out that by using steps of posttranslational modification (PTM) the intracellular accumulation of CPPs can be increased. For instance, when we introduced a CaaX amino acid motif to the CPP sequence, we obtained peptides that interact with prenyltransferases and affect the downstream signalling of Ras proteins in pancreatic cancer cells [5].

In another approach, we created PTM-CPPs bearing a palmitoylation sequence. *S*-palmitoylation plays a crucial role in regulating protein function, trafficking, and localization and is catalysed by a family of palmitoyl transferases which modify cysteine residues within a highly conserved, catalytic DHHC motif. We generated DHHC-CPPs, tested their bioactivity in different cell lines and observed altered localization and function of distinct palmitoylated proteins.

This work will highlight our results on bifunctional PTM-CPPs, which, in our opinion, represent interesting chemical tools not only to investigate posttranslational modification, but also to use them as drugs that selectively alter the PTM machinery.

**References**


[1] L. Feni, *et al.*, *Bioconjug Chem.* **2019**, 30, 2011-2022., [2] A. Negrete-Hurtado, *et al.*, *Nat Commun.* **2020**, 11, 1535., [3] J. Grabeck, *et al.*, *Molecules.* **2022**, 27, 6656., [4] I. Raote, *et al.*, *Nat Commun.* **2024**, 15, 3302., [5] K. Klimpel, *et al.*, *FEBS J.* **2021**, 288, 2911-2929.



世話人： 中瀬 生彦
（大阪公立大学 大学院理学研究科 生物化学専攻）
連絡先：i-nakase@omu.ac.jp