Science Frontier: Biological Chemistry Seminar

How to improve antimicrobial activity of a membrane-active peptide

Dr. Ines Neundorf

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

Specialty field： peptide science（cell-penetrating peptides, antimicrobial peptides）

Date & Time：15th October (Wed.) 15:00-16:00
Venue：Nakamozu campus
A13 build. 3F room 323

No prior registration is required
Please come direct to the venue

Antimicrobial peptides (AMP) have been evolved as promising alternatives to commonly used antibiotics. Usually, these peptides act by permeabilizing cell membranes of pathogenic bacteria, whereas being harmless to mammalian cells. In this work, we generated and screened a small synthetic library of membrane-active peptides to identify the active residues and to discover novel AMPs with high activity. Peptides with increased hydrophobicity were tested against various bacterial strains, and hits were further optimized leading to four generations of peptides, with the last also comprising fluorinated amino acid building blocks. We highlight new candidates, particularly those from generation 4, with promising antimicrobial activities against pathogens and when immobilized on titanium surfaces. Moreover, we recently generated shorter peptides by rational amino acid substitutions. New hit peptides were further modified by introducing a triazole-bridge into the backbone. We found this strategy as highly suitable to enhance antibacterial activity and hypothesize that bringing the peptide into an alpha helical structure improves its interaction with bacterial membranes. Since for some novel peptides we also detected anticancer activity, they may present a valuable and promising source for the development of future therapeutics with antibacterial activity and beyond.

References

[1] Grabeck J, Mayer J, Miltz A, Casoria M, Quagliata M, Meinberger D, Klatt AR, Wielert I, Maier B, Anna Maria Papini AM, Ines Neundorf. ACS Inf. Dis. **2024;** 10(8):2717-2727.

[2] Drexelius M, Reinhardt A, Grabeck J, Cronenberg T, Nitsche F, Huesgen PF, Maier B, Neundorf I. Multistep optimization of a cell-penetrating peptide towards its antimicrobial activity. Biochem J. **2021**;478(1):63-78.

Organizer：Ikuhiko Nakase
（Department of Biological Chemistry,
Graduate School of Science, Osaka Metropolitan University）
E-mail： i-nakase@omu.ac.jp