DATE: Day 18 Month 04 Year 2026

SUMMARY of
FY2025 RESEARCH RESULTS REPORT
For International Collaborative Research with IPR, The University of Osaka

Research Title		**Discovery of cyclic peptide-based antibiotics targeting bacterial lipid A or peptidoglycans, part I**
Applicant	**Name**	**Wei-chieh Cheng**
	Affiliation	**Genomics Research Center, Academia Sinica, Taiwan**
	Present Title	**Professor**
Research Collaborator (Host PI)		**Prof. Hironobu Hojo**

Summary

Bacterial cell wall including components in the outer membrane (toward Gram negative bacteria) and peptidoglycan (toward Gram positive, Gram negative, and mycobacteria) is a complicated and essential part for bacterial survival. Indeed, for example, targeting enzymes involved in peptidoglycan (PGN) biosynthesis is a promising strategy for antibiotic development. However, the mutation-prone nature of PGN-synthesizing enzymes and the emergence of drug-resistant strains such as MRSA pose significant challenges, prompting a shift toward targeting PGN-related biomolecules or substrates like Lipid II, naturally exhibiting fewer resistance occurring.

Lipid II has been validated as an effective target for antibiotics like vancomycin (Van) and teixobactin (Tex). The latter is a highly promising antibacterial depsipeptide consisting of a rare L-allo-enduracididine amino acid, important for the antibacterial activity of Tex. Recently, a new PGN-based label-free affinity screening (PLAS) platform with the assistance of mass spectrometry has been developed in our lab (unpublished dada, the provisional patent). It offers a robust binding affinity assay for easily screening Lipid II binders and realizing the contribution of fragments. Likewise, lipid A, an essential component in the outer membrane of Gram-negative bacteria, is a known and attractive target. Currently, several naturally occurring cyclic peptides have been reported to target Lipid A or LPS.

In this collaboration project with Prof. Hironobu Hojo, we have successfully established several assay platforms and prepared the polymyxin and teixobactin model study. Now, we are systematically studying the interactions between cyclic peptides or their analogues and Lipid II, Lipid A or their fragments. We believe this collaboration project will illustrate the essential interaction relationships, which might guide us how to tackle down the serious antibiotic drug resistance issue soon.

***Deadline: May 11, 2026**
***Please submit it to E-mail: tanpakuken-kyoten@office.osaka-u.ac.jp.**
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