화학과 세미나

김양미 교수
건국대학교 생명공학과

Structural Insights for Targeting Fatty Acid and Aryl Polyene Biosynthesis and Membrane of Carbapenem-Resistant Acinetobacter baumannii

Bacterial secondary metabolites play a critical role in the primary defense against environmental stress. While developing effective antibiotics against virulent carbapenem-resistant Acinetobacter baumannii (CRAB), we identified biosynthesis gene clusters (BGC) responsible for aryl polyenes (APEs) biosynthesis only from clinically isolated CRABs. This cluster contains two β-ketosynthases (KS) and two distinctive acyl carrier proteins (ApeE and ApeF) within a series of open reading frames. We investigated the pivotal roles of these ACPs and their interaction with KS through NMR spectroscopy and molecular dynamics simulation. ApeE features a unique structural configuration, characterized by a glycine-rich loop, an unusually long α2α3-loop, and a specialized hydrophobic surface pocket crucial for its initial benzoylation by benzoyl-ACP synthetase. Backbone dynamics analyses revealed significant conformational exchanges in these loops, promoting efficient chain flipping. Conversely, ApeF primarily functions in transferring malonyl groups by interacting with the malonyl-CoA transacylase involved in fatty acid synthesis (FAS) pathway. The dynamic interplay between ApeO-ApeC and the ACPs enhances the elongation of the rigid APE chain on ApeE via the back-transfer of APE intermediates to KS. These findings clarify the molecular mechanism of the APE BGC and its metabolic crosstalk with FAS, informing strategies to develop antibiotics that target these biosynthetic enzymes and the bacterial membrane for treatment of CRAB infections. Additionally, guided by structure–activity relationships, we design peptide antibiotics that target the CRAB membrane and modulate TLR4-mediated inflammatory signaling; these molecules represent promising candidates for addressing CRAB-associated infections.

Date : 2026년 6월 11일 (목) 오후 5시
Location : 과학관 B133호
Host : 연세대학교 화학과