

Biosynthesis and Engineering of Cyclic Peptide Antibiotics

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Abstract

The genome sequencing efforts of the first decade of the 21st century have revealed that ribosomally synthesized and post-translationally modified peptides (RiPPs) constitute a very large class of peptide natural products. These molecules are produced in all three domains of life, their biosynthetic genes are ubiquitous in the currently sequenced genomes, and their structural diversity is vast. Lanthionine-containing peptides (lanthipeptides) are examples of this growing class and many members are highly effective antimicrobial agents that display nanomolar minimal inhibitory concentrations (MICs) against pathogenic bacteria (lantibiotics). These peptides are posttranslationally modified to install multiple thioether crosslinks. During their biosynthesis, a single enzyme typically breaks 8-16 chemical bonds and forms 6-10 new bonds with high control over regio- and chemoselectivity. This presentation will discuss investigations of the mechanisms of these remarkable catalysts as well as their use for the generation of non-natural cyclic peptide libraries.