An iterative type I polyketide synthase initiates the biosynthesis of the antimycoplasma agent micacocidin.

Kage H, Kreutzer MF, Wackler B, Hoffmeister D, Nett M (2013) An iterative type I polyketide synthase initiates the biosynthesis of the antimycoplasma agent micacocidin. *Chem Biol* 20, 764-771.

Abstract

Micacocidin is a thiazoline-containing natural product from the bacterium Ralstonia solanacearum that shows significant activity against Mycoplasma pneumoniae. The presence of a pentylphenol moiety distinguishes micacocidin from the structurally related siderophore yersiniabactin, and this residue also contributes to the potent antimycoplasma effects. The biosynthesis of the pentylphenol moiety, as deduced from bioinformatic analysis and stable isotope feeding experiments, involves an iterative type I polyketide synthase (iPKS), which generates a linear tetraketide intermediate from acyl carrier protein-tethered hexanoic acid by three consecutive, decarboxylative Claisen condensations with malonyl-coenzyme A. The final conversion into 6-pentylsalicylic acid depends on a ketoreductase domain within the iPKS, as demonstrated by heterologous expression in E. coli and subsequent site-directed mutagenesis experiments. Our results unveil the early steps in micacocidin biosynthesis and illuminate a bacterial enzyme that functionally resembles fungal polyketide synthases.

Beteiligte Forschungseinheiten

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