Structural basis of head to head polyketide fusion by CorB.

Zocher G, Vilstrup J, Heine D, Hallab A, Goralski E, Hertweck C, Stahl M, Schäberle TF, Stehle T (2015) Structural basis of head to head polyketide fusion by CorB. *Chem Sci* 6(11), 6525-6536.

Details

Abstract

Corallopyronin A is a polyketide derived from the myxobacterium *Corallococcus coralloides* with potent antibiotic features. The gene cluster responsible for the biosynthesis of corallopyronin A has been described recently, and it was proposed that CorB acts as a ketosynthase to interconnect two polyketide chains in a rare head-to-head condensation reaction. We determined the structure of CorB, the interconnecting polyketide synthase, to high resolution and found that CorB displays a thiolase fold. Site-directed mutagenesis showed that the catalytic triad consisting of a cysteine, a histidine and an asparagine is crucial for catalysis, and that this triad shares similarities with the triad found in HMG-CoA synthases. We synthesized a substrate mimic to derivatize purified CorB and confirmed substrate attachment by ESI-MS. Structural analysis of the complex yielded an electron density-based model for the polyketide chain and showed that the unusually wide, T-shaped active site is able to accommodate two polyketides simultaneously. Our structural analysis provides a platform for understanding the unusual head-to-head polyketide-interconnecting reaction catalyzed by CorB.

Beteiligte Forschungseinheiten

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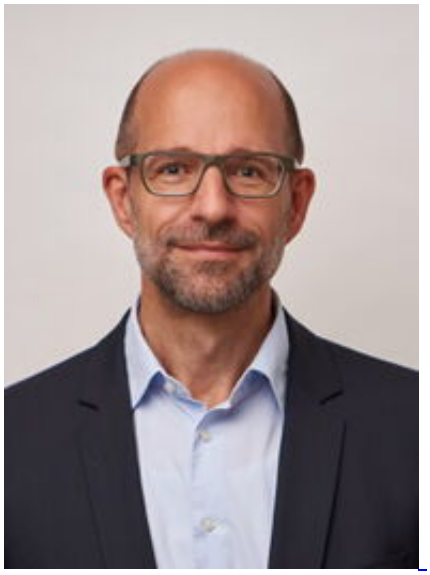

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Identifier

doi: 10.1039/C5SC02488A