Polyketide proofreading by an acyltransferase-like enzyme.

Jensen K, Niederkrüger H, Zimmermann K, Vagstad AL, Moldenhauer J, Brendel N, Frank S, Pöplau P, Kohlhaas C, Townsend CA, Oldiges M, Hertweck C, Piel J (2012) Polyketide proofreading by an acyltransferase-like enzyme. *Chem Biol* 19(3), 329-339.

Details

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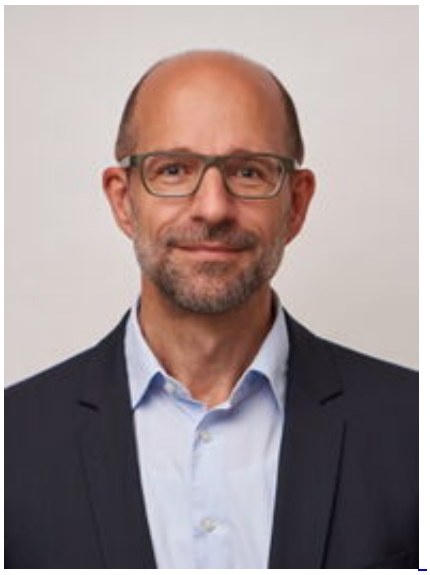
Abstract

Trans-acyltransferase polyketide synthases (trans-AT PKSs) are an important group of bacterial enzymes producing bioactive polyketides. One difference from textbook PKSs is the presence of one or more free-standing AT-like enzymes. While one homolog loads the PKS with malonyl units, the function of the second copy (AT2) was unknown. We studied the two ATs PedC and PedD involved in pederin biosynthesis in an uncultivated symbiont. PedD displayed malonyl- but not acetyltransferase activity toward various acyl carrier proteins (ACPs). In contrast, the AT2 PedC efficiently hydrolyzed acyl units bound to N-acetylcysteamine or ACP. It accepted substrates with various chain lengths and functionalizations but did not cleave malonyl-ACP. These data are consistent with the role of PedC in PKS proofreading, suggesting a similar function for other AT2 homologs and providing strategies for polyketide titer improvement and biosynthetic investigations.

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