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Full Paper

The Thioesterase Bhp is Involved in the Formation of β-Hydroxytyrosine during Balhimycin Biosynthesis in *Amycolatopsis balhimycina*

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KEYWORDS

antibiotics • balhimycin • beta-hydroxytyrosine • glycopeptides • thioesterases • vancomycin

ABSTRACT

The putative hydrolase gene *bhp* from the balhimycin biosynthetic gene cluster has been cloned and overexpressed in *Escherichia coli*. The corresponding enzyme Bhp was purified to homogeneity by nickel-chelating chromatography and characterized. Although Bhp has sequence similarities to hydrolases with "haloperoxidase"/perhydrolase activity, it did not show any enzymatic activity with standard "haloperoxidase"/perhydrolase substrates (e.g., monochlorodimedone and phenol red), nonspecific esterase substrates (such as *p*-nitrophenyl acetate, *p*-nitrophenyl phosphate and *S*-thiophenyl acetate) or the model lactonase substrate dihydrocoumarin. However, Bhp could be shown to catalyse the hydrolysis of *S*-β-hydroxytyrosyl-*N*-acetyl cysteamine thioester (β-OH-Tyr-SNAC) with 15 times the efficiency of *S*-**L**-tyrosyl-*N*-acetyl cysteamine thioester (**L**-Tyr-SNAC). This is in agreement with the suggestion that Bhp is involved in

balhimycin biosynthesis, during which it was supposed to catalyse the hydrolysis of β-OH-Tyr-*S*-PCP (PCP=peptidyl carrier protein) to free β-hydroxytyrosine (β-OH-Tyr) and strongly suggests that Bhp is a thioesterase with high substrate specificity for PCP-bound β-OH-Tyr and not a "haloperoxidase"/perhydrolase or nonspecific esterase.

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