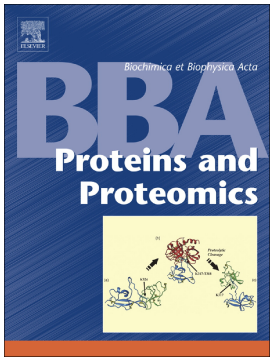

CYP106A2 – a versatile biocatalyst with high potential for biotechnological production of selectively hydroxylated steroid and terpenoid compounds

Daniela Schmitz, Simon Janocha, Flora Marta Kiss, Rita Bernhardt

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CYP106A2 – a versatile biocatalyst with high potential for biotechnological production of selectively hydroxylated steroid and terpenoid compounds

Daniela Schmitz, Simon Janocha, Flora Marta Kiss, Rita Bernhardt*

*corresponding author

Department of Biochemistry, Saarland University, Campus B2.2, 66123 Saarbruecken, Germany

E-mail: ritabern@mx.uni-saarland.de

Phone: (+49) 681-302-4241

Fax: (+49) 681-302-4739

Abstract

CYP106A2 from *Bacillus megaterium* ATCC13368, was identified in the 1970s as one of the first bacterial steroid hydroxylases responsible for the conversion of progesterone to 15β-hydroxyprogesterone. Later on it has been proven to be a potent hydroxylase of numerous 3-oxo-Δ^4 as well as 3-hydroxy-Δ^5-steroids and has recently also been characterized as a regioselective allylic bacterial diterpene hydroxylase. The main hydroxylation position of CYP106A2 is thought to be influenced by the functional groups at C3 position in the steroid core leading to a favored 15β-hydroxylation of 3-oxo-Δ^4-steroids and 7β-hydroxylation of 3-hydroxy-Δ^5-steroids. However, in some cases the hydroxylation is not strictly selective, resulting in the formation of undesired side-products. To overcome the unspecific hydroxylations or, on the contrary, to gain more of these products in case they are of industrial interest, rational protein design and directed evolution have been successfully performed to shift the stereoselectivity of hydroxylation by CYP106A2. The subsequently obtained hydroxylated steroid and terpene derivatives are especially useful as drug metabolites and drug precursors for the pharmaceutical industry, due to their diverse biological properties and hardship of their chemical synthesis. As a soluble prokaryotic P450 with broad substrate spectrum and hydroxylating capacity, CYP106A2 is an outstanding candidate to establish bioconversion processes. It has been expressed with respectable yields in *Escherichia coli* and *Bacillus megaterium* and was applied for the preparative hydroxylation of several steroids and terpenes. Recently, the application of the enzyme was assessed under process conditions as well, depicting a successfully optimized process development and getting us closer to industrial scale process requirements and a future large scale application.