Structural Studies of Prenyltransferases and Industrial Enzymes

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Abstract

We have obtained several crystal structures of prenyltransferases1,3 for antibiotic drug design and industrial enzymes (e.g. xylanase, phytase and mannanase)4-8 for enzyme engineering purpose within these years. For example, we have solved the structure of a bacterial diterpene synthase, tuberculosinol/iso-tuberculosinol synthase (Rv3378c) from Mycobacterium tuberculosis, a virulent factor which is considered as a novel target for anti-tuberculosis therapies. This phosphatase adopts the same fold as found in the Z- or cis-prenyltransferases. We also obtained complex structures containing the tuberculosinyl diphosphate substrate and bisphosphonate inhibitors. These structures together with the results of site-directed mutagenesis suggest an unusual mechanism of action involving two Tyr residues. Given the similarity in local and global structure between Rv3378c and the M. tuberculosis cis-decaprenyl diphosphate synthase (DPPS; Rv2361c), the possibility exists for the development of inhibitors that target not only virulence but also cell wall biosynthesis. Some other cases for industrial enzyme engineering will be presented here, too.

Keywords – prenyltransferase, industrial enzymes, xylanase, crystal structure

References

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