Poster Presentation

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Structural analysis of E. coli 6-carboxytetrahydropterin synthase

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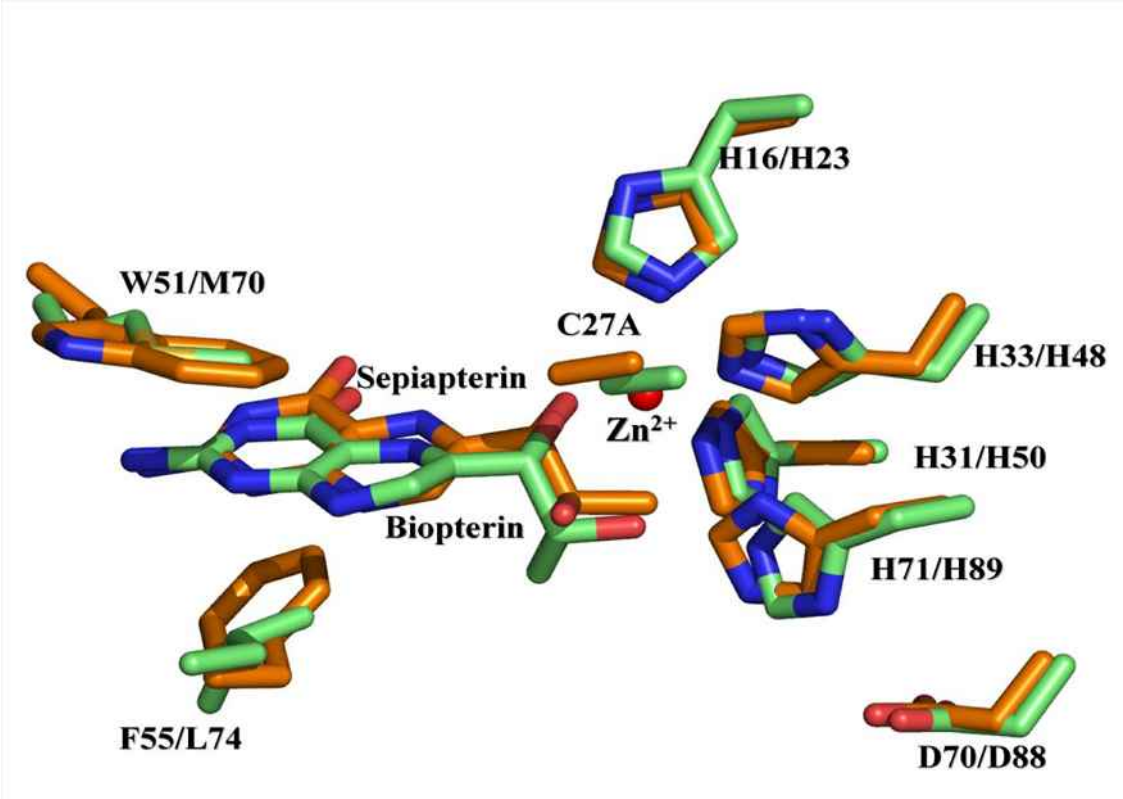
The Escherichia coli 6-carboxytetrahydropterin synthase (eCTPS), a homolog of 6-pyruvoyl tetrahydropterin synthase (PTPS), possesses a much stronger catalytic activity to cleave the side chain of sepiapterin in vitro rather than the genuine PTPS activity and catalyzes the conversion of dihydroneopterin triphosphate to 6-carboxy-5,6,7,8-tetrahydropterin in vivo. We have determined crystal structures of a wild type apo-eCTPS and a Cys27Ala mutant eCTPS complexed with sepiapterin up to 2.3 and 2.5 Å, respectively. The structures are highly conserved at the active site and the Zn2+ binding site. However, comparison of the eCTPS structures with those of mammalian PTPS homologs revealed that two specific residues Trp51 and Phe55, not existing in the mammalian PTPS, kept the substrate bound by stacking it with their side chains. Replacements of these two residues by site-directed mutagenesis to the residues, Met and Leu, existing only in mammalian PTPS, converted the eCTPS to have the mammalian PTPS activity. Our studies confirm that these two aromatic residues in eCTPS play an essential role in stabilizing the substrate and for the specific enzyme activity different from the original PTPS activity. These aromatic residues Trp51 and Phe55 are a key signature of bacterial PTPS enzymes that distinguish them from mammalian PTPS homologs.



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