Structure-based Functional Analysis of Prenyltransferases: *Trans*-type OPPs from *T. maritima* and *Cis*-type UPPs from *E. Coli*

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Isoprenoids are an extensive group of natural products with diverse structures consisting of various numbers of five-carbon isopentenyl pyrophosphate (IPP) units. The enzymes responsible for the synthesis of linear isoprenyl pyrophosphates can be classified as *cis*- and *trans*-isoprenyl pyrophosphate synthase (IPPs) according to the stereochemical outcome of their products. The C_{40} product of octaprenyl pyrophosphate synthase (OPPs) constitutes the side chain of ubiquinone in *Thermotoga maritima*. Among the *cis*-polyprenyl pyrophosphates, the C_{55} product of the bacterial undecaprenyl pyrophosphate synthase (UPPs) serves as a lipid carrier in cell wall peptidoglycan biosynthesis.

OPPs is composed entirely of α-helices joined by connecting loops and is arranged with 9 core helices around a large central cavity. An elongated hydrophobic tunnel between D and F α-helices contains two DDxxD motifs on the top for substrate binding and is occupied at the bottom with one large residue F132. From the biochemical studies, F132 is the key residue for determining the product chain length.

The structures of *Escherichia coli* UPPs were determined previously as an apo-enzyme, in complex with Mg^{2+}/sulfate/Triton, and with bound FPP. In further search of its catalytic mechanism, the wild-type UPPs and the Asp26Ala mutant are crystallized in a new trigonal unit cell with Mg^{2+}/IPP/FsPP (farnesyl thiopyrophosphate, an FPP analogue) bound to the active site. Our results here improve the understanding of the prenyltransferases reaction significantly.

Keywords: prenyltransferase, crystal structure, metal ion