Poster Presentation

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Crystal structure of archaeal phosphopantothenate synthetase

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Bacteria/eukaryotes share a common pathway for coenzyme A biosynthesis which involves two enzymes, pantothenate synthetase and pantothenate kinase, to convert pantoate to 4'-phosphopantothenate. These two enzymes are absent in almost all archaea. Recently, it was reported that two novel enzymes, pantoate kinase (PoK) and phosphopantothenate synthetase (PPS), are responsible for this conversion in archaea[1]. In archaea, pantoate is phosphorylated by PoK to produce 4-phosphopantoate (PPo), and then condensation of PPo and β-alanine is catalyzed by PPS, generating 4'-phosphopantothenate. Here, we report the crystal structure of PPS from the hyperthermophilic archaeon, Thermococcus kodakarensis and its complexes with ATP, and ATP and 4-phosphopantoate (PPo). PPS forms an asymmetric homodimer, in which two monomers composing a dimer, deviated from the exact 2-fold symmetry, displaying 4°-13° distortion. Two active sites in PPS dimer are located near the rotation axis. Due to the asymmetricity of PPS dimer molecule, two active sites in PPS dimer are not equivalent. The structural features are consistent with the mutagenesis data and the results of biochemical experiments previously reported. Based on the structures of PPS, PPS/ATP complex, and PPS/ATP/PPo complex, we discuss the catalytic mechanism by which PPS produces phosphopantoyl adenylate (PPA), which is thought to be a reaction intermediate.

[1] *Y. Yokooji, et al., J. Biol. Chem. 2009, 284, 28137-28145*

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