Study of Substrate-Complexed Formylglycinamide Ribonucleotide Amidotransferase

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Formylglycinamide ribonucleotide amidotransferase, also known as PurL, catalyzes the fourth step of the purine biosynthetic pathway. PurL catalyzes the ATP-dependent synthesis of formylglycinamidine ribonucleotide from formylglycinamide ribonucleotide and glutamine [1]. Two types of PurLs have been detected. The first type, found in eukaryotes and Gram-negative bacteria, consists of a single polypeptide chain (140 kDa) and is designated large PurL. The second type, small PurL, (80 kDa) is found in Gram-positive and archea bacteria and requires two additional gene products (PurS and PurQ) for activity.

The proposed reaction mechanism of PurL remains mostly uncharacterized [2]. PurL is also a member of a protein superfamily that contains a novel ATP-binding domain [3]. To characterize the active site of the enzyme, structures of several complexes of small PurL from *Thermotoga maritima* were determined. These complexes show a conformational change in the protein not seen in the native structures [4]. They also provide insight into the positioning of the substrates in the active site and the identification of catalytically important residues, thereby elucidating aspects of the mechanism, as well as the signature sequence of the novel ATP-binding domain.

[1] Buchanan, Hartman, *Adv. Enzymol. Relat. Areas Mol. Biol.,* 1959, **21**, 199-261. [2] Schrimsher *et al., Biochemistry,* 1986, **25**, 4366. [3] Li *et al*., *Structure,* 1999, **7**, 1155. [4] Anand *et al.*, *Biochemistry,* 2004, **43**, 10328.

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