Stucture of *S. typhimurium* Formylglycinamide Ribonucleotide amidotransferase

Ruchi Anand^a, Aaron A. Hoskins^b, JoAnne Stubbe^b, Steven E. Ealick^a, ^aDept. of Chemistry and Chemical Biology, Cornell Univ., Ithaca, NY 14853. ^bDept. of Chemistry and Biology, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA. E-mail: ra62@cornell.edu

Formylglycinamide ribonucleotide amidotransferase (FGAR-AT) catalyzes the ATP-dependent conversion of formylglycinamide ribonucleotide, and glutamine to formylglycinamidine ribonucleotide (FGAM) and glutamate in the purine biosynthetic pathway. In eukaryotes and Gram negative bacteria, FGAR-AT is encoded by the purL gene as a multidomain protein. In Gram positive bacteria and archaebacteria FGAR-AT is a complex of three proteins: PurS, PurL and PurQ. We have determined the structure of FGAR-AT from Salmonella. typhimurium at 1.9 Å resolution. The structure reveals four domains: an N-terminal domain structurally homologous to a PurS dimer, a linker region, an FGAM synthetase domain homologous to an aminoimidazole ribonucleotide synthetase dimer, and a triad glutaminase domain. A structural ADP molecule was found bound. A glutamylthioester intermediate was found in the glutaminase domain at C1135. The N-terminal domain is hypothesized to form the channel through which ammonia passes from the glutaminase domain to the FGAM synthetase domain.

Keywords: formylglycinamide ribonucleotide amidotransferase, ATP-grasp motif, protein evolution