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Crystal Structure of PurO from *Methanobacterium thermoautotrophicum*. You-Na Kang^a, Robert H. White^b, Steven E. Ealick^{a*}, ^aDept. of Chemistry and Chemical Biology, Cornell Univ., Ithaca, NY, 14853, USA. ^bDept. of Biochemistry, Virginia Tech, Blacksburg, VA 24061, USA.

Inosine 5'-monophosphate cyclohydrolase (IMPCH) catalyzes the cyclization of 5-formaminoimidazole-4-carboxamide ribonucleotide (FAICAR) to IMP in the final step of *de novo* purine biosynthesis. Two major types of this enzyme have been discovered to date; PurH in Bacteria and Eukarya, and PurO in Archaea. The structure of MTH1020 from *Methanobacterium thermoautotrophicum* was previously solved without functional annotation (PDB 1KUU) but shows high sequence similarity to the archaeal IMPCH (PurO). We determined the crystal structures of MTH1020 in complex with either IMP or AICAR. Based on the sequence analysis, structures, and biochemical data, MTH1020 is confirmed as an archaeal IMPCH, thus designated as MthPurO. MthPurO has α - β - β - α core structure showing an N-terminal nucleophile (NTN) hydrolase fold. The active site is located at the deep pocket on the surface and contains residues strictly conserved within PurOs. Biochemical studies show that R30 and E104 act as critical residues for catalysis. Comparisons of the two types of IMPCH, PurO and PurH, revealed that there are no similarities in sequence, structure, or the active site architecture, suggesting they are evolutionarily not related with each other.