Structure of the dimeric form of CTP synthase from Sulfolobus solfataricus

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CTP synthase catalyzes the last committed step in de novo pyrimidine-nucleotide biosynthesis. Active CTP synthase is a tetrameric enzyme composed of a dimer of dimers. The tetramer is favored in the presence of the substrate nucleotides ATP and UTP; when saturated with nucleotide, the tetramer completely dominates the oligomeric state of the enzyme. Furthermore, phosphorylation has been shown to regulate the oligomeric states of the enzymes from yeast and human. The crystal structure of a dimeric form of CTP synthase from Sulfolobus solfataricus has been determined at 2.5 Å resolution. A comparison of the dimeric interface with the intermolecular interfaces in the tetrameric structures of Thermus thermophilus CTP synthase and Escherichia coli CTP synthase shows that the dimeric interfaces are almost identical in the three systems. Residues that are involved in the tetramerization of S. solfataricus CTP synthase according to a structural alignment with the E. coli enzyme all have large thermal parameters in the dimeric form. Furthermore, they are seen to undergo substantial movement upon tetramerization.

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