Poster Presentation

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Structural insights into archeal-type SAHase from Thermotoga maritima

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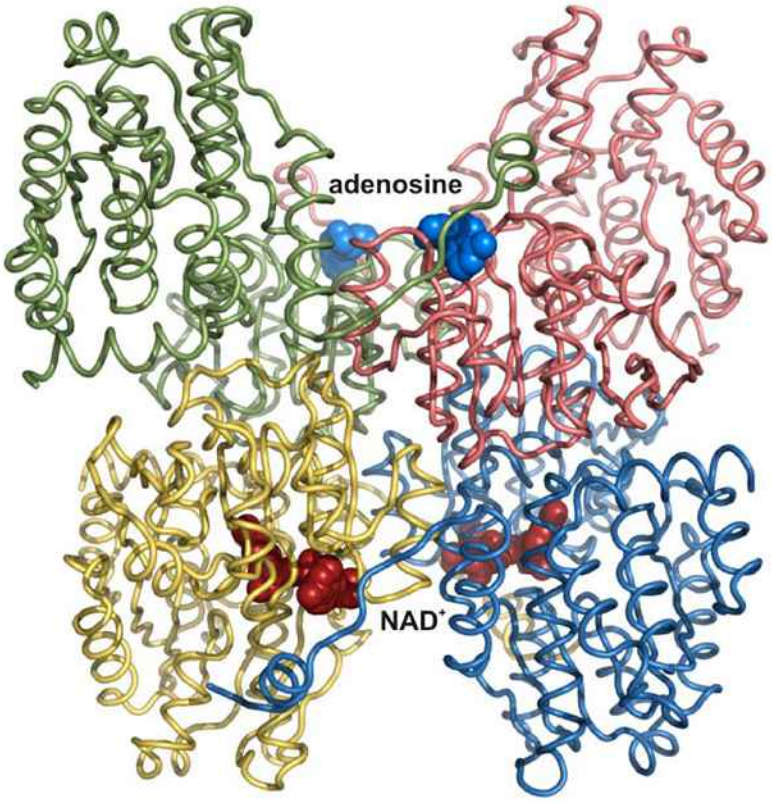
S-adenosyl-L-homocysteine hydrolase (SAHase) catalyzes the reversible breakdown of S-adenosyl-L-homocysteine (SAH) to adenosine (Ado) and homocysteine (Hcy). SAH is formed in methylation reactions that utilize S-adenosyl-L-methionine (SAM) as a methyl donor. By removing the SAH byproduct, SAHase serves as a regulator of SAM-dependent biological methylation reactions.[1] Thermotoga maritima is a thermophilic bacterium, but its genome carries a number of archeal genes as a consequence of massive gene transfers related to adaptation to the high-temperature environment.[2] sahh is one of many genes of archeal origin found in T. maritima. Crystals of recombinant SAHase from T. maritima in complex with adenosine were obtained by the hanging drop vapor diffusion method. The crystals are monoclinic, space group C2, with a = 120.4, b =105.5, c = 85.5 Å, β=108.8° and diffract X-rays to 1.80 Å. The crystal contains two protein molecules in the asymmetric unit. The enzyme is active as a homotetramer with a molecular weight of about 180 kDa. The crystal contains two protomers in the asymmetric unit, which exist in both, open and closed conformations. The complete tetrameric enzyme molecule is generated in the crystal lattice through the operation of the crystallographic twofold axis. In contrast to other SAHase structures, only two subunits contain a tightly bound NAD+ cofactor, however their closed conformations exclude the possibility of substrate binding. The other two subunits are in open conformation and bind adenosine molecule in the cofactor binding site. Herein, lack of the cofactor molecule excludes the possibility of an enzymatic reaction. In contrast to other SAHases, the C-terminal domain from adjacent protomer does not participate in the binding of the NAD+. Results presented here indicate a different structural organization of archeal type SAHases.

[1] *P.K. Chiang, Pharmacology & Therapeutics, 1998, 77, 115-134,* ***[2]*** *K.E. Nelson et al. Nature, 1999, 399, 323-329*



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