Crystal Structure of an Archaeal Dihydroorotase

Jacqueline Vitali[1], Jay Nix[2], Haley Newman[3], Aditya Singh[4], Michael Colaneri[5]

[1]Cleveland State University [2]Molecular Biology Consortium, [3]Cleveland State University, [4]Cleveland State University, [5]SUNY Old Westbury

jackie.vitali@gmail.com

Dihydroorotase (DHOase) is a zinc metalloenzyme that functions in the pyrimidine nucleotide biosynthesis. In this paper we report the x-ray structural analysis of the DHOase from the archaeon Methanococcus jannaschii. The crystals are P3221, a = b = 111.3 Å and c = 101.2 Å. The structure was solved by molecular replacement and final Rwork = 0.179 and Rfree = 0.213 at a resolution 1.9 Å (limit for CC1/2 > 0.30).

This is the first archaeal DHOase studied by X-ray diffraction and has similarities and differences from the other known DHOases. This study showed that archaeal DHOases form a separate subtype of long DHOases and are most closely related to bacterial type I. However, they also share common features with the other subclasses. In particular, they have a long flexible loop similar to bacterial type II, III and human CAD and differ from type I that have a short flexible loop. It has two Zn ions in the active site in contrast to some type I that have only one Zn. Contrary to our expectations (Vitali et al, 2017) the two Zn ions are bridged by a carboxylated lysine similar to bacterial type II, III and human CAD and differ from type I that that use an aspartate invariant in this subclass. The active site is shown in Figure 1. The M. jannaschii DHOase is a monomer in contrast to most DHOases that are dimers.

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References

Vitali, J. Singh, A.K. and Colaneri, M.J. (2017) The Protein Journal 36, 361-373.

‡Present address: Department of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77555, USA, adsingh@utmb.edu

Fig. 1. The active site of M. jannaschii DHOase superimposed on a 2mFo-DFc map contoured at 1.7σ.

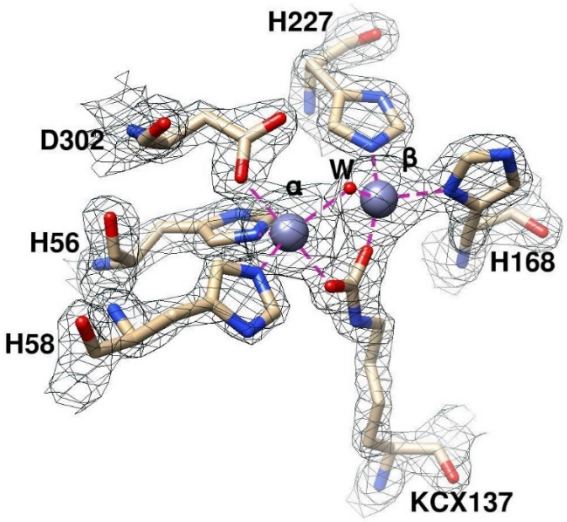

Figure 1