

Crystal Structure of Human HMG-CoA lyase

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3-Hydroxy-3-methylglutaryl-CoA (HMG-CoA) lyase (EC 4.1.3.4) catalyzes the divalent cation dependent cleavage of HMG-CoA to form acetyl-CoA and acetoacetate. This reaction is a key step in ketogenesis and the final step in leucine catabolism. Human HMG-CoA lyase has been previously cloned and overexpressed in *Escherichia Coli*. Crystals of the lyase containing a competitive inhibitor have been obtained with PEG 8K using sitting-drop vapor diffusion method. The crystals belong to the monoclinic space group C2, with unit cell parameters $a=197.0\text{\AA}$, $b=116.1\text{\AA}$, $c=86.8\text{\AA}$, and $\beta=122.5^\circ$. The native data set has been collected which is 99.8 % complete to 2.1\AA . The calculated V_m is $2.34\text{\AA}^3\text{Da}^{-1}$, with a solvent content of 43.2%, which corresponds to three dimers of the enzyme in the asymmetric unit (each dimer molecular weight, 65 kDa). One heavy atom derivative (Hg) has been obtained and the search for additional derivatives is in progress.

Keywords: HMG-CoA lyase structure, fatty acid metabolism, ketogenesis