

## Crystal Structure Studies of NADP<sup>+</sup> Dependent Isocitrate Dehydrogenase From *Thermus Thermophilus* Exhibiting A Novel Terminal Domain

### Abstract

NADP(+) dependent isocitrate dehydrogenase (IDH) is an enzyme catalyzing oxidative decarboxylation of isocitrate into oxalosuccinate (intermediate) and finally the product  $\alpha$ -ketoglutarate. The crystal structure of *Thermus thermophilus* isocitrate dehydrogenase (TtIDH) ternary complex with citrate and cofactor NADP(+) was determined using X-ray diffraction method to a resolution of 1.80 Å. The overall fold of this protein was resolved into large domain, small domain and a clasp domain. The monomeric structure reveals a novel terminal domain involved in dimerization, very unique and novel domain when compared to other IDH's. And, small domain and clasp domain showing significant differences when compared to other IDH's of the same sub-family. The structure of TtIDH reveals the absence of helix at the clasp domain, which is mainly involved in oligomerization in other IDH's. Also, helices/beta sheets are absent in the small domain, when compared to other IDH's of the same sub family. The overall TtIDH structure exhibits closed conformation with catalytic triad residues, Tyr144-Asp248-Lys191 are conserved. Oligomerization of the protein is quantized using interface area and subunit-subunit interactions between protomers. Overall, the TtIDH structure with novel terminal domain may be categorized as a first structure of subfamily of type IV.