Dual Substrate Recognition of Acetylornithine Aminotransferase

Ikuko Miyahara[a,b] , Mitsuyoshi Matsumura[a,b], Masaru Goto[a,b], Rie Omi[a,b], Ken Hirotsu[a,b], Hiroyuki Mizuguchi[c], Hideyuki Hayashi[c], Hiroyuki Kagamiyama[c], *[a]Graduate School of Science, Osaka City University. [b]Harima Institute/SPring-8, The Institute of Physical and Chemical Resaech(RIKEN) Hyogo, Japan. [c]Osaka Medical School, Japan.* E-mail: miyahara@sci. osaka-cu.ac.jp

Acetylornithine aminotransferase (AcOAT) is a pyridoxal 5'-phosphate(PLP)-dependent enzyme. The enzyme catalyses the fourth reaction on the arginine biosynthetic pathway, AcoAT reversibly catalyze the transamination reaction in which the α-amino group of N-acetyl-L-ornithine is transferred to N-acetyl-L-glutamate ν-semialdehyde to produce 2-oxoglutarate and L-glutamate. AcOAT is distinguished from other typical aminotransferases in that the δ-amino group of acetylornithine forms a Schiff base with the cofactor PLP, although glutamate forms a Schiff base between its α-amino group and the cofactor. This implies that the α-carboxylate and N-acetyl group of acetylornithine and the γ-carboxylate of glutamine are on the phosphate side of the cofactor.

The crystal structure of native AcOAT from *Thermus thermophilus* HB8 and its complexes N-(5'- phosphopyrydoxyl) -N-acetylornithine and N-(5'-phosphopyrydoxyl)- L-glutamate have been solved and refined to *R*-factors 19.5, 22.6, and 18.1% at 1.35, 2.05, and 2.25Å. No significant change in the overall structure in AcOAT was observed on binding of the ligands. The active site residues do not show any significant changes in side-chain conformations except for Phe140 and Glu197.

Keywords: x-ray crystallography of biological macromolecules, substrate binding, aminotransferases