**The *E. coli* PDHc E1 Component Complex with a Reaction Intermediate Analogue**

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The thiamin diphosphate (ThDP) dependent E1 component of the pyruvate dehydrogenase multienzyme complex (PDHc) catalyzes the decarboxylation of pyruvate and subsequent acetyl transfer to a lipoyl-lysine residue from the E2 component. Biochemical studies of the H407A E1 variant clearly indicated the importance of this residue to the overall reaction of the multienzyme complex. The specific activity of this variant is only 0.15% with respect to the native enzyme. In the native E1 crystal structure the loop region containing the residue H407 was unobserved due to disorder. Superposition of the E1 component and yeast transketolase (TK) structures indicates a general structural similarity and it is clear that if this region becomes ordered as in TK, the H407 residue can come very close to the ThDP and can interact with substrate or reaction intermediates. The crystal structures of the native and H407A variant of *E. coli* PDHc E1, both with a reaction intermediate analogue in its active site, have been determined to a resolution of 2.1 and 1.85Å respectively. Comparison of these two structures clearly indicates that the presence of the substrate analogue in the active site induces conformational changes in its vicinity.

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