Conformational Motions of a Tetraglycine Active Site Loop in Formyl-CoA Transferase

Nigel G. J. Richards, Sang-Bae Lee & Cory G. Toyota

Department of Chemistry, University of Florida, Gainesville, FL 32606

The formyl-CoA transferase (FRC) from *Oxalobacter formigenes* catalyzes the synthesis of oxalyl-CoA from oxalate and formyl-CoA [3]. The structures of several intermediates in the mechanism of the acyl transfer reaction have been characterized using X-ray crystallography [1,2]. These studies have revealed large-scale changes in the conformation of both bound intermediates and a tetraglycine active site loop that take place during catalysis (Figure). In this poster we will outline the use of normal-mode analysis (NMA) methods [4] to evaluate the extent to which the conformational motions of the tetraglycine loop are a consequence of intrinsic protein dynamics or substrate binding. We find that coenzyme A binding does not significantly influence the motional properties of individual residues in the tetraglycine loop, suggesting that intrinsic protein motions are exploited in substrate binding. In addition, these computational findings will be correlated with the steady-state kinetic properties exhibited by a series of FRC mutants in which glycines in the loop are systematically replaced by alanine residues. We thank NIH/NIDDK for financial support (DK61666).

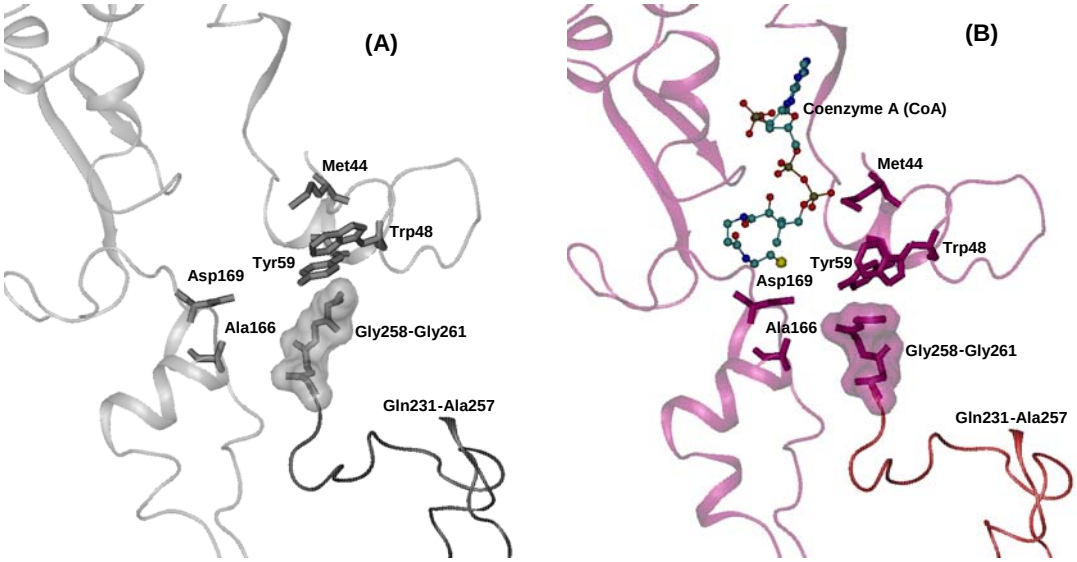

Figure. Structural representations of key active site residues and the tetraglycine loop (Gly258-Gly261) in (A) the apoenzyme of FRC, and (B) the FRC/CoA complex. Coenzyme A is drawn as a "ball and stick" model. Crystallographic water molecules are not shown for clarity.

References

1. Berthold, C., Toyota, C. G., Richards, N. G. J., & Lindqvist, Y. (2008) *J. Biol. Chem.* **282**, 6519-6529.
2. Jonsson, S., Ricagno, S., Lindqvist, Y., & Richards, N. G. J. (2004) *J. Biol. Chem.* **279**, 36003-36012.
3. Svedruzic, D., Jonsson, S., Toyota, C. G., Reinhardt, L. A., Ricagno, S., Lindqvist, Y., & Richards, N. G. J. (2005) *Arch. Biochem. Biophys.* **433**, 176-192.
4. Tama, F., & Brooks, C. L., III (2006) *Annu. Rev. Biophys. Biomol. Struct.* **35**, 115-133.