Kinetic and Mechanistic Characterization of the Formyl-CoA Transferase from *Oxalobacter formigenes*.

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*Oxalobacter formigenes* is an obligate anaerobe that colonizes the human gastro-intestinal tract, and which employs oxalate breakdown to generate ATP in a novel process involving the interplay of two coupled enzymes and a membrane-bound oxalate:formate antiporter. Formyl-CoA transferase is a critical enzyme in oxalate-dependent ATP synthesis, and is the first Class III CoA-transferase for which a high-resolution, three-dimensional structure has been determined [1]. We now report the first detailed kinetic characterizations of recombinant, wild type formyl-CoA transferase, and a number of site-specific mutants, which suggest that catalysis proceeds via a series of anhydride intermediates. Further evidence for this mechanistic proposal is provided by the X-ray crystallographic observation of an acylenzyme intermediate [2] that is formed when formyl-CoA transferase is incubated with oxalyl-CoA. The catalytic mechanism of formyl-CoA transferase is therefore established, and is almost certainly employed by all other members of the Class III CoA-transferase family.

Figure 1: View showing the interactions of the oxalyl-aspartyl anhydride with residues in the FRC dimer. The letter designation (A or B) in the numbering scheme indicates the FRC monomer in which the residue is located.

References