

Insight into Structure and Functions of of Acyl CoA Binding Protein of Leishmania major

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Abstract : Acyl-CoA binding protein (ACBP) is a housekeeping protein which functions as an intracellular carrier of acyl-CoA esters. Given the fact that the amastigote stage (blood stage) of Leishmania depends largely on fatty acids as the energy source, of which a large part is derived from its host, these proteins might have an important role in its survival. In Leishmania major, genome sequencing suggests the presence of six ACBPs, whose function remains largely unknown. For functional and structural characterization, one of the ACBP genes was cloned, and the protein was expressed and purified heterologously. Acyl-CoA ester binding and stoichiometry were analyzed by isothermal titration calorimetry and Dynamic light scattering. Our results shed light on high affinity of ACBP towards longer acyl-CoA esters, such as myristoyl-CoA to arachidonoyl-CoA with single binding site. To understand the binding mechanism & dynamics, Nuclear magnetic resonance assignments of this protein are being done. The protein's crystal structure was determined at 1.5Å resolution and revealed a classical topology for ACBP, containing four alpha-helical bundles. In the binding pocket, the loop between the first and the second helix (16 - 26AA) is four residues longer from other extensively studied ACBPs (PfACBP) and it curls upwards towards the pantothenate moiety of CoA to provide a large tunnel space for long acyl chain insertion.

Keywords : acyl-coa binding protein (ACBP), acyl-coa esters, crystal structure, isothermal titration, calorimetry, Leishmania

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