TOWARDS THE STRUCTURE DETERMINATION OF THE LMM BINDING DOMAIN OF MYOSIN BINDING PROTEIN C (MyBPC) BY NMR

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MyBPC comprises ~2% of myofibrillar protein being present in the A-bands of all vertebrate striated muscles. Mutations in the cardiac MyBPC gene (*MYBPC3*) are implicated in familial hypertrophic cardiomyopathy (FHC), with an incidence of 20-45%. MyBPC is constituted of a unique polypeptide chain composed by 10 (skeletal) or 11 (cardiac) globular domains homologous to immunoglobulin (Ig) and fibronectin type III (FnIII) motifs, and has both structural and regulatory roles. The N-terminal portion is involved in the regulation of muscle contraction in a Ca^{2+} dependent manner, while the C-terminal has a structural role. In the last decade, there were several attempts to determine the structure of the myosin-binding domain (C10) of MyBPC. Protein aggregation and low solubility prevented structural solution. In the present work we show partial resonance assignments of C10 in solution. HSQC spectrum indicates that there is equilibrium between a major well-folded conformational state and a minor unfolded state. At this condition we acquired triple resonance spectra, such as CBCANH, CBCACONH, HNCA, HNCOCA, which enabled us to get chemical shifts values of HN, Hα, Cα and Cβ. The data is compatible with the expected secondary structure, validating the homology model. To obtain full assignment and structure we will need to stabilize the protein in a unique conformation.