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Folding dynamics of a family of beta-sheet proteins[1]

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Fatty acid binding proteins (FABP) consist of ten anti-parallel beta strands and two small alpha helices. The beta strands are arranged into two nearly orthogonal five-strand beta sheets that surround the interior cavity, which binds unsaturated long-chain fatty acids. In the brain isoform (BFABP), these are very important for the development of the central nervous system and neuron differentiation. Furthermore, BFABP is implicated in the pathogenesis of a variety of human diseases including cancer and neuronal degenerative disorders. In this work, site-directed spin labeling combined with EPR techniques have been used to study the folding mechanism of BFABP. In the first series of studies, we labeled the two Cys residues at position 5 and 80 in the wild type protein with an EPR spin marker; in addition, two singly labeled mutants at positions 5 and 80 in the C80A and C5A mutants, respectively, were also produced and used as controls. The changes in the distances between the two residues were examined by a pulsed EPR method, DEER (Double Electron Electron Resonance), as a function of guanidinium hydrochloride concentration. The results were compared with those from CW EPR, circular dichroism and fluorescence measurements, which provide the information regarding sidechain mobility, secondary structure and tertiary structure, respectively. The results will be discussed in the context of the folding mechanism of the family of fatty acid binding proteins.

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