PRELIMINARY CHARACTERIZATION OF THE UNFOLDED STATE OF THE FBP11WW1 DOMAIN.

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The formin binding protein 11 (FBP11) is a protein with a modular architecture, including two WW domains, protein-protein interaction modules that recognize proline rich motifs. Due to its WW domains FBP11 is able to bind to the proteins huntingtin and MeCP2 and was implicated in Huntington`s disease and Rett syndrome respectively. The WW domain is folded as a three-stranded antiparallel ß-sheet structure and is the smallest natural ß-protein known (ca. of 40 aminoacid residues), thus is often used as prototype for understanding the mechanisms of the ß-folding. In the present work we have used CD, NMR and fluorescence spectroscopies to characterize the unfolded state of the first WW domain of FBP11. Signals observed in the near-UV region of the CD spectrum as well as the maximum wavelength of fluorescence emission and the signal dispersion observed in the NMR spectrum evidence the presence of residual tertiary structure involving a cluster of aromatic residues in the presence of 8M Urea or 5M GdnHCl. This result demonstrate the importance of long-range hydrophobic interactions, as the first events in the structure nucleation of FBP11WW1 domain. Further NMR techniques are being applied to better elucidate the structure and dynamics of the FBP11WW1 domain in the presence of chaotropic agents.