HUMAN FEZ1 HAS FEATURES OF A NATIVE UNFOLDED PROTEIN AND ITS INTERACTION WITH OTHER PROTEINS IS REGULATED BY PHOSPHORYLATION THROUGH PROTEIN KINASE C

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The Fasciculation and Elongation protein Zeta 1 (FEZ1) is the mammalian orthologue of the *Caenorhabditis elegans* protein UNC-76, necessary for axon growth in the nematodes neurons. FEZ1 interacts among others with Protein Kinase C (PKC) and regulatory proteins involved in microtubule associated transport or transcriptional regulation. Here, we performed low-resolution structural analyses of both the whole protein FEZ1 as well as its N- and C-terminal fragments, using analytical gel-filtration, circular dichroism and fluorescence spectroscopy and Small Angle X-Ray Scattering. The results confirmed previous pull-down and yeast two-hybrid data that had shown FEZ1 dimerization and suggest further that the protein may be part of the growing class of native unfolded proteins. Furthermore, we performed *in vitro* phosphorylation assays of FEZ1 employing three classes of PKCs and different PKC inhibitors. Interaction tests between phosphorylated FEZ1 and several selected interacting proteins demonstrated that the interaction with some of these proteins is abrogated upon phosphorylation of FEZ1. FEZ1 phosphorylation occurs along the whole protein sequence, but is especially clustered in its C-terminal region. Although phosphorylation did not cause any significant structural changes, as detected by spectroscopic methods, it clearly affects interactions with other proteins and possibly the cellular localization of FEZ1. Supported by: FAPESP, CNPq and the LNLS.