Disulfide driven folding for a conditionally disordered protein

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Conditionally disordered proteins are either ordered or disordered depending on the environmental context. The substrates of the mitochondrial intermembrane space (IMS) oxidoreductase Mia40 are synthesized on cytosolic ribosomes and diffuse as intrinsically disordered proteins to the IMS, where they fold into their functional conformations; behaving thus as conditionally disordered proteins. It is not clear how the sequences of these polypeptides encode at the same time for their ability to adopt a folded structure and to remain unfolded. Here we characterize the disorder-to-order transition of a Mia40 substrate, the human small copper chaperone Cox17. Using an integrated real-time approach, including chromatography, fluorescence, CD, FTIR, SAXS, NMR, and MS analysis, we demonstrate that in this mitochondrial protein, the conformational switch between disordered and folded states is controlled by the formation of a single disulfide bond, both in the presence and in the absence of Mia40. We provide molecular details on how the folding of a conditionally disordered protein is tightly regulated in time and space, in such a way that the same sequence is competent for protein translocation and activity [1].

References

[1] - H. Fraga, J. Pujols, M. Gil-Garcia, A. Roque, G. Bernardo-Seisdedos, C. Santambrogio, J.J. Bech-Serra, F. Canals, P. Bernadó, R. Grandori, O. Millet, S. Ventura, Disulfide driven folding for a conditionally disordered protein. Scientific Reports. 7(1):16994.