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FOLDING MECHANISM OF E-PROTEINS TRANSACTIVATION DOMAIN AFTER ITS INTERACTION WITH KIX DOMAIN OF CBP TRANSCRIPTION COACTIVATOR

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Intrinsically disordered proteins, incapable to form tight ordered structure due to self-organization, could form compact structure with interaction with partners, if free energy of occurring complex is less than free energy of protein and partner before interaction. In particular, intrinsically disordered transactivation domain of E-family proteins undergoes a conformational transition coil-helix after its interaction in with the KIX domain of the CBP transcription coactivator. In this paper, the conformational changes of TAD and its L20P mutant form were characterized in various solvents. This allowed us to establish a folding mechanism of this domain. It was shown that macromolecular crowding conditions, change in pH ionic strength of the solution, and the presence of osmolytes (sarcosine, taurine) does not cause compaction of the TAD structure. At the same time, a significant ordering of the TAD structure was detected in solutions of TMAO and alcohols. These data allowed us to conclude that the TAD ordering is due to its dehydration. Accordingly, we assumed that TAD folding after its binding to binding to KIX is also due to the displacement of water from the TAD environment. To test this hypothesis, the structure of the L20P TAD mutant form was studied in different solvents. It is known that this mutation weakens the interaction of E-family proteins with KIX. It was shown that the L20P structure does not practically change in solutions of alcohols. These data confirmed our assumption about the ordering of TAD after its interacting with KIX due to the dehydration of the TAD.

Key words: intrinsically disordered proteins, self-organization, compact structure, dehydrotation