Structural and stability studies of hsp90 co-chaperone p23 suggested that the C-terminal stabilizes the ß-sheet folded domain.

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p23 acts as a co-chaperone for Hsp90 by regulating Hsp90 ATPase cycle and substrate release. p23 is formed by an ß-sheet folded domain, which is responsible for interacting with Hsp90 dimer, and a charged C-terminal region with unclear function which seem to be unstructured or flexible. We present results on the use of spectroscopic and hydrodynamic techniques to study p23 and C-terminus truncation mutant (p23_1-117). Both proteins were expressed in fusion with a poli-His tag and purified by affinity chromatography. His-tags were cleaved by thrombin and the proteins were further purified by ionic exchange chromatography. Circular dichroism analysis suggested that p23 is mainly formed by ß-sheet. p23 tertiary structure was investigated either by circular dichroism or intrinsic emission fluorescence spectroscopy, which showed that the tryptophan residues were buried into the protein. It is interesting to mention that the p23 C-terminal truncation showed higher circular dichroism signal at 230 nm, a p23 characteristic signal, suggesting that the C-terminal disturbs the ß-sheet folded domain. On the contrary of showed by the literature, our thermal-induced unfolding experiments suggested that the presence p23 C-terminus region increased the p23 thermal stability. Both wild-type and truncated mutant behaved as asymmetric monomers in analytical ultracentrifugation experiments, but C-terminal truncation reduced p23 asymmetry. Throughout molecular modeling, a p23 model was generated showing that the C-terminus would fold partially as an a-helix structure. The predicted hydrodynamic data for this model agreed with that of experimental data. The results lead us to conclude that the p23 C-terminus influence the stability of the p23 ß-sheet folded domain.

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