CONFORMATIONAL STUDIES OF HUMAN HSP90 CO-CHAPERONE P23

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p23 acts as a co-chaperone for Hsp90 by regulating Hsp90 ATPase cycle and substrate release (induces conformational changes that stimulates Hsp90-substrate dissociation). p23 is formed by an beta-sheet structured amino-terminal domain, which is responsible for interacting with the Hsp90 dimer, and an unstructured carboxi-terminal region with unclear function. We present results on the use of spectroscopic and hydrodynamic techniques to study the human p23, which was expressed in fusion with a poli-His tag and purified by affinity chromatography. The tag was cleaved by thrombin and the protein further purified by ionic exchange chromatography. Circular dichroism analysis suggested that human p23 is mainly formed by beta-sheet. Both circular dichroism and emitted intrinsic fluorescence spectroscopy were used in order to investigate the tertiary structure of p23 and showed that the tryptophan residues seem to be well buried into the protein. Analytical ultracentrifugation experiments also confirmed the folded characteristic of the protein by showing that it was a compact, although asymmetric, monomer. The information generated was used in combination with molecular modeling to generate a model for the structure of human p23. Our results may help to explain the mechanism by which p23 regulates the function of Hsp90.

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