Structural and stability studies of p23, a co-chaperone of Hsp90


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Hsp90 is a highly conserved and abundant molecular chaperone that is essential for folding, assembly, and maintenance of many proteins. The activity of Hsp90 N-terminal ATPase domain is regulated by several co-chaperones, as p23 that binds and stabilizes the ATP-bound state of Hsp90 and inhibits ATP hydrolysis maintaining the interaction between Hsp90 and many client proteins. Additionally, p23 may be involved in the stimulation of Hsp90-substrate dissociation. Co-chaperone p23 is a small acidic protein formed by a β-sheet folded domain and an unstructured C-terminal tail. The β-sheet domain is responsible for the interaction with Hsp90 and also for binding partially unfolding proteins. The functional role of the C-terminus tail is under investigation and may be essential for its chaperone activity and to regulate Hsp90 chaperone activity. Caspase 3 (and 8) degrades p23 releasing a 19 kDa degradation product (p231-142) that is stable and functional in apoptotic cells. We present a biophysical investigation on human p23 WT and truncated p23 mutants (p231-117 and p231-131). The recombinant proteins were produced pure and folded as asymmetric monomers. Thermal-induced unfolding experiments followed by circular dichroism and differential scanning calorimetry showed that WT p23 unfolded thru two transitions and that p231-117 and p231-131 were substantially less stable than p23. A discussion on the role of the C-terminus in the structural and functional aspects of p23 is presented.