

NETWORKS OF PROTEIN FOLDING PATHWAYS IN THE CELL: THE REGULATION OF MOLECULAR CHAPERONES BY CO- CHAPERONES

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Molecular chaperones are proteins that act as facilitators and quality control factors for the correct folding and assembly of other proteins within the cell. They are therefore vital for ensuring that the structural integrity of the cellular protein machinery is maintained under normal physiological conditions, but also under conditions of cell stress. Under certain conditions, the major molecular chaperones, heat shock protein 70 (Hsp70) and heat shock protein 90 (Hsp90) are able to act on their own as molecular chaperones, modulated only by the prevailing metabolic conditions of the cell such as ATP concentration. However, over the last ten years it has become evident that the cellular functions of Hsp70 and Hsp90 are regulated by a cohort of co-chaperone proteins that provide a layer of complexity to the system. Several different co-chaperone-directed protein folding pathways have been identified, that are interconnected to form a well organized chaperone network within the cell. I will present and discuss some of the recent key findings of the Chaperone Research Group, Rhodes University. We have been investigating certain co-chaperones that regulate Hsp70, and that integrate Hsp70 protein folding pathways with Hsp90 protein folding pathways. We have conducted molecular and mechanistic analyses of certain structural protein-protein interaction domains, and the specificity determinants involved in the interaction of co-chaperones with their partner chaperones. The implications of our findings will be discussed in the context of the role of molecular chaperones in biology, medicine and protein biotechnology.

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