

**P001** Functional domain mapping of the HSP70 cochaperone HSP70  
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The human DnaJ (HSP40) proteins HSP40A and HSP40B can regulate the ATPase activity and substrate binding of HSP70. HSP40A and HSP40B are expressed in neuronal tissues but, have different intracellular localization due to the prenylation of HSP40B. The proteins are enriched in photoreceptors where HSP40B is present at the site of rhodopsin production. In cultured cells HSP40B has a dramatic inhibitory effect on the normal cellular processing of rhodopsin apoprotein, causing its retention in the ER and an increase in inclusion formation. This modulation of rhodopsin processing is dependent on the correct sub-cellular targeting of prenylated HSP40B to the cytosolic face of the ER.

In this study we delineate the region of HSP40B responsible for the inhibition of normal rhodopsin processing, using domain deletion mutants. Residues 160-274 of HSP40B contain the domain responsible for ER retention and increased inclusion formation. Within this putative domain is a region that is highly conserved within a subfamily of type II DnaJ proteins. This may represent a novel chaperone domain.

Furthermore, using a yeast two-hybrid screen we have shown that HSP40B interacts with ubiquitin fusion proteins Uba52 and Uba80. Ubiquitin binding by HSP40 proteins is dependent on a ubiquitin interaction motif at residues 249-266 of HSP40B, which is necessary and sufficient for the interaction. These data suggest the HSP40B/rhodopsin interaction may be relevant to the degradation of rhodopsin by the ubiquitin proteasome system.