FUNCTIONAL CHARACTERISATION OF MOLECULAR CHAPERONES: BRAIN-ENRICHED HUMAN HSP40 (Hsj1a) AND MALARIAL HSP40 (Pfj4).

Caryn McNamara, William S. Nicoll and Gregory L. Blatch

Chaperone Research Group, Department of Biochemistry, Microbiology and Biotechnology, Rhodes University, Grahamstown, South Africa

Hsp40 and Hsp70 are families of 40-kDa and 70-kDa heat shock proteins, respectively, that consist of certain members that are over-expressed under stress conditions, and others that are constitutively expressed. The Hsp70/Hsp40 chaperone system is known to confer cytoprotection *in vivo* to cells by aiding protein folding under normal conditions, and by reducing protein denaturation when cells are under heat or other stresses. We are analysing the functional similarities of two potentially related Hsp40 molecular chaperones: a known brain-enriched human protein, Hsj1a, and a *Plasmodium falciparum* protein, Pfj4. These proteins both have a J-domain, glycine-phenylalanine rich region and a similar C-terminal domain. The C-terminal domain of Hsj1a contains an Ubiquitin Interaction Motif (UIM) implicating it in the protein degradation pathway, and we are currently investigating the presence of a UIM in Pfj4. We have constructed chimeric protein constructs replacing the J-domains in two prokaryotic Hsp40 homologues (*Escherichia coli* DnaJ and *Agrobacterium tumiefaciens* DnaJ) with the J domains of Hsj1a and Pfj4. We will present the results of *in vivo* complementation assays using an *E. coli dnaJ cbpA* mutant strain to determine whether the chimeric J-domain proteins are functional and specific in their chaperone activity. Amino acid substitutions will be performed on key J domain residues known to be of importance in the interaction of Hsp40s with Hsp70s to determine the roles of these residues in the chimeric proteins. If these two proteins are sufficiently dissimilar in their mechanism of interaction and specificity, then the malarial protein may prove to be a potential target for anti-malarial drug design in the future.

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