IN VIVO ANALYSIS OF THE CHAPERONE ROLE OF *PLASMODIUM FALCIPARUM* HEAT SHOCK PROTEIN 70

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Molecular chaperones are proteins that assist other proteins to attain their correct three dimensional conformations. The heat shock protein 70 (Hsp70) family of proteins is one of the most important groups of chaperones. They are involved at all levels of protein biogenesis, and also prevent and reverse protein misfolding under physiological stress conditions. We are interested in the Hsp70 chaperone machinery of the malaria parasite, *Plasmodium falciparum*, that is known to over-express heat shock proteins including Hsp70 in response to thermal stress. In this study we investigated the in vivo role of *P. falciparum* Hsp70 (PfHsp70). Our results show that PfHsp70 has chaperone cytoprotective features as it was able to functionally replace E. coli DnaK (*E. coli* Hsp70 homologue) in an *E. coli dnaK* mutant strain. Two amino acid residues in the linker region that are necessary for the PfHsp70 function were identified. Chimeric proteins that consist of the swapped ATPase and substrate binding domains of PfHsp70 and DnaK were used to investigate the possibility of interdomain communication between Hsp70s from the two organisms. Whilst KPf, the chimera that had the ATPase domain of E. coli DnaK and PfHsp70 substrate binding domain, was able to complement for DnaK function, the reverse chimera PfK could not. The functional substitution of PfHsp70 for DnaK, despite their low amino acid sequence identity, suggests that they may have a similar three-dimensional structure and that certain functional characteristics of Hsp70 proteins are conserved in eukaryotic and prokaryotic homologues. This study also challenges the notion that the substrate binding domain of Hsp70 determines functional specificity. As future work we envisage using PfHsp70 and its Hsp40 co-chaperone PfJ to improve the solubility of heterologously expressed recombinant *P. falciparum* proteins, most of which aggregate when overproduced in *E. coli*. We also intend to investigate PfHsp70s ability to refold a model protein substrate *in vitro*.

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