Poster #27

Regulation of Human Ah receptor Signaling by Chaperone Proteins in a Yeast Model System.

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Chaperones control the functions of their specific protein substrates through direct interactions that often involve regulation of conformation, localization, and stability. We have used a yeast model system to explore the role of chaperone proteins in human Ah (dioxin) receptor signaling. These experiments are feasible due to the strong conservation of chaperones among diverse species. Two Hsp90 co-chaperone proteins, Cpr7 and Cns1, were identified through functional genetic assays as factors that positively modulate Ah receptor signaling. Co-precipitation experiments conducted with recombinant proteins demonstrated a physical interaction between the yeast Cpr7 protein and Ah receptor *in vitro*. Genetic deletion experiments revealed that the tetratricopeptide repeat (TPR) domain of Cpr7 was sufficient to restore Ah receptor signaling in a cpr7-deleted strain. The yeast Cpr7 and Cns1 proteins share sequence similarity with the TPR-containing region of human XAP2 (also called ARA9 and AIP), a protein that was previously identified as a component of Ah receptor-Hsp90 complexes. Our results suggest that these yeast proteins may be performing a similar function to the human XAP2 protein in the Ah receptor signaling pathway. In general, these studies illustrate the utility of studying human Ah receptor signaling in a yeast model system.