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The Effects of the STF-083010 Inhibitor and Chaperone 4-PBA on the Unfolded Protein Response

The unfolded protein response (UPR) is a cellular stress response that regulates the expression of genes that maintain homeostasis in the endoplasmic reticulum (ER). Perturbations of this organelle can lead to an accumulation of unfolded or misfolded proteins, which then activates UPR pathways such as the IRE1 (Inositol-requiring enzyme 1) pathway. In response to the insufficiency of the ER's protein-folding capacity, IRE1 splices *Xbp1* mRNA, resulting in the active form of the protein, which enhances the expression of molecular chaperons to help protein folding and protein degradation machinery to rid the cell of misfolded proteins. We investigated the effects of the IRE1 inhibitor STF-083010 and the chemical chaperone 4-PBA on UPR activity by measuring the promoter activity of honey bee *Hsc70-3* gene, which encodes a chaperone. Since STF-083010 directly inhibits the IRE1 pathway and 4-PBA inhibits UPR pathways as a whole, 4-PBA should result in the reducing ER stress due to the accumulation of chaperons, while IRE1 will have a direct affect on *Hsc70-3* if it is an IRE1 target. The promoter activity of the *Hsc70-3* promoter in *Drosophila Melanogaster* S2 cells treated with DTT was determined from a dual luciferase assay. Increasing concentrations of STF-083010 and chaperone 4-PBA showed a decrease in the promoter activity. The presence of 4-PBA is effective in reducing ER stress, while the STF-83010 inhibitor directly halts the IRE1-dependent promoter activity pathway. Since UPR plays a central role in human diseases, we can hypothesize that this cellular stress response pathway contributes to bee health. Future experimental investigations will be centered in furthering our understanding of the UPR in this critical species.