Cell Death and the Unfolded Protein Response with Cholera Toxin

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Cholera toxin causes a diarrheal response in patients by inducing chloride efflux from intestinal epithelial cells, but it does not kill the intoxicated epithelial cells. Cholera toxin also activates the unfolded protein response (UPR) in intoxicated cells which improves the efficiency of intoxication. Prolonged UPR activation is known to cause apoptosis in cells, but cholera toxin does not cause cell death. The goal of this research project was to gain more information about how cholera toxin activates the UPR without generating an apoptotic effect. This was accomplished by studying two chemicals which act similarly to cholera toxin within the cell. Both Thapsigargin and Dithiothreitol (DTT) induce the UPR. Thapsigargin induces the UPR by blocking the calcium pumps within the cell while DTT induces the UPR by cleaving disulfide bonds. The chemicals were added to Chinese Hamster Ovary (CHO) cells and compared to the effect of cholera toxin on the cells. Dimethyl Sulfoxide, (DMSO), a drug which causes stress on the cells, was added to the CHO cells alone as a negative control. A colorimetric assay which detects mitochondrial respiration (MTS assay) was performed on the cells to assess cell viability after intoxication. DTT and Thapsigargin killed more cells than cholera toxin but fewer cells than DMSO, which indicates that cholera toxin activates and utilizes the UPR in a different way than DTT and Thapsigargin.

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