Can Oxidative Stress Increase Transcriptional Mutagenesis and Aggregate Apha-Synuclein Protein?

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The aim of this project was to discover whether or not oxidative stress could cause DNA damage in cells deficient of Ogg1 and if so, to see if that would increase transcriptional mutagenesis. First a plasmid was nucleofected into the knockout cells with the Alpha-Synuclein sequence on it. Then cells were treated with Rotenone, a chemical that shuts down complex I in mitochondria, causing oxidative stress. RNA was made from these treated and untreated cells at different time points and then sequenced. It was found that this decreased cell growth but did not show a change in RNA mutations. The next chemical used was Glucose Oxidase (GO), which produces hydrogen peroxide. RNA was isolated from treated and untreated nucleofected-cells of different GO concentrations at 2 and 24 hours. This treatment decreased cell survival. RNA from the GO treated cells was sequenced but no mutations were found. A GFP-Synuclein plasmid was also put into the cells and examined to see if this GO treatment produced aggregated protein using fluorescent microscopy. There was expression of the Synuclein-GFP protein and signs of mutated protein. Western analsyis did show oligomers of Alpha-Synuclein in GO-treated cells. These results suggests transcriptional mutagenesis is not implicated in the causation of neuro-degenerative diseases such as Parkinson's disease, where it has already been proven that the presence of aggregate Alpha-Synuclein in the neurons of patients with Parkinson's disease damages the neurons. This research could lead to the discovery of causes and cures to these types of diseases.

Awards Won:

Air Force Research Laboratory on behalf of the United States Air Force: First Award of $750 in each Intel ISEF Category