CALIFORNIA STATE SCIENCE FAIR
2010 PROJECT SUMMARY

Name(s)

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Project Number

S1817

Project Title

Multi-Drug Resistance and the Mechanism of Orlistat-Induced Cell Death in Ovarian Carcinoma

Abstract

Objectives/Goals

The purpose of this study is to investigate the pathway(s) of orlistat induced cellular death in ovarian cancer cells by comparing the effects of Orlistat on drug resistant and drug sensitive ovarian cancer cells.The primary objective is to evaluate GRP78 (and endoplasmic reticulum stress indicator) shows greater expression in drug sensitive ovarian cancer cells compared to multidrug resistant ovarian cancer cells during drug treatment.

Methods/Materials

Multi-drug resistant and drug sensitive cells were used as the basis of comparison for the orlistat treatment. A Trypan Blue exclusion and a sulforhodamine B assay (SRB) were performed to test cell viability. A SDS-PAGE gel electrophoresis separated out the proteins of interest and a western blot was used to probe for the protein GRP78. RT-PCR with GRP78 primers were used to measure GRP78 expression. A SDS PAGE gel electrophoresis was also conducted, then stained with Coomassie or SYPRO Ruby to differentiate protein expression.

Results

The western blots and the RT-PCR show that there are similar levels of GRP78 expression in both the drug resistant and drug sensitive cell lines both before and after treatment with orlistat. The SYRPO Ruby stain showed different protein expressions between the drug resistant and drug sensitive cell lines both with and without orlistat treatment. One of these proteins was Identified as heterogeneous nuclear ribonucleoprotein isoform C, which was down regulated after orlistat treatment in both the drug sensitive and drug resistant cell lines.

Conclusions/Discussion

The data does not support the hypothesis that orlistat uses a endoplasmic reticulum stress induced pathway with regard to cellular death. It is possible that the biological mechanism(s) which causes the differences in GRP78 protein expression between the drug resistant and drug sensitive cell lines, plays a major role in the effectiveness of orlistat.The use of the coomassie and SYPRO Ruby stains are the first steps to proteomic analysis of the cells under orlistat treatment

Summary Statement

Orlistat does not use a endoplasmic reticulum stress induced pathway with regard to cellular death.

Help Received

Worked in the lab of Dr. Jason Bush