CALIFORNIA STATE SCIENCE FAIR
2009 PROJECT SUMMARY

Name(s)
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Project Number
S1817

Project Title
Mechanisms of Survival Against a Fatty Acid Synthase Inhibitor in Multidrug Resistant Ovarian Cancer

Abstract

Objectives/Goals
The main objective of this project is to define the biological mechanism(s) by which multidrug resistance (MDR) to a fatty acid synthase inhibitor occurs. Hopefully this investigation will improve the understanding of the MDR phenomenon to better refine the treatment regimen for women diagnosed with ovarian cancer.
Hypothesis
Multidrug resistant ovarian cancer cells treated with orlistat will undergo less cell death compared to drug sensitive ovarian cancer cells.
If GRP78 shows greater expression in drug sensitive ovarian cancer cells compared to multidrug resistant ovarian cancer cells during drug treatment then drug resistance to orlistat must be related to preventing endoplasmic reticulum stress.

Methods/Materials
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.

Results
After treatment with either orlistat or doxorubicin, the drug sensitive cell lines will die during the duration of the treatment with either drug, while the drug resistant cell lines continue to proliferate. Following 72 hours of treatment with orlistat, the multidrug resistant ovarian cancer cells, NCIADR, began to grow, showing a resistance to the orlistat, while the sensitive cells, OVCAR 8, continued to die.

Conclusions/Discussion
The first hypothesis, that multidrug resistant ovarian cancer cells treated with orlistat will undergo less cell death compared to drug sensitive ovarian cancer cells, was supported by several experiments including the Trypan blue exclusion and the SRB cell assays. The Coomassie stain showed changes in protein concentration and it is possible that these proteins may be related to drug resistance against the drug orlistat. 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 after treatment with orlistat. This does not support the hypothesis that drug resistance is related to the prevention of ER stress. It also appears that there is no increase in GRP78 expression after treatment with the drug orlistat compared to the untreated in both the drug resistant and drug sensitive cell lines.

Summary Statement
The main objective of this project is to define the biological mechanism(s) by which multidrug resistance to a fatty acid synthase inhibitor occurs.

Help Received
Jason Bush PhD, California State University Fresno