CALIFORNIA STATE SCIENCE FAIR
2005 PROJECT SUMMARY

Name(s)
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Project Number
S1421

Project Title
Discovery of Novel Histone Deacetylase Inhibitors for Breast Cancer

Abstract

Objectives/Goals
The purpose of this project is to determine whether Histone Deacytelayse (HD) inhibitors, 51 novel compounds, are effective compounds against MDA-MB-435 breast cancer cells. Effectiveness is determined by whether the compound surpasses a certain toxicity; thereupon it will be an active compound that kills breast cancer cells. HD Inhibitors are effective because they bind onto the histones causing hyperacetylation, which is when many acetyl groups attach onto the histone, forcing the DNA to unravel. This forces the DNA to be transcribed, but it is an unregulated transcription of DNA, in effect the DNA malfunctions. The cell cycle is arrested and apoptosis occurs. We hypothesize these novel small-molecule compounds to works against breast cancer based on docking studies.

Methods/Materials
With a breast cell culture, trypsinizning the cells removes the cells off of the flask. Then, the amount of cells present can be determined by counting the cells under a microscope. After plating the cells into a 96 well plate, prepared compounds are added into each well. An incubation period of 48 hours is needed so that the drugs can be incorporated into the newly dividing cells. MTT assay is then used to stain cells that are metabolically active, which in this case, is a purple stain. The color will help determine the amount of cells alive in each well, as with the intensity of the purple coloring.

Results
The dose response demonstrates that compounds HD 38, HD 39, and HD 42 displays activity on the MDA-MB-435 breast cancer cells. The IC50s found for the compounds implies a good set, where the lowest concentration that destroys the cancer cells is determined to be below 20 µM (micro-molar). The IC50s of HD 38, HD 39, and HD 42 are 2.3, 2.2, and 14 µM (micro-molar) respectively. The IC50 value is the concentration of each compound that eliminates 50% of the cells, and this is the standard that is needed to determine how potent a compound is. The compounds are proven to be active based on their toxicity, which illustrates that they do inhibit the site of the histone attachment site with the DNA.

Conclusions/Discussion
Compounds HD 38, HD 39, and HD 42, are potential anti-cancer compounds. These compounds are acting as histone deacetylase inhibitors to eliminate MDA-MB 435 Breast Cancer Cells.

Summary Statement
To determine if the newly developed novel Histone Deacytelayse inhibitors are potential anti-cancer compounds for MDA-MB 435 breast cancer .

Help Received
Lab equipment at University of Southern at the Department of Pharmaceutical Sciences