CALIFORNIA SCIENCE & ENGINEERING FAIR
2018 PROJECT SUMMARY

Name(s)

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Project Number

S0527

Project Title

Cholesterol Control: The Effect of Bisphosphonates on Cellular LDL Uptake

Abstract

Objectives/Goals

The goal of this study was to determine the secondary effects of bisphosphonates, a class of drugs primarily used to treat osteoporosis or other bone-related diseases, on cellular LDL uptake. It was hypothesized that nitrogenous bisphosphonates (NBP) but not non-nitrogenous bisphosphonates (BP) would increase cellular LDL uptake by decreasing de novo cholesterol synthesis by inhibiting FDPS in the mevalonate pathway.

Methods/Materials

Hep-G2 cells (human hepatocellular carcinoma) were used as a model system for LDL uptake in this study, and etidronate and alendronate were selected as the BP and NBP, respectively. Cells were grown on 96-well plates for 48 hours and subsequently treated with 0 (control), 1, 10, or 100 uM etidronate or alendronate for 24 hours. Cells were incubated with 20 ug/mL Dylight 550-labeled human LDL in serum-free media for 4 hours, after which LDL uptake was measured at 540/570 nm in the microplate reader. LDL Receptor (LDLR) was tagged with a Dylight 488-conjugated antibody via indirect immunofluorescent straining and was measured at 485/535 nm in the microplate reader.

Results

Statistical analysis of the results was carried out using Student's t-test (n=11). LDL uptake was significantly increased in wells treated with 10 uM alendronate ($p=0.016$), and 1 and 10 uM etidronate ($p=0.023$, 0.049), and a similar pattern was observed in the LDLR data. Uptake did not increase as expected in either 100 uM etidronate or alendronate treatments, which was likely due to toxicity (a subsequent viability assay via propidium iodide staining revealed an order of magnitude decrease in viable cell counts at those concentrations).

Conclusions/Discussion

The increase in LDL uptake as a result of treatment with both BP and NBP points to either the existence of interactions between BP and the mevalonate pathway, or alternative mechanisms through which both impact cellular cholesterol production or LDL uptake. Further research should focus on elucidating the cellular mechanisms responsible for these changes. Additionally, these initial results suggest that for individuals requiring treatment for both osteoporosis and high LDL cholesterol, treatment with bisphosphonates alone (without statins) may be sufficient, and corroborate patient studies that have correlated bisphosphonate usage with a decrease in serum LDL concentration as measured in blood tests.

Summary Statement

I studied the effects of nitrogenous and non-nitrogenous bisphosphonates on LDL uptake in hepatic cells.

Help Received

My scientific research teacher, Mr. Vander Veen, reviewed my research plans and experimental design. All procedures were performed at the laboratory facilities available at my high school under his supervision. Materials were purchased by my high school.