

Determining Small Molecule Inhibitors of Calpain To Promote Cholesterol Efflux in Macrophage-Derived Foam Cells

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Heart disease is the leading cause of death for both men and women in the United States, and is responsible for a third of deaths worldwide. Most cardiovascular disease is caused by the accumulation of plaque in the artery walls, otherwise known as atherosclerosis. When cholesterol settles into the wall of the artery, macrophages migrate to the area and trap the cholesterol, becoming foam cells and creating plaques. One of the primary proteins involved in the cholesterol influx process is calpain, an intracellular calcium dependent protease. Molecular docking was used to identify a top small molecule inhibitor of calpain which should promote cholesterol efflux from cells and reduce foam cell formation. Among a variety of atheroprotective compounds that were screened, quercetin was found to be a top performing compound, with an average binding affinity of -64.826 kcal/mol. An Amplex Red Cholesterol Assay was used to quantify cholesterol efflux from lipid laden J774a.1 macrophage-like cells, treated with 100uM of quercetin. These values will then be compared against piperine (50 uM), which is known to improve cholesterol efflux capabilities. The results of the Amplex Red showed that the foam cells treated with quercetin had a higher level of cholesterol efflux in comparison to piperine. More trials will be run, and a Western blot for an associated protein (CD36) will be done. Data collection is ongoing.

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