AZELNIDIPINE ATTENUATES INFLAMMATORY RESPONSES, SUPEROXIDE AND RELEVANT SIGNALING PATHWAYS INDUCED BY AMYLOID-BETA IN MOUSE CEREBRAL ENDOTHELIAL CELLS

Tao Teng

James Lee, Thesis Supervisor

ABSTRACT

Alzheimer’s disease (AD) is a debilitating neurodegenerative disease with no known cure. The cause and progression of AD is still unclear. Over the years, studies have shown that one of the earliest cytotoxic effects is the production of reactive oxygen species (ROS) and inflammation induced by the amyloid-β peptide in microglial cells, endothelial cells and neurons. The focus of this thesis is to study the effects of Azelnidipine (ALP), which is a Calcium channel blocker, on Aβ-induced oxidative stress and its downstream pathways in mouse immortalized cerebral endothelial cells (bEnd.3). In AD, Aβ_{1-42} induces oxidative stress through the activation of ERK 1/2 pathway, phosphorylation of cPLA2 and production of intercellular superoxide anions. Furthermore, Aβ_{42} has been shown to induce the translocation of NF-κB into the nucleus of bEnd.3 cells causing an inflammatory response. Here, ALP is utilized to reduce the ROS and inflammatory effects of Aβ_{42} in bEnd.3 cells. The results show that ALP is effective in reducing the Aβ_{42} induced superoxide anion production, ERK 1/2 activation, cPLA2 phosphorylation and NF-κB translocation into the nucleus of bEnd.3 cells. Thus, ALP may be an effective treatment to alleviate the debilitating effects of AD. Finally, this research implicates that there may be cross-talk between the ERK 1/2 pathway and NF-κB translocation into the bEnd.3 nucleus.