Moving Towards the Cure: The Effect of Neuroinflammation and Microglial Activity on Alzheimer's Pathology and the Development of Therapeutics for Their Mitigation in the TG4510 Mouse Model (A Third Year Study)

Chandar, Jay

The purpose of this experiment was to investigate the effects of neuroinflammation and microglial activity on the progression of Alzheimer’s and to develop therapeutics with RNA-Interference. The researcher hypothesized that RNA molecules directly involved in microglial activity, such as ITGAX, IL1ß, TREM2, and Calgranulin B will show increased levels that parallel the temporal progression of Alzheimer’s, and that their breakdown through RNA Interference will decrease levels of neurofibrillary tangle and amyloid beta plaque formation Using many processes, including Cell Culture, quantitative Real Time Polymerase Chain Reaction, and Mouse Behavioral Analysis, positive results were obtained. IL1ß, ITGAX, TREM2, and Calgranulin B paralleled the temporal progression of Alzheimer’s pathology, showing increased levels in older age groups. This supports the researcher’s hypothesis, showing that as the disease progresses, the micro-glial RNA molecules' overexertion increased, establishing their relationship with Alzheimer’s. T-tests showed statistical significance increased temporally as well, supporting the researcher’s hypothesis. RNA Interference in mouse neuronal cells stimulated for increased microglial activity showed a statistically significant decrease in the amount of hyper-phosphorylated tau protein.This leads to prevention of neuronal death due to prevention of neurofibrillary tangle formation. Those stimulated for increased microglial activity, but were not treated had a statistically significant increase in hyper-phosphorylated tau protein. RNA Interference is being performed on the TG4510 mouse model for IL1ß and ITGAX. If these results can be supported with further trials, this form of gene therapy can provide an effective treatment for Alzheimer's.