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Regulation of Amyloid β Precursor Protein by Iron Treatment and Mir-106b Alterations

Alzheimer's Disease (AD) is a neurodegenerative disorder believed to be triggered by the aggregation of amyloid-β peptides (Aβ) into senile plaques in the neocortical and subcortical regions of the brain. Within these regions of the brain, elevated exogenous concentrations of zinc, copper, aluminum, and iron were found to be linked to the regulation of the amyloid beta deposits. Additionally, studies have shown that Aβ levels can be not only regulated at the transcriptional or translational levels by growth factors and proinflammatory cytokine, but also post-transcriptionally by microRNAs (miRNAs). In a study performed by Lukiw and Pogue in 2007, it was shown that metals, such as iron and aluminum, regulate a specific set of miRNAS found to be downregulated in AD brain.

Several studies have found iron(II) ions and mir-106b levels to regulate the formation of the amyloid-β precursor protein (APP-β), but the relationship between the two remains unknown. In order to investigate the connection between iron(II) metal concentrations and mir-106b in neuronal cells, our lab created lucfierase constructs of the 3'UTR of the amyloid beta precursor protein that contained the mir-106b binding site. The vector was then transfected into SHS-Y5Y neuronal cell to quantify and determine expression of APP-β at varying levels of mir-106b and iron(II) concentrations. Our results, thus far, have shown that decreased levels of mir-106b increase APP-β and increased levels of iron(II) metal increase APP-β concentrations.