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Rohan Gopinath

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**Potential Role of MicroRNA-758 in the Pathogenesis of Alzheimer’s Disease**

*Rohan Gopinath*

Mentor: Jungsu Kim

Alzheimer’s disease (AD) is a neurodegenerative disease that is the most common cause of dementia in the elderly. Abnormal accumulation of amyloid beta (Aβ) peptide in the brain has been hypothesized to trigger pathogenic cascades that eventually lead to AD. Aβ peptide is generated by the sequential proteolytic cleavage of amyloid precursor protein (APP) by β- and γ-secretase. The proteolytic activity of β-secretase, also known as β-site APP cleaving enzyme1 (BACE1), is altered by cholesterol dysregulation. ATP-binding cassette transporter A1 (ABCA1) plays a critical role in maintaining cholesterol homeostasis. Thus, regulation of ABCA1 levels has been identified as a potential therapeutic target for AD. Recently, microRNAs (miRNAs) have been identified as important regulators of disease-related genes in diverse settings such as AD. In particular, miR-758 has been identified as a miRNA that post-transcriptionally controls ABCA1 levels. First, we identified miR-758 as a regulator of ABCA1 with multiple predicted binding sites on the 3’UTR region of its mRNA transcript. Next, we found that miR-758 represses endogenous ABCA1 levels in both HT22 and H4 WT cells. The suppression of ABCA1 by miR-758 leads to subsequent increase in production of Aβ peptide. Furthermore, miR-758 was identified as a novel regulator of cAMP response element binding protein (CREB), a transcription factor integral in forming spatial memory. In both HT22 and H4 WT cells, miR-758 was found to repress endogenous CREB levels. In conclusion, we suggest that miR-758 represses ABCA1 expression which leads to subsequent increase in Aβ peptide levels. In addition, miR-758 was shown to decrease CREB levels which could lead to the loss of spatial memory associated with AD. Thus, miR-758 may play a critical role in AD pathogenesis and warrants further studies.