Jumping Genes: A Potential Molecular Target for Alzheimer's Disease Intervention

Chen, Isabelle (School: Barrington High School)

Alzheimer's Disease(AD) affects more than 6 million people in the US, by causing degeneration of the brain cells, deficiency of cognition and mobility, and even death. As aging progresses, symptoms of AD worsen and therefore, become harder to treat. Thus, an understanding of molecular mechanisms is needed for early detection and intervention of AD. Retrotransposon LINE1, a type of jumping gene, comprises about 17 percent of our genome and is associated with the pathogenesis of various diseases. In this work, I characterized the upregulation of LINE1 RNA in AD mice (APP/PS1) brains through RNA extraction, reverse transcription PCR, and qPCR. I found that LINE-1 RNA was upregulated in the middle section and, in particular, the brain's hippocampus in the AD mouse model. I found that IL-1b, a pro-inflammatory cytokine in the body, was upregulated in the same regions as LINE-1. I found that 3TC (Lamivudine), a nucleotide reverse transcriptase inhibitor, inhibited LINE-1 up-regulation and IL-1b in the midbrain and hippocampus of AD mice. Furthermore, 3TC oral administration previously corrected the mobility deficiency of AD mice. Thus, my data reveals a molecular mechanism by which retrotransposon LINE-1 is highly activated in the middle part of the brain during AD pathogenesis. The activation of LINE-1 leads to upregulation of pro-inflammatory cytokine IL-1b, brain tissue degeneration, and AD pathogenesis. Since 3TC is an FDA-approved drug to treat HIV, my data suggests that it may be repurposed for AD intervention.