DLG4 in Synaptic Plasticity

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Introduction
Alzheimer's disease is a form of dementia that worsens over time, causing impairment in different areas of mental functions, the most well-known being memory loss. Many efforts are being made to slow the progression of Alzheimer's as it has no known cure. Examining genes that are expressed differently in various stages of Alzheimer's may be an efficient method to determine target genes as potential cures. One such gene is DLG4, which maintains cell polarity. DLG4 is connected to MAGUK family of genes which were found to be related to synaptic formation and plasticity of the brain, and also to NMDA receptor which plays a significant role in synaptic plasticity. Considering these roles, DLG4 was further studied to observe its connection to Alzheimer's disease.

Methods
Dataset GSE28146 was downloaded from the NCBI website [2]. Our dataset was an analysis of sections of gray matter from 30 human subjects (n=30) in different stages of Alzheimer's, including control groups. We used cygwin and unix commands to condense the data into values just for the moderate and severe Alzheimer's patient groups. We then performed a student t-test with a p-value less than 0.01 on R to separate the data into genes that were upregulated and downregulated in severe Alzheimer's patients in comparison to the moderate group. Next, we visualized the connections between genes that were upregulated in severe Alzheimer's patients, and between genes that were downregulated with Cytoscape plugins, BiNGO and String, using a significance level of 0.05.

Results
Based on BiNGO visualization results, DLG4, involved with maintaining cell polarity, had many connections in the given downregulated genes. Furthermore, String visualization results indicated that DLG4 had connections to 10 other genes, more than other genes in the group. These findings proved that DLG4 was a significant enough gene to study.
DLG4 is a part of the MAGUK family of genes, which play a large role in synaptic formation and plasticity [3]. DLG4 is also used by the NMDA receptor along with DLG2 to help in the clustering of receptors and ion channels. This NMDA receptor plays a large role in synapse plasticity, and even memory as well, as the calcium that flows through it (postsynaptic calcium) is critical to plasticity [4]. Opening the NMDA receptors leads to a higher postsynaptic calcium concentration, creating long-term potentiation [5]. A lack of the DLG4 gene can disrupt the NMDA receptor pathways, which in turn leads to memory loss that can be seen in Alzheimer's patients.

Conclusion
Data suggests DLG4 is connected to memory loss through the NMDA receptor and postysynaptic calcium concentrations. Using this knowledge, scientists can potentially target this gene to slow the progression of Alzheimer's disease.

Keywords: Alzheimer's disease, DLG4, MAGUK, NMDA receptor, synaptic plasticity

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Grace is an 18 year old student from Ann Arbor, Michigan. She recently graduated from Huron High School this past month, where she was co-president of the Huron Gidas Club. Next fall, she will be attending Michigan State University, and will be majoring in genomics and molecular genetics.
She discovered her passion for science and genomics through Dr. Inhan Lee's organization, miRcore, during the summer between her sophomore and junior year of high school. Even though she started later than her peers, she was able to catch on quickly, and found that she always wanted to know more about everything related to genomics.
During her senior year of high school, and with the help of Dr. Lee, she entered the Southeast Michigan Science Fair for the first time in her life. After placing second with a project based on determining which chromosome could best predict how individuals would respond to certain toxins, she went on to compete in the International Science Fair in L.A., where she was able to meet and gain inspiration from teenagers from around the world. She hopes to continue her research as soon as she gets her graduation gift - a laptop that can actually handle all of the computing.