At an incidence of about 1 case per 800 live births, Down syndrome is the most common genetic development disorder. Down syndrome is caused by a trisomy of chromosome 21 (having three copies instead of two copies) [1]. This extra copy of chromosome 21 is a result of abnormal cell division of either the sperm or egg cell during development and can cause several neuronal abnormalities in affected individuals throughout their developmental years [2]. Down syndrome cannot be cured, and symptoms will stay with individuals for the rest of their lives. The current support and treatment can only help affected individuals manage their symptoms. Although several genes may be involved, the upregulation of the *DYRK1A* gene due to the third copy of chromosome 21 has been associated with cognitive defects in Down syndrome and other neurodegenerative disorders. *DYRK1A* encodes for the dual-specificity tyrosine-(Y)-phosphorylation-regulated kinase 1A protein and plays a role in reduced neurogenesis and premature neuronal differentiation of neuro-progenitor cells [3]. Although the ­DYRK1A protein is known to decrease transcriptional activity of the NFAT pathway, *it is still unclear how overexpressed DYRK1A protein leads to premature neuronal differentiation.*

My **primary goal** is to gain a better understanding of how the overexpression of the *DYRK1A* gene and its inhibitory nature leads to premature neuronal differentiation. The findings in this study may illustrate novel pathways that could be targeted for gene therapy in an effort to treat Down syndrome and other neurodegenerative diseases. My **hypothesis** is that DYRK1A’s inhibitory nature downregulates neuronal development pathways without effecting normal cell division, causing premature differentiation of neuro-progenitor cells. I will use the common mouse (*Mus musculus)*, specifically the Ts65dn strain, due to its roughly 1.5-fold expression of human homologs in chromosome 21.

**Aim 1: Characterize and identify essential sequences on DYRK1A that are critical for its function in neuronal development pathways.**

**Approach:** In mice with overexpression of *DYRK1A,* I will use CRISPR to remove highly conserved regions of DYRK1A. Then, DYRK1A’s ability to carry out its function will be observed in modified cells. Specifically, I will look at neurons and to see if any abnormalities have occurred in development.

**Rationale:** Since DYRK1A is known to reduce neurogenesis, removing regions of the gene that may play a role in its functionality could stop the reduced neurogenesis. If we know the specific sequences that are essential to DYRK1A’s function, this could help with understanding the mechanism of how DYRK1A interacts with proteins and genes.

**Hypothesis:** Specific regions of DYRK1A are dedicated to its function, specifically, the region that encodes for the P-kinase will be essential for DYRK1A’s inhibitory function.

**References:**

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