A Differential Gene Expression and Alternative Splicing Analysis of ALS-Causing Mutations

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Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder characterized by death of upper and lower motor neurons and progressive paralysis of the extremities. ALS is a complex disease caused by a mutation on one of over twenty-five genes including C9orf72, FUS, and TDP-43. Symptoms include glutamate imbalance, protein aggregation, and RNA metabolism deregulation but the exact etiology of the disease remains ambiguous. Various types of ALS present as the same disease but their differences have not been studied in depth. Detecting similarities could provide scientific insight into predominant disease-phenotype causing mechanisms and deregulation. Bioinformatics analysis includes a genome wide examination of biological RNA-sequencing data. iPSC derived motor neuron RNA-seq data of patients with C9orf72 ALS, FUS ALS, and TDP-43 ALS was obtained through Sequence Read Archive. A STAR Alignment and DESeq2 were performed to analyze gene expression. rMATS and Maser were utilized to investigate abnormal isoform expression. The resulting data from each mutation group was compared, and enrichment analysis was completed using DAIVD. A small number of commonalities were discovered between all mutations suggesting that treatment dependent on specific gene mutation may be beneficial to patients with ALS. The most significantly deregulated pathways involved the extracellular matrix, transcription, and cell-cell adhesion. As the search for treatment continues, the deregulated pathways identified in this novel study should be considered and targeted because they may be a root cause of the cascade of symptoms leading to motor neuron degradation and patient death.

Awards Won:
Fourth Award of $500