In Amyotrophic Lateral Sclerosis (ALS) Patient Tissue, UG Rich RNA Is Not Preferentially Soluble as Predicted

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Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disorder for which there is no cure. In 97% of sporadic ALS patients, TDP-43 forms insoluble protein aggregates dysregulating RNA metabolism, a condition known as TDP-43 proteinopathy. Last year my research showed that UG rich RNA was sufficient to mitigate TDP- 43 induced locomotor dysfunction in Drosophila. UG rich RNAs were preferentially soluble in flies with TDP-43 proteinopathy. This current project explores whether UG rich RNA is also preferentially soluble in postmortem ALS patient spinal tissue, and if pathways dysregulated in ALS experience altered solubility in the patient tissues. Differential expression analysis from RNA sequencing data of patient genes was provided, and Rstudio was used to determine UG richness of the soluble and insoluble genes. DAVID screened pathways that were enriched in the soluble or insoluble fractions of the genes. Different UG binding motifs were analyzed, and results were based on the cumulative number of different sized UG repeats. Soluble genes were not significantly enriched for UG sequences (mean UG total score of 145), however, the insoluble genes were (mean total score of 165). When quantifying larger UG repeats, insolubilization did not significantly correlate to UG richness. These results refute the hypothesis, indicating that total UG richness relates to solubility in a TDP-43 independent manner. Nicotine addiction RNAs (an ALS related pathway) and neuroactive ligand receptor RNAs, experienced altered solubility. Altered solubility in the nicotine addiction RNAs may suggest a mechanism for why smoking has been linked to an increased risk of ALS.

Awards Won:
Arizona State University: Arizona State University ISEF Scholarship
University of Arizona: Renewal Tuition Scholarship