UG-Rich RNA Is Key to Alleviating Neurodegeneration in a Drosophila Model of Amyotrophic Lateral Sclerosis (ALS)

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Amyotrophic Lateral Sclerosis (ALS) is a devastating, neurodegenerative, adult-onset disorder, for which there is no known cure. In approximately 97% of sporadic ALS patients, a protein called TDP-43 forms insoluble aggregates resulting in dysregulation of RNA metabolism", a condition known as TDP-43 pathology. Research using a Drosophila melanogaster model has identified a dally-like protein (dlp) whose production is inhibited due to TDP-43 pathology. Increased expression of this protein rescues the locomotive function in these fly models. What is unclear, however, is whether the rescue occurs because of the increased levels of the dlp, or because of the increased levels of UG-rich RNA necessary to make the protein. This project investigated the role of UG-rich RNA in the rescue of motor function in Drosophila larvae that have locomotor dysfunction induced by TDP-43 pathology. Virgin female fruit flies were crossed with males to produce progeny with both TDP-43 pathology and overexpression of UG-rich RNA. Larval turning was used to determine the locomotor function of these flies relative to the controls. Results showed that the average turning time for larvae whose genotype included ALS and overexpression of a UG-rich RNA (20 seconds) were significantly lower than the average turn time for larvae with ALS but no UG-rich RNA (60 seconds). The data supported the hypothesis that overexpression of UG-rich RNA is sufficient to alleviate locomotor dysfunction in Drosophila with TDP-43 induced ALS.

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