OFFICIAL ABSTRACT and CERTIFICATION

Towards an Animal Model to Study Sporadic ALS

Amyotrophic lateral sclerosis (ALS) is a complex and presently incurable disease that causes progressive degeneration of motor neurons. About ten percent of cases are attributed to genetic factors while ninety percent are sporadic with unknown causes. Thus, animal models created by genetic means cannot be studied to learn about sporadic ALS, so another method for inducing ALS must be discovered. The incorporation of D. melanogaster models of neurodegeneration holds tremendous promise for discovery of therapeutic targets. In order to induce ALS-like motor impairment, the light-sensitive protein Mito-Killer Red was expressed in the mitochondria of fly motor neurons. Mito-Killer Red photoactivation is known to release hydrogen peroxide; herein the neuromuscular junctions of instar 3 larvae. Motor function was examined before and after photoactivation. Larvae were then dissected and processed for immunostaining of the neuromuscular junction and fluorescence microscopy imaging. Photoactivation caused a slight but not statistically significant effect on motor function (P=.10) and the structure of the neuromuscular junction (P=.13). On average, the Mito-Killer larvae performed 2.4 times worse than the controls at the 90 minute mark and 2.5 times worse at the 120 minute mark. The structural integrity of the neuromuscular junction decreased by 11.7%. To confirm this relationship, future studies should use larger sample sizes and find ways to increaseintensity of ALS symptoms. This study is an important step towards a model for sporadic ALS, which has the potential to provide insight into the underlying causes of sporadic ALS and allow for the development of drug screening protocols.

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1. As a part of this research project, the student directly handled, manipulated, or interacted with (check ALL that apply):

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