Video Article

Characterization of an ALS-linked mutant model of neurodegeneration in Caenorhabditis elegans

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Abstract

Protein aggregation is associated in numerous neurodegenerative diseases, yet exactly how these misfolded protein aggregates contribute to neuronal malfunction remains poorly understood. Much of our current understanding of neurodegeneration has come from animal models. The major form of motor neuron degeneration, Amyotrophic Lateral Schleorsis (ALS), has been studied extensively in mouse models which recapitulate the characteristic clinical phenotypes, including limb paralysis and muscle deterioration. Transgenic mouse models of ALS reveal multiple possible sites of physical toxicity, including Endoplasmic Reticulum, mitochondria, and axonal traffic. To test for primary sites of SOD1 induced neuronal toxicity, then, we sought to express mutant human SOD1 in neurons of c.elegans in order to assess for a minimal target of the protein's toxic effects which could then be further studies in mammalian systems. Here we characterize the creation, development, and utilization of a novel worm model of ALS that expresses the mutant SOD1 protein, G85R, and whose observable phenotype closely resembles the symptoms of ALS seen in mammals. Pan-neuronal expression of the mutant SOD1, G85R, forms well-defined aggregates when viewed under fluorescent microscope. The behavioral change associated with the mutant protein is further evaluated through quantitative measures including escape response, movement distance following prodding, and thrashing in liquid media. Using this locomoter defect as a read-out of protein induced toxicity, it is then possible to harness the genetic power of c.elegans by performing large-scale screens for modifiers of neurodegeneration which may reveal neurtoxic mechanisms of relevant human diseases.

Disclosures

No conflicts of interest declared.