

THE CURE TO ALS IS FLYING AROUND YOU: USING FRUIT FLIES TO INVESTIGATE A FATAL DISEASE

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RESEARCH QUESTION

What is the role of the fruit fly gene CG12299 and how does it affect the pathogenesis of ALS?

ABSTRACT

When the fruit fly gene CG12299 was mutated in a fruit fly model of amyotrophic lateral sclerosis (ALS), it has been shown to reduce the severity of an ALS model-associated phenotype, resulting in an appearance approaching that of an unaffected fly. This suggests that CG12299 plays a role in the pathogenesis of ALS and determining its function could lead to a better understanding of ALS and the development of novel therapeutics for the treatment of ALS. In this project, we predict the function of CG12299 using multiple literary and database searches, and propose its role in ALS. We then design multiple experiments which could determine the function of CG12299.

WHY FRUIT FLIES

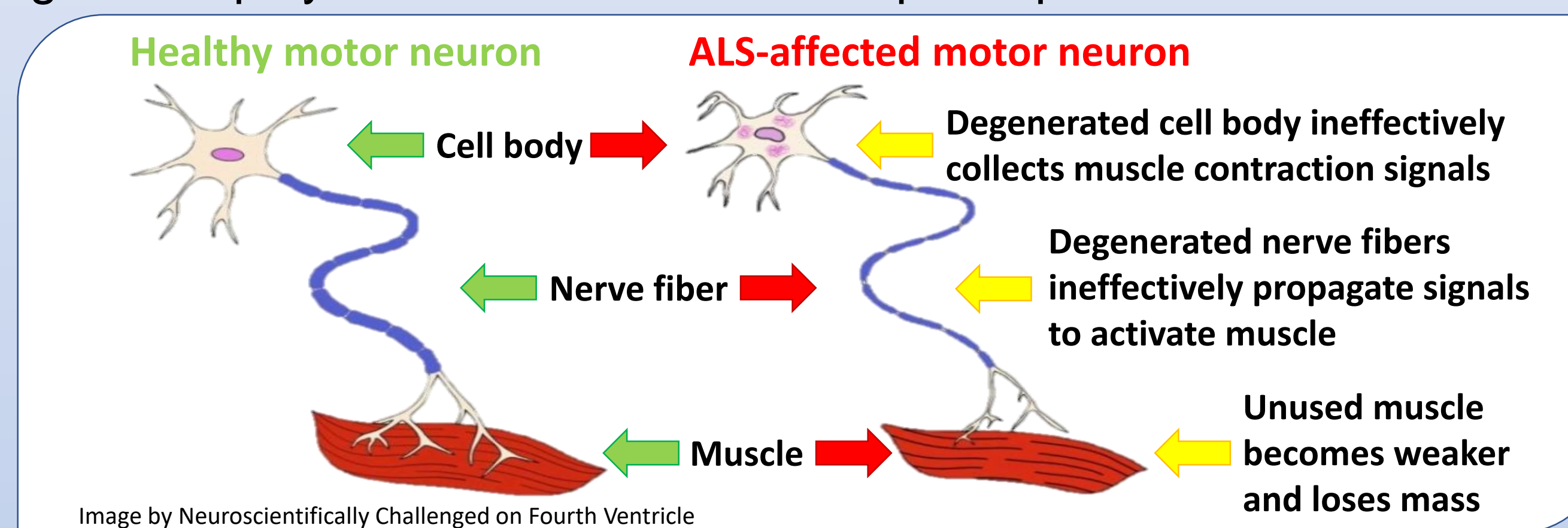
The common fruit fly (*Drosophila melanogaster*) has been used for over a century as a model organism. Two benefits of using fruit flies are:

- It has a fully sequenced genome
- It contains at least 75% of the genes that are found in the human genome.

However, the function of many different genes in the fruit fly genome still remain uncharacterized. One such gene is CG12299.

AMYOTROPHIC LATERAL SCLEROSIS

Amyotrophic lateral sclerosis (ALS) is a disease in which the neurons controlling voluntary muscles die, leading to ALS affected individuals unable to control their arms, legs, and eventually the diaphragm and intercostal muscles that control breathing. It is believed that genetics plays a role in an individual's predisposition to ALS.



METHODS

Gene Selection

To identify possible genes which influence ALS, we located journal articles in which a fruit fly model of ALS was used and different strains of fruit flies carrying various gene mutations were then bred to these ALS-modelling flies. Enhancement or suppression of ALS model-associated traits indicates that the gene mutated plays a role in ALS pathogenesis.

Function prediction

We used multiple online tools which gave us clues in determining the function of CG12299.

Basic Local Alignment Search Tool (BLAST) was used to compare the molecular sequence of the CG12299 protein to other known protein sequences across different species. *Drosophila* Interactions Database (DroID) was used to determine what proteins interact with CG12299 within the cell. Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) was used to map the interactions among CG12299 and its protein interactors. FlyBase was used to determine the areas of expression of CG12299 protein across the body of the fly.

RESULTS

- BLAST showed that brown rats also possess a protein made with the same molecular sequence, and that the highest concentration of this protein is made in the brain
- DroID showed that CG12299 interacts with 2 proteins which either produce or are found at the cellular skeleton (officially termed the "cytoskeleton"), and 4 proteins involved with neuron creation or guidance
- STRING search showed that two proteins which interact with CG12299 and also interact with each other are highly concentrated in neuronal cells
- FlyBase search showed that the highest concentration of CG12299 was in neuronal cells

DISCUSSION

As we have concluded that CG12299 plays a role in the creation of the cellular skeleton in neuronal cells, the failure of this gene to synthesize its gene product will result in the inability of neuronal cells in maintaining their structure, ultimately leading to neuronal cell death. This neuronal cell death is a key hallmark of ALS.

PROPOSED NAME

As CG12299 is believed to be involved in the development of long, chain-like structural elements, we have decided to name the gene **Spiderman**. Without Spiderman, the cell would not be able to make the long chains that support the structure of the cell.

