Gene discovered that can protect against severe muscle disease

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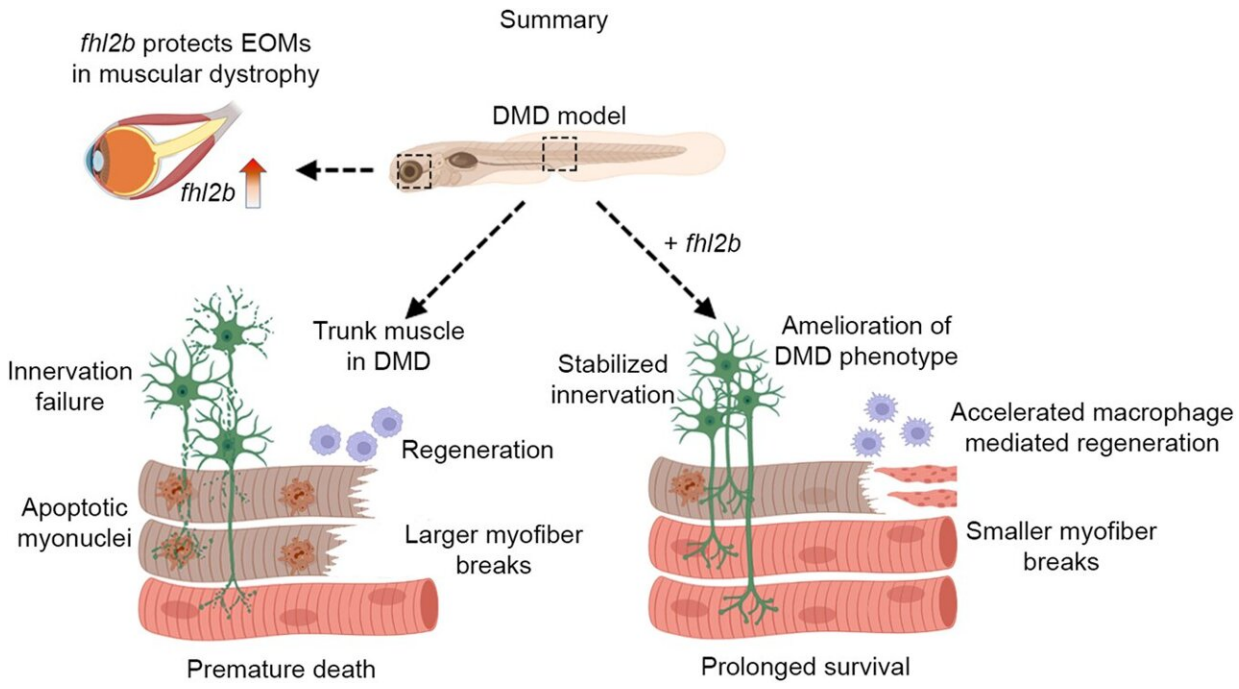

Model for fhl2b mediated rescue of muscular dystrophy. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-46187-x

A specific gene may play a key role in new treatments that prevent muscle in the body from breaking down in serious muscle diseases, or muscular dystrophies. This is shown in a new study carried out at Umeå University, Sweden, which has been published in *Nature Communications*.

Protein expressed by the gene naturally prevents the muscles around the eye from being affected when other muscles in the body are broken down during muscular dystrophies. In the study, genetic scissors were used on the gene that is expressed in all muscles. The effects were that muscular dystrophin was alleviated throughout the body.

"You could say that the eye muscles function as both an eye-opener for understanding the disease and as a door opener to a treatment for the whole body," says Fatima Pedrosa Domellöf, professor of eye diseases at Umeå University and one of the study's authors.

Muscular dystrophies are a group of congenital genetic diseases that affect muscle tissue and often lead to severe disability and greatly reduced life expectancy. Despite intensive research, there are still no effective treatments for patients suffering from muscular dystrophy.

It has previously been discovered that the muscles that control eye movements are not affected by muscular dystrophy, even in otherwise severe disease processes. In people affected by muscular dystrophies, the muscles in the body atrophy while the muscles of the eye remain resistant despite having the same gene defect. However, it has been unclear what this resistance of the eye's musculature is due to.

The study from Umeå University now sheds light on this phenomenon. It turns out that a specific gene plays a key role. This gene, fhl2b, is expressed in eye muscles throughout life, but not in other muscles on the body. In addition, this gene expression in the eye muscles was increased in experiments on zebrafish affected by muscular dystrophy, suggesting that this protects against muscle breakdown.

To test the hypothesis, the researchers tested overexpressing the fhl2b gene in all muscle tissue of zebrafish with the serious muscle disease called Duchenne muscular dystrophy. The results showed that the

zebrafish's muscles were saved and became significantly stronger, and that the fish survived longer.

"There is a long way to go before we arrive at new treatment methods. But the results mean that we have a clear track for further research on how we can use the specific gene and protein to slow down this painful disease progression," says Jonas von Hofsten, associate professor at Umeå University and researcher in the study.

In the study, the researchers used genetically-modified zebrafish to investigate how muscular dystrophies affect eye muscles compared to other body muscles. By using Crispr/Cas9 genetic scissors, new genetic disease models were created.

More information: Nils Dennhag et al, fhl2b mediates extraocular muscle protection in zebrafish models of muscular dystrophies and its ectopic expression ameliorates affected body muscles, *Nature Communications* (2024). DOI: 10.1038/s41467-024-46187-x

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