Qeios

Peer Review

Review of: "VPS13D Mutations Affect Mitochondrial Homeostasis and Locomotion in Caenorhabditis elegans"

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The authors have contributed to developing a C.elegans model to study VPS13D-related SCAR4 disease. Using CRISPR/Cas9 gene editing, they generated disease-relevant mutants and a C-terminal deletion. They conducted fertility and locomotion assays in these models. Based on observations in human and fly models, they focused on mitochondria and performed mitochondrial morphology and UPR assays. Additionally, they addressed the genetic interaction between vps-13D and fzo-1.

Comments:

1. In Figure 3, the authors show mitochondrial morphology changes. The quantifications do not reflect the images presented here. Mitochondrial circularity marks changes in mitochondrial fragmentation. In the images, the null and C-terminal deletion animals show drastic changes in the mitochondrial circularity. The disease-relevant mutations show visible changes in the circularity, though not as drastic as the null or C-terminal deletion. The authors could include quantifications that better reflect their observations. For example, they could include circularity measurement as a quantification, which might be performed using ImageJ.

2. The N3017I variant has stronger changes in locomotion and mitochondrial UPR compared to the N2454S and R3144Q. The authors could provide a biological relevance for this effect. Does N3017I cause severe disease in humans compared to other variants? Is it present at an important protein domain that leads to this increased toxicity?

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Declarations

Potential competing interests: No potential competing interests to declare.