Korte Engelse samenvatting

The rare neurodegenerative disease Chorea-Acanthocytosis (ChAc) is caused by mutations in the VPS13A gene leading to absence of the VPS13A protein in patients. Lack of VPS13A causes neuronal cell death and patients develop movement disorders. Currently, no treatment is available and patients die prematurely. Knowledge about de underlying disease mechanisms of ChAc is limited and here we aimed to gain more insight in the localization and function of VPS13A. For this we used fruit flies in which we knocked out the Vps13 gene in several ways, including the gene editing technique CRISPR/Cas9. Those flies can therefore serve as a model organism for the disease. Mutated flies had a shortened life span, developed motor problems and showed disturbances in protein homeostasis. In addition, those flies showed vacuoles in the brain characteristic for neurodegeneration. Next to a role for Vps13 in the central nervous system, it is also important in the ovaries of fruit flies in which the protein is enriched and is surrounding nuclei that need to be removed. Here Vps13 is required for proper and timely removal of those nuclei through the formation of a specific membrane structure. Using human cell lines we found that VPS13A binds to different cellular organelles and is important for establishing contact sites between different membranes. An increase in cellular lipid content caused relocalization of the protein. This thesis provides insights in the localization and function of VPS13A and contributes to the body of knowledge about the cellular processes in which VPS13A plays a role.

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