Fruit flies give researchers new insights into the 'highway of the nerve cells'

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The nervous system is the internet of the human body and can in the same way transfer signals over long distances very quickly. Some of the

most important elements in this signaling are the axons. They are projections of the nerve cells which send signals to other nerve cells or muscles. For instance, axons that jut out from nerve cells in the spinal cord can be over one meter long.

Researchers from the Faculty of Health and Medical Sciences at the University of Copenhagen have now in a new study examined how signal molecules are transported in the axons.

"We have found out, that the protein Rab2 has to be present and functioning properly in order for the nerve cells to send effective signals between the central nervous system and the body. When we remove the protein in fruit flies we can see that the signal molecules are accumulate in the axons like in a traffic jam," explains visiting researchers Viktor Karlovich Lund from the Department of Neuroscience.

Same or similar mechanism in humans

The researchers investigate the transport of signal molecules in axons because there are multiple illnesses in humans where the transport is inhibited. This is true for neurodegenerative diseases such as Alzheimer's and Parkinson's disease, Amyotrophic lateral sclerosis (ALS) and neuropathy. Changes in the Rab2 gene are also connected to autism spectrum disorders.

Even though one has to be careful drawing conclusions between species, the researchers think that they have good reason to believe that their discovery is also relevant in humans.

"We share around 75 percent of disease-related genes with fruit flies. Beyond that, we know that the genes coding for Rab2 look alike in many different species—they have a high degree of evolutionary conservation. This makes us quite convinced that the same mechanism or one very

similar exists in the human nervous system," says Ole Kjærulff, Associate Professor at the Department of Neuroscience.

The glue between cargo and engine

The signaling works by signaling molecules being transferred from one end of the axons to other nerve cells.

"Some types of signals require that the signal molecules first travel very far in the same cell. They are packaged into small organelles with a membrane around them and then they are transported op to one meter or more. This requires a complex machinery where everything needs to run smoothly," says Ole Kjærulff.

Inside the axons the 'cargo' is pulled by motor proteins that can be compared to small locomotives.

"Our best guess is that the Rab2 protein is the link between the motor proteins driving forward and the cargo being pulled. Almost like a molecular glue holding everything together," says Viktor Karlovich Lund.

The researchers hope that their new discovery can be the foundation for new attempts to create drugs targeting neurodegenerative diseases and neuropathy.

More information: Viktor Karlovich Lund et al, Rab2 drives axonal transport of dense core vesicles and lysosomal organelles, *Cell Reports* (2021). DOI: 10.1016/j.celrep.2021.108973

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