MedicalXpress

Has a possible new lead been found in the fight against neurodegenerative diseases?

November 24 2014

Good communication between brain cells is vital for optimal (mental) health. Mutations in the TBC1D24 gene inhibit this process, thereby causing neurodegeneration and epilepsy. Fruit flies with a defect in Skywalker, the fruit fly variant of TBC1D24, are being used as a model for neurodegeneration. Researchers from VIB and KU Leuven have succeeded in completely suppressing neurodegeneration in such fruit flies, by partially inhibiting the breakdown of 'defective' proteins in brain cells.

Patrik Verstreken (VIB/KU Leuven): "These unexpected results offer us a new line of approach for research into communication between brain cells. We feel that in time it should be possible to help patients with mutations in the TBC1D24 gene, by partially inhibiting transport to the lysosomes (compartments in the cell that digest various molecules)."

A good model for the study of neurodegenerative diseases

We know that mutations in the TBC1D24 gene cause a brain disorder that brings with it conditions including extensive neurodegeneration, epilepsy, mental retardation and hearing problems. Patrik Verstreken and his colleagues have developed fruit flies with mutations in the Skywalker gene, the fruit fly version of TBC1D24. These fruit flies display similar symptoms to patients with brain disorders.

Patrik Verstreken explains: "These fruit flies are not only a suitable model for investigating what goes wrong in the brain, but also for exploring how this can be tackled. For instance we are attempting to reduce or eliminate the symptoms in the fruit flies with mutations in Skywalker by introducing further changes to their DNA. If successful, it means that we have new starting points for our research into neurodegeneration."

Need for "contaminated, defective" proteins

Brain cells communicate with one another at a synapse. Ana Clara Fernandes, Valerie Uytterhoeven and their colleagues, led by Patrik Verstreken, were screening for genes with a potential impact on communication between brain cells. In the process they came across HOPS complex genes. The HOPS complex ensures that contaminated, defective proteins at the synapse (where brain cells communicate with one another) are transported to the lysosome, the compartment of the cell responsible for breaking down the proteins.

When the VIB researchers cut out half of the HOPS complex genes in their fruit fly model for neurodegeneration, the flies were found to be no longer ill. Initially this seems rather strange, because a less active HOPS complex means that the transport of defective proteins to the degradation site is not working as well as it should. This research has shown, however, that defective proteins also play a role at the synapse. These surprising results offer a new line of approach for research into brain disorders.

Provided by VIB (the Flanders Institute for Biotechnology)