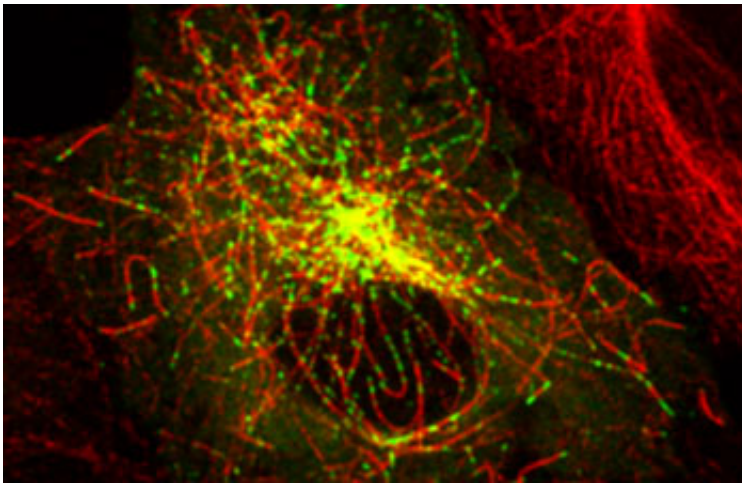


# Effects of high-risk Parkinson's mutation are reversible

October 15 2014, by Amy Pullan

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A microscope image of a cultured cell

Mutations in a gene called LRRK2 carry a well-established risk for Parkinson's disease, however the basis for this link is unclear.

The team, led by Parkinson's UK funded researchers Dr Kurt De Vos from the Department of Neuroscience and Dr Alex Whitworth from the Department of Biomedical Sciences, found that certain drugs could fully restore movement problems observed in fruit flies carrying the LRRK2 Roc-COR Parkinson's mutation.

These drugs, deacetylase inhibitors, target the transport system and reverse the defects caused by the faulty LRRK2 within nerve cells. The

study is published today (15 October 2014) month in *Nature Communications*.

Dr De Vos, a Lecturer in Translational Neuroscience at the world-leading Sheffield Institute for Translational Neuroscience (SITraN), said: "Our study provides compelling evidence that there is a direct link between defective transport within nerve cells and movement problems caused by the LRRK2 Parkinson's mutation in flies."

Co-investigator Dr Alex Whitworth explained: "We could also show that these neuronal transport defects caused by the LRRK2 mutation are reversible.

"By targeting the transport system with drugs, we could not only prevent movement problems, but also fully restore movement abilities in fruit flies who already showed impaired movement marked by a significant decrease in both climbing and flight ability."

The LRRK2 gene produces a protein that affects many processes in the cell. It is known to bind to the microtubules, the cells' transport tracks. A defect in this transport system has been suggested to contribute to Parkinson's disease. The researchers have investigated this link and have now found the evidence that certain LRRK2 mutations affect transport in nerve cells which leads to movement problems observed in the fruit fly (*Drosophila*).

The team then used several approaches to show that preventing the association of the mutant LRRK2 protein with the microtubule transport system rescues the transport defects in [nerve cells](#), as well as the movement deficits in fruit flies.

Dr De Vos added: "We successfully used drugs called deacetylase inhibitors to increase the acetylated form of  $\alpha$ -tubulin within

microtubules which does not associate with the mutant LRRK2 protein. We found that increasing microtubule acetylation had a direct impact on cellular axonal transport.

"These are very promising results which point to a potential Parkinson's therapy. However, further studies are needed to confirm that this rescue effect also applies in humans."

Dr Beckie Port, Research Communications Officer at Parkinson's UK, which helped to fund the study, said: "This research gives hope that, for people with a particular mutation in their genes, it may one day be possible to intervene and stop the progression of Parkinson's.

"The study has only been carried out in [fruit flies](#), so much more research is needed before we know if these findings could lead to new treatment approaches for people with Parkinson's."

**More information:** *Nature Communications* 5, Article number: 5245  
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