



# Parkinson Association of Orange County

## Genetic Mutations Linked to Parkinson's Disease

Researchers have discovered how genetic mutations linked to Parkinson's disease might play a key role in the death of brain cells, potentially paving the way for the development of more effective drug treatments.

In the new study, published in *Nature Neuroscience*, a team of researchers from University College London, the University of Cambridge and the University of Sheffield showed how defects in the Parkinson's gene *Fbxo7* cause problems with "mitophagy" —an essential process through which our bodies are able to get rid of damaged cells.

Mitochondria are the "energy powerhouses" of cells. Their function is vital in nerve cells which require a great deal of energy in order to function and survive. Dysfunctional mitochondria are potentially very harmful and, normally, cells dispose of the damaged mitochondria by ingesting them, a process called mitophagy.

Most of what we know about the mitophagy process comes from the study of the familial forms of Parkinson's, one of the most common diseases of the brain. Over the last three years, two genes associated with familial Parkinson's disease, *PINK1* and *Parkin*, have been reported to play a role in mitophagy.

This new study shows just how central the role of mitophagy is and how mutations in *Fbxo7* are also linked with the disease and interfere with the *PINK1-Parkin* pathway. In people with Parkinson's, genetic mutations cause defects in mitophagy, leading to a build-up of dysfunctional mitochondria. This is likely to explain, at least partially, the death of brain cells in Parkinson's patients with these mutations.

One of the lead authors, Dr Helene Plun-Favreau from the UCL Institute of Neurology, said: "These findings suggest that treatment strategies that target mitophagy might be developed to benefit patients with Parkinson's disease in the future."

Dr Plun-Favreau, who was recently awarded a grant from the National Institute for Health Research (NIHR) University College London Hospitals Biomedical Research Centre, said: "What makes the study so robust is the confirmation of defective mitophagy in a number of different Parkinson's models, including cells of patients who carry a mutation in the *Fbxo7* gene."

Co-author Dr Heike Laman, University of Cambridge, said: "This research focuses the attention of the PD community on the importance of the proper maintenance of mitochondria for the health of neurons. We are really only at the very beginning of this work, but perhaps we can use this information to enable earlier diagnosis for Parkinson's disease patients or design therapies aimed at supporting mitochondrial health."

Professor Nicholas Wood, Neuroscience programme director for the NIHR University College London Hospitals BRC, said: "It is very exciting to see how detailed biological work of this type can highlight a single pathway that contributes to Parkinson's disease. This presents the opportunity of more rationale drug design for many forms of parkinsonism."

Professor Hugh Perry, chair of the Neurosciences and Mental Health Board at the Medical Research Council said: "This study raises interesting questions about precisely how brain cells die in a Parkinson's patient: the process which is key to understanding the disease's progression. The more we understand about the basic molecular events which contribute to the onset and progression of Parkinson's disease, the better placed we will be to develop treatments to stop it in its tracks."