

# Studying alpha-synuclein in a realistic model of Parkinson's



## Project information

Lead researcher	Dr Richard Wade-Martins
Location	University of Oxford
Cost	£212,058 over 3 years
Start date	September 2010
Type of project	Project grant
Project code	G-1003

## Project background

Alpha-synuclein is a protein that's found all over the brain, and that seems to play a critical role in Parkinson's. At the moment we don't understand enough about what that role is, or even how it usually works. So, in order to find a cure we need to know what the protein typically does in the brain. We also need to know what changes happen to alpha-synuclein in Parkinson's, both in the areas that control voluntary movement and in the non-motor brain areas affected by the condition. To do that, we need to develop new and better animal models of Parkinson's as one of our key research priorities.

- **How do we know alpha-synuclein is important?** Alpha-synuclein is the main component of sticky clumps of protein called Lewy bodies that form inside the nerve cells that die in Parkinson's. People who inherit specific variations in the gene for alpha-synuclein have an increased risk of developing the condition. And recent genetic research suggests that the protein also plays a role for the 95% of people with non-inherited Parkinson's too.
- **Why do we need new animal models?** Parkinson's develops over time and spreads through the brain, but we can't study how this happens in people living with Parkinson's

– they need their brains! Looking at the brain after people have died doesn't tell us what happened in earlier stages of the condition. And currently animals with Parkinson's-like symptoms don't develop Lewy bodies or non-motor symptoms such as trouble sleeping, constipation or low mood. So we need animal models that can accurately mimic the changes that happen inside the brain over time.

### What the researchers are doing

Dr Wade-Martins and the team at the Oxford Parkinson's Disease Centre have genetically engineered mice to have the same type of alpha-synuclein that humans do. They hope that these animals may eventually develop the Lewy bodies that are found in the human brain. Their preliminary research shows that the human alpha-synuclein is present in all the brain areas affected by Parkinson's. So in this project they have a number of goals. The team will carry out detailed brain imaging of the mice to try to detect the earliest changes that may be related to Parkinson's and then compare this with brain tissue from people who had Parkinson's. They'll investigate any changes in the way dopamine is used by nerve cells before any Lewy bodies develop. They'll track any build-up of alpha-synuclein and measure how this affects both dopamine use and how well the animals can carry out a range of motor and non-motor tests.

### How the research will help people with Parkinson's

At the end of the project we should know more about which comes first: changes to alpha-synuclein or changing dopamine use by nerve cells. This will help us understand the earliest stages of Parkinson's better. We should also know more about how the condition progresses with time and about the non-motor symptoms that people develop. We'll also have a more realistic animal model of Parkinson's that can be used in other research projects. All of these elements will lead us closer to a cure.

## For more information, please talk to the Research Team

Call	<a href="tel:02079639313">020 7963 9313</a>
Email	<a href="mailto:research@parkinsons.org.uk">research@parkinsons.org.uk</a>
Write	Parkinson's UK, 215 Vauxhall Bridge Road, London SW1V 1EJ