

# Linking alpha-synuclein to Parkinson's



Maria Grazia

## Project information

Lead researcher	Prof Maria Grazia Spillantini
Location	University of Cambridge
Cost	£127,997 over two years
Start date	October 2011
Type of project	Project Grant
Project code	G-1102

## Project background

Alpha-synuclein is a protein that plays an important role in the development of Parkinson's. It's found inside all brain cells but we don't yet know much about what it does. We do know that it makes up the main part of sticky clumps of protein called Lewy bodies that are found inside the nerve cells that die in Parkinson's. A small number of people have the inherited form of Parkinson's due to mutations or changes in their alpha-synuclein gene.

Researchers have shown that development of Lewy bodies leads to a decrease in the amount of the normal alpha-synuclein protein inside the cell. And what is interesting is that Parkinson's can also develop when the normal protein is present in larger amounts than usual.

- **Dopamine is a chemical that's important in the way that nerve cells communicate with each other.** And previous research has shown that the amount of dopamine manufactured by cells decreases before the cells start to die. Proteins called SNAREs control the way the chemical is released from nerve cells as the cells send signals between each other.
- **Accumulation of alpha-synuclein molecules to form aggregates can affect how SNAREs work.** And when the SNAREs don't function correctly, dopamine is not released from the nerve cells. This can lead to slow nerve cell death.

- **The formation of aggregates of alpha-synuclein is a two step process.** Firstly, a few molecules come together to form oligomers. These then clump together to form much larger filaments that make up the Lewy bodies that are characteristic of Parkinson's.

Prof Spillantini and her team have developed a mouse model of Parkinson's that contains a form of alpha-synuclein that is more prone to aggregation and so replicates some of the features seen in the brains of people with Parkinson's. In another Parkinson's UK-funded project (project code: G-0701), they used this model to show that alpha-synuclein forms aggregates in the nerve terminals where nerve cells communicate with the other through release of dopamine.

### What the researchers are doing

In this study, Prof Spillantini and her team will use the mouse model as well as post-mortem brain tissue from people with Parkinson's to see which form of alpha-synuclein is toxic – the smaller oligomers that are formed initially or the larger filaments that give rise to the aggregates of the protein. Once they have this information they will test a number of drugs to see which ones can either stop the oligomers being formed or dissolve them. This would allow SNARE to function properly and dopamine can be released as normal.

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

This study will give us more information about what alpha-synuclein does in nerve cells. If the alpha-synuclein aggregates play an important role at the synapse, preventing their formation or dissolving them with drugs may therefore restore normal dopamine release. This could lead the way forward to a new treatment to slow down or halt the death of nerve cells and ultimately bring us closer to a cure for Parkinson's.

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

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