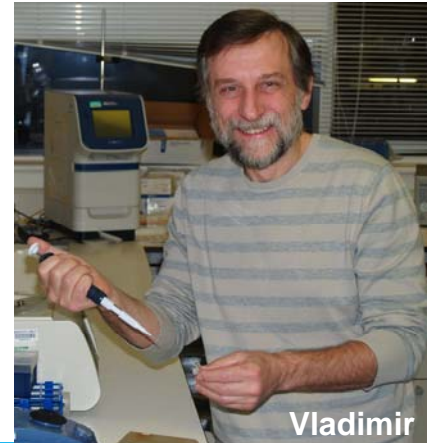


What does alpha-synuclein do in nerve cells?



Project information

Lead researcher	Prof Vladimir Buchman
Location	University of Cardiff
Cost	£184,778 over 3 years
Start date	April 2011
Type of project	Project grant
Project code	G-1006

Project background

Alpha-synuclein is a protein that's one of the key players in Parkinson's. It's normally found in cells all over the body. However in Parkinson's it also forms clumps inside the specific nerve cells that produce the chemical dopamine. People with Parkinson's lack dopamine in a part of the brain that helps control movement because the dopamine-producing nerve cells there die. We don't fully understand the role that alpha-synuclein plays in these cells, but some research has reported that it may be important in ensuring that dopamine is released by the nerve cells in the proper manner. And inherited variations in the gene for alpha-synuclein can lead to young-onset Parkinson's, so we know the protein must play a critical role.

- **Lewy bodies are the clumps of protein that are found inside the nerve cells that die in Parkinson's.** While they're mainly made up mainly of alpha-synuclein. they also contain other proteins in smaller amounts. We think that the alpha-synuclein first starts to band together on its own. It forms what are knows as 'fibrils'. The fibrils then join up, together with the other proteins that make up Lewy bodies.
- **Recent research suggests that alpha-synuclein fibrils are toxic to nerve cells.** Once the Lewy bodies appear in the nerve cells, they become less well able to work normally and eventually die.

- **The levels of normal alpha synuclein decrease in cells which contain Lewy bodies.** The clumping of the alpha synuclein really has two effects. Not only does it give rise to the generation of Lewy bodies but there is also a decrease in the amount of the normal form of the protein inside the cell. However, while we know that Lewy bodies are harmful, we don't know what the effect of decreased amounts of normal alpha synuclein will have on a cell, how it works or how fragile it may become.

What the researchers are doing

In this project, Prof Buchman and his group are asking the question whether the decrease in the levels of the normal alpha synuclein protein will cause nerve cells to work less efficiently. They will generate mice which have normal amounts of the protein in their nerve cells while they are growing up. Then, using sensitive biochemical techniques, they will suddenly turn it off. This will be similar to what happens when all of the alpha synuclein in the cell clumps together into Lewy bodies. But this study will allow us to find out what are the effects of the decrease in the alpha synuclein alone as no toxic Lewy bodies will be formed.

How the research will help people with Parkinson's

We need a cure for Parkinson's. At the moment the best we have are various drugs that treat the symptoms. But none of them stop the dopamine-producing nerve cells from dying. If we could stop the nerve cell death and perhaps even reverse the damage in cells that have begun to be affected by Parkinson's, we'll be well on the way to people living free of symptoms. So we need to find out what are the key factors that cause specific nerve cells in the brain to become more fragile and die in Parkinson's. Using this information, we can concentrate on vital processes inside the cell that we may be able to target with drugs to slow down, halt or even prevent the death of nerve cells.

For more information, please talk to the Research Team

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