

Using skin cells to tell us more about Parkinson's



Project information

Lead researcher	Dr Oliver Bandmann
Location	University of Sheffield
Cost	£226,181 over three years
Start date	April 2011
Type of project	Project grant
Project code	G-1007

Project background

LRRK2 – pronounced lark 2 – is the most common gene associated with Parkinson's. A mutant form of the LRRK2 gene which is used to make the LRRK2 protein, can cause the death of nerve cells, although we don't know the reason for this. However, some research that has previously been carried out suggests that this may be due to a decrease in the cells ability to produce enough energy to allow it to work normally.

- **Mitochondria play an essential role in all cells**, providing the energy needed to live and function properly. They are effectively the tiny energy-producing batteries that are present inside cells. Nerve cells have very high energy demands because of the huge amount of work they do, which means their mitochondria have to work extra hard. This makes them very vulnerable to factors that may be harmful. In Parkinson's, mitochondria don't seem to work properly.
- **It is difficult to study nerve cells in the brain.** However, certain genes which are responsible for the working of the cell, such as LRRK2, are also present in other cells in the body. These include skin cells (called fibroblasts) which can be used to investigate what role particular proteins play in the cell.

- **Not everybody with the altered form of LRRK2 will develop Parkinson's.** So we need to find out the reason for this and why some people are more vulnerable. This will give us ideas of how we may be able to prevent nerve cells from dying.

What the researchers are doing

Dr Bandmann's team want to find out more about how mutations in LRRK2 may influence a cell's ability to make energy to work properly. In particular, they want to find out why only some people with the altered form of LRRK2 will develop Parkinson's. So they'll use a number of approaches. Firstly, they will turn off LRRK2 to see what effect this has. This may have a similar effect to cells having a mutant form of the protein. They then want to see whether they can "rescue" the cells – to prevent them from dying. Because skin cells are easy to grow in the lab, they can treat them in various ways – modifying their genes, or adding drugs – to see whether these can protect against the cells dying. They will also compare cells from people with altered LRRK2 but who don't have Parkinson's. This will help us to understand better why some people develop the condition. They will also use skin cells to screen for drugs that can overcome the decrease in the cell's ability to produce enough energy to work properly.

How the research will help people with Parkinson's

One of the key components of the Parkinson's UK research strategy is to understand why people get Parkinson's. This research will ask why some people with a mutant form of a gene develop Parkinson's, while others don't. This may, for example, be due to their ability to cope with a decrease in the cell's production of energy. But they will also use the system to screen for drugs that can potentially overcome the problem. These could slow down, halt or prevent the death of nerve cells and help us to develop more effective treatments for the condition and ultimately lead us closer to a cure.

For more information, please talk to the Research Team

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