Developing a test to monitor the early signs of Parkinson's


Richard

Project information	
Lead researcher	Dr Richard Wade-Martins
Location	University of Oxford
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Project code	K-1003

Project background

Having studied the 5% of people who have inherited Parkinson's from their parents, we know that at least two key proteins play an important role in the condition. Variations in the genes for alpha-synuclein and LRRK2 (pronounced 'lark 2') lead to a build-up of proteins inside nerve cells that make the chemical dopamine. These clumps of protein are called Lewy bodies and may be related to the death of the dopamine cells. When most of these cells have died, the movement-related symptoms of Parkinson's begin. Now, the most recent research has found that LRRK2 and alpha-synuclein are also affected in the 95% of people who have the non-inherited form of Parkinson's. So we really need to piece together the detective work done so far on these proteins to in order to spot the condition early and develop drugs that can stop the condition.

- **LRRK2 may be the key to the death of dopamine-producing nerve cells.** Recent research in animals has shown that when LRRK2 is over-active, alpha-synuclein is more likely to clump together. Another recent discovery is that preventing LRRK2 from working protects the dopamine nerve cells and stops them from dying so quickly.

- **Monitoring LRRK2 activity could tell us whether Lewy bodies are starting to form.** LRRK2 is only active when two copies of the protein are bound together. So it could be possible to monitor LRRK2 activity by looking for pairs of the protein that are locked together. This has proved a successful technique in other areas of research but has never been tried before for Parkinson's.
- **DNA can be designed to detect specific proteins.** A newly developed technique allows researchers to detect pairs (or small groups) of proteins only when they are very close together (as they would be if the proteins were bound together). This means that researchers can see and count how many clusters of protein are inside a cell.

What the researchers are doing

Dr Wade-Martins and the team at the Oxford Parkinson's Disease Centre are designing new strings of DNA that they hope can be used to detect LRRK2 and alpha-synuclein. They are trying out several different variations in order to find out which ones do the best job of finding active pairs of LRRK2 or small clumps of alpha-synuclein. They can then use the new test in models of Parkinson's both in the lab dish and in animals with Parkinson's-like symptoms to find out what's happening inside the nerve cells.

How the research will help people with Parkinson's

At the moment there is no way to detect the early stages of Parkinson's. And we don't yet have a drug that can stop the dopamine-producing nerve cells from dying. Having a test that can reliably find active LRRK2 or small clumps of alpha-synuclein will bring both of those goals much closer. This kind of test could be used to find active LRRK2 in the blood or cerebrospinal fluid of people at risk of Parkinson's, enabling treatment to begin as early as possible. It could also make it faster and easier to find a drug that can stop LRRK2 from working, and so perhaps find a permanent cure for the condition.

For more information, please talk to the Research Team

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