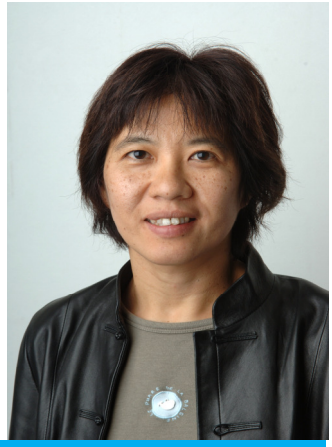
Why are dopamine-producing nerve cells vulnerable in Parkinson's?



Project information	
Lead researcher	Dr Siew-Lan Ang
Location	National Institute of Medical Research London
Cost	£189,017 over three years
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Type of project	Project grant
Project code	G-0906

Project background

Dopamine is an important chemical that's used by nerve cells to communicate with each other. Although it's used by nerve cells in several different brain regions, it's only the dopamine-producing cells in the part of the brain that controls movement that begin to die in Parkinson's. The major goal of Parkinson's research is to find a cure. But before this can happen we need to know more about why specific dopamine-producing nerve cells die.

- **Not all dopamine-producing nerve cells are the same.** Dopamine-producing cells are different in individual parts of the brain**.** They each have a distinct genetic make-up that makes some of them more susceptible to factors that contribute to the death of nerve cells in Parkinson's
- **Specific genes play a key role in how individual nerve cells work.** Researchers can use specialised genetic techniques to find out what these genes are and how they work. Previous research has shown that the nerve cells affected by Parkinson's contain two genes called Robo1 and Robo2. However, other dopamine-producing cells in a neighbouring part of the brain only contain the Robo1 gene.

What the researchers are doing

In order to develop new therapies for Parkinson's we need to understand why only certain nerve cells are die. This is not only determined by the chemicals that they produce (such

as dopamine) but also by specific genes that they contain. The aim of this project is to try to understand the roles of the two Robo genes. These genes are very important in the development of specific dopamine-producing nerve cells. Because they are only present in some dopamine-producing nerve cells, they may provide a clue as to why some dopamine-producing nerve cells die in Parkinson's while others don't.

Progress so far

- One technique to help us understand the role of specific genes in cells is to make mutant mice that are missing one or both of these genes. The researchers have initially generated mice that are missing either Robo1 or Robo2.
- Nerve cells in the mice which have no Robo1 don't develop correctly and the connections between neighbouring nerve cells are not stable. However, these problems are not seen in the mice which are missing Robo2.

What is the next stage?

The next stage is to investigate why an effect is only seen in mice which have no Robo1. This is particularly important given that the cells affected in Parkinson's have both Robo genes. So the researchers will make animals without both of the genes to see what effect this has on the dopamine-producing nerve cells in the different parts of the brain. They also want to find out what the Robo genes do and how will this influence whether particular dopamine-producing nerve cells die.

How the research will help people with Parkinson's

If we can understand why specific nerve cells die, this may help to provide new ways of developing drugs to slow down, halt or even reverse the process.

For more information, please talk to the Research Team

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