

Can zebrafish help us to understand early onset Parkinson's?



Project information

Lead researcher	Dr Oliver Bandmann
Location	University of Sheffield
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Project background

One in every 20 people diagnosed with Parkinson's is under the age of 40. When the diagnosis comes this early in life, the condition is known as early onset Parkinson's. Scientific research has discovered that inheriting a mutation in a gene called *parkin* from both parents can lead to early onset Parkinson's. But we don't yet know exactly how mutations in *parkin* result in the death of nerve cells that produce the chemical dopamine (the chemical that is missing from people with Parkinson's, causing the common symptoms of tremor, slow movement and stiffness in many people with the condition). We also don't know how inheriting one copy of the mutated gene affects a person's risk of developing Parkinson's later in life.

Some facts about genes and proteins:

- **Genes tell cells in the body which proteins to make.** The gene called *parkin* is like a blueprint that tells dopamine-producing nerve cells to make the parkin protein that is vital for nerve cells to work normally. People with early onset Parkinson's who have a mutant form of the gene are likely to have inherited a copy from both parents – we all have two copies of each gene, one from each of our parents. The result is that the nerve cells can't work very efficiently and this leads to the death of dopamine-producing nerve cells in a part of the brain called the substantia nigra.

- **Proteins work together, so changes to one may affect how other proteins work.**
We know that inheriting the mutant form of *parkin* from both parents leads to Parkinson's but sometimes a person may only inherit one copy of the gene. We don't know what effect this will have. We need to find out the role of the parkin protein inside the cell and how it interacts with other proteins and genes.
- **Zebrafish have a *parkin* gene that is very similar to the human gene.** It is possible for scientists to study how genes and proteins work by seeing what happens in animals who have been modified to have the mutant form of *parkin* that is associated with Parkinson's.

What the researchers are doing

Dr Bandmann's team will investigate what happens to zebrafish that have changes in their *parkin* gene. They are trying to answer four different questions -

- 1) Does a lack of the parkin protein make the dopamine-producing nerve cells more fragile?
- 2) What is the effect of inheriting one copy of the mutated gene along with one normal copy?
- 3) How does a lack of the parkin protein affect other genes and proteins in the nerve cell?
- 4) Does a lack of parkin change how efficient the dopamine-producing nerve cells work and whether they are more fragile than normal cells?

How the research will help people with Parkinson's

This study will give us new information about how genes might lead to a cure for Parkinson's, both for people with early onset Parkinson's and for people who develop the condition later in life. Although only a small number of people with Parkinson's have a mutant form of the *parkin* gene, this research will help us to understand what happens when a nerve cell dies. We can use this information to identify ways in which new drugs could overcome these problems and slow down or stop the death of nerve cells that occurs in Parkinson's UK.

For more information, please talk to the Research Team

Call	020 7963 9313
Email	research@parkinsons.org.uk
Write	Parkinson's UK, 215 Vauxhall Bridge Road, London SW1V 1EJ