Stemming the flow: Stem cell study reveals how Parkinson's spreads

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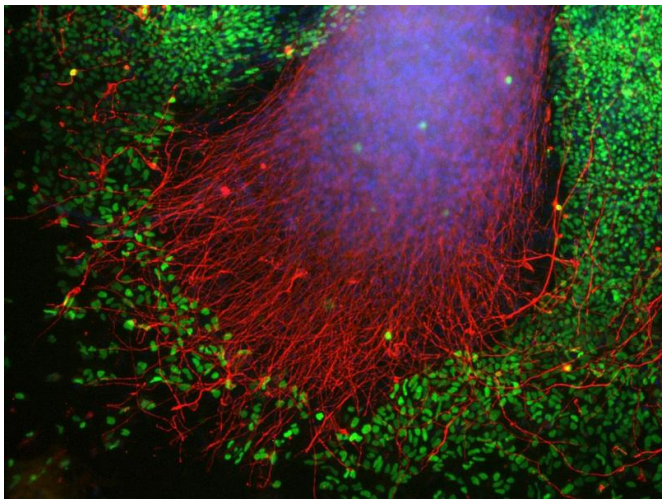

Stem cells being turned into brain cells affected by Parkinson's. Credit: Parkinson's UK

Stem cell research published today offers up new clues as to how Parkinson's spreads from cell to cell, a process which has evaded researchers for decades.

The research, published in *Stem Cell Reports*, is the first to link the release of alpha synuclein, a naturally occurring protein that plays a central role in the development of Parkinson's, with its most common genetic risk factor - GBA-1 - shedding new light on its role in the progression of the devastating neurological condition and its symptoms.

The study, carried out at the Parkinson's UK-funded Oxford Parkinson's Disease Centre, studied cells from two groups of participants - a group with Parkinson's carrying the GBA1 genetic mutation and a control group without the condition.

By studying stem cells and brain cells created from the skin of participants, scientists discovered for the first time that the GBA1 mutation creates problems with how proteins, in particular alpha-synuclein, are processed and recycled in cells. When someone has a GBA1 mutation, protein recycling does not work properly in the cell, creating a build-up of alpha synuclein, which is released into the brain - contributing to the spread of Parkinson's.

The physical and motor symptoms of Parkinson's emerge when around 70% of cells have been lost in the part of the brain called the substantia nigra. Physical symptoms can include a tremor, slowness of walking and stiffness. When the condition spreads to other areas of the brain, Parkinson's dementia and cognitive problems develop.

These new findings offer an insight into how and why excess alpha-synuclein is released into the brain and opens up new pathways of investigation into targeting treatments that could stop this process - with the goal of halting or minimising the severity of the condition.

Professor Richard Wade-Martins, Head of Oxford Parkinson's Disease Centre, and lead researcher on the Parkinson's UK-funded study said:

"Our brain cells work like a complex manufacturing unit, building new proteins to carry out activities and recycling proteins that get damaged. We already know that Parkinson's may spread when alpha-synuclein escapes from affected cells into the brain, where it can then get taken up by other cells. Thanks to this study, for the first time we know how the protein is released, giving us new clues on how this spread happens.

"Most importantly, these findings open up new avenues into investigating potential new therapies or treatments that could stop the spread of alpha-synuclein and slow the condition's progression."

Parkinson's UK Director of Research, Dr Arthur

Roach which funded the study said:

"People with Parkinson's and their families are living with the constant uncertainty of how the condition will affect them both mentally and physically in the future. In addition to the well-known problems with movement and balance, up to 80% of people with Parkinson's will go on to develop dementia, affecting their ability to reason and plan as well as their concentration, attention, memory and language.

"This study is a good example of how studying a genetic form of the condition can provide important insights into what is thought to be a fundamental feature of all forms of Parkinson's. These findings offer new ideas on how we could stop the condition in its tracks - changing the lives of the 127,000 people in the UK, and seven million worldwide, living with Parkinson's."

More information: Fernandes et al., ER Stress and Autophagic Perturbations Lead to Elevated Extracellular a-Synuclein in GBAN370S. Parkinson's iPSC-Derived Dopamine Neurons, *Stem Cell Reports* (2016), dx.doi.org/10.1016/j.stemcr.2016.01.013

Provided by Parkinson's UK