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Unfolding pathogenesis in Parkinson's

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The study, published in the *Journal of Clinical Investigation*, reveals that damaged alpha-synuclein proteins (which are implicated in Parkinson's disease) can spread in a 'prion-like' manner, an infection model previously described for diseases such as BSE (mad cow disease).

"This is a significant step forward in our understanding of the potential role of cell-to-cell transfer of alpha-synuclein in Parkinson's disease pathogenesis and we are very excited about the findings", says Professor Patrik Brundin at Lund University, Sweden, who led a team of investigators from research centres in Denmark, France and Portugal.

A previous observation that aggregated alpha-synuclein protein gradually appears in healthy young neurons transplanted to the brains of Parkinson's patients initially gave rise to the group's hypothesis of cell-to-cell protein transfer. The theory has now been tested in several cell culture experiments. Dr Christian Hansen, one of the key investigators, explains the importance of the new findings:

"We have now shown that alpha-synuclein not only can transfer from one cell to another, but also that the transferred protein can seed aggregation of alpha-synuclein in recipient cells as well. This could be an important mechanism for the spread of the pathology."

Transplant trials in mice, performed by Dr Elodie Angot, lead investigator for animal modelling in the study, strengthened the theory of cell-to-cell transfer: "Six months after Parkinson's disease model mice were transplanted with healthy dopamine neurons, we found that the new

brain cells contained human alpha-synuclein, indicating cell-to-cell transfer from the host brain to the transplants."

These findings add further support to the research group's hypothesis that protein aggregates crossing cellular membranes contribute to the pathogenesis of neurodegenerative diseases. Patrik Brundin concludes, "We are one step closer to understanding how the neuropathology spreads throughout the nervous system in Parkinson's disease, which opens up avenues for new treatments. Hopefully, in the future we will be able to inhibit this spread and slow down the relentless disease progression and worsening of symptoms in patients."

More information: 'α-Synuclein propagates from mouse brain to grafted dopaminergic neurons and seeds aggregation in cultured human cells', *J Clin Invest.* doi:10.1172/JCI43366

Provided by Lund University