Molecule capable of halting and reverting neurodegeneration caused by Parkinson's disease identified

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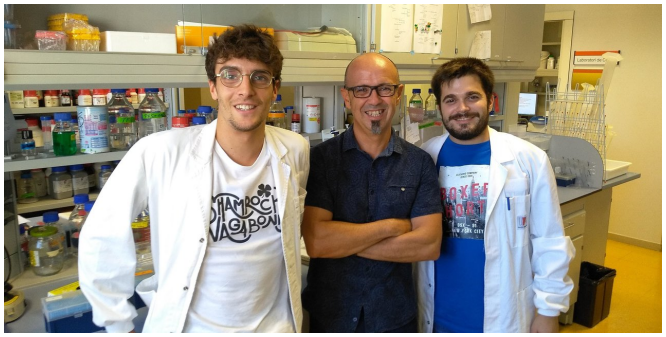

Jordi Pujols, Salvador Ventura and Samuel Peña at the UAB. Credit: Universitat Autònoma de Barcelona

The small SynuClean-D molecule interrupts the formation of the alpha-synuclein amyloid fibres responsible for the onset of Parkinson's disease, and reverts the neurodegeneration caused by the disease. The study, headed by Universitat Autònoma de Barcelona researchers, was published in *PNAS*.

Parkinson's disease is the second most common incurable neurodegenerative disorder after Alzheimer's disease. It is characterised by the accumulation of protein deposits in dopaminergic neurons in the form of amyloid fibres. These aggregates are formed mainly by the alpha-synuclein protein and in a very complex manner, which makes it complicated to identify molecules which could prevent or revert the process and the neurodegeneration associated with it.

A scientific collaboration led by researchers at the Institute of Biotechnology and Biomedicine (IBB) of the Universitat Autònoma de Barcelona has identified a molecule which halts and reverts this neurodegeneration. After analysing over 14,000 molecules, they found the SynuClean-D molecule, which inhibits the aggregation of the alpha-synuclein protein and breaks the already formed amyloid fibres, thus preventing the initiation of the process causing the onset of the neurodegenerative Parkinson's disease.

Through experiments conducted with the small Caenorhabditis elegans worm, one of the most commonly used animal models in neurodegenerative diseases, researchers were able to verify that by administering it through food, the molecule was capable of notably reducing alpha-synuclein aggregations, preventing the spread of toxic aggregates and therefore avoiding the degeneration of dopaminergic neurons.

"Everything seems to indicate that the molecule we identified, the SynuClean-D, may provide therapeutic applications for the treatment of neurodegenerative disases such as Parkinson's in the future", UAB researcher and coordinator of the study Salvador Ventura points out.

To identify SynuClean-D researchers developed a methodology capable of indentifying the alpha-synuclein aggregation inhibitors among thousands of molecules. Once identified, an in vitro biophysical characterisation was conducted of their inhibiting activity and tests were run to discover their behaviour with human neural cell cultures, before testing it in animal models of the disease (the Caenorhabditis elegans worm). These animals express the alpha-synuclein in the muscle or in dopaminergic neurons. The experiments demonstrated that the administration of the identified inhibitor reduced protein aggregation, improving the mobility of the animal and protecting it from neural degeneration.

More information: Jordi Pujols et al. Small

molecule inhibits ?-synuclein aggregation, disrupts amyloid fibrils, and prevents degeneration of dopaminergic neurons, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1804198115