

Identification of potential target protein aggregates for treating Alzheimer's

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The aggregation of alpha-synuclein proteins in Parkinson's disease and tau proteins in Alzheimer's disease is intimately linked to the progression of these neurodegenerative diseases. These aggregates propagate from one neuronal cell to another, attaching themselves to the cells.

They multiply during this propagation. It has already been shown that the propagation and amplification of these protein aggregates are harmful

and contribute to the progression of these diseases.

Understanding the formation of these aggregates, their propagation and their multiplication in the [cells](#) of the central nervous system offers potential for treatments: it would make it possible to target these processes and to act on their consequences.

Protein propagation

The key step in the propagation of the pathogenic aggregates is the attachment of aggregates released from affected neuronal cells to the membranes of unaffected cells. Having already identified the targets of pathogenic aggregates of the alpha-synuclein protein (Shrivastava et al., 2015 *EMBO-J*), the team at the Neurodegenerative Diseases Laboratory (CNRS/CEA/Université Paris-Sud , MIRCen, Fontenay-aux-Roses), in collaboration with the Ecole normale supérieure, Sorbonne University and Inserm, has just identified the targets of tau protein aggregates. The targets are the sodium / potassium pump and glutamate receptors, two essential proteins for the survival of neurons The experiment was carried out on mouse neurons in culture.

Neuron membrane modification

The researchers also showed that the pathogenic aggregates modify the neuron membranes by redistributing the [membrane](#) proteins. The integrity of the membrane—and particularly of the synapses, the essential nodes for communication between neurons—is affected. These changes have a deleterious effect on the neurons because they cause abnormal communication between the neurons, as well as their degeneration.

This work therefore explains the early malfunctioning of the synapses

and the degradation of normal communication observed in the neuronal networks as the [disease](#) progresses.

Toward new treatments

It also paves the way for the development of new treatment strategies based on protecting the integrity of the synapses, restoring the activity of the tau protein membrane receptors through the use of decoys to prevent harmful interaction between the pathogenic tau [protein](#) aggregates and their neuron membrane targets. These therapeutic approaches could be developed using human [neurons](#), since researchers at the laboratory have just developed cultures of this type in collaboration with the I-Stem (Institute for Stem Cell Therapy & Exploration of Monogenic Diseases, AFM-Téléthon/Insem/Génopole/University of Evry-Val-d'Essonne) laboratory and Sorbonne University. This latter study is also published on 10 January 2019, in *Stem Cell Reports*.

Provided by CEA

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