Targeting Alpha-Synuclein for Treating Multiple System Atrophy

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Country

France

Title of project or programme

Targeting Alpha-Synuclein for Treating Multiple System Atrophy

Source of funding information

ANR

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€ 234,000

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01/12/2014

Total duration of award in years

4

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Research Abstract
Multiple system atrophy is a fatal disorder with severe motor impairment and dysautonomia affecting over 30,000 people in Europe. Accumulation of a-synuclein in oligodendrocytes plays a pivotal role, leading to glial and neuronal dysfunction and degeneration. These features are recapitulated in the PLP-SYN mouse model expressing a-synuclein in oligodendrocytes. This project aims at counteracting disease progression by targeting key mechanisms contributing to a-synuclein accumulation. Using complementary in-vitro and in-vivo models, we will test the efficacy of: 1) increasing a-synuclein clearance by activating autophagy with rapamycin, 2) reducing seeding of aggregation by preventing its cleavage with VX-765, 3) reducing a-synuclein aggregation using the oligomer inhibitor anle138b, and 4) preventing a-synuclein

propagation via active and passive immunotherapy using AFFITOPE®. Finally, we will test the combination of the most promising strategies to obtain synergistic therapeutic effect. Efficacy readouts will include oxidative stress, unfolded protein response (in-vitro), cell survival, monomeric, oligomeric and post-translational modifications of a-synuclein (in-vitro and in-vivo), astroglial and microglial activation, as well as motor deficits (in-vivo). This project involves academic partners with strong expertise in multiple system atrophy and industrial partners with innovative therapeutic candidates. This unique combination at the European level will allow a rapid translation of successful strategies into clinical trials.

Further information available at:

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Investments < €500k

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France

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