Laboratory title : CNRS UMR 5293 - Erwan Bézard

Supervisor

Name : Wassilios MEISSNER

Thesis title : Establishment of a non-human primate model and biomarker research in Parkinson's disease

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Contact

Firstname : Wassilios Name : MEISSNER

E-mail : wassilios.meissner@u-bordeaux.fr

phone number : 0557575693

Fax :

Abstract

The clinical differential diagnosis between Parkinson's disease (PD) and atypical parkinsonian disorders including multiple system atrophy (MSA) can be difficult. Therefore, there is a great need for the development of biomarkers to improve the accuracy of diagnosis. Furthermore, no treatments are available to slow down the neurodegenerative process. Previous clinical neuroprotection trials have failed in part because of the limitations of preclinical models in terms of translational value (probability of success in patients after validation in animals) and the lack of biological markers as objective outcomes to measure treatment efficacy in patients.

Accumulation of abnormally folded alpha-synuclein (aSyn) is the main mechanism of the underlying neurodegenerative process in PD and MSA. Several promising treatment strategies for PD and MSA targeting aSyn are in preclinical development. We propose the validation of an innovative non-human primate model, based on the inoculation with PD- or MSA-patient derived aSyn. We expect a better translational value of this model better. In parallel, we propose the development of biomarkers for the diagnosis and the evaluation of neuroprotective strategies in patients.

The objectives of this translational project are threefold:
1) To characterise the aSyn aggregation pattern in cerebrospinal fluid (CSF) in PD and its most relevant differential diagnosis MSA of existing patient cohorts.
2) To monitor longitudinal changes of CSF levels of distinct aSyn species as known progression markers in innovative non-human primate models of PD and MSA.
3) To assess the effect of compounds with putative neuroprotective properties on CSF aSyn pattern in the non-human primate model of PD.

Qualification required

An experience in the techniques of immunohistochemistry, western blot and molecular biology are very welcome.