Laboratory title : CNRS UMR 5293 - Erwan Bézard

Supervisor

Name : Benjamin DEHAY

Thesis title :
Cross-sectional study of Parkinson’s disease-related neurodegenerative and spreading mechanisms

Keywords : Parkinson’s disease, neurodegeneration, spreading mechanisms

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Abstract

Neurodegenerative diseases are characterized by a selective neuronal vulnerability with degeneration in specific brain regions, and deposits of misfolded proteins. Alzheimer’s (AD) and Parkinson’s (PD) diseases are the most prevalent neurodegenerative diseases. They are characterized by severe neuronal losses in several brain regions leading to (i) inexorable impairments of memory and other cognitive functions in AD and (ii) paralysis-like syndrome in PD. The neuropathological landmark of PD is defined by the presence of Lewy Bodies (LB) that are intraneuronal proteinacious cytoplasmic inclusions, which alpha-synuclein is the major protein component. In the past two years, another hallmark has been added, as aggregation-prone protein may act as prions. Evidence for a role of alpha-synuclein acting in a potentially prion-like manner has emerged from in vitro and recently by ourself in vivo studies to explain how alpha-synuclein can undergo spontaneous self-aggregation, propagate from cell to cell, and initiate the formation of aggregates, all of which associated with neuronal cell death. The proposed PhD research project, taking advantage of a translational approach in place in the laboratory, aims at i) defining and characterizing the kinetics of the prion-like LB-induced neurodegeneration in rodents and non-human primates ii) establishing the specific vulnerability of the nigro-striatal dopaminergic system to uptake and propagate alpha-synuclein for PD and (iii) correlating pathological observation with measures of parkinsonian symptoms / imaging alterations.

Qualification required

Extreme motivation, availability, curious mindset, rock-solid knowledge of neurodegenerative disease pathophysiology, fluent in English. In vivo experience and molecular biology, biochemistry and cell biology technical aspects are very welcome.