

Internship Proposal Academic Year 2019-2020

1. Host team:

Research Unit (e.g. Department or Institute): CNRS CEA UMR 9199, Laboratory of Neurodegenerative Diseases

Research Unit Director: Emmanuel BROUILLET

Research Team Director: Gilles BONVENTO

Team name: Cell-cell interactions in neurodegenerative diseases

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2. Internship project title:

Role of glial cells in the propagation of toxic tau species

3. Internship Description :

Tauopathies, whose prototypical example is Alzheimer's disease (AD), form a set of neurodegenerative diseases that are characterized by a pathological aggregation of Tau protein in neurons, but also in the glial cells according to the pathologies. In the case of AD, Tau aggregates occur in a well-characterized spatio-temporal pattern, known as Braak stages, and strongly correlated with the severity of symptoms. In order to study the phenomena of propagation of pathological forms of Tau, we have developed a model of gene transfer overexpression of different forms of this protein. This has allowed us to show recently that highly aggregated insoluble forms of the pathological protein are much less toxic than soluble oligomers [1]. In addition, recent data from the literature converge to designate neuroinflammation, and in particular microglial cells, as a major player in the etiology of AD. The current goal of our research is thus to establish the link between tauopathy and neuroinflammation using the AAV-derived gene transfer tools that we have developed and which will be now applied to cellular and animal models of tauopathies.

As part of this project, the student selected for this internship will have to implement techniques of cell biology, molecular biology and quantitative histology.

1. d'Orange et al., Potentiating tangle formation reduces acute toxicity of soluble tau species in the rat. *Brain*, 141:535, 208.