

Internship Proposal Academic Year 2018-2019

1. Host team :

Research Unit (e.g. Department or Institute) : MIRCen, Institut François Jacob, CEA Fontenay aux Roses

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Team name : Preclinical therapies for neurodegenerative diseases

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2. Internship project title:

Impact of neuronal tauopathy on astrocytes

3. Internship Description :

The role of astrocytes in neurodegenerative diseases has long been overlooked. Yet, these cells play important supportive functions for neurons. In Alzheimer's disease patients and animal models, signs of astrodegeneration have been reported, suggesting that astrocytes supportive functions may be seriously impaired and may contribute to pathology (1,2,3). The Tau protein is now identified as a key player in the pathological cascade of many Tauopathies, where it can accumulate in both neurons and astrocytes. Here, we will determine whether the aggregation of Tau that first develops in neurons, secondarily affects astrocytes. We first aim at understanding how astrocytes come to display Tau aggregates since they normally synthesize low levels of this protein. A second aim is to evaluate astrocytic morphology, survival and functions in the presence of soluble or insoluble Tau species.

We have recently developed in vivo models of Tauopathies in rodents showing neuronal Tauopathy with varying degrees of aggregation (4). These are induced by local injection of AAV Tau vectors in the hippocampus of adult mice. Surprisingly, while our AAVs transduce neurons only, these models also display astrocytic tauopathy. During the internship, histological analysis will determine the severity of Tau pathology in neurons and astrocytes, and how it affects the morphology and survival of astrocytes in vivo.

1. Togo T and Dickson DW. Acta Neuropathol. 2002, 104:398
2. Piacentini R et al, Glia. 2017, 65:1302
3. Kovacs et al, Brain Pathol. 2017, 27:675
4. d'Orange et al, Brain, 2018, 141:535