Master de Sciences et Technologies
Mention Biologie Intégrative et Physiologie
Parcours : Neurosciences
Responsable : Professeur Régis Lambert

Internship Proposal
Academic Year 2019-2020

1. Host team:

Research Unit (e.g. Department or Institute): CNRS CEA UMR 9199
Research Unit Director: Emmanuel BROUILLET
Research Team co-Director: Gilles BONVENTO
Team name: Cell-cell interactions in neurodegenerative diseases

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2. Internship project title:

Primary cilia signalling in Huntington's Disease human astrocytes

3. Internship Description:

Mutation in the Huntingtin protein (HTT) underlies the neurodegenerative disorder, Huntington disease (HD). This devastating disorder is characterized by progressive degeneration in the basal ganglia and cerebral cortex. Primary cilia are slender protuberances that project from the cell body. They are present in all cell types including neurons and astrocytes and act as sensory organelles to receive signals that regulate cellular behaviour and physiology and plays important roles in brain development and diseases. HTT is present at the base of the primary cilia and is required for ciliogenesis. Defects in primary cilia were detected not only in cellular mouse models of HD but more importantly in HD patients.

The extent to which cilia defect contributes to symptoms in HD patients is unknown. Over the past decades, the true complex nature of human astrocytes has been progressively exposed; suggesting astrocytes are key players in neurodegenerative diseases including HD. Our working hypothesis is that cilia defect contributes to HD via the impairment of astrocytic function in the brain of patients.

The rationale of this project is to take advantage of the properties of human pluripotent stem cells (hPSC) to model human astrocytes functions alone and human astrocyte-neuron interactions in vitro. More specifically, we will study whether and how cilia dysfunctions are linked to HTT loss or HD mutations in hPSC-astroglial derivatives of human iPS lines. Our long term goal is to determine to what extent cilia defect contributes to symptoms in HD patients mediated by dysfunctional astrocytes.