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) : Institute du Cerveau et la Moelle Epinière
Research Unit Director : Alexis Brice
Research Team Director : Drs.Stéphane Haïk and Marie-Claude Potier
Team name : « Alzheimer disease and prion disease »

Address : 47 Bd de l'Hôpital, 75013 Paris

Supervisor of the Research Intern for this project : Dr. Susana Boluda
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2. Internship project title:

Search for a molecular signature in patients with rapidly progressive Alzheimer's disease

3. Internship Description :

The internship would be for 6 months

Context:

Alzheimer's disease (AD), the most frequent cause of dementia, is characterized by the extracellular aggregation of Aβ peptides assembling in plaques and the intracellular aggregation of Tau protein forming neurofibrillary tangles. The most frequent clinical presentation of AD is a progressive cognitive decline with mean disease duration of 8 years. However, AD can be clinically diverse. Specifically, there is a group of patients with a fast progression of the disease and atypical clinical presentation that resembles prion disease.

In prion diseases, the clinical diversity is mainly caused by the existence of different strains of the pathological protein PrP^{SC}. A prion strain is defined as the alternative conformation that a protein can acquire during its folding and aggregation and that is able to induce a specific disease when transmitted to a host. This different folding pattern or conformation gives the protein a molecular signature (electrophoretic mobility, protease resistance, sedimentation velocity) that is characteristic of each strain.

In AD, we postulate that the presence of different strains of any of the two proteins involved in the disease, Aβ and/or tau, contributes to its clinical diversity and particularly to the rapidly progressive AD (rpAD).

Objective:

The main goal of the project is to identify within patients with rpAD a specific tau biochemical signature that may suggest the presence of a specific tau strain. To this aim, we will compare using different approaches the biochemical properties of abnormal tau protein in different clinical subsets of sporadic AD cases including rpAD. The project forms part of a larger integrative project in the team.

Methods

Patient's brain extracts will be prepared and analyzed by different biochemical techniques: separation of tau assemblies by sedimentation velocity in sucrose gradient; protease digestion of tau fibrils; epitopes mapping using a panel of tau-specific antibodies. Results of biochemical analysis will be correlated with clinical and neuropathological data. The student will work with human brain tissue in specialized infrastructures and will benefit from the technical support and the supervision of a multidisciplinary team with expertise in neuropathology, biochemistry, animal and cellular models of AD.