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

Internship Proposal
Academic Year 2018-2019

1. Host team :

Research Unit (e.g. Department or Institute) : Centre de Recherche INSTITUT DE LA VISION UM 80 UPMC - UMR S 968 Inserm - UMR 7210 CNRS

Research Unit Director : Pr. José-Alain SAHEL

Research Team Director : Dr. Serge Picaud

Team name : *Transmission de l'information visuelle, pharmacotoxicité rétinienne et neuroprotection*

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2. Internship project title:

Retinal dysfonction in Alzheimer disease mice model

3. Internship Description :

Alzheimer's disease is the most common aging-associated neurodegenerative disease; it represents 50 to 70% of all dementia cases and according to the World Alzheimer Reports, 46 million people live with dementia. Nowadays, Alzheimer disease is considered as a public health priority by the World Health Organization due to the high costs associated with care and treatments. The main pathological hallmarks of Alzheimer disease are the presence of extracellular Aβ-plaques, intracellular inclusions of hyperphosphorylates tau proteins and brain atrophy associated to neuron and synapse loss.

Recently, different studies of Alzheimer patients have shown a reduction of the retinal nerve fiber layer thickness and a decrease in retinal blood flow rate and venous diameter. Different publications have reported the presence of Aβ-plaques in the retina, although others only reported

the presence of hyperphosphorylated tau proteins. Furthermore, Koromyo-Hamaoui group claim that the accumulation of plaques starts in retina before brain. Thus, pathological alterations in the retina represent a good candidate for developing new biomarker for Alzheimer disease diagnosis. To note, the retina is considered a very convenient circuit for assessing information processing and neurodegenerative pathologies thanks to its easy optical assessment, the possibility to record its natural activity *in vivo* by measuring electroretinograms (ERGs) or even *in vitro* on multielectrode array. The retina is by far the most accessible part of the vertebrate central nervous system (CNS) and one of the most convenient models to study neural circuit pathologies. The complexity of the retinal circuit is such that all neurotransmitters (glutamate, GABA, Glycine, Acetylcholine, Dopamine, Serotonin…) present in the brain are also present in the retina.

In the present project, we propose to assess at a functional and histological level *in vivo* and *in vitro* the state of the retina at different ages in an animal model of the Alzheimer disease. The occurrence and development of visual dysfunction will be investigated in the APP/PS1 transgenic mice by measuring visual acuity overtime. A correlation between retinal dysfunction and *in vivo* appearance of β-amyloid plaques will be evaluated in mice model. Such a project on an animal model of Alzheimer disease can provide conditions for testing different therapeutic strategies on this disease model. It can also provide new ways for detecting the disease development in patients prior to major neurologic symptom.