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): Neuroscience Department at Institut Pasteur, Paris
Research Unit Director : Dr David DiGregorio
Research Team Director : Dr Uwe Maskos
Team name : Integrative Neurobiology of Cholinergic Systems

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Supervisor of the Research Intern for this project : Isabelle Cloëz-Tayarani (PhD, HDR)
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2. Internship project title:

A new humanized mouse model with grafted human neural precursors to study the role of nicotinic receptors in early stages of Alzheimer's disease.

3. Internship Description:

Alzheimer's disease (AD) is the most common neurodegenerative disorder which has been characterized by a progressive loss of cognitive abilities and memory as well as the loss of specific neuronal populations in cortex and hippocampus. These two regions are particularly vulnerable in the early stages of AD. An accumulation of β-amyloid peptide (Aβ) to form amyloid plaques occurs within the brain. However, the direct link between such accumulation and the progression of AD is still unknown. Initial studies in the laboratory have clearly shown the existence of a direct interaction between Aβ and nicotinic acetylcholine receptors (nAChR), that may take place in the normal physiology of the brain, and in AD as well. As a follow-up to our initial studies, the aim of the internship is to investigate the interaction of Aβ with nAChR and the involvement of these receptors in pathogenesis of AD. The functional properties of the human form of alpha7 nAChR subtype together with its brain anatomical localization render this subtype of particular interest. Consequently, one important objective is to clearly identify the interaction of human alpha7 nAChR with Aβ, within the cortex and hippocampus. The project consists in the implantation of human neuronal precursors expressing human alpha7 nAChR in a murine model of AD (Lombardo et al, Neurobiology of Aging *46*, 221-34, 2016; Koukouli et al, Aging *8*, 3430-48, 2016) with subsequent analysis of morphological and functional phenotypes. Experimental approaches will include cell culture, immunofluorescence labeling, histology, cell grafting into the developing mouse brain.