Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2024-2025

Laboratory/Institute: Grenoble Institut Neurosciences (GIN) **Director:** Dr. E. Barbier
Team: Neuropathologies et Dysfonctionnements synaptiques **Head of the team:** Pr. Alain Buisson

Name and status of the scientist in charge of the project: Dr. Yves Goldberg & Dr. Fabien Lanté

HDR: yes
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Program of the Master's degree in Biology: Neurosciences and Neurobiology

Title of the project: How Alzheimer disease Amyloid-β peptide (Aβ) modulates the K+/Cl- cotransporter (KCC2) expression and function in hippocampal glutamatergic neurotransmission

Objectives (up to 3 lines): The aim of the project will be to study the link between changes in KCC2 expression induced by Aβ and alterations of glutamatergic transmission, loss of synaptic density and morphological changes of dendritic spines

Abstract (up to 10 lines):

Alzheimer's disease (AD) likely begins with the cerebral accumulation of toxic oligomers of the beta amyloid peptide (Aβo), which impair the persistence and plasticity of neuronal synapses. Recent results from our lab indicate that Aβo targets a synaptic pathway that connects KCC2, a crucial regulator of the excitation / inhibition balance, and cofilin, an actin-binding protein with a central role in cytoskeletal dynamics, especially at synapses. Our goal here is to understand how Aβo affects the trafficking of KCC2; how this relates to cofilin (dys)regulation; and what is the net effect of cofilin activation and inactivation on synaptic actin assembly and post synaptic currents. In this M2 project we will address these questions in cultured mouse neurons by combining the use of a photo-regulatable (optogenetic) variant of cofilin with confocal microscopy, patch-clamp electrophysiology, and biochemical analyses.

Methods (up to 3 lines):

In this M2 project we will address these questions in cultured mouse neurons by combining the use of a photo-regulatable (optogenetic) variant of cofilin with confocal microscopy, patch-clamp electrophysiology, and biochemical analyses.

Up to 3 relevant publications of the team:

Rolland M et al; Effect of Aβ oligomers on neuronal APP triggers a vicious cycle leading to the propagation of synaptic plasticity alterations to healthy neurons. Journal of Neuroscience 2020 Jul 1;40(27):5161-5176.

Rush T et al; Synaptotoxicity in alzheimer's disease involved a dysregulation of actin cytoskeleton dynamics through cofilin 1 phosphorylation. Journal of Neuroscience 2018 38:10349–10361.

Frandemiche ML et al ; Activity-dependent tau protein translocation to excitatory synapse is disrupted by exposure to amyloid-beta oligomers. J Neuroscience. 2014 Apr 23;34(17):6084-97

Requested domains of expertise (up to 5 keywords):

Electrophysiology, Confocal microscopy, Molecular Biology, Immunofluorescence.