

**Master 2 internship project
Year 2026-2027**

Laboratory/Institute: Grenoble Institut Neurosciences - GIN **Director:** E. Barbier
Team: Neuropathologies and Synaptic Dysfunctions **Head of the team:** A. Buisson
Name and status of the scientist in charge of the project: Fabien Lanté, MCF UGA
HDR: yes ☒ no ☐
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Program of the Master's degree in Biology:

- ☐ Microbiology, Infectious Diseases and Immunology ☐ Biochemistry & Structure
☐ Physiology, Epigenetics, Differentiation, Cancer ☒ **Neurosciences and Neurobiology**

Title of the project: Kv2 channels: converging role in cognitive deficits associated with epileptic encephalopathies and Alzheimer's disease.

Objectives (up to 3 lines): Analyze the consequences of changes in Kv2.1 expression and localization in an Alzheimer disease mouse model (APP-PS1) and on neurons expressing Kv2.1 mutants involved in epileptic encephalopathies

Abstract (up to 10 lines):

Patients with epilepsy suffer not only from seizures, but also from reduced quality of life due to cognitive impairments. Alzheimer's disease (AD) on the other hand is characterized by progressive cognitive decline and altered neuronal excitability with a significant risk of early occurring comorbid epilepsy. Both seizures and cognitive morbidities may result from a common alteration of neuronal excitability. However, the mechanisms to be targeted have not yet been fully identified. Published data and our preliminary results suggest that the delayed rectifier K⁺ channel Kv2.1 represent a new molecular candidate. Changes in Kv2.1 expression or localization could underly neuronal hyperexcitability and altered active dendrite properties in AD and epilepsy, contributing to impaired cognitive function. In this project, we aim to experimentally test this hypothesis for the first time. We will employ electrophysiological (patch-clamp) and imaging (confocal and super-resolution microscopy, biphoton calcium imaging) to analyze the consequences of changes in Kv2.1 expression and localization in an AD mouse model (APP-PS1) and on neurons expressing Kv2.1 mutants involved in epileptic encephalopathies.

Methods (up to 3 lines):

We will employ electrophysiological (patch-clamp) and imaging (confocal and super-resolution microscopy, biphoton calcium imaging)

Up to 3 relevant publications of the team:

- 1) Rolland M et al; Effect of A β 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.
- 2) 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.
- 3) 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.