Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2026-2027

Laboratory/Institute: Grenoble Institut Neurosciences - GIN **Director:** E. Barbier
Teams: Myologie Cellulaire et Pathologies **Head of the team:** I. Marty
Neuropathologies et Dysfonctionnements Synaptiques **Head of the team:** A. Buisson

Name and status of the scientist in charge of the project:
Jean-Christophe Deloulme, CRHC Inserm **HDR: yes X no ☐**

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Program of the Master's degree in Biology:

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

Title of the project: Role of Central Nervous System RyR1 Calcium Channel Functions in Neurodegenerative Diseases and Malignant Hyperthermia.

Objectives (up to 3 lines): This project aims to determine the role of RyR1 in central nervous system function and to assess the impact of malignant hyperthermia-associated mutations on neuronal activity. It will investigate the consequences of *RYR1* deletion or mutation on thermoregulation, brain connectivity, and calcium signaling.

Abstract (up to 10 lines): The ryanodine receptor type 1 (RyR1) is a key intracellular calcium channel essential for skeletal muscle function, but it is also expressed in specific regions of the central nervous system, where its role remains poorly understood. Emerging evidence suggests that RyR1 contributes to neuronal calcium signaling and may be involved in the pathophysiology of malignant hyperthermia and neurodegenerative diseases. However, the impact of RyR1 dysfunction in the brain, as well as the consequences of disease-associated mutations, is still largely unknown. This project aims to clarify the role of RyR1 in central nervous system function and to determine how its alteration affects brain physiology, with a particular focus on thermoregulation, neural circuit integrity, and disease mechanisms. Ultimately, it seeks to establish RyR1 as a key player linking calcium homeostasis to neurological disorders.

Methods (up to 3 lines): The project combines conditional mouse models, viral-mediated gene deletion, and knock-in models to investigate the role of RyR1 in the brain. Brain structure and connectivity will be assessed using anatomical and diffusion MRI, while neuronal calcium signaling and synaptic function will be analyzed by two-photon calcium imaging and electrophysiology. Behavioral, molecular, and in vivo rescue approaches will further evaluate the impact of RyR1 dysfunction and disease-associated mutations.

This project is co-led by J. Fauré, a geneticist and muscle specialist, F. Lanté, an electrophysiologist, and J.-C. Deloulme, a neuroanatomist.

Up to 3 relevant publications of the team:

Deloulme at al. Structural interhemispheric connectivity defects in mouse models of BBSOAS: Insights from high spatial resolution 3D white matter tractography. Neurobiol Dis. 2024

Maino A, et al. Identification of a novel de novo RYR1 variant associated with malignant hyperthermia : A case report. Eur J Anaesthesiol. 2026

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.

Requested domains of expertise (up to 5 keywords):

Neuronal calcium signaling ; Brain MRI ; Synaptic plasticity ; Mouse models of neurological diseases