

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

Laboratory/Institute: Grenoble Institut Neurosciences - GIN

Director: E. Barbier

Team: Myologie Cellulaire et Pathologies

Head of the team: I. Marty

Name and status of the scientist in charge of the project: Anne Petiot, CR1 Inserm

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: Oxydative stress and ER stress in RyR1-related myopathies

Objectives (up to 3 lines):

The project aims at a better understanding of the mechanism of action of antioxidant and inhibitor of ER stress treatments in RyR1-related myopathies.

Abstract (up to 10 lines):

RyR1-related disorders (RyR1-RD) represent the most common congenital myopathies, with a severity ranging from generalized muscle weakness to perinatal lethality, with a possible neurological involvement, and are due to mutations in the *RYR1* gene encoding the main intracellular calcium channel of skeletal muscle also expressed in some neurons. Due to its large size, the huge number of mutations in the *RYR1* gene and the restricted number of patients, therapeutic approaches are limited up to now to physical therapy. Our group has produced and characterized a mouse model (so called RyR1-Rec) in which a muscle specific reduction in the RyR1 expression induces the apparition of a progressive myopathy mimicking the patients' disease. In preliminary studies, we evaluated antioxidants and endoplasmic reticulum (ER) stress inhibitors as potential therapeutic agents and assessed their effects on muscle strength in this mouse model. The project aims to gain a better understanding of the mechanisms of action of these two classes of compounds in the RyR1-Rec model, with the ultimate goal of identifying more effective therapeutic candidates for the treatment of RyR1-RD.

Methods (up to 3 lines):

Primary muscle cell culture, immuno-fluorescence, western blot, RTqPCR, biochemical assays, functional assay (calcium imaging....).

Up to 3 relevant publications of the team:

Tourel A, Reynaud-Dulaurier R, Brocard J, Fauré J, Marty I, Petiot A. **RyR1 Is Involved in the Control of Myogenesis.** Cells. 2025 Jan 21;14(3):158. doi: 10.3390/cells14030158.

Beaufils M, Melka M, Brocard J, Benoit C, Debbah N, Mamchaoui K, Romero NB, Dalmas-Laurent AF, Quijano-Roy S, Fauré J, Rendu J, Marty I. **Functional benefit of CRISPR-Cas9-induced allele deletion for RYR1 dominant mutation.** Mol Ther Nucleic Acids. 2024 Jun 17;35(3):102259. doi: 10.1016/j.omtn.2024.102259.

Master's degree in Biology – Chemistry-Biology Department

Pelletier L, Petiot A, Brocard J, Giannesini B, Giovannini D, Sanchez C, Travard L, Chivet M, Beaufiles M, Kutchukian C, Bendahan D, Metzger D, Franzini Armstrong C, Romero NB, Rendu J, Jacquemond V, Fauré J, Marty I. **In vivo RyR1 reduction in muscle triggers a core-like myopathy.** Acta Neuropathol Commun. 2020 Nov 11;8(1):192. doi: 10.1186/s40478-020-01068

Requested domains of expertise (up to 5 keywords):

Interest in cell biology and in deciphering physio-pathological mechanisms.