Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2025-2026

Laboratory/Institute: Grenoble Institut Neurosciences **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, Inserm Researcher
HDR: yes ☐ **no** x

Address: Bâtiment Edmond J. Safra, chemin Fortuné Ferrini, 38700 La Tronche, France
Phone: 33 4 56 52 05 71 **e-mail:** anne.petiot@univ-grenoble-alpes.fr

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:

Therapeutic approaches for RyR1-related myopathies

Objectives (up to 3 lines):

The project aims at a better understanding of the mechanism of action of antioxidant treatment in RyR1-RD 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 experiments, we tested an antioxidant as a potential therapy and observed a spectacular improvement of muscle strength in this mouse model. The project aims at a better understanding of the mechanism of action of the antioxidant in our model, in order to further identify more efficient therapeutic molecules that could be used as a treatment for RYR1-RD.

Methods (up to 3 lines):

In vivo animal experimentation, primary muscle cell culture, immuno-fluorescence, western blot, immunoprecipitation , 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.

Pelletier L, Petiot A, Brocard J, Giannesini B, Giovannini D, Sanchez C, Travard L, Chivet M, Beaufils 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/s40478-020-01068-4.

Requested domains of expertise (up to 5 keywords):

Interest in cell biology and in deciphering physio-pathological mechanisms