Master 2 internship project  
Year 2020-2021

**Laboratory/Institute:** Grenoble Institut Neurosciences - GIN  
**Team:** Myologie cellulaire et pathologies - CMyPath

**Director:** Prof. F. Saudou  
**Head of the team:** Dr. I. Marty

**Name and status of the scientist in charge of the project:** A. Petiot, CR1 INSERM  
**HDR:** no

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**Program of the Master's degree in Biology:**
- ☐ Immunology, Microbiology, Infectious Diseases  
  - ☐ Integrative Structural Biology
- X Physiology, Epigenetics, Differentiation, Cancer  
  - X Neurosciences and Neurobiology
- ☐ Planta International

**Title of the project:**
Therapeutic development for RyR1-related myopathies using a mouse model?

**Objectives (up to 3 lines):**
The purpose of this work is to characterize the effect of a therapeutic chemical (the N acetyl Cysteine) "in vivo" as well as "in vitro" in order to offer therapeutic perspectives for congenital myopathies

**Abstract (up to 10 lines):**
Congenital myopathies are characterized by impairment of skeletal muscles calcium release leading to muscle weakness. An inducible and muscle-specific mouse model of congenital myopathy has been established in our laboratory to better understand the physio-pathology and especially the importance of the Ryanodine receptor-1 (RyR1) in these myopathies. RyR1 is the calcium channel responsible for the release of calcium from the sarcoplasmic reticulum to the cytosol, and so the muscle contraction. Our previous results show that our mouse model presents close similarities with human disease, characterized by loss of muscle strength and weight, and constitutes so a good model to test therapeutic approaches. The purpose of this work is to study "in vivo" as well as "in vitro" the effect of a therapeutic chemical (the N Acetyl Cysteine) in order to offer therapeutic perspectives for congenital myopathies

**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:**

- **'Dusty core disease' (DuCD): expanding morphological spectrum of RYR1 recessive myopathies.**

- **Dynamics of triadin, a muscle-specific triad protein, within sarcoplasmic reticulum subdomains**

- **Functional Characterization of a Central Core Disease RyR1 Mutation (p.Y4864H) Associated with Quantitative Defect in RyR1 Protein.**

**Requested domains of expertise (up to 5 keywords):**
Interest in cell biology and in deciphering physio-pathological mechanisms.