

**Master 2 internship project
Year 2023-2024**

Laboratory/Institute: Grenoble Institut Neurosciences - GIN

Director: E. Barbier

Team: Cellular myology and pathologies

Head of the team: Dr I. Marty

Name and status of the scientist in charge of the project: Dr Anne-Sophie Nicot, MCU

HDR: yes no

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Program of the Master's degree in Biology:

Microbiology, Infectious Diseases and Immunology Structural Biology of Pathogens
 Physiology, Epigenetics, Differentiation, Cancer Neurosciences and Neurobiology

Title of the project: Skeletal muscle under the light of new cellular tools

Objectives:

The project aims at revisiting the protein content of triads, which are skeletal muscle peculiar membrane structures essential for excitation-contraction coupling, with state-of-the-art cellular, biochemical and imaging tools. This will enlighten new functions for this structure and new candidate genes for muscle diseases.

Abstract:

In skeletal muscle, triads are composed of an invagination of the plasma membrane, the transverse tubule, flanked by two terminal cisternae of the sarcoplasmic reticulum (SR) which are calcium storage sites. Action potentials transmitted by nerves activate channels at triads, leading to intracellular SR calcium release and sarcomere contraction. Despite their central role for muscle, the mechanisms governing the dynamics of triads, as well as their extensive functions remain mysterious. To elucidate those mechanisms, proteins localized at triads under stimulations will be identified using the recently developed technique of proximity-dependent biotinylation identification (BioID).

The master student will be in charge of the confirmation of a selected list of proteins with biochemical technics and super-resolution microscopy. The function at triads of the best candidate will then be studied *in cellulo* and in mouse skeletal muscle through gene inactivation by CRISPR-Cas9 and overexpression.

Methods:

Methods used will include molecular biology (plasmid cloning, CRISPR-Cas9), biochemistry, cell culture and microscopy, *in cellulo* and *in vivo*.

Up to 3 relevant publications of the team:

- Sébastien et al. (2020) Dynamics of triadin, a muscle-specific triad protein, within sarcoplasmic reticulum subdomains. *Mol Biol Cell*. 31(4):261-272.
- Osseni et al. (2016) Triadin and CLIMP-63 form a link between triads and microtubules in muscle cells. *J Cell Sci*. 2016. 129(20):3744-3755.

Requested domains of expertise: molecular biology, biochemistry, cell biology