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Involvement of SH3KBP1 in the modulation of myofiber integrity via autophagy regulation

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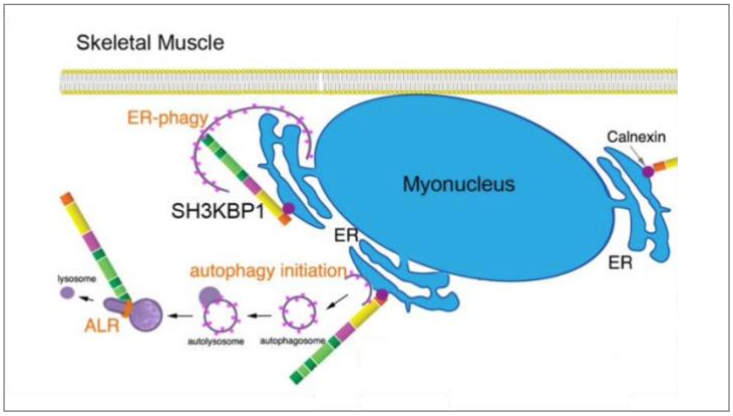
Research project:

Muscle dysfunction is implicated in a plethora of human diseases and in sarcopenia, i.e. muscle atrophy with age, which constitutes the leading cause of loss of ambulation and independence. This project aims at identifying important pathways for muscle intracellular organization, under physiological and pathological conditions. The function of the muscle fiber (myofiber) is supported by a precise positioning of its organelles and nuclei.



We identified SH3KBP1 (SH3 domain-containing kinase-binding protein 1) as a new factor controlling myonuclear positioning, endoplasmic reticulum (ER) and T-tubule organization.

We aim at characterizing the pathways regulating the organization and functionality of myofibers, focusing on ER and T-tubule remodeling and on associated functions such as

autophagy in physiological or pathological (CentroNucleoMyopathies) contexts (ANR Atrorescue funding).

The proposed internship will focus on the biological functions of SH3KBP1 related to its modulation of ER architecture with a special focus on the autophagic pathway and notably ER-phagy process, but also autophagic lysosome reformation. Depending on the project progress, an analysis of the different processes identified could also be carried out in cellular models of centronuclear myopathies.

Methods:

- Cell biology (muscle cell line and primary cell culture, transfection)
- Biochemistry (western blots, co-immunoprecipitation)
- Molecular biology (cloning, sequencing)
- Microscopy (immunofluorescence, live cell imaging)

References:

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