MASTER BMC LYON Biologie Moléculaire Cellulaire

Université Claude Bernard Lyon 1

MASTER 2 BMC
PARCOURS GENOPATH
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Titre du sujet de stage : Characterization of muscle aging in *Caenorhabditis elegans*

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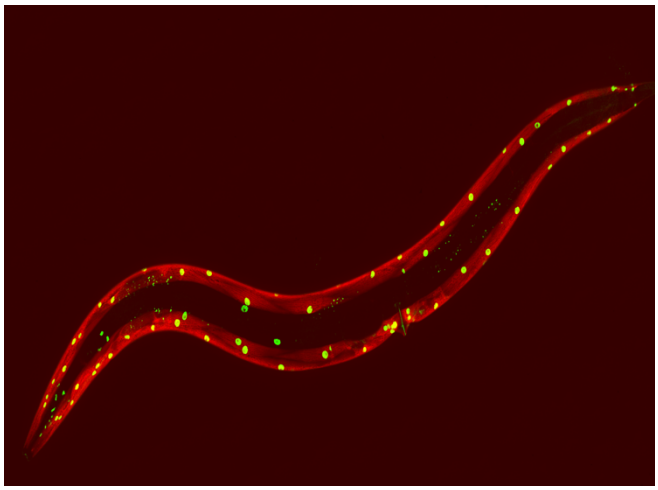
Sujet de stage :
Ageing is one of the most important challenges that modern societies have to struggle in order to prevent the burden of age-associated diseases and dependency. Longitudinal studies showed that physical performance is the most predictive criterion for mortality in the elderly. Thus, deciphering the limiting factors that cause muscle aging is a major public health issue.
Our project aims to identify mechanisms responsible for muscle aging by novel approaches taking advantage of *C.elegans* powerful genetic tools
The short lived *C.elegans* nematode (adult's lifespan is only 3 weeks long) was instrumental in uncovering the first molecular pathway associated with an increased lifespan in many species[1]. However, little is known about ageing at tissue scale, as the regulation of aging has mainly been addressed through the study of longevity so far.
C.elegans possess striated muscle cells with highly conserved structure of sarcomeric contractile units. We recently described a stereotyped sequence of molecular and cellular events that characterize muscle aging and that correlate with the progressive muscle loss of function with age. Those changes include a sharp decrease in some sarcomeric transcripts in early adulthood, followed by the progressive fragmentation of muscle mitochondria and a blockade of autophagy. **Interestingly those features are also observed upon human aging in both skeletal and cardiac muscle .** To identify causative factors of muscle aging we initially used a candidate approach and identified the transcription factor SRF as a conserved regulator of muscle aging between worms and mammals. **We next designed innovative strategies, based on a genetic screen and a transcriptomic approach** in order to uncover genes that affect muscle aging **in an unbiased manner** (unpublished).



The student will participate in:
- the characterization of novel biomarkers of muscle aging and
- a genetic screen for the identification of novel actors of muscle aging.

Technologies utilisées : : the student will become familiar with a number of techniques routinely used in the lab including:- confocal microscopy and image processing - *C. elegans*

handling and basic genetics, complementation tests, microinjection... - molecular biology and cloning by Gibson technology - CRISPR technology for genome engineering - manipulation of the Wormbase database, Image J software...

Mots clés : Aging, Muscle, C.elegans, CRISPR, Cellular and molecular biology

Publications d'intérêt : *Related references from the team:*

-Mergoud Dit Lamarche, et al. UNC-120/SRF independently controls muscle aging and lifespan in *Caenorhabditis elegans*. **Aging Cell** 17, e12713 **(2018).**
-Solyga M and Solari F. DAF-2 receptor signaling pathway: a key role in muscular aging. **Med Sci** (Paris) Oct;36(10):938-841. **(2020).**
- Roy et al.DAF-2/insulin IGF-1 receptor regulates motility during aging by integrating opposite signaling from muscle and neuronal tissues. **Aging Cell**, July, **(2022).**
-Roy et al., Aging gracefully: time and space matter . Aging , **May**, (2023)