Offre de stage de M2 – IPHC UMR7178 – CNRS/Université de Strasbourg

Mechanically assisted muscle preservation in brown bears: bio-inspiration to better combat muscle atrophy in humans

The loss of skeletal muscle mass under a wide range of conditions, from disuse to ageing and different diseases, is associated with poor prognosis, reduced quality of life, and increased mortality. Yet, despite the current pandemic of sedentary lifestyle and the aging of populations, and although basic knowledge of the cellular and molecular mechanisms of muscle atrophy has been continuously growing, there is no efficient therapy for muscle atrophy. *Therefore, new research strategies are needed to stimulate the development of innovative therapies.*

Torpor and hibernation are powerful hypometabolic strategies that allow animals to survive periods of low resource availability and weather challenge. The torpid state favors an energy-saving strategy, involving a controlled reduction in metabolic rate and body temperature. It is also characterized by numerous adaptive physiological, cellular and molecular processes, some of which are triggered to protect key organs of hibernators. In particular, the muscle mass and muscle strength is well maintained during hibernation, i.e. in the face of conditions known to trigger atrophy in humans (food deprivation and physical inactivity). In hibernating bears, several key mechanisms for muscle preservation have been proposed, including an antioxidant strategy, a myogenic microRNA response, the possible role of some lipid molecules and other circulating anti-atrophy factors that are still to be identified. *This project will go a step further to test the hypothesis of a mechanical control of muscle maintenance in hibernating brown bears.* Mechanical stimuli are indeed known to play a major role in the regulation of skeletal muscle mass, but nothing is known during hibernation. *This project will characterize seasonal changes in muscle proteomic profiles in bears, specifically* paying attention to a series of mechanotransduction-related pathways.

Hypothesis: The comparison of the muscle proteome in hibernating and summer-active individuals should underline if genome reprogramming has involved a response similar to that to mechanical stimuli.

Methodology: State-of-the-art proteomics protocols will be used on brown bear muscles to identify and quantify proteins/peptides. Today, improvements of mass spectrometry (MS) instrumentation (e.g. in terms of high speed, resolution, sensitivity), bioinformatics tools and the increased rate of genome sequencing, including for non-model species have opened the way to shotgun analysis in any species through state-of-the-art proteomic analytical approaches such as data-independent acquisition (DIA) mass spectrometry, with a very high level of reproducibility. MS equipment is already available in our lab, and MS data will fill the bioinformatics workflow we have already developed. Among other complementary assays, gene expression (using qPCR, Western Blot or immunohistochemistry) will complete the picture, especially for targets suspected to be difficult to detect (e.g., a few nuclear and membrane proteins).

Expected outcome: This project is an integral part of a much broader research program which seeks to define new therapeutic and preventive levers for preserving muscle mass in humans. Target populations include emaciated or obese people, patients confined to hospital for long periods, the elderly, patients suffering from catabolic pathologies and astronauts. We expect this project will highlight innovative target pathways/molecules to better fight muscle atrophy.

Required skills

- Interest for muscle physiology and bioinspired approaches
- Interest for labwork, including mass-spectrometry-based methods
- Skills with statistical analysis using R

Contact

Envoi des candidatures (CV et lettre de motivation) : fbertile@unistra.fr