Central inflammation, skeletal muscle contractile properties, and gene expression – Functional relevance in cancer cachexia

Supervisor. Professor Damien Freyssenet
E-mail. damien.freyssenet@univ-st-etienne.fr

Where? Jean Monnet University Saint Etienne (https://www.univ-st-etienne.fr/fr/index.html). Jean Monnet University is a multidisciplinary University that offers a wide range of academic programs aligned with society and its regional environment, while promoting high-quality research. The University welcomes nearly 20,000 students and 1,500 staff members. It is composed of five faculties, three institutes, one department of political and territorial studies, one engineering school, six doctoral schools, and 24 research teams.
Laboratoire Interuniversitaire de Biologie de la Motricité (https://libm.univ-st-etienne.fr/fr/index.html). The LIBM brings together researchers in the fields of biology, physiology, biomechanics, neuroscience, and engineering sciences applied to physical activity, sport, and health. The various biological aspects of motor function are studied through multi-scale research, ranging from the cell to the human organism.

Subject. Cancer-associated cachexia is characterized by a progressive loss of muscle mass and strength. Clinically, cachexia has a profound impact on patients' quality of life, increases the risk of surgical complications, and reduces tolerance to anticancer treatments. Although systemic inflammation induced by tumor growth is recognized as a key driver of cachexia, its effects on the central nervous system remain poorly understood.
Hypothesis and objectives. We hypothesize that tumor growth–induced systemic inflammation alters central nervous system activity and contributes to the development of cachexia. Our objectives are to: (1) characterize the central inflammatory state at different stages of cachexia, and (2) determine whether central inflammation is associated with the emergence of molecular markers of cachexia in skeletal muscle, as well as with reduced muscle strength.
Experimental design. $Apc^{Min/+}$ mice, a well-established murine model of cancer cachexia, will be studied at 15 weeks (moderate cachexia), and 20 weeks of age (severe cachexia) to assess central inflammation (Objective 1). To address Objective 2, central inflammation will be induced in healthy mice via intracerebroventricular injection of an inflammatory agent. Transcriptomic analyses of skeletal muscle and assessments of muscle contractile properties (strength, contraction velocity, and endurance) will be performed to evaluate the effects of central inflammation on muscle force production and gene expression. In addition, microglial depletion will be carried out to determine whether glial cells serve as a central relay for systemic inflammatory signals in $Apc^{Min/+}$ mice.
Expected outcomes. By addressing cancer-associated cachexia from a fully innovative perspective, this project aims to generate novel conceptual insights that may support the development of new therapeutic strategies to combat cachexia.

Candidate profile. The candidate should be motivated to develop an integrative approach to cancer cachexia, drawing on physiology as well as on cellular and molecular biology. The candidate, with a scientific background, must have an excellent academic record at Bachelor's and Master's level. Theoretical knowledge of biology tools (RT-qPCR, enzymology, Western blot, immunohistochemistry, epifluorescence microscopy) is required. He or she must already have completed a research internship, have a solid background in statistics. He or she must also possess the interpersonal skills necessary for teamwork.