A translational approach to the mechanisms of sarcopenia in humans: redefining skeletal muscle fibre types in the era of omics

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Research Areas: Physiology; Cell Biology; Regenerative Medicine; Translational Medicine

Project Overview

Skeletal muscle is the most abundant and adaptable tissue in the human body. Its ability to adapt to physical activity, inactivity, ageing, and disease is fundamental to maintaining mobility, independence, and quality of life. However, ageing-induced loss of skeletal muscle mass and function (termed sarcopenia) represents a major and growing societal and healthcare challenge worldwide. Despite decades of research, the cellular and molecular mechanisms driving sarcopenia remain incompletely understood.

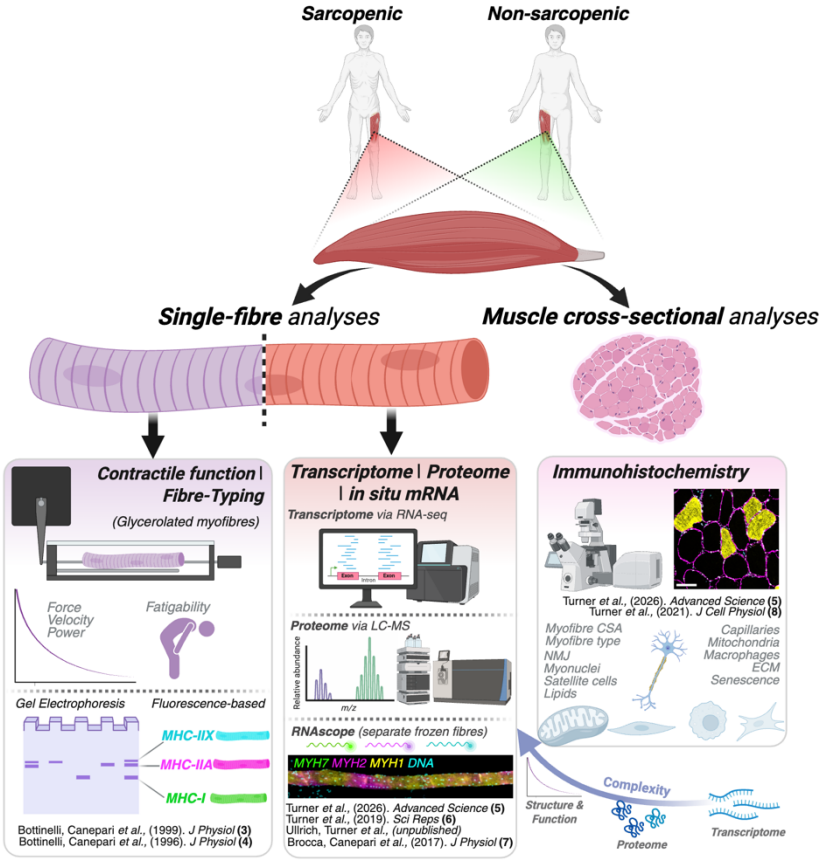
Scientific Background

Human skeletal muscle cells (myofibres) are traditionally classified as either "slow" (type 1) or "fast" (type 2A and 2X) fibres according to their differing myosin heavy chain isoforms and associated functional characteristics [1]. Changes in fibre-type composition (e.g., proportion of fast versus slow fibres) have traditionally been considered a key mechanism underlying muscle (mal)adaptation in health and disease. Recent advances in single-cell and single-nucleus omics technologies have challenged traditional concepts of muscle fibre identity within established fibre classes. Indeed, emerging evidence in ageing [2] and our own preliminary data suggests that muscle (mal)adaptations are not simply characterized by shifts between slow and fast fibres or by myofibre atrophy, but rather by transitions between distinct cellular sub-states within the same fibre type. These cellular sub-states are associated with extensive gene expression remodeling that may play a central role in the development of age-related and disuse-induced muscle wasting.

Research Objectives

This PhD project aims to characterise skeletal muscle fibre heterogeneity by integrating physiological measurements performed *in vivo* and *ex vivo* with cutting-edge omics technologies. The successful PhD candidate will investigate:

1. **The functional properties of individual human muscle fibres**, including force production, shortening velocity, and fatigue resistance.
2. **The molecular heterogeneity within established fibre types** using single-fibre transcriptomics and proteomics.
3. **The relationship between muscle fibre function and molecular phenotype**, linking physiological outcomes with cellular and molecular signatures.



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