UNIVERSITÀ DEGLI STUDI DI PADOVA

SMECC - Skeletal Muscle-Endothelial Cell Crosstalk in Muscle Plasticity and Disease

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The maintenance of skeletal muscle mass and function is critically important in various conditions, including aging, cancer, muscular dystrophies, and more. It presents a considerable societal concern, impacting not only individual health but also imposing substantial healthcare expenditures. Despite its clinical relevance, there are currently no fully effective treatments to prevent or reverse muscle wasting due to an incomplete understanding of the involved mechanisms. While much attention has been given to intracellular signalling regulating muscle size, such as the Akt-mTORC1 pathway, the role of muscle perfusion and paracrine interactions between muscle fibers and endothelial cells (ECs) remains poorly understood. Recent studies point to the strong interconnection between muscle fibers and ECs, highlighting their reciprocal influence on each other's function. This project aims to illuminate these interactions, exploring how changes in muscle mass influence protein homeostasis in ECs and how alterations in ECs' proliferation and permeability impact muscle physiology. To address these questions, we will utilize cutting-edge technologies including molecular biology, animal phenotyping, histology, omics, and advanced bioimaging techniques such as tissue clearing and light sheet fluorescence microscopy, while employing innovative models to elucidate the mechanisms underlying in vivo changes in a cell-type specific manner. We will use novel tissue-specific mouse lines, such as MetRS mice, to monitor protein homeostasis within defined time windows, allowing for the study of muscle-EC crosstalk. The anticipated outcomes of this project include a deeper understanding of how ECs and muscle fibers communicate during changes in muscle size and function. By exploring these interactions, we aim to uncover key molecular mechanisms that govern muscle-EC interplay, enhancing our knowledge of ECs' role in muscle biology and guiding future therapeutic strategies.

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