Title
Microvascular dysfunction and mitochondrial impairment in aging and disuse: integrated in vivo and molecular investigations

PI and Laboratory
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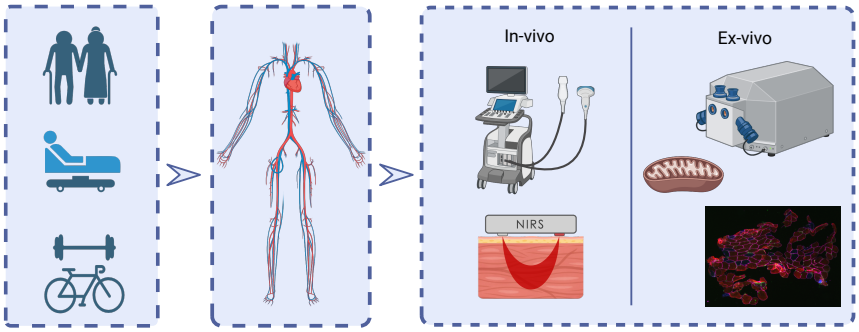
Research Theme/Topic
Human Physiology, Aging, Disuse, Skeletal Muscle, Mitochondria, Microcirculation

Main Abstract
Aging and disuse represent major drivers of functional decline in skeletal muscle, with vascular dysfunction and mitochondrial impairment playing central mechanistic roles. Age-related alterations in vascular function include reduced endothelial responsiveness, capillary rarefaction, and diminished perfusion, which limit oxygen delivery and extraction. Similarly, disuse leads to rapid deterioration in microvascular reactivity and mitochondrial oxidative capacity. Despite their shared features, the interactions between vascular and mitochondrial dysfunction in these conditions remain poorly defined.



This project aims to investigate how aging and physical inactivity impair skeletal muscle microvascular and mitochondrial function, using both in vivo non-invasive techniques (such as near-infrared spectroscopy, NIRS) and ex vivo/in vitro analyses of muscle biopsies. In vivo, we will assess microvascular reactivity, muscle blood blow and fractional O_2 extraction during exercise via ultrasound and NIRS in young and older adults, and in individuals undergoing step reduction or bed rest. Mitochondrial function will be evaluated in vitro via high-resolution respirometry, Western blotting of oxidative phosphorylation complexes, and RT-PCR for mitochondrial biogenesis markers (e.g., PGC-1α, NRF1, TFAM).

By combining vascular and mitochondrial endpoints, the study will clarify whether impaired oxygen delivery, utilization, or their mismatch is the primary driver of functional decline. Importantly, we will explore whether the combination of vascular and mitochondrial markers better explains muscle deconditioning than either domain alone. The project will generate mechanistic insights relevant to age-related frailty, disuse syndromes, and the optimization of countermeasures (e.g., exercise and pharmacological mimetics).

Techniques
In vivo: ultrasound, NIRS, metabolic cart, transthoracic bioimpedance

Ex vivo/in vitro: High-resolution respirometry, confocal microscopy, Western blot, RT-PCR

References

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