Skeletal Muscle Interstitium and Microvascular Blood Flow: A Window into the Mechanisms behind Age-Related Anabolic Resistance to Nutrients?

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Age-related skeletal muscle loss is thought to stem from suboptimal nutrition and resistance to anabolic stimuli such as exercise and amino acids. Although the etiology of age-related anabolic resistance is uncertain, its hallmark characteristics of reduced protein synthesis and/or elevated circulating amino acid concentrations suggest two general, non-exclusive mechanisms: 1) a reduced capacity for protein synthesis (utilization defect) and 2) a reduced availability of amino acids to cells for protein synthesis (delivery defect).
Notably, an elevated circulating concentration of amino acids does not necessarily indicate greater delivery to skeletal muscle, as the amino acids must also diffuse from the capillaries into the interstitial fluid and be transported from the interstitial fluid into skeletal muscle before becoming available for protein synthesis. However, other factors such as the role of skeletal muscle microcirculatory (nutritive) blood flow may also contribute to the anabolic resistance of skeletal muscle, though methodological barriers have greatly limited the in-depth investigation of these regulatory mechanisms.
We recently utilized microdialysis sampling of the skeletal muscle interstitium during periods of rest, exercise, amino acid provision, and pharmacologic blood flow enhancement to provide a window into the mechanisms regulating the stimulation of muscle protein synthesis, and whether age and microvascular flow impacts the normal response to anabolic stimuli. Since exercise and a mixed meal each have been shown to markedly increase muscle microvascular perfusion and capillary recruitment (expanding the endothelial surface for nutrient exchange), we studied whether this expansion is an important physiological response to facilitate nutrient delivery and utilization for muscle protein synthesis in healthy older and younger humans. We also employed a novel technique, contrast enhanced ultrasound, to measure skeletal muscle microvascular blood flow during these metabolically diverse conditions.
We will demonstrate the importance of the interstitial milieu as well as the hemodynamic response in age-related anabolic resistance, and will present data suggesting that age-related anabolic resistance to amino acids is not mediated *via* reduced amino acid availability. We will also present data demonstrating that pharmacologic enhancement of the aging vasculature is responsive to exogenous NO, and that equalizing the hyperemic response between young and old restores normal muscle anabolism.