Title: A Multi-Scale Approach to Studying the Microvasculature in Skeletal Muscle

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Structured Abstract:

The A.C. Burton Lab for vascular research has a multitude of ongoing studies including both basic research and applied research. On the basic research side, we are developing new experimental tools, techniques, and multiple experimental models. The development of these tools and techniques enable us to derive, investigate, and translate complexed questions involving pathological changes in vasculature which is associated with disease states. On the applied side, we are studying metabolic disease, stress & depression, how these three things differ with sexual dimorphism, and how all the previously mentioned conditions may change with aging. Using intravital video microscopy (IVVM), we can assess microvascular network structure, the integrated hemodynamics involved, as well as local/systemic effects to pharmaceuticals, in situ. Therefore, both extrinsic vascular signaling (sympathetic nervous signaling & circulating hormones) and intrinsic mechanisms (myogenic tone, shear stress, structural support, and pharmacological reactivity) remain intact while measuring the previously mentioned parameters of interest. Additionally, isolated vessels (ex vivo) can be used to study the intrinsic mechanisms, independent of any extrinsic signaling, which allows us to understand what is happening at the vascular level with detail that cannot be obtain using IVVM. With this multi-scale approach, we can draw conclusions from our data with a high level of confidence.

Although most of previous work focuses primarily on the extrinsic signals of the vasculature, such as adrenergic control, our future research projects will focus more on intrinsic factors such as studying mechanosensitive ion channel proteins which are transmembrane proteins capable of responding to mechanical stress over a wide dynamic range of external mechanical stimuli. These transmembrane channel proteins are located in both the smooth muscle and the endothelial layer of blood vessels and have been shown to play important roles in myogenetic reactivity and tone as well as the sensation of shear stress created by blood flowing against the lumen walls. Using chemical stimulators and inhibitors, we intended to asses the transmembrane protein's role, using the both in-situ and ex-vivo techniques, in vascular stability and reactivity. We will be the first lab to study the role of these mechanosensitive ion channel proteins with this level of functional detail. Our primary objective is to understand the basic science behind these proteins and their role in the vasculature. Further, we intend to translate these finding into our applied research models to observe how the role of these proteins may change with metabolic disease, stress, or depression in an effort to provide further insight for the associated vasculopathies with the ultimate goal of using those insights to contribute to their treatment and/or alleviation.