

The skeletal muscle endothelium: the barrier within

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Studies of endocrinology and metabolism rely on the vascular system to deliver hormones and nutrients to the area of interest, yet blood vessels are a dynamic variable that can be impacted by disease. In addition to blood supply to the area and distribution through tissue, the endothelial barrier regulates access to muscle as both a structural barrier and a modifiable permeable gateway. The endothelium in each tissue is different, such that some tissues are exposed to blood components more readily than others. Therefore, to understand the true impact of the distribution and delivery of blood, it is necessary to understand the local, interstitial environment, which is what the tissue is exposed to. Measuring interstitial fluid is difficult, and there are few accurate techniques available. We use the hindlimb lymph vessels to sample the interstitial fluid in the canine model under inhaled isoflurane anesthesia. Even in healthy individuals, the level of insulin in the skeletal muscle interstitium is approximately half that of the blood. Blood flow defects induced by disease states, such as insulin resistance, cardiovascular disease and diabetes, can impact the amount of insulin getting to the tissue, and thus contribute to the metabolic impairments associated with these diseases. We have investigated different dietary interventions that can induce similar levels of obesity but have differing effects on metabolism and interstitial insulin levels, at least partly due to their reported effects on the endothelium. Therefore, interventions that target the vasculature, whether by increasing delivery or by altering permeability, may provide a novel approach to improve metabolism and metabolic disease.