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“Mitochondrial Bioenergetics of Collecting Lymphatic Vessels in Healthy and After Injury”

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Lymphatic transport of fluid, proteins and metabolites from the interstitium back to the blood circulation occurs through phasic and tonic contractions of the vessel. Impaired contractility results in the accumulation of proteins and fluid in the interstitium leading to lymphedema. Molecular mechanisms responsible for the impairment of lymphatics are not well understood due to the complex regulation by mechanical and chemical stimuli. This gap in our understanding underpins the lack of a medical therapy to prevent or treat lymphedema. Our previous studies have shown that lymphatic muscle cells isolated from a sheep lymphatic injury model exhibited increased oxidative stress and altered oxidative phosphorylation, but currently little is known about the metabolism of cells within intact collecting lymphatic vessels in healthy and pathological states. To this end we surgically removed the rat popliteal and inguinal lymph nodes and partially associated lymphatic vessels. Increase of inflammatory, oxidative stress markers as well as decrease of mitochondrial defense markers were evaluated immunohistochemically and contractile pattern of the remaining lymphatics was assessed by NIR Imaging for up to 4 weeks after injury. Contraction frequency of lymphatics from injured hind limb compared to naive was increased by 114.9%±8.7, packet amplitude and packet transport was decreased by 46.5%±4.3 and 22.9%±2.9 respectively. Mitochondrial bioenergetics of excised vessels was assessed by Seahorse XF Extracellular Flux Analyzer using the Mito-stress test. Maximal respiration, ATP production, and proton leak increases by 51.8% ± 9.3, 53.1± 8.2, 21.7 ± 3.7 in injured lymphatics compared to sham and naïve animals. Understanding how collecting lymphatics metabolize energy sources, respond to injury, oxidative stress can lead to future therapies for preventing and treating lymphatic pump failure.