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BSSE Seminar

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Mechanosensitivity of Lymphatic Vessels: A Clue Towards Understanding Lymphatic Dysfunction

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ABOUT THE SPEAKER

Anish Mukherjee is currently pursuing his PhD in Bioengineering at Georgia Institute of Technology in the Laboratory of Lymphatic Biology and Bioengineering. He completed his MS in Electrical and Computer Engineering from Georgia Tech and BE in Electrical Engineering from Jadavpur University. His research interests encompass the mechanics of lymphatic vessels in relation to pathologies in the tissue microenvironment, especially lymphedema. He has received the American Heart Association Predoctoral Fellowship which supports his current work.

ABSTRACT

The lymphatic system is a secondary circulatory system comprised of a network of interconnected vessels and nodes that serves to maintain tissue fluid balance, and also plays a role in immune response and lipid transport. The transport of lymph through the lymphatic system is achieved by intrinsically contractile vessel segments called lymphangions, which are separated by valves to promote a unidirectional flow of lymph. The most common dysfunction associated with impaired lymphatic vessel contractility is lymphedema, a debilitating condition characterized by a unilateral swelling of the extremities. Breast cancer related surgery may be a cause of lymphedema, which is thought to adversely affect the mechanical microenvironment of the lymphatic vessels, thereby disrupting lymphatic function. The present work delves into the role of mechanosensitivity (the functional response of lymphatic vessels to imposed forces) in dictating the physiological and pathological response of lymphatic vessels to changes in their microenvironment. The mechanosensitivity of lymphatic vessels to oscillatory shear stresses (OSS) was quantified using isolated thoracic ducts, specifically in the context of the entrainment of lymphatic vessels to oscillatory forces. The results show that the entrainment of the lymphatic vessels to the OSS is dependent on the frequency and amplitude of the stimulation, as well as the intrinsic contractility and mechanosensitivity of the vessel. Optimum mechanical conditions were identified for the modulation of lymphatic contractility. This behavior was further recapitulated in lymphatic vessels in vivo, by applying temporally and spatially varying oscillatory pressure on rat tail lymphatic vessels. Measurements on lymphatic function were performed in vivo using near infrared (NIR) imaging. Rodent tail lymphatic injury models have also been developed to study the changes in mechanosensitivity of lymphatic vessels in response to a pathological microenvironment. Preliminary studies into the MAPK pathway proteins indicate p38 as a potential player in the mechanotransduction cascade leading to OSS sensitivity. The work is intended to highlight the importance of lymphatic vessel mechanosensitivity to the oscillatory microenvironment as an important factor in the functioning and coordination of lymphangions, and as a potential hallmark of lymphatic dysfunction.