**Mass Transport in the Lymphatic Vessels and Nodes**

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The lymphatic system has many recognized important roles in normal physiology and in a variety of disease conditions. In addition to returning fluid from interstitial tissue spaces to the blood circulation, it also serves as an important transport route for immune cells. Lymph nodes are important sites for cellular interactions involved in immunity, inflammation and fluid balance. Transport phenomena and/or breakdowns in lymphatic system performance are crucial, or at least involved in, cardiovascular diseases, cancer, obesity and injury resolution. Despite the importance in so many causes of death and disability, little is actually known about transport mechanisms in this obscure system.

We have developed models of lymphatic system pumping based on a multiscale approach, combined with a unique experimental skill set. In addition to the general insight on lymphatic pumping, we have elucidated the phenomena by which the lymphatic system is able to generate negative interstitial tissue pressures while still generating positive fluid flow out of those tissues. Our results indicate the importance of a crucial but largely unexplored factor in pumping: the unique abilities of lymphatic muscle cells (LMC) to contract over a wide range of vessel diameters. Our current experimental and modeling work is focused on quantifying this parameter better.

We have also analyzed fluid flow patterns in lymph nodes. These are highly compartmentalized structures in which leukocytes process antigens, foreign bodies and tumor cells. There are also specialized direct communication ports with the blood circulation in which fluid and cells can traverse in either direction. Under normal conditions, approximately 90% of the flow goes around the main part of the lymph node via the subcapsular sinus and medullary sinus. With vaccination, the flow distribution shifts to send more flow into the B and T cell regions. These flow patterns are crucial in establishing and maintaining chemokine concentration gradients, which trigger the movement of several types of immune cells and cancer cells.

The results of this research will include the most advanced model of lymphatic transport and function to date, the ability to predict the effects of interventional procedures, and the optimization of those procedures for the benefit of the numerous patients suffering from lymphatic associated diseases.