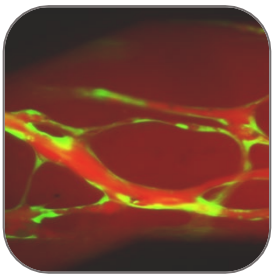
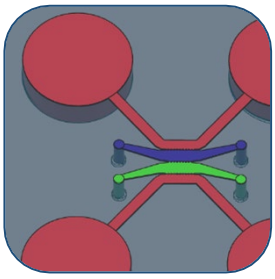
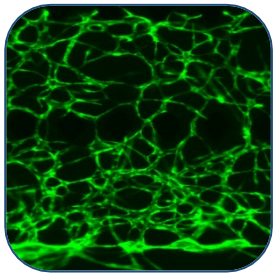
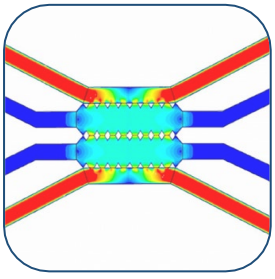




µMechanoLymph

Elucidating the impact of mechanobiological stimulation on lymphatic uptake with organ-on-a-chip technology





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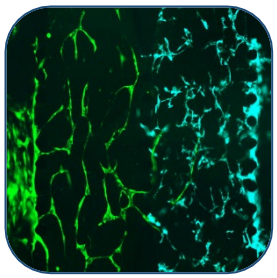
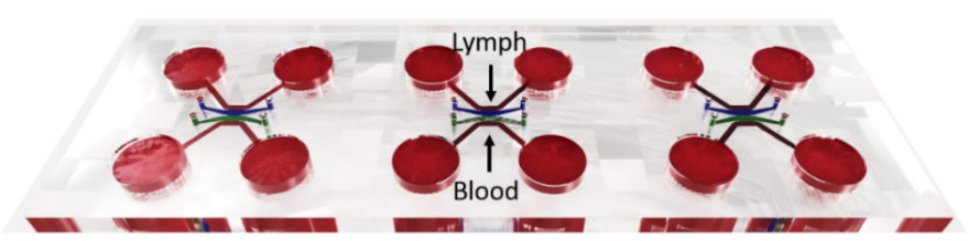


Project description

After decades of being referred to as the body's sewage system, the lymphatic system has recently been recognized as a key player in numerous physiological and pathological processes. As an essential site of immune cell interactions, the lymphatic system is a crucial identified as a potential target for next-generation drug delivery approaches to define novel treatments for cancer, infection, and inflammatory diseases. Despite this potential of lymphatic-targeted drug delivery, scientific progress is currently hampered by (a) insufficient *in vitro* cell-based assays lacking the necessary biologic complexity and (b) unreliable *in vivo* animal models. Within this Ph.D. project, an advanced chip-based microvascular model incorporating biomechanical cues will be established to overcome these limitations and gain a deeper understanding of molecule distribution between the blood and the lymphatic circulatory systems. To achieve this goal, microfluidics technology, biomechanical stimulation, and 3D cell biology are combined to engineer a microphysiological replica of the blood-lymphatic interface to study the lymphatic hyaluronic acid uptake route.

This study will address the following research questions: 1) Can a chip-based blood-lymph interstitial interface model reproduce physiologic interstitial flow conditions to study molecule movement from the bloodstream into the interstitial space to subsequent uptake into the lymphatic system and 2) to what extent do lymphatic endothelial cells actively transport molecules across the lymphatic endothelium via receptor-mediated transport (LYVE-1, hyaluronan) and vesicular (clathrin, albumin) transport. Using TUW rapid microfluidic prototyping technologies, an organ-on-a-chip device containing two interconnected hydrogel-chambers housing blood and lymphatic endothelial cells and supporting cells will be developed. The microfluidic blood/lymphatic interface will be utilized to evaluate the response of the microphysiological system to biomechanical stimuli, track dynamic transport processes of hyaluronic acid, and identify the role of LYVE-1 and CD44 in lymphatic hyaluronic acid uptake. To date, no microphysiological system capable of recapitulating the biomechanical microenvironment of the blood-lymph interstitial space exists. This study engineers such a system to subsequently study the role of receptor-mediated hyaluronic acid uptake into the lymphatics. Hyaluronic acid is a promising linker molecule for drug delivery due to its biocompatibility and abundance of linker sites.



Keywords: organ-on-a-chip; lymphatic system; mechanobiology; vasculature; transport studies