Microsystems Engineering for Bridging Angiogenesis with Mechanopathology

Jonathan Song
The Ohio State University, Columbus, OH
Department of Mechanical and Aerospace Engineering; Comprehensive Cancer Center

Solid tumors are characterized by uncontrolled growth of new blood vessels. This process known as tumor angiogenesis produces aberrant blood vessels that are tortuous and leaky which impairs forward moving blood flow and results in elevated interstitial fluid pressure (IFP). Although these determinants of tumor blood flow have been established to contribute to the molecular origins of cancer, our understanding of how the mechanical forces associated with the unique flow patterns of tumor blood vessels is lacking due in large part to the limitations of existing model systems to experimentally manipulate flow dynamics *in vivo* or mimic 3-D tissue-level function *in vitro*. To overcome these limitations, we use microscale engineering technology to reconstitute the microarchitecture of living tissue *in vitro* to investigate the role of fluid mechanical forces, such as intravascular shear stress and transvascular interstitial flow, in guiding new vessel formation. Using this approach, we showed that physiological levels of shear stress (3 dyn/cm^2) attenuates vascular endothelial growth factor (VEGF) induced angiogenesis compared to static conditions. This finding may help explain why local regions of flow stasis contribute to the tortuous nature of tumor blood vessels. Another important finding was that interstitial flow helps potentiate VEGF-induced angiogenesis and anastomosis which confirms the observation that angiogenesis is enhanced in regions of elevated interstitial flow such as at the peri-tumor margin. Collectively, these findings help establish a fluid mechanical basis for the characteristics of tumor blood vessels that can be exploited for therapeutic benefit to help stop tumor progression.