Joint Department of

BIOMEDICAL ENGINEERING

UNC CHAPEL HILL | NC STATE UNIVERSITY

Coulter Seminar Series Presents

"Vasculature-on-chip models for studying metastasis and the tumor microenvironment"

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Dr. Shelton earned her B.S. and M.S. degrees in Environmental Sciences and Engineering at the University of North Carolina before joining the UNC-NCSU Joint Department of Biomedical Engineering for her Ph.D. During her doctoral studies under the guidance of Paul Dayton, she developed ultrasound contrast imaging and analysis methods to identify tortuous vasculature for improved cancer diagnosis. She earned a F99K00 award from the NIH to continue her studies of the vascular tumor microenvironment through a postdoctoral fellowship at Massachusetts Institute of Technology with Roger Kamm, with a co-appointment at Dana-Farber Cancer Institute with David Barbie. Her current research is in the development of vascularized microphysiological devices to model interactions between multiple cell types within the tumor microenvironment for the identification of biomarkers of disease and opportunities for therapeutic intervention.

ABSTRACT

Microphysiological systems or "organ-on-chip" devices are three-dimensional models of simplified biological tissues that have expanded the types of hypotheses that can be explored in vitro. My work focuses on vascularized models of the tumor microenvironment to understand how the endothelial barrier interacts with circulating cells and stroma in order to investigate factors that drive growth, metastasis, and resistance to therapy. One illustration of the capabilities of these models is the observation of metastasis-on-chip. By perfusing cells through vascular models in the presence of plasma proteins, we can determine how the clotting cascade influences the extravasation of cancer cells. Additionally, I have developed vascularized models of the tumor microenvironment using cells from surgical resections to generate patient-specific devices. In this model, cancer-associated fibroblasts altered several functional indicators of endothelial phenotype including vascular morphology, barrier function, angiogenesis, and immune cell recruitment, likely through cytokine signaling. One major challenge of performing in vitro immunotherapy studies arises from non-specific activation of T cells that occurs when mixing cells from different donors. Therefore, the combination of patient-specific cells and engineered vasculature will enable new immune-oncology studies, including basic science, precision medicine trials, and enabling rapid testing and translation of novel immunotherapies.

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