



Engineering Tumor Microenvironments on a Chip to Model Early Events in Breast and Ovarian Cancer Metastasis

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The tumor microenvironment is a dynamic and multifaceted ecosystem in which biochemical and mechanical cues jointly regulate cell behavior, tumor heterogeneity, and disease progression. My lab develops engineered "tumor-on-a-chip" systems to reconstruct the 3D tumor microenvironment and dissect how cell-cell interactions, fluid flow, and interfacial mechanics influence early metastatic events. In this talk, I will first introduce our approach for the rapid and accessible fabrication of organ-on-a-chip devices using epoxy-coated 3D printed molds. This workflow enables the generation of high-fidelity, biocompatible PDMS-based devices in a scalable, reproducible, and imaging-compatible format. I will then discuss how we are leveraging this technology to reverse-engineer solid breast tumors composed of heterogeneous cancer cell and immune cell subpopulations, including macrophages, to model how tumor-immune interactions shape cell plasticity and collective invasion. Finally, I will present our novel peritoneal cavity-on-a-chip, designed to mimic the primary route of ovarian cancer spread. In this model, individual ovarian cancer cells and clusters can be injected into fluid-filled peritoneal cavities to emulate circulating tumor cells that shed from the ovary during disease progression. Using live-cell imaging, we examine how these cells interact with, and infiltrate, the surrounding mesothelium to initiate metastatic colonization. Together, these approaches establish versatile experimental platforms to study dynamic cell and tissue-level behaviors, providing new strategies to model,

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predict, and ultimately control metastatic progression.

Dr. Susan E. Leggett is an Assistant Professor of Bioengineering at the University of Illinois Urbana-Champaign and an Associate Member of the Cancer Center at Illinois. Dr. Leggett earned her Ph.D. in Pathobiology from Brown University and completed postdoctoral training in Chemical and Biological Engineering at Princeton University, where she was a Clinical and Translational Science Fellow. At Illinois, Dr. Leggett leads an interdisciplinary research program that integrates tissue engineering, mechanobiology, and advanced live-cell imaging. Her laboratory develops engineered three-dimensional tumor-on-a-chip models to uncover how biochemical and mechanical cues in the tumor microenvironment drive cancer cell plasticity, therapeutic resistance, and metastasis. Her work bridges fundamental mechanobiology with translational oncology to identify new strategies for predicting and controlling cancer progression. Leggett's research is supported by the Cancer Center at Illinois, the Siteman Cancer Center, the Elsa U. Pardee Foundation, and the National Science Foundation.

