

# CARNEGIE MELLON UNIVERSITY BME 2024 FALL SEMINAR SERIES

## Cancer Mechanotherapy: Harnessing Cellular Mechanotransduction to Understand and Treat Metastatic Cancer



### PRESENTED BY

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### SCHEDULE

**Porter Hall (PH) 100**

**Thursday,  
October 3, 2024  
(9:30-10:30AM)**

Many types of cancer metastasize via the bloodstream, where circulating tumor cells (CTCs) originating from the primary tumor can travel through the circulation or lymphatic system and engraft in distant organs. Previously, our laboratory found that cancer cells exposed to physiological levels of fluid shear stress (FSS) are dramatically more susceptible to undergoing apoptosis via TRAIL protein, inspiring a new therapeutic drug delivery approach to target metastatic cells in the circulation. The FSS response of CTCs and their neutralization by nanoscale liposome conjugation to the surface of circulating immune cells has been demonstrated with in vitro cell line experiments, orthotopic mouse models of metastasis, and analysis of primary CTC aggregates isolated from metastatic cancer patients. We learned that this shear stress response is primarily mediated by Piezo1 activation, and is modulated by interactions with aggregated stromal cells such as cancer-associated fibroblasts. Interestingly, we also discovered that FSS activation of Piezo1 dramatically enhances the activation of T cells and dendritic cells, which may have important implications for various immunotherapy applications. Our ongoing research is also exploring whether cellular mechanosensors can be non-invasively stimulated using focused ultrasound, to improve clinical outcomes in cancer.

