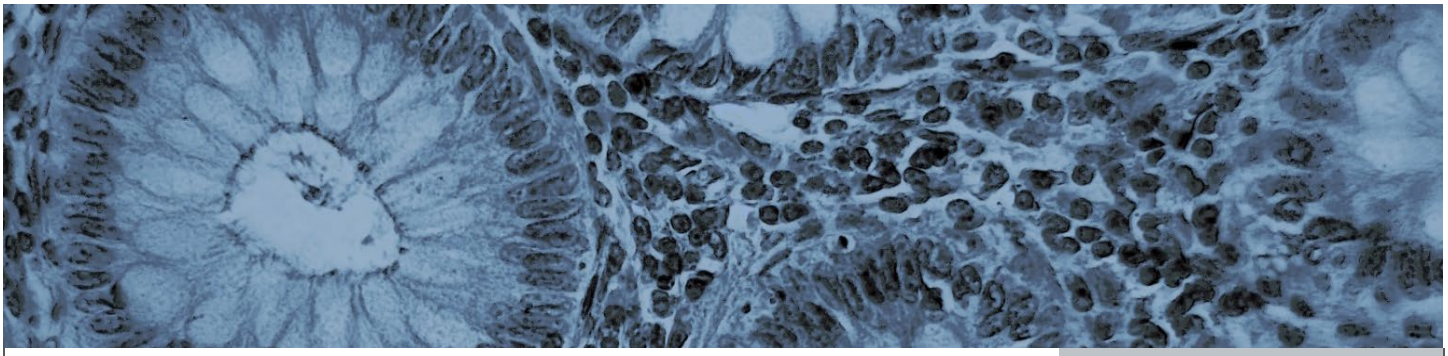

Physical mechanisms of signaling in the tumor microenvironment

Thursday, October 1, 2020
11:30 AM to 12:30 PM
https://us02web.zoom.us/j/89067192135?pwd=NUVtY0JmWm9iWHlQcmVuN3dWRHdDZz09

Biochemical signal transduction networks integrate environmental cues and mediate cellular responses. With a few exceptions, the goal of controlling these processes for therapeutic benefit has remained frustrating. An area of current interest is in cancer immunity where mobilizing immune cell responses within the complex chemical, physical, and mechanical tumor microenvironment is a potent treatment option. Understanding activation mechanisms of immune cells and tumor evolution are needed to push therapeutic efforts forward. We recently introduced a molecular impulse-response assay to quantify how individual cells receive and integrate binding events into behavioral outcomes. Importantly, this assay enables direct visualization of individual cell activities with high spatial and temporal resolution. I will discuss two cellular systems in which we have been measuring mechanistic features of signal processing. Using single molecule imaging, we map the stochastic series of binding events experienced by single T cells to discrete, signaling protein condensates, and that cell's activation decision. In the case of mammary epithelial cells, we have measured the contributions of environmental mechanics to effector protein recruitment, signaling domain dynamics, and signaling propagation in the MAP kinase pathway. In both of these systems, spatial organization and the temporal sequence of events profoundly modulate the cellular responses. I will discuss how the molecular impulse-response assay quantifies cellular signaling thresholds and creates actionable insights for therapeutic developments.

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