Using microfluidics to study multi-cell interactions in metastatic cancer

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Metastatic cancer often involves a sequence of events: the separation of individual cells from the primary tumor, migration through host tissue under the action of biochemical gradients and physical factors such as interstitial flow, intravasation into the vascular system, extravasation at a remote site, and the colonization, growth and vascularization of a peripheral tumor. Each of these processes involves a complex set of signaling events among multiple cell types in a variety of microenvironmental settings. Studies have been performed using various designs of a microfluidic platform to simulate several stages of metastasis: epithelial-mesenchymal transition (EMT), migration through the extracellular matrix, angiogenesis, intravasation, and extravasation. Selected results will be presented addressing several of these phenomena. Studies of intravasation show how the presence of accessory cells (e.g., macrophages) appear to be necessary for vascular wall crossing. Extravasation, in contrast, appears to occur readily with no need for other cell types, and occurs soon after contact with the endothelial monolayer. Tumor vascularization is influenced by secreted factors from tumor cells and by local interstitial flows. Examples will focus on the critical role of mechanobiology in these behaviors.