Engineering platforms to quantitatively measure contact inhibition of locomotion in a fibrillar *ex vivo* environment

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Metastasis accounts for 90 percent of all cancer–related deaths. This process, driven by cell migration, involves cancer cells escaping from the primary tumor, invading the local tissue and forming secondary tumors in remote areas of the body. Healthy cells do not exhibit this ability because their locomotion is inhibited by contact with another cell. Contact inhibition of locomotion (CIL) is suppressed in cancer cells, one distinctive feature that allows them to become metastatic. The principle goal of the proposed thesis is to engineer a novel *ex vivo* platform to quantitatively measure CIL and use it to identify molecular mediators that facilitate local invasion during metastasis. Micropatterns provide a unique environment to study CIL because they mimic aspects of *in vivo* cell migration along fibers and force pairwise collisions between cells.

We recently used a micropatterning approach to develop a 1D platform to study homotypic CIL. Time-lapse microscopy was used to quantitatively compare CIL in normal mammary epithelial cells and metastatic breast cancer cells. Cells were confined to micropatterned lines that varied in width from one to two cell diameters (18 - 33 microns). Pairwise interactions between cells were scored as bouncing or sliding collisions. The fraction of sliding collisions was measured as a representative metric of CIL and reported as a function of patterned line width. A statistically significant difference was observed in normal and metastatic cells. Furthermore, examination of results with respect to normalized cell diameter revealed that the ability of metastatic cells to invade was size-independent whereas the few sliding events observed in normal cells occurred only when adequate space was available. Further testing using this platform as a phenotypic assay will be conducted in the context of the Eph/ephrin signaling system to elucidate its role in contributing to the loss of CIL in tumor progression. By analyzing cell-cell interactions in this context, quantitative differences between measured characteristics and expression levels can be used to identify critical expression levels of signaling molecules that regulate metastasis. Our system provides a useful tool to gain insights that can help develop novel therapeutic strategies.