Impact of Narrow Constraint on Single Cell Motion

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Carcinoma progression is associated with of a loss of epithelial characteristics in tumor cells, combined with a gain in mesenchymal ones, a process known as the epithelial-to-mesenchymal transition (EMT) [1]. During carcinoma development and invasion, epithelial cells assume an elongated morphology and disarranged polarity in order to migrate and degrade the surrounding extra-cellular environment, intravasate into the lymphatic and circulatory system, and reach distant tissues and organs [2]. At a molecular level, tumor tissues appear to exhibit an abnormal expression of epithelial markers together with a higher expression of proteins associated to cell migration [3].
In this study, we assess the potential invasiveness of five human breast carcinoma cell lines through single cell migration assays in confinement. For this purpose, we use a novel microfluidic device to investigate the ability of both mesenchymal and epithelial breast carcinoma cells to deform and migrate through narrowing microstructures upon chemoattractant stimulation. We find that normal epithelial cells are able to migrate through the narrowest micro-constrictions as the more invasive mesenchymal cells. We also demonstrate that migration of epithelial cells through a highly compressive environment can occur in absence of a chemoattractive stimulus, thus evidencing that they are just as prone to react to mechanical cues as invasive cells.
We then evaluate the expression of vimentin and cytokeratin (CK) intermediate filaments (IFs) in our cell lines through immunostaining and western blots, and observe how the IF cytoskeletal network responds to the compressive stress applied by narrow micro-channels, and whether differences in IF protein expression affect the migratory behavior of our cells. We find no remarkable difference between the mechanical behaviors of the keratin and vimentin networks during migration through our micro-constrictions. Moreover, since vimentin positive mesenchymal cells did not display invasive behavior, while other vimentin negative cells did, we conclude that vimentin protein expression does not strongly correlate to single cells invasive behavior in confinement.

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