**Crosstalk between matrix metalloproteases (MMPs) and the actomyosin cytoskeleton in breast cancer**

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Abstract: During cancer progression, the extracellular matrix (ECM) of various epithelial tissues undergoes stiffening induced by increased deposition and crosslinking of the fibrillar protein collagen I. Cancer cells invade through these dense matrices using two modes of invasion: (i) mesenchymal mode, wherein cells degrade the ECM using matrix metalloproteinases (MMPs); (ii) amoeboidal mode, wherein cells squeeze through the matrix using actomyosin contractility. While it is assumed that MMPs are only required for mesenchymal motility, increasing evidence points to a cross-modulation between the two. In our work, we have probed this cross-modulation in MDA-MB-231 cells. When cultured on polyacrylamide hydrogels of varying stiffness, MDA-MB-231 cells spread extensively and mechanically adapt to their underlying substrate by stiffening their cortex and increasing their contractility. Concomitant with this, cells secrete increasing amount of soluble MMPs, MMP2 and MMP9. Interestingly, treatment of cells with the broad spectrum MMP inhibitor GM6001 leads to cell rounding, cell softening and reduction in cell contractility. Similar results are also observed when cells are incubated with the adhesive peptide RGD. Thus far, our results suggest that the crosstalk between MMPs and the actomyosin contractility is mediated by integrins. Future studies will be focused on understanding the implication of this crosstalk in breast cancer invasion.