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Mechanical properties of metastatic breast cancer cells invading into collagen I matrices[1]

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Mechanical interactions between cells and the extracellular matrix (ECM) are critical to the metastasis of cancer cells. To investigate the mechanical interplay between the cells and ECM during invasion, we created thin bovine collagen I hydrogels ranging from 0.1-5 kPa in Young's modulus that were seeded with highly metastatic MDA-MB-231 breast cancer cells. Significant population fractions invaded the matrices either partially or fully within 24 h. We then combined confocal fluorescence microscopy and indentation with an atomic force microscope to determine the Young's moduli of individual embedded cells and the pericellular matrix using novel analysis methods for heterogeneous samples. In partially embedded cells, we observe a statistically significant correlation between the degree of invasion and the Young's modulus, which was up to an order of magnitude greater than that of the same cells measured in 2D. ROCK inhibition returned the cells' Young's moduli to values similar to 2D and diminished but did not abrogate invasion. This provides evidence that Rho/ROCK-dependent acto-myosin contractility is employed for matrix reorganization during initial invasion, and suggests the observed cell stiffening is due to an attendant increase in actin stress fibers.

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