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Cell migration through connective tissue in 3-D

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A prerequisite for metastasis formation is the ability of tumor cells to invade and migrate through connective tissue. Four key components endow tumor cells with this ability: secretion of matrix-degrading enzymes, firm but temporary adhesion onto connective tissue fibers, contractile force generation, and rapid remodeling of cytoskeletal structures. Cell adhesion, contraction, and cytoskeletal remodeling are biomechanical parameter that can be measured on single cells using a panel of biophysical methods. We use 2-D and 3-D traction microscopy to measure contractile forces; magnetic tweezer microrheology to estimate adhesion strengths, cytoskeletal stiffness and molecular turn-over rates; and nanoscale particle tracking to measure cytoskeletal remodeling. On a wide range of tumor cell lines we could show that cell invasiveness correlates with increased expression of integrin adhesion receptors, increased contractile force generation, and increased speed of cytoskeletal reorganization. Each of those biomechanical parameters, however, varied considerably between cell lines of similar invasivity, suggesting that tumor cells employ multiple invasion strategies that cannot be unambiguously characterized using a single assay.