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**Stem cell cytoskeleton is slaved to active motors** FLORIAN REHFELDT, ANDRE BROWN, ADAM ENGLER, DENNIS DISCHER, University of Pennsylvania — Cells feel their physical microenvironment through their adhesion and respond to it in various ways. Indeed, matrix elasticity can even guide the differentiation of human adult mesenchymal stem cells (MSCs) [Engler et al. *Cell* 2006]. Sparse cultures of MSCs on elastic collagen-coated substrates that are respectively soft, stiff, or extremely stiff were shown to induce neurogenesis, myogenesis, and osteogenesis. Lineage commitment was evaluated by morphological analysis, protein expression profiles, and transcription microarrays. Differentiation could be completely blocked with a specific non-muscle myosin II (NMM II) inhibitor, suggesting that contractile motor activity is essential for the cells to sense matrix elasticity. Current studies by AFM and near-field fluorescence imaging show that NMM II inhibition in stem cells on rigid glass surfaces promotes actin-rich dendritic outgrowth resembling neurite extension. Dynamic cell studies have been conducted to elucidate the complex molecular interplay of the contractile apparatus in response to selected physical and biochemical stimuli. Additional insight is being gained by using AFM to investigate the local elasticity of the cell's cytoskeletal force sensing machinery.

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