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Matrix elasticity directs stem cell lineage specification

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Adhesion of stem cells - like most cells - is not just a membrane phenomenon. Most tissue cells need to adhere to a "solid" for viability, and over the last decade it has become increasingly clear that the physical "elasticity" of that solid is literally "felt" by cells. Here we show that Mesenchymal Stem Cells (MSCs) specify lineage and commit to phenotypes with extreme sensitivity to the elasticity typical of tissues [1]. In serum only media, soft matrices that mimic brain appear neurogenic, stiffer matrices that mimic muscle are myogenic, and comparatively rigid matrices that mimic collagenous bone prove osteogenic. Inhibition of nonmuscle myosin II activity blocks all elasticity directed lineage specification, which indicates that the cytoskeleton pulls on matrix through adhesive attachments. Results have significant implications for 'therapeutic' stem cells and have motivated development of a proteomic-scale method to identify mechano-responsive protein structures [2] as well as deeper physical studies of matrix physics [3] and growth factor pathways [4].

[1] A. Engler, et al. Matrix elasticity directs stem cell lineage specification. Cell (2006).
[2] C.P. Johnson, et al. Forced unfolding of proteins within cells. Science (2007).
[3] A.E.X. Brown, et al. Multiscale mechanics of fibrin polymer: Gel stretching with protein unfolding and loss of water. Science (2009).
[4] D.E. Discher, et al. Growth factors, matrices, and forces combine and control stem cells. Science (2009).