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Matrix elasticity directs stem cell differentiation in 3D too ALLISON ZAJAC, FLORIAN REHFELDT, DENNIS DISCHER, University of Pennsylvania — Microenvironments appear important in stem cell lineage specification but can be difficult to adequately characterize or control with soft tissues. Naive mesenchymal stem cells (MSCs) are shown here to specify lineage andcommit to phenotypes with extreme sensitivity to tissue level elasticity. Soft matrices that mimic brain are neurogenic, stiffer matrices that mimic muscle are myogenic, and comparatively rigid matrices that mimic collagenous bone prove osteogenic. During the initial week in culture, reprogramming of these lineages is possible with addition of soluble induction factors, but after several weeks in culture, the cells commit to the lineage specified by matrix elasticity, consistent with the elasticity-insensitive commitment of differentiated cell types. Inhibition of nonmuscle myosin II blocks all elasticitydirected lineage specification–without strongly perturbing many other aspects of cell function and shape. The results have significant implications for understanding physical effects of the in vivo microenvironment and also for therapeutic uses of stem cells.

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