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Matrix elasticity perturbation and Lamin-A/C expression in stem cells modulate their mechanics and lineage specification[1] IRENA IVANOVSKA, DENNIS DISCHER, University of Pennsylvania — Commitment of stem cells to different lineages is regulated by many cues in their local microenvironment. They are particularly sensitive to the mechanical properties of their extracellular matrix. Nuclear lamins are fibrous proteins providing structural function and transcriptional regulation in the cell nucleus. In particular Lamin A/C levels could influence cellular mechanical sensitivity. Here we show that perturbation of the extracellular matrix and nucleus mechanics can direct stem cells lineage specification. We studied the behavior of human mensechymal stem cells (hMSC) cultured on thin highly ordered collagen nanofilms. To tune the mechanical properties of the nanofilms we used the enzyme transglutaminase as a crosslinking agent. AFM imaging and manipulation is used to examine the nano topography and mechanical properties of the films and cells. Film stiffening affects cells morphology, cytoskeleton organization and their elastic response. hMSCs cultured for two weeks on collagen nanofilms initially tune their stiffness with matrix elasticity but later continuously change it with time. We observed upregulation of osteogenic markers on cross-linked films and increased lamin A/C expression. We show that manipulating Lamin-A/C expression in stem cells also directs cell lineage with knockdown favoring adipogenesis and over expression favoring osteogenesis. We found positive correlation between matrix and nucleus mechanics and that they have a synergistic effect on hMSCs differentiation potential.

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