ELASTICITY OF EXTRA-CELLULAR MATRIX DIRECTS STEM CELL DIFFERENTIATION

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Microenvironments and niches appear important in stem cell differentiation but can be difficult to adequately characterize or control with soft tissues. It also appears that many differentiated cell types 'feel' the softness of their matrix through contractile mechanisms [1], but any influence of matrix elasticity on stem cell differentiation is unknown. Mesenchymal stem cells are shown here to differentiate in response to tissue elasticity under otherwise uniform media and adhesion conditions. Differentiation occurs with coupled regulation of non-muscle myosin II activity as well as cytoskeletal organization. Soft matrices that mimic brain are neurogenic, while stiffer matrices that mimic muscle [2] are myogenic, and comparatively rigid matrices that mimic collagenous bone prove osteogenic. Elasticity-dependent expression profiles correlate Ras family activators with lineage-specific transcription factors and implicate an adhesion-contractile balance in differentiation. Inhibition of myosin-II and the Rho-GTPase ROCK indeed abrogate elasticity-directed differentiation. Biophysical metrics document the increases in cell contractility with matrix stiffness and fit within a simple chemomechanical model that quantifies differentiation of stem cells directed by matrix elasticity. The results highlight the critical importance of matrix mechanics to cell state.

References

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