Effect of Matrix Polarity on Fate Specification of Human Mesenchymal Stem Cells

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Abstract: Human stem cells hold the potential of almost unimaginable medical breakthroughs for the treatment of a variety of diseases. However, their use as a therapy is hampered by the limited understanding of the mechanisms by which cells integrate environmental stimuli. Efforts to understand extracellular biophysical cues have demonstrated the critical role of cell geometrical parameters and mechanical signals in determining the ultimate fate of stem cells. The goal of this contribution was to dissect the interplay between cell shape polarity and matrix stiffness in stem cell lineage specification. To accomplish this goal, microcontact printing was employed to create polar and nonpolar hydrogels of varying stiffness moduli. Human mesenchymal stem cells (hMSCs) were confined to the hydrogels at the single cell level and were given the choice to differentiate along adipogenic and osteogenic routes. Our results demonstrated that on soft matrices, polarity exerted a significant effect on osteogenesis. On the contrary, cell shape polarity had negligible effects on the stiff matrices. The insight gained from this project provide a rational basis for designing stem cell culture systems that will facilitate their use in research and clinical settings.