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PROBING MECHANISMS OF MECHANO-SENSITIVE DIFFERENTIATION IN MESENCHYMAL STEM CELLS

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Adult mesenchymal stem cells (MSCs) have recently been shown to be responsive to the properties of their adjacent extracellular niche, most notably physical parameters such as topography and elasticity. Elasticity varies dramatically between tissues that MSCs inhibit, which drives elasticity-based differentiation into neurons, muscle, bone, etc. However within tissues, distinct elasticity gradients, brought on by pathological conditions, e.g. myocardial infarction ~ 8.67 ± 1.50 kPa/mm, or through normal tissue variation, e.g. 0.58 ± 0.88 kPa/mm, could drive MSC migration. In fact, MSCs appear to undergo directed migration up elasticity gradients, or "durotax," as shallow as 0.96 kPa/mm, indicating a 'differentiation hierarchy' since when given the choice, MSCs will durotax into the stiffest regions of the niche and then differentiate based on niche elasticity. As cells move up the gradient, they do so by deforming their niche to determine it's elasticity, but the molecular mechanism that converts this biophysical signal into a biochemical one which the nucleus can interpret is yet unresolved. We have identified several focal adhesion-related proteins may be capable of force-induced conformational changes, e.g. vinculin. Upon the application of different amounts of traction stress *in situ* by MSCs, an appropriate amount of stretching results in the exposure of cryptic MAPK binding sites within vinculin and suggests that vinculin, among other focal adhesion proteins, may be sensitive to physical ECM properties and thus able to relay information leading to differentiation of stem cells.