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Physical Control of Stem Cells via Matrix Elasticity FLORIAN REHFELDT, DENNIS DISCHER, University of Pennsylvania — Most of our cells reside in soft tissue, but it has only become clear over the last decade that substrate elasticity exerts a major influence on cell motility, contractility, and overall cell function. The mechanical properties of the matrix can even direct the differentiation of human adult stem cells as reported by our group recently (Engler et al. Cell 2006). Basically, the greater the resistance to matrix deformation, the larger the force with which the cell pulls on the matrix, driving the assembly of cytoskeleton and adhesions. For a deeper understanding of the molecular mechanisms of force generation and transduction, various biophysical and biochemical tools must be combined with well-defined extracellular matrix (ECM) models. Past studies have been conducted mostly with synthetic and uncharged polyacrylamide (PA) gel matrices, motivating more bio-relevant gel models. We have developed such a biocompatible hydrogel system of widely and finely tunable elasticity using hyaluronic acid (HA), which is ubiquitous in development and in particular adult tissues. The effective Young's modulus E of these negatively charged hydrogels measured by AFM can be finely tuned by variation of cross-linker and HA concentration yielding a stiffness of 0.1 kPa to 150 kPa. E scales with the concentration of HA to the power of n=2.6 and is a biphasic function of cross-linker concentration. We will describe the influence of these unique gels on stem cell differentiation.

Florian Rehfeldt
University of Pennsylvania

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