Tissue cells must survive as well as specialize. We have been studying two broad aspects of both topics with a wide range of experiments and modeling. Our focus on ‘survival’ centers on the innate immune system, which efficiently terminates – more often than not – all manner of foreign cells and particles while sparing ‘Self’ cells. A reductionist based materials approach is taken to the decision of macrophages to destroy or not. We simulate, synthesize, and demonstrate in vivo as well as in vitro that a short peptide found in a protein on all cells can mark even plastic particles as ‘Self’ and prevent their phagocytic clearance. We exploit the peptide in anti-cancer applications and elucidate its folding and function. In a second set of studies, we have focused on the influence in differentiation and systematics of tissue rheology, recognizing that tissues can be very soft like fat and brain, or increasingly stiff like striated muscle and bone [Discher Science 2009]. Cells (that survive) feel and respond to the elasticity differences [Engler Cell 2006], and we now find the signaling propagates all the way into the lamina of the nucleus, which amplifies matrix cues. Proteomic profiling of tissue nuclei has revealed that Lamin expression increases more than 30-fold and in near-proportion to micro-elasticity of adult tissue. With adherent adult stem cells in vitro, matrix elasticity is shown to affect expression of nucleoskeleton proteins, with low levels of Lamin s amplifying soft matrix toward a soft tissue lineage while high levels amplify stiff matrix to promote a rigid tissue lineage.


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