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**Best Stiffness for Striation: Effect of Matrix Stiffness on Myocytes and Stem Cells** DENNIS DISCHER, ADAM ENGLER — Contractile myocytes provide a test of the hypothesis that cells sense their mechanical as well as molecular microenvironment, altering expression, organization, and/or morphology accordingly. Here, myoblasts and stem cells were cultured on collagen strips attached to glass or polymer gels of varied elasticity. MyoD expression and morphology peaks on gels with stiffness typical of normal muscle (passive Young's modulus $E$ ~9-15 kPa). While fusion of myoblasts into myotubes occurs independent of substrate flexibility, myosin/ actin striations emerge later only on gels with the same tissue-like $E$. On glass and much softer or stiffer gels, including gels emulating stiff or fibrotic muscle, cells do not striate. In addition, myotubes grown on top of a compliant bottom layer of glass-attached myotubes (but not softer fibroblasts) will striate, whereas the bottom cells will only assemble stress fibers and vinculin-rich adhesions. Unlike sarcomere formation, adhesion strength increases monotonically versus substrate stiffness with strongest adhesion on glass. These findings have major implications for in vivo introduction of stem cells into diseased or damaged striated muscle of altered mechanical composition.

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