

In This Issue

Best stiffness for striation

A small change in substrate stiffness can deter striated muscle differentiation, as shown on page 877 by Engler et al. As stiffness changes of this magnitude are not uncommon in diseased tissues, injections of stem cells may be useless unless the target environment is also treated.

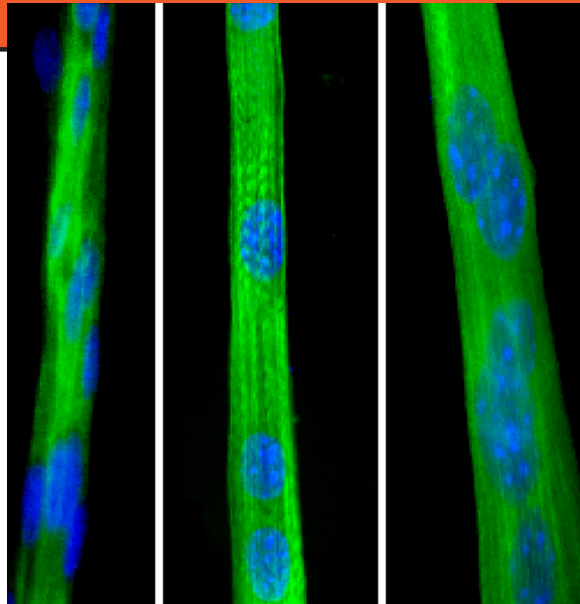
Muscular dystrophy patients suffer from stiffened muscle tissue. Although muscle precursors are abundant in *mdx* mice, a muscular dystrophy model, they fail to regenerate injured muscle. The new article shows that this failure may be due to their overly stiff environment, which prevents skeletal muscle striation.

Skeletal muscle precursors spread, assumed a spindle shape, and fused into multinucleated cells when grown on surfaces within a wide range of stiffness. However, striation—the alignment of actin and myosin into repeated units—was blocked if the substrates were either too soft (e.g., fibroblasts or weak gels) or

too stiff (e.g., glass).

Adhesions were strongest on the stiffest substrate. Differentiation therefore requires enough adhesion to sense the matrix stiffness, but not so much that cytoskeletal changes leading to striation are inhibited. What translates forces felt at adhesion sites into differentiation is unknown, but the membrane-bound scaffold protein N-RAP is one possibility, as it both nucleates actin filaments and regulates transcription.

Striation was most prominent on substrates within just 25% of the stiffness of normal muscle. The authors found that *mdx* muscle is stiffer than this optimal range, and thus may inhibit



Striation (middle) is inefficient on too soft (left) or too hard (right) surfaces.

differentiation of its own precursors. If cardiac muscles are similarly sensitive, careful application of antifibrotics may be needed before injections of precursor cells can regenerate tissue damaged by heart attacks. ■