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Effect of ECM Stiffness on Integrin-Ligand Binding Strength
GAWAIN THOMAS, QI WEN, Department of Physics, Worcester Polytechnic Institute, Worcester, MA — Many studies have shown that cells respond to the stiffness of their extracellular matrix (ECM). However, the mechanism of this stiffness sensing is not fully understood. We believe that cells probe stiffness by applying intracellular force to the ECM via the integrin-mediated adhesions. The linkage of integrins to the cytoskeleton has been modeled as a slip clutch, which has been shown to affect focal adhesion formation and hence force transmission in a stiffness dependent manner. In contrast, the bonds between integrins and ECM have been characterized as "catch bonds." It is unclear how ECM viscoelasticity affects these catch bonds. We report, for the first time, the effects of ECM stiffness on the binding strength of integrins to ECM ligands by measuring the rupture force of individual integrin-ligand bonds of cells on collagen-coated polyacrylamide gels. Results show that the integrin-collagen bonds of 3T3 fibroblasts are nearly four times stronger on a stiff (30 kPa) gel than on a soft (3 kPa) gel. The stronger integrin bonds on stiffer substrates can promote focal adhesion formation. This suggests that the substrate stiffness regulates the cell-ECM adhesions not only by affecting the cytoskeleton-integrin links but also by modulating the binding of integrins to the ECM.

Gawain Thomas
Department of Physics, Worcester Polytechnic Institute, Worcester, MA

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