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Characterization of cellular traction forces at the single-molecule level ALEXANDER DUNN, Department of Chemical Engineering, Stanford University — The ability of cells to generate and respond to mechanical cues is an essential aspect of stem cell differentiation, embryonic development, and our senses of touch and hearing. However, our understanding of the roles of mechanical force in cell biology remains in its infancy, due largely to a lack of tools that measure the forces generated by living cells at the molecular scale. Here we describe a new technique termed Molecular Force Microscopy (MFM) that visualizes the forces exerted by single cellular adhesion molecules with nm, pN, and sub-second resolutions. MFM uses novel FRET-based molecular tension sensors that bind to a glass coverslip and present a binding site for integrins, a ubiquitous class of cell adhesion proteins. Cell-generated forces stretch the MFM sensor molecules, resulting in decreased FRET with increasing load that can be imaged at the single-molecule level. Human foreskin fibroblasts adhere to surfaces functionalized with the MFM probes and develop robust focal adhesions. FRET values measured using MFM indicate forces of between 1 and 4 pN per integrin, thus providing the first direct measurement of the tension per integrin molecule necessary to form stable adhesions. The relatively narrow force distribution suggests that mechanical tension is subject to exquisite feedback and control at the molecular level.

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