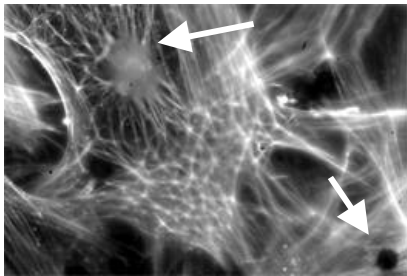


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**STIFFENING OF HUMAN AIRWAY SMOOTH MUSCLE CELLS AND
CYTOSKELETAL REORGANIZATION IN RESPONSE TO MECHANICAL
STIMULATION AND CONTRACTILE ACTIVATION**

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The stiffening of human airway smooth muscle cells may impede the ability for lung inflations to dilate the airways and reverse bronchoconstriction as occurs in asthma. Using magnetic twisting cytometry (*Science*, 260:1124-7,1993) and fluorescent imaging of the cytoskeleton (CSK) of human airway smooth muscle cells we found that the cells stiffen following mechanical stimulation, and that the CSK reorganized at the sites of mechanical stimulation. Ferromagnetic beads (3.5 μm) coated with RGD peptide were bound to integrins (primarily to $\beta 1\alpha 5$) on the cell surface. Beads were oscillated by sinusoidal magnetic fields of 20 Gauss, imposing stresses of $\sim 55 \text{ dyn/cm}^2$ at 0.1 Hz for 5 min. At 24 ± 5 min following stimulation, cell elasticity (E) was elevated by $30 \pm 3\%$ ($p < 0.05$), while viscosity (R) was unchanged. Increases in E may be attributed to reorganization of the actin CSK or development of focal adhesions. Administration of Cytochalasin D (1 $\mu\text{g/ml}$) which severed actin filaments decreased E to $36 \pm 7\%$ of control, with no alteration in R, while administration of Jasplakinolide at 10 μM (which stabilizes actin filaments) prevented any stiffening by mechanical stimulation or by histamine activation. Mechanical stimulation led to increased expression of vinculin staining at some of the beads with further increases following activation with histamine. Cells given histamine (10^{-5}M), and subjected to 15 min of continuous mechanical stimulation showed increased localization of actin filaments (phalloidin staining) to some of the beads (arrow top), but not to all beads (arrow right).

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