Cell stretch and deformation induce ATP release from A549 alveolar cells

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Physical forces are important regulators of normal lung function. Cell distortion, for example, is a predominant physiological stimulus for surfactant secretion in the alveolus, which may involve mechanosensitive release of ATP, a major surfactant secretagogue. ATP release induced by stresses that are relevant in the lung, such as cell stretch, or cell distortion has not been extensively investigated. In this study effect of cell stretch on ATP release was examined in real-time by imaging ATP-dependent bioluminescence of extracellular luciferase with high-sensitivity CCD camera. Modest stretch (<10%, 1-s duration) of cells grown in a flexible chamber produced a transient ATP release that was restricted to few active cells. The number of responding cells increased dose-dependently with the applied stretch (10-25%), but did not involve cell damage. In parallel experiments, cells were subjected to deformation by passing an air bubble over the cell monolayer in a flow-through chamber. Such stimulation induced reversible non-lytic cell deformation, transient intracellular Ca^{2+} elevation, and significant ATP release, as determined by off-line luciferin-luciferase bioluminescence assay. ATP release was reduced in BAPTA-loaded cells, and was completely abolished by N-methylmaleimide suggesting involvement of exocytosis. Experiments demonstrate that physiologically-relevant stimuli induce mechanosensitive ATP release from lung epithelial cells.