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may emerge as a powerful tool to analyze whether cancer cells may be able to break down the endothelial cell barrier by altering endothelial cells mechanical properties.

3806-Pos
Feeling for Cells with Light: Illuminating the Role of Biomechanics for Cancer Metastasis
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Light has been used to observe cells since Leeuwenhoek's times; however, we use the forces caused by light described by Maxwell's surface tensor to feel for the cellular cytoskeleton. The cytoskeleton a compound of highly dynamic polymers and active nano-elements inside biological cells is responsible for a cell's stability and organization. It mechanically senses a cell's environment and generates cellular forces sufficiently strong to push rigid AFM-cantilevers out of the way. The active cytoskeleton is described by a new type of polymer physics since nano-sized molecular motors and active polymerization overcome the inherently slow, often glass-like brownian polymer dynamics. The optical stretcher exploits the nonlinear, thus amplified response of a cell's mechanical strength to small changes between different cytoskeletal proteomic compositions as a high precision cell marker that uniquely characterizes different cell types. Consequentially, the optical stretcher detects tumors and their stages with accuracy unparalleled by molecular biology. As implied by developmental biology the compartmentalization of cells and the epithelial-mesenchymal transition that allows cells to overcome compartmental boundaries strongly depend on cell stiffness and adhesiveness. Consequentially, biomechanical changes are key when metastatic cells become able to leave the boundaries of the primary tumor.

3807-Pos
Refrigerated Versus Fresh Human Red Blood Cells Response to Sheer Stress
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By fully calibrating 1064 nm infrared laser traps we have studied the mechanical deformations caused by shear stress on healthy human RBCs. In this study we have investigated how the mechanical deformation of RBCs to such a stress varies when we use fresh and refrigerated RBC (at 4°C for a period of about 2 weeks). Fresh and refrigerated red blood cells from a healthy donor are suspended in the donor's blood plasma. Then the cells are subjected to viscose drag force by translating the microscope stage holding the blood sample while the cells are kept trapped by the laser to cause sheer deformation on the cells. Under these conditions the areal, longitudinal, and transverse deformations of the cells as a function of the sheer stress have been investigated. The results for these deformations have revealed significant difference with a nonlinear behavior as a function of the net force acting on the cells. Moreover, the results indicate the elasticity of the cells drastically decreases due to refrigeration.

3808-Pos
How Deep Cells Feel
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Cellular organization within a multicellular organism requires a cell to assess its relative location, taking in multiple cues from its microenvironment. A cell engages ECM and actively probes the matrix, sensing in deformation the elastic resistance that seems to characterize different tissues, and so to assess how far the feedback extends - by analogy to the 'princess and the pea'fairy tale - we have generated substrates of different elasticity and different thickness on top of rigid supports. The elastic properties of our gels are characterized by AFM-based micro-rheology - a tool that probes at the cellular scale, and mesenchymal stem cells (MSCs) are studied because these cells have proven particularly sensitive to matrix elasticity and microenvironment in terms of their adhesion, their morphology, and even - after days - their differentiation. Cell morphology changes generally take hours, and we find that spread area, focal adhesions and cytoskeleton organization of MSCs on thin and soft gels resemble structures in cells on thick and stiff gels. Thickness sensitivity decreases with stiffness, and initial computational modeling of cell and matrix mechanics lends insight into the sub-cellular sensitivity. Furthermore, continuity of deformation from matrix into the cell and around the cytoskeleton-caged and linked nucleus also suggests mechanisms to affect processes such as differentiation. The results ultimately show that even if one's cells are not of royal descent, they seem to feel the difference between stiff or soft and thick or thin surroundings.

3809-Pos
Fibroblasts Sense Substrate Viscosity
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Mechanosensitivity of fibroblasts, their ability to sense and respond to viscoelastic changes in their surrounding environment, is believed to critically affect cell adhesion and morphology and to play an important role in multiple cellular processes, such as cell differentiation and migration. Previous studies in cellular mechanoresponse using μm-thick polymeric films suggest that fibroblasts mainly sense changes in substrate elasticity. Here we present comparable experiments using a biomembrane-mimicking substrate which show that plated fibroblasts may respond similarly to changes in substrate viscosity. These 8-40nm thick substrates consist of stacks of multiple, polymer-interconnected lipid bilayers where cell-linker fluidity and substrate viscosity are tuned through the degree of stacking. In this experimental system, the amount of frictional coupling affecting substrate viscosity is reduced with increasing distance between the outermost (cell-exposed) lipid bilayer and underlying glass. The integrity of the multi-bilayer system, containing mobile laminin linkers, in the presence of plated cells is confirmed through combined differential interference contrast (DIC) microscopy and fluorescence recovery after photobleaching. Optical microscopy (DIC, phase contrast, EPI-fluorescence) data of GFP-actin transfected cells illustrate profound changes in adsorption, phenotype, and cytoskeletal organization, in response to substrate viscosity. Furthermore the impact of substrate viscosity on projected cell area and cellular migration is discussed.

3810-Pos
Control of Extracellular Matrix Organization through Coupled Mechanical and Chemical Inputs
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The extracellular matrix (ECM) is a critical cellular component that provide structural support and organization as well being linked to a variety of cell responses including motility, proliferation, and apoptosis. Fibronectin (FN) is an ECM protein that is secreted by many mammalian cells as a soluble dimer and assembles into insoluble multimeric fibrils at the cell surface. This specific extracellular component has been linked to wound healing, cell adhesion, blood coagulation, cell differentiation and migration, maintenance of the cellular cytoskeleton, and tumor metastasis. In addition, FN is constantly subjected to mechanical and chemical stimulations, resulting in a highly dynamic microenvironment that is constantly being remodeled by the cell. While many studies have examined FN organization through various modes of chemical stimulation, there is limited work on examining the effects of mechanical stimulation or in examining the coupled affects of mechanical and chemical stimulation. In our present study we used a custom fabricated device to probe the effects of mechanical and chemical stimulation on FN organization. We exposed single cells to equibiaxial stretching and observed an increase in localized FN fibrils relative to unstimulated cells. The response patterns of the FN were markedly distinct when examining intracellular versus extracellular organization. We also perturbed this system by coupling the mechanical stimulation with chemical stimulation by exposing cells to equibiaxial stretching while inhibiting Rho activity. These dual mode stimulated cells revealed similar responses to cells exposed to mechanical stimulation in that increased FN fibrils was observed, indicating mechanics may play more of a dominate role in ECM organization with respect to Rho activity. These results have implications in a variety of fields including biophysics, cell mechanics, and mechanotransduction.

3811-Pos
Cell-Matrix De-Adhesion Dynamics Reflect Contractile Mechanics
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Measurement of the mechanical properties of single cells is of increasing interest both from a fundamental cell biological perspective and in the context of disease diagnostics. In this study, we show that tracking cell shape dynamics during trypsin-induced de-adhesion can serve as a simple but extremely useful tool for probing the contractility of adherent cells. When treated with trypsin, both $SW13^{-/-}$ epithelial cells and U373 MG glioma cells exhibit a brief lag period followed by a concerted retraction to a rounded shape. The time-response of the normalized cell area can be fit to a sigmoidal curve with two characteristic time constants that rise and fall when cells are treated with blebbistatin and nocodazole, respectively. These differences can be attributed to actomyosin-based cytoskeletal remodeling, as evidenced by the prominent buildup of stress fibers in nocodazole-treated $SW13^{-/-}$ cells, which are also two-fold stiffer than untreated cells. Similar results observed in U373 MG cells highlights the direct association between cell stiffness and the de-adhesion response. Faster de-adhesion is obtained with higher trypsin concentration, with nocodazole treatment further expediting the process and blebbistatin treatment blunting the response. A simple finite element model confirms that faster contraction is achieved with increased stiffness.