mechanosensing studies. Specifically, the dBFP allows us to analyze dual receptor crosstalk by quantifying the spatiotemporal requirements and functional consequences of the up- and down-stream signaling events. In this work, the utility and power of the dBFP has been demonstrated with four important dual receptor systems that play key roles in immunological synapse formation, shear-dependent thrombus formation, and agonist driven blood clotting respectively.

1601-Pos Board B510

Mechanical Property Change of Red Blood Cell Membrane under Photosensitizer Mediated Oxidative Stress of CIS Porphyrin

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Various cytoskeletal networks have been investigated to understand the cell mechanics because it can directly apply for therapeutic researches of immune or cancer disease. However, due to a lack of sufficient signal-transduction measurement techniques, even for the well-studied red blood cell (RBC), the relationships between the cytoskeleton physiology and mechanical properties of the cell membrane – i.e., ''signaling'' – are still not well understood. Here, we applied a newly designed micropipette manipulation technique to make dynamic membrane elasticity measurements in the presence of a therapeutic photosensitizer-mediated oxidant, cis-porphyrin. We found that the shear modulus of the RBC was dynamically changed from 6.7 $\pm$ 0.5 x 10^{-6} N/m (absence of the porphyrin) to a non-measureable or plastic-like behavior value (presence of 0.05 μM porphyrin and irradiation) with the degree of oxidative stress controlled by the irradiation. We also found that the porphyrin oxidative stress could induce unique morphological change before hemolysis of the RBC. We hypothesize that dynamical cytoskeletal network reformation with oxidative stress could cause these behaviors. Therefore, to visualize the network proteins, we also applied the techniques of Stimulated Emission Depletion (STED) microscopy. We consider that this further characterization of the mechanical properties of the RBC membrane will help to understand more complicated cytoskeletal network of immune, cancer or even neuron cells for therapeutic development in the future. More details will be shown at the meeting.

1602-Pos Board B511

Cell Growth Rate Dictates the Onset of Glass to Fluid-Like Transition and Long Time Super-Diffusion in an Evolving Cell Colony

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Collective migration dominates many phenomena, from cell movement in living systems to abiotic self-propelling particles. Studying early stages of tumor evolution, we clarify the principles involved in cell dynamics and highlight their implications in understanding similar behavior in seemingly unrelated soft glassy materials and possibly chemokine-induced migration of CD8+ T cells. We performed simulations of tumor invasion using a minimal three-dimensional model, taking into account cell elasticity and adhesive cell-cell interactions to establish that cell growth rate-dependent tumor expansion leads to the emergence of distinct topological niches. Cells at the periphery move with a higher velocity perpendicular to the tumor boundary, while the movement of interior cells is slower and isotropic. The mean square displacement, $\Delta(t)$, of cells exhibits glassy behavior at times comparable to the cell cycle time, but, exhibit super-diffusive behavior, $\Delta(t) \sim t^{\alpha}$, at longer times. We establish the universality of super-diffusion in a class of seemingly unrelated non-equilibrium systems. Our findings for the collective migration, which also suggests that tumor evolution occurs in a polarized manner, are in quantitative agreement with in vitro experiments. Although set in the context of tumor invasion, our findings should be relevant in describing collective motion in growing cell colonies especially in active systems where creation and annihilation of particles play a role.

1603-Pos Board B512

The Apical Constriction Force of Madin-Darby Canine Kidney (MDCK) Cells

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The dominant thinking of the mechanism for the apical constriction is the purse-string model which explains the shrinkage of apical area is due to the contractile force from circumferential actomyosin bundle around the apical surface. However, recent studies of morphogenesis gastrulation in *Drosophila* and *Xenopus* hasve shown that the apical constriction of ventral furrow cells can be is driven by pulsed actomyosin contraction within medio-apical surface. Here we used MDCK cysts, which consist of cellular monolayers enclosing a fluid-filled lumen, to study apical constriction. We found that the tight junctions, which form continuous belt structure at subapical regions of a cell, become tortuous as cysts mature. We quantified the tortuous tight junctions and found that the tight junctions become straighter when we disrupt the actomyosin contractility with pharmaceutical perturbation. Together with theoretical simulations based on Surface Evolver®, we can explain the morphological change by the change of apical surface tension. In addition, we performed laser ablation at the apical face and found that the apical surface area increase after ablation. The expansion rate increase with increasing tortuosity and decreasing apical area of the cells. This observation fits our model of actomyosin contractility on the apical surface. Our proposed cytoarcheture of medioapical actomyosin network may shed light to how cytoskeleton regulates the paracellular transportation of tight junctions.

1604-Pos Board B513

A Breakdown of Cellular Mechanisms Required for Cell and Focal Adhesion Area Sensitivity to Substrate Stiffness

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Cell spread area and focal adhesion (FA) sizes are known to increase with substrate stiffness (Yeung et al., *Cell Motil. Cytoskeleton*., 2005). Different models have been developed, some of which can predict increases in cell spread area with substrate stiffness while others can predict increases in only the FA area. Here, we systematically add one mechanism at a time to start recapitulating both these behaviors together. We start with an adapted model (Walcott et. al. *Biophysical J.,* 2011) of FA growth implemented in a 2D cell that spreads at a constant rate. This model demonstrates that while the total FA area increases with substrate stiffness the cell spread area is not sensitive to the stiffness. In order for the cell spread area to increase with substrate stiffness the spreading model must include a coupling between the spreading rate, the FA complex evolution, and intracellular stresses (Vernerey & Farsad, *J. Math. Bio.,* 2013). When the spreading rate is coupled with cellular stresses and FA evolution, we demonstrate the ability of our model to qualitatively reproduce the increase in cell spread area and FA area with substrate stiffness. Further we try to generate biological insight on the role of the model parameters in their ability to reproduce cellular behavior for various experimentally studied cellular systems such as 3T3 fibroblasts and human mesenchymal stem cells. Based on this we also articulate the gaps in the current model and make a case for potentially bringing in additional mechanisms that can account for the role of stress fiber orientation (Deshpande et al, *PNAS,* 2006) which can enhance our ability to understand the interplay between the different mechanisms in predicting cellular responses across a broader range of cell types.

1605-Pos Board B514

Magneto-Active Substrates for Local Mechanical Stimulation of Living Cells

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Cells can feel and react to the mechanical properties of their environment such as stiffness or geometry by translating mechanical cues into biochemical ones, inducing biochemical and mechanical responses. This process, called mechanotransduction, drives critical functions such as cell differentiation, proliferation and migration. In order to assess to which extend cellular response depends on the temporal and spatial characteristics of the stimulation, it is essential to control temporally and spatially the mechanical cues. Methods have been proposed to apply global and continuous deformations, or local deformations though discrete substrates. Here we propose a novel method to apply mechanical stimuli in a local and dynamic way to cells plated on the continuous surface of deformable substrates. These substrates are made of a soft elastomer (PDMS) in which iron micro-pillars are embedded and actuated by two electromagnets. The amplitude of the surface deformation is controlled by the input current in the coils, and monitored by tracking fluorescent particles underneath the surface. Traction Force Microscopy (TFM) allows us to estimate the stress generated by the pillars, and the cellular mechanical response. Cells adhering to the magneto-active substrates can be stimulated both in