The cortical myosin web determines mechanical integrity of non-confluent epithelia

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Abstract

Epithelia are continuously exposed to mechanical stresses like tension and shear. While the mechanisms by which confluent cells sense and react to mechanical stress is well studied, little is known about the regulation of mechanical integrity of non-confluent cells. During morphogenesis, wound healing or migration, epithelial cells are frequently not surrounded by other cells or a tight matrix. We have recently shown that in these scenarios, epithelial cells form a characteristic cortical acto-myosin network that organizes the apical cell surface. Based on our preliminary results we hypothesized that this cortical web is able to generate and coordinate forces to confer mechanical stability to non-confluent cells.

Using optical flow and spatio-temporal correlation analysis, we were able to identify and characterize oscillatory rearrangements in the cortical acto-myosin web, with constant cycles between states of low and high contractility. These oscillations exhibited characteristic periods of around 175 s and were modulated by myosin light chain activity and Ca^{2+}/Calmodulin signaling. Using laser ablation and combined fluorescence and atomic force microscopy we could show that the observed acto-myosin oscillations strongly correlated with periodic softening/stiffening cycles of the cell cortex.

In summary, we characterized a novel facet in the complex interplay between cellular organization and mechanical forces acting on cells. The dynamic acto-myosin network on the apical surface of epithelial cells is likely to be a key determinant for their mechanical integrity. In addition, contractile oscillations are likely to play an important role in mechano-transduction and future work will focus on the regulatory pathways that can modulate oscillation parameters.