Physical forces driving migration, division and folding of epithelial sheets

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Biological processes such as morphogenesis, tissue regeneration, and cancer invasion are driven by collective migration, division, and folding of epithelial tissues. Each of these functions is tightly regulated by mechanochemical networks and ultimately driven by physical forces. I will present maps of cell-cell and cell-extracellular matrix (ECM) forces during cell migration and division in a variety of epithelial models, from the expanding MDCK cluster to the regenerating zebrafish epicardium. Force maps show that cells dividing in a migrating epithelium exert large cell-ECM forces during cytokinesis. These forces point towards the division axis and are exerted through paxillin-rich focal adhesions that connect the cytokinetic ring to the underlying ECM. Large forces at these adhesions are associated with failure of cytokinesis and polyploidy, indicating that abnormal cell-matrix adhesion at the cleavage furrow impedes abscission. Time lapse analysis of force maps further reveals that cell-cell forces determine the duration of the cell cycle and mitosis. Finally, I will present direct measurements of epithelial traction, tension, and luminal pressure in three-dimensional epithelia of controlled size and shape. Strikingly, we found that epithelial tension in the free-standing curved monolayers is constant up to 200% strain, indicating active mechanisms of tensional homeostasis.