Internship

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Mechanical regulation of tissue homeostasis

Our multidisciplinary team « Cell mechanics and adhesion » is co-supervised by RM. Mège (Biologist) and B. Ladoux (physicist). Our research aims at understanding how living cells interact with their environment. In particular, we are studying the cooperation between adhesion, bio-mechanical and bio-chemical signaling for the adaptation of living cells to changes in their environment.

Epithelial cell sheets act as a covering for most of the internal and external surfaces of the body. The primary role of the epithelium is a protective barrier against physical damage and infection attack. In order to perform these functions, the integrity of the epithelial cell sheet must be maintained by balancing cell renewal and removal. Deteriorating, damaged, or unnecessarily cells are targeted for elimination by apoptosis – the process of programmed cell death – allowing them to be eliminated without causing damage to the neighboring healthy cells, such as inflammation. The removal of cells in excess through extrusion is important to prevent accumulation of cells and tumor formation. Such events strongly depend on intercellular interactions and in particular, interactions between the dying cell and its neighbours. However, the role of mechanical cues on cell extrusion mechanisms remains poorly understood even though the extrusion of cells relies on active tension including cell-cell interactions and tissue density fluctuations. Therefore the most challenging problem is to determine the relative contributions of mechanical and biochemical processes during cell extrusion and to understand how the integration of biomechanical signals leads to a global response at the cellular or multicellular scales. We recently showed that mechanics played an important role in cell extrusion mechanisms *(Kocgozlu et al. Current Biol 2016; Saw et al. Nature 2017)*.

We will use experimental in vitro approaches for understanding of how extrusion arise from the interaction of the epithelium with its mechanical environment. We will study how extrusion can be influenced by external force application on epithelia, and how cells respond to different rates and types of force application (shear, compression, or stretch). Passive mechanical environment parameters such as substrate stiffness and curvature have also been shown to significantly influence collective cell migration and epithelial architecture. In parallel, we will analyze changes in cell shape, nucleus deformation, cytoskeleton remodeling and cell-cell junctions. Our project will involve a multidisciplinary approach combining microfabrication, experimental cell biology, functional live cell imaging, tissue dynamics, computational image processing and biophysical approaches. We anticipate that our results will provide mechanistic insight into epithelial homeostasis and tumorigenesis.

Methods: *soft lithography techniques, particle imaging velocimetry (PIV), molecular biology, cell culture, immunofluorescence microscopy, live cell microscopy and/or in cell biophysics and Image analysis.*