Master 2 + PhD Project:

The mechanical assembly of stratifying skin epithelia

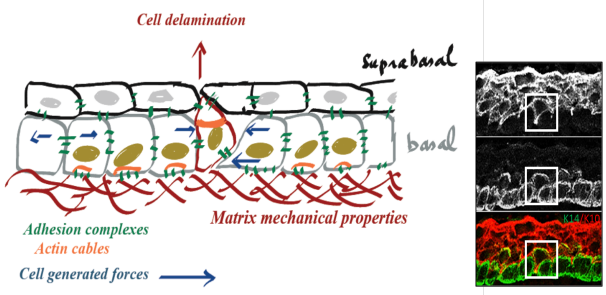
Supervisor:
Name: Dr. LADOUX BENOIT
E-mail: benoit.ladoux@ijm.fr
Host Laboratory:
Affiliation: CNRS and Paris Diderot
Lab Name : Institut Jacques Monod
Address : "Cell Adhesion and Mechanics", Institut Jacques Monod, Université Paris Diderot & CNRS.
http://www.ijm.fr/en/research/research-groups/cell-adhesion-and-mechanics/
Partners or collaborations :
Name: René-Marc Mège (Cell biologist), Affliliation: Same team (Institut Jacques Monod, Paris)
Other collaborations: Carien Niessen (Koln, Germany)

Project description :

Epithelia are assemblies of multiple cells that are crucial for barrier function and tissue integrity to protect against challenges from the environment. To maintain tissue homeostasis in the face of these challenges, **epithelia balance cell renewal with cell death**. Whereas simple epithelia are monolayered, the skin epithelium, **the epidermis, is a stratified epithelium**. **Both types of epithelia renew through a continuous flow of dividing and extruding cells**, but whereas in simple epithelia those extruding cells are either lost or reinsert into the monolayer, delaminating stem cells of stratified epithelia differentiate while integrating into a suprabasal layer. Little is known on the cell- and tissue- mechanics of basal cell delamination and generation or renewal of a suprabasal layer. We would like **to address the molecular and mechanical principles that govern cell delamination and subsequent formation of an adhesive distinct suprabasal differentiated layer to generate a basal/suprabasal fate boundary.** We hypothesize that the mechanical and adhesive state of an epithelial determines whether an epithelial monolayer will generate a suprabasal layer to undergo stratification.

To this end, we will ask what adhesive, cytoskeletal and mechanical properties are shared between extrusion and stratification, what are the key determinants of stratification and what governs the establishment and maintenance of a boundary between basal and suprabasal layers of the epidermis. We will follow these processes in mouse keratinocytes within *in vitro* monolayer and multilayered systems as well as *in vivo* and compare findings to one of the best characterized *in vitro* model systems for cell extrusion, the MDCK monolayer.

We will combine quantitative assessment of forces, convergence-divergence fields, nematic ordering, extensility/compressibility, cell shape dynamics in fixed and live cell imaging and image analysis and micropatterning. Our *in vitro* **pluri-disciplinary, quantitative approach** is expected to provide insight **how mechanical properties of the tissue** participate in **1) cell delamination from the basal layer**, while **2) maintaining a homeostatic partitioning between basal and suprabasal layers** of epidermis. The innovative approaches that we will develop and apply, will not only provide insights into skin biology and cell extrusion in other epithelia, but also in the general area of the physics of life matter.



Schematic of epidermal cell delamination and stratification in relation with the biomechanical environment and in vivo example (box) of delaminating cell