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Titre du projet : **Epithelial behaviour in microfabricated 3D environment and consequences on tissue homeostasis**

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Epithelial monolayers have to constantly and collectively adapt to microenvironment properties to maintain its organized state. The intestinal epithelium displays a simple and regular architecture, where proliferative and differentiated cells are distributed in distinct areas: the crypt and the villus, respectively. Therefore, the maintenance of the functional integrity of the intestinal epithelium requires a tight coordination between stem cell niche homeostasis, cell proliferation, cell progression along the crypt-villus axis, cell polarization and cohesion. Control of intestinal morphogenesis has long been shown to be triggered by morphogens and downstream signaling pathways in the crypt-villus axis. However, recent experimental evidence have led to recognition that tissue mechanical properties direct various cell functions including cell proliferation, migration and differentiation. Only very recent studies concern the role of mechanics for intestinal epithelial regulation.

The need of culture systems to study the multicellular behaviours during tissue morphogenesis where one could control different parameters provoked the development of biomimetic cultures. Microfabrication techniques offer new perspectives in making well-defined structured surfaces on a small scale and can be used to mimic 3D cellular environments *in vitro* in close physiological conditions. **We improve culture systems that mimic crypt-villus axis. We combine 3D soft-matter microfabrication techniques and primary intestinal crypt cultures isolated either from genetic mouse models or from biopsies of patients with intestinal disease. We concentrate on understanding the physical cues regulating intestinal cell proliferation and differentiation along the crypt/villus axis.**

We investigate the influence of substrate topography on the stem cell behaviour and consequences on epithelial differentiation. We determine which topographical parameter(s) is required to induce changes in stem cell homeostasis as well as in epithelial sheet expansion and differentiation on 3D devices in physiological conditions. We identify mechanisms through which epithelial cells are able of modulating their organization and terminal differentiation according with tissue physical properties, chemical signature of the underlying substrate. The study takes place in a multidisciplinary lab at the crossroad between developmental biology, cell biology and physics, and combines microfabrication, cell biology and cell imaging technics. This work, while being focused on intestinal epithelium, will pave the way for future studies in other epithelia and in mechanotransduction fields.

Publications de l'équipe, relatives au stage proposé

- Xi W, Saw TB, Delacour D, Lim CT and Ladoux B. Active behaviours of epithelial tissues in a mechanical environment. *Nature Reviews Materials*. In press.
- Gaston C, Salomon J, Goulet O and Delacour D.
The Congenital Tufting Enteropathy, or when the intestine is under low tension. *Médecine/Sciences*, 33(8-9):694-697.
- Salomon J, Gaston C, Magescas J, Duvauchelle B, Campeotto F, Canioni D, Sengmanivong L, Mayeux A, Michaux G, Poirier F, Minc N, Schmitz J, Brousse N, Ladoux B, Goulet O and Delacour D.
Contractile forces at tricellular contacts modulate epithelial organization and monolayer integrity. *Nature Communications* (2017), 8:13998.
- Xi W, Sonam S, Beng Saw T, Ladoux B, Lim CT. Emergent patterns of collective migration under tubular confinement. *Nature Communications* (2017), 8(1):1517.
- Delacour D, Salomon J, Robine S and Louvard D
The plasticity of the brush border: the yin and the yang of intestinal homeostasis. *Nature Reviews Gastroenterology and Hepatology* (2016), 13(3) :161-174.