2016-05

IC-**3i** International PhD Program

PhD thesis project

2017 Call for application

Migration of Epithelial Cells in Gut Homeostasis Role of Microenvironment

General information

Call	2017
Reference	2016-05-VIGNJEVIC&DESCROIX
Keyword(s)	cell migration, extracellular matrix, gut, fibroblasts, microfabrication

Director(s) and team

Thesis director(s)	Danijela Vignjevic &Stéphanie Descroix
Research team	Cell Migration & Invasion
Research department	Subcellular Structure and Cellular Dynamics

Description of the PhD thesis project

The entire intestinal epithelium is renewed every week due to cell division in the crypts coupled with cell migration towards the villi and loss of cells by apoptosis at the tip of villi. However, the mechanism responsible for the migration of intestinal cells remains largely unknown.

The basal surface of single-layer epithelium is underlined by the basement membrane, a thin and dense sheet-like structure. The basement membrane provides structural support for the epithelium, promotes cell adhesions, maintains cell polarity and has a role in compartmentalization of the tissue by separating epithelium from the stroma. One of the major components of the stroma are fibroblasts surrounded by the network of extracellular matrix (ECM). Fibroblasts play a role in gut homeostasis by producing growth factors, cytokines and ECM proteins. Whether they play a role in epithelium renewal and more specifically in epithelial cell migration remains unknown.

The goal of the PhD project is to unravel the role of stroma (basement membrane and fibroblasts) in epithelial cell migration during homeostasis using multi-disciplinary approach that combines animal models, cell biology and microfabrication. The project is based on collaborative efforts between two teams, cell biologists (Danijela Vignjevic) and physicist/chemists (Stephanie Descroix). The broad objective of Vignjevic's team is to understand how epithelial cells interact with their microenvironment during migration, in homeostasis and cancer invasion. They use the gut as a model system and their research strategy combines molecular and cell biology techniques with live-cell imaging. In particular, they use 3D *in vitro* cell cultures; ex vivo tissue slices and different transgenic mouse models to study cell migration in the living animal. S. Descroix works in a multidisciplinary team focused on the development of innovative tools for biology and medicine. They are experts in microfabrication, microfluidics and organs on chip.

International, interdisciplinary & intersectoral aspects of the project

This interdisciplinary project relies on complementary approaches developed by cell biologists, physicists and chemists aiming to investigate gut homeostasis and it is part of a broader project funded by ANR. Grafting of the specific molecules on 3D ECM scaffolds will be done in a collaboration with start-up company Alveole. A successful development of an *in vitro* cell-based model of intestine that mimics the mechanical, structural, physiological properties of the gut could accelerate pharmacological development, and potentially reduce animal testing. In addition, tools generated through this project will also be beneficial for other research fields, such as developmental biology, cancer metastasis and microbe-host interactions.

Recent publications

1. Yamada A, Renault R, Chikina A, Venzac B, Pereiro I, Coscoy S, Verhulsel M, Parrini MC, Villard C, Viovy JL and **Descroix S**.
Transient microfluidic compartmentalization using actionable microfilaments for biochemical assays, cell culture and organs-on-chip
Lab Chip, 2016, 16, 4691-4701

2. Glentis A, Gurchenkov V, Matic **Vignjevic D**.
Assembly, heterogeneity, and breaching of the basement membranes.
Cell Adh Migr. 2014;8(3):236-45. Review.

3. Elkhatib N, Neu MB, Zensen C, Schmoller KM, Louvard D, Bausch AR, Betz T, **Vignjevic DM.**
Fascin plays a role in stress fiber organization and focal adhesion disassembly.
Curr Biol. 2014 Jul 7;24(13):1492-9.

4. Verhulsel M, Vignes M, Descroix S, Malaquin L, **Vignjevic DM**, Viovy JL.
A review of microfabrication and hydrogel engineering for micro-organs on chips.
Biomaterials. 2014 Feb;35(6):1816-32. 2.

5. Schoumacher M, Goldman RD, Louvard D, **Vignjevic DM**.
Actin, microtubules, and vimentin intermediate filaments cooperate for elongation of invadopodia. J Cell Biol. 2010 May 3;189(3):541-56.

Expected profile of the candidate

Applicants should have a strong desire to explore cell biological phenomena in an *in vivo* context, and to develop physiologically relevant 3D *in vitro* models using microfabrication approaches. While cell biology background is strongly recommended, background in microfabrication is a plus but not compulsory. The project highly relies on microscopy and live imaging techniques, for which the applicant should have either experience or a strong motivation to learn. Applicants should show solid capacity for independent and creative thinking.