Master Biologie Moléculaire et Cellulaire 'BMC',
Université de Paris - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2020-2021

Unité INSERM ou CNRS ou Université : Institut Jacques Monod UMR 7592 **Intitulé Equipe : Cell Adhesion and Mechanics** **ED d'appartenance :BioSPC & PIF** **Responsable de l'Equipe :Ladoux/Mège**	**Responsable du Stage : Benoit Ladoux** **Contacts** Adresse :IJM, Batiment Buffon, 15 rue Hélène Brion, 75013 Paris Email :benoit.ladoux@ijm.fr Tel :0143576121

Titre du projet : Mechanical control of epithelial cell death and extrusion

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras) :

Epithelial cell sheets act as a covering for most of the internal and external surfaces of the body. While the epithelial barrier function needs to be maintained, epithelial cells are constantly challenged by their environment, which can lead to cell elimination. Understanding how cell fate -live, death, or transformed- is determined within epithelia and how this leads to the competition and/or extrusion of cells from the epithelium is key to understanding important homeostatic and pathologic processes such as aging and cancer development. Recent studies including ours have shed light on the crucial coupling of cell shape, collective cell behaviors and mechanical stress to biochemical signaling for cell extrusion and delamination, but a great deal remains to be elucidated. The role of the mechanical environment in cell extrusion is largely unexplored. **Here, we thus propose to adress the impact of mechanical forces at cell-matrix and cell-cell adhesions on epithelial cell extrusion and delamination *in vitro* environments.**

We propose to characterize the impact of a controlled mechanical environment on cell extrusion. We will further determine the type of extrusion induced when the balance between cell-cell and cell-matrix adhesion is impaired. To tackle this hypothesis, we will study how extrusion is influenced by external force application on epithelia, and how cells respond to different rates and types of force application (shear, compression, or stretch). Our project involves 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.

Publications de l'équipe relatives au projet de stage (max 5)

T. Chen, A. Callan-Jones, E. Fedorov, A. Ravasio, A. Brugues, H. T. Ong, Y. Toyama, B. C. Low, X. Trepat, T. Shemesh, R. Voituriez & B. Ladoux, Large-scale curvature sensing by directional actin flow drives cellular migration mode switching, Nature Physics, 15, 393-402 (2019).

T. B. Saw, A. Doostmohammadi, V. Nier, L. Kocgozlu, S. Thampi, Y. Toyama, P. Marcq, C. T. Lim, J. M. Yeomans* & B. Ladoux*, Topological defects in epithelia govern cell death and extrusion, Nature, 544, 212-216 (2017).

L. Kocgozlu, T. B. Saw, A. P. Le, M. Shagirov, E. Wong, R-M. Mège, C. T. Lim, Y. Toyama & B. Ladoux, Epithelial cell packing induces distinct modes of cell extrusions, Current Biology, 26, 2942-2950 (2016).