Extracellular matrix proteins and integrins' interaction using a biomimetic model

Supervisors: Nicolas Rodriguez and Guillaume Perry

Context:

Extracellular matrix (ECM) plays an important role in controlling the cell local environment. This is particularly true for basement membranes which separate epithelial and endothelial tissues within various species since the emergence of *Metazoans*. Basement membranes (BM) are mainly composed of two intertwined sheet-like scaffolds formed by Type IV Collagen (Col4) and Laminins respectively. Formation of BM has been widely studied in *in vivo* models such as *C. Elegans* and *Drosophila melanogaster* (Jayadev and Sherwood, *Current Biology*, 2017). These model organisms are highly used in developmental biology to study BM genesis using genetic modification to insert fluorescent reporters within ECM proteins composing BM (Sherwood, *J. Cell Biol.* 2017, 210:3,369–372). Nevertheless, the results obtained are not directly transferable to mammals as mammalian BM proteins are more complex. Moreover, the basic underpinning mechanisms of BM formation remain elusive particularly the interactions between cellular receptors (integrins) and extracellular matrix proteins (collagen and laminins) particularly in mammals.

This limited knowledge does not enable *in vitro* engineering of basement membrane using bottom-up approach. Better understanding the interaction mechanisms and physicochemical characterization of the resulting assembly, would enable the use of this assembly as new biomaterial for tissue engineering and overcome the limitations of *in vivo* models (Perry *et al.*, *Integr. Biol.*, 2018). We previously demonstrated *in vitro* that Col4 binds to a specific subset of integrins that are included in a lipid bilayer. Moreover, using Quartz Crystal Microbalance with dissipation measurement (QCM-D), we showed that this binding is mediated by divalent cations and depends on their concentration within the buffer. The nature of the integrin and divalent cations also affects the viscoelasticity of the resulting assembly.

This internship proposal aims to study these mechanisms using a complementary method (Fluorescent Recovery After Photobleaching, FRAP) and confocal microscopy.

Scientific questions:

During this internship, we expect to answer the following questions:

- Are integrin mobile on the lipid bilayer?
- Are the laminin/integrin and Col4/integrin complexes mobile on the lipid bilayer?
- How does Ca^{2+} concentration influence the interaction between Col and integrin?

To answer these questions, we aim to image in real time the mobility of different BM proteins and integrin complexes in different conditions.

Expected contributions:

- Optimize and write detailed protocols for the experimental setup
- Acquire technical skills with the relevant characterization tools (Samples preparation, Confocal microscopy, FRAP setup, image processing, data processing)
- Present during the bimonthly team meeting
- Read scientific literature

If interested, please send your CV, cover letter and academic transcripts to:
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Team:

We previously studied the interaction dynamics between Type IV collagen/laminin and integrins in various conditions using Quartz Crystal Microbalance (QCM) at LRS in collaboration with CPCV (Sophie Cribier). However, there are still unanswered questions regarding the interactions in specific conditions. We will further characterize these interactions in specific conditions using supported lipid bilayers and fluorescently labelled proteins

Candidate profile:

We are looking for a M2 student with a background in biophysics, biochemistry or molecular biology. Previous experiences in microscopy, python coding and image processing will be a plus. Depending on the results, a PhD project based on the internship could be considered.