**Master 2 internship project**

**Year 2021-2022**

**Laboratory/Institute:** IAB **Director:** Pierre Hainaut

**Team:** DYSAD **Head of the team:** Corinne Albiges-Rizo

**Name and status of the scientist in charge of the project:** Dr Emmanuelle PLANUS (MCU-HC-UGA) and Dr Olivier DESTAING (CR-CNRS) **HDR: yes X no ☐**

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**Program of the Master’s degree in Biology:**

**X** Immunology, Microbiology, Infectious Diseases **☐** Structural Biology of Pathogens

**X** Physiology, Epigenetics, Differentiation, Cancer **X** Neurosciences and Neurobiology

**Title of the project: Characterization and regulation by optogenetics of molecular machineries involved in the mechanisms of matrix degradation implicated in physiological and pathological invasion processes.**

Objectives (up to 3 lines):

This project aims to understand the cellular mechanisms implicated in the degradation of the extracellular matrix to support the process of invasion. To do so, we will characterize the functions of the molecular machineries involved and their regulators by genetic and optogenetic approaches combined with quantification and live imaging of extracellular matrix degradation.

Abstract (up to 10 lines):

The process of cell invasion is essential in multiple physiological (development, immune scanning, tissue repair, bone remodeling, neurogenesis…) and pathological (metastasis, inflammation) situations. Cell invasion supposes to couple cell movements with an intense ability of reorganization and degradation of the extracellular matrix (ECM) through specific types of adhesive structures, the invadosomes. Indeed, invadosomes support cell invasion by coupling adhesive and extracellular matrix degradative functions, which are apparently two antagonist cellular processes. Our lab developed the concept that both functions are in fact tightly regulated in space and time to achieve an effective and local invasion by the cell. Today, we propose that the degradation of the ECM is under the control of different molecular machineries gathered at the vicinity of invadosomes. We propose to identify, characterize and control the interplay between the machineries. To do so, we developed new state of the art approaches to finely investigate the degradation processes in 2 and 3D environments, but also in physiological and pathological invadosomes. Thus, we propose to characterize the differences between physiological and pathological invadosome funtions in order to develop new strategies that will either favorize immune cell invasion or decrease cancer cell invasion.

Methods (up to 3 lines):

Molecular biology, cell engineering (infection and Cell sorting), live imaging, zymography, optogenetics activation

Up to 3 relevant publications of the team:

1-Control of SRC molecular dynamics encodes distinct cytoskeletal responses by specifying its signaling pathway usage. Kerjouan A, Boyault C, Oddou C, Hiriart-Bryant E, Pezet M, Balland M, Faurobert E, Bonnet I, Coute Y, Fourcade B, Albiges-Rizo C, **Destaing O**\*. **J Cell Sci.** 2021 Jan 25;134(2):jcs254599.

2- Cross-talk between the calcium channel TRPV4 and reactive oxygen species interlocks adhesive and degradative functions of invadosomes. Vellino S, Oddou C, Rivier P, Boyault C, Hiriart-Bryant E, Kraut A, Martin R, Coute Y, Knölker HJ, Valverde AM, Albiges-Rizo C, **Destaing O**\*. **J Cell Biol.** 2021 Feb 1;220(2):e201910079.

3-DNA mechanotechnology reveals that integrin receptors apply pN forces in podosomes on fluid substrates. Glazier R, Brockman JM, Bartle E, Mattheyses AL, **Destaing O\*, Salaita K\***. **Nat Commun.** 2019 Oct 18;10(1):4507.

4-Roles of paxillin family members in adhesion and ECM degradation coupling at invadosomes. Petropoulos C, Oddou C, Emadali A, Hiriart-Bryant E, Boyault C, Faurobert E, Vande Pol S, Kim-Kaneyama JR, Kraut A, Coute Y, Block M, Albiges-Rizo C, **Destaing O**.\* **J Cell Biol.** 2016 Jun 6;213(5):585-99.

# 5- Functional and structural consequences of epithelial cell invasion by Bordetella pertussis adenylate cyclase toxin

[Christelle Angely](https://pubmed-ncbi-nlm-nih-gov.proxy.insermbiblio.inist.fr/?sort=date&term=Angely+C&cauthor_id=32392246), [Daniel Ladant](https://pubmed-ncbi-nlm-nih-gov.proxy.insermbiblio.inist.fr/?sort=date&term=Ladant+D&cauthor_id=32392246), [**Emmanuelle Planus**](https://pubmed-ncbi-nlm-nih-gov.proxy.insermbiblio.inist.fr/?sort=date&term=Planus+E&cauthor_id=32392246), [Bruno Louis](https://pubmed-ncbi-nlm-nih-gov.proxy.insermbiblio.inist.fr/?sort=date&term=Louis+B&cauthor_id=32392246), [Marcel Filoche](https://pubmed-ncbi-nlm-nih-gov.proxy.insermbiblio.inist.fr/?sort=date&term=Filoche+M&cauthor_id=32392246), [Alexandre Chenal](https://pubmed-ncbi-nlm-nih-gov.proxy.insermbiblio.inist.fr/?sort=date&term=Chenal+A&cauthor_id=32392246), Daniel Isabey

**PLoS One** 2020 May 11;15(5):e0228606

6- ICAP-1 monoubiquitylation coordinates matrix density and rigidity sensing for cell migration through ROCK2-MRCKα balance. Bouin AP, Kyumurkov A, Régent-Kloeckner M, Ribba AS, Faurobert E, Fournier HN, Bourrin-Reynard I, Manet-Dupé S, Oddou C, Balland M, **Planus E\*, Albiges-Rizo C**\*. . **J Cell Sci.** 2017 Feb 1;130(3):626-636.

Requested domains of expertise (up to 5 keywords):

Cell culture, microscopy, biochemistry, surface treatment, image analysis, cell biology, synthetic biology