**Master 2 internship project**

**Year 2025-2026**

**Laboratory/Institute:** IAB **Director:** C. Arnoult

**Team:** INVADE **Head of the team:** Destaing/Faurobert

**Name and status of the scientist in charge of the project:** Eva Faurobert, DR CNRS

 **HDR: yes ☐X no ☐**

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

**☐** Microbiology, Infectious Diseases and Immunology **☐** Biochemistry & Structure

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

**Title of the project: Role of mechanotransduction on the epigenetic control of endothelial identity in the context of vascular malformations CCM**

Objectives (up to 3 lines):

We will address the synergistic roles of mechanical cell forces and transcription factors activity in the pathogenesis of Cerebral Cavernous Malformations using in vitro 2D models.

Abstract (up to 10 lines):

Our lab focusses on the mechanical aspects of a cerebrovascular disease named Cerebral Cavernous Malformations (CCM) that is characterized by capillary-venous angiomas and recurrent bleedings. These vascular malformations form stacks of angiogenic and malformed capillaries composed of mosaics of mutant and wild-type endothelial cells (ECs). The goal of this proposal is to elucidate **how cell mechanics and epigenetics interplay** in controlling cell fate decisions in the CCM pathology. Our lab has shown that a loss of CCM proteins has a profound effect on EC mechanics and disrupts the mechanical homeostasis of the endothelium and the expression profile of numerous genes leading to a senescence associated with a secretory phenotype (SASP) (Vannier et al. Angiogenesis 2021). In a recent work, we showed that mechanically hyperactive senescent mutant ECs recruit wild-type ECs and reprogram them into proliferative cells (Shapeti et al. Nature Comm. 2024). During this internship, the student will participate in a research program ongoing in the lab that aims at unravelling how forces exerted by hyperactive mutant cells lead to reprogramming of neighboring cells, a question also relevant in cancer and aging.

Methods (up to 3 lines):

Cell biology (culture, infection, transfection), Immunofluorescence, cell imaging techniques (epifluorescence, confocal microscopy, live microscopy), micropatterning.

Up to 3 relevant publications of the team:

-Pham VC, Rödel CJ, Valentino M, Malinverno M, Paolini A, Münch J, Pasquier C, Onyeogaziri FC, Lazovic B, Girard R, Koskimäki J, Hußmann M, Keith B, Jachimowicz D, Kohl F, Hagelkruys A, Penninger JM, Schulte-Merker S, Awad IA, Hicks R, Magnusson PU, Faurobert E, Pagani M, Abdelilah-Seyfried S. Epigenetic regulation by polycomb repressive complex 1 promotes cerebral cavernous malformations. EMBO Mol Med. 2024 Nov;16(11):2827-2855.

-Apeksha Shapeti, Jorge Barrasa-Fano, Abdel Rahman Abdel Fattah, Janne de Jong, José Antonio Sanz-Herrera, Mylène Pezet, Said Assou, Emilie de Vet, Seyed Ali Elahi, Adrian Ranga, Eva Faurobert\*, Hans Van Oosterwyck\*. [Force-mediated recruitment and reprogramming of healthy endothelial cells drive vascular lesion growth](https://www.biorxiv.org/content/10.1101/2023.11.27.568780v1), Nat Commun. 2024 Oct 6;15(1):8660

- Vannier DR, Shapeti A, Chuffart F, Planus E, Manet S, Rivier P, Destaing O, Albiges-Rizo C, Van Oosterwyck H, Faurobert E\*. CCM2 deficient endothelial cells undergo a ROCK dependent reprogramming into senescence associated secretory phenotype. Angiogenesis, 2021, Nov;24(4):843-860. [doi: 10.1007/s10456-021-09809-2](https://link.springer.com/article/10.1007/s10456-021-09809-2)

Requested domains of expertise (up to 5 keywords):

Academic knowledge on cell biology, epigenetics, mechanosensitive transcription factors, mechanotransduction, intracellular signaling.

We are seeking a motivated candidate for joining our dynamic team and potentially interested in continuing with a PhD.