**Master 2 internship project**

**Year 2024-2025**

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

**Team:** Hainaut **Head of the team:**

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

 **HDR: yes ☐X no ☐**

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

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

**☐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 epigenetic factors activity in the pathogenesis of Cerebral Cavernous Malformations using in vitro 2D models.

Abstract (up to 10 lines):

Epigenetic regulatory circuits control transcription factor activity. This has been widely recognized as a central molecular mechanism involved in many physiological, and disease-related processes. Therefore, understanding what triggers epigenetic changes and how this impacts the transcription of the genome is critical for understanding diseases. 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. 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 cell mechanics and disrupts the mechanical homeostasis of the endothelium and the expression profile of numerous genes involved in the pathogenesis of the disease. Importantly, in preliminary work, we identified the histone acetyl-transferases p300 and CBP as crucial epigenetic factors downstream of ROCK1/2. As p300 and CBP are known to regulate the mechano-dependent transcription factors YAP/TAZ, we will investigate how they interplay in mutant endothelial cells and how mechanical inputs (ECM stiffness and fluid shear stress) regulate their dialog.

Methods (up to 3 lines):

Cell biology, Immunofluorescence, live microscopy, micropatterning, microfluidic

Up to 3 relevant publications of the team:

- 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) bioRxiv 2023.11.27.568780; doi: https://doi.org/10.1101/2023.11.27.568780 (accepted in Nature Com).

- 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, mechanotransduction, intracellular signaling.