**Master 2 internship project**

**Year 2025-2026**

**Laboratory/Institute:** HP2 **Director:** Jean Louis Pépin (HP2)

**Team:** axis 2, vascular consequences of hypoxia **Head of the team:** JL Cracowski / A Briancon-Marjollet

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

Dr Anne Briançon-Marjollet

 **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: Impact of PCSK9 on vascular consequences of intermittent hypoxia: in vitro study using a microfluidic system**

Objectives (up to 3 lines):

To characterize the role of PCSK9 in the vascular consequences of intermittent hypoxia exposure, as a model of Obstructive Sleep Apnea, in an in vitro system using intermittent hypoxia coupled to microfluidic control of shear stress.

Abstract (up to 10 lines):

Obstructive sleep apnea (OSA) is a chronic respiratory condition with systemic severe repercussions, including vascular remodeling leading to atherosclerosis. In particular, we are interested in endothelial permeability as an early mechanism leading to atherosclerosis. Our preliminary results suggest that the PCSK9 protease is overexpressed in OSAS patients and could be implicated, in vitro, in IH-induced endothelial permeability and transendothelial migration of monocytes. The main objective of this internship is to use an anti-PCSK9 antibody (evolocumab) to better characterize the involvement of PCSK9 in IH-induced endothelial permeability and monocyte adhesion, both in vitro and in vivo. In vitro, we will evaluate endothelial activation, monocyte adhesion and LDL internalization in a microfluidic system able to combine shear stress and hypoxia exposure. In vivo we will use mice exposed to IH to investigate the therapeutic potential of evolocumab on IH-induced vascular remodeling. If our hypothesis are validated, PCSK9 inhibitors may become a new pharmacologic tools to prevent the vascular consequences of OSA.

Methods (up to 3 lines):

Cell culture (endothelial cells), microfluidic culture with shear stress

Quantitative PCR and western blot on cells and aorta samples from mice

Immunohistology: cryosections, immunostaining, followed by image analysis

 (Note that animal exposure to IH and aorta samples collection will be completed before the beginning of the M2 internship, that will only include sample analysis).

Up to 3 relevant publications of the team:

1.Harki O, Tamisier R, Pépin JL, Bailly S, Mahmani A, Gonthier B, Salomon A, Vilgrain I, Faury G, **Briançon-Marjollet A**. VE-Cadherin cleavage in sleep apnoea: new insights into intermittent hypoxia-related endothelial permeability. *European Respiratory Journal* 2021 May6:2004518. (IF: 24.9, Q1, top 5%)

2.Harki O, BoeteQ, PépinJL, ArnaudC, BelaidiE, FauryG, KhouriC, **Briançon-Marjollet****A**. Intermittent hypoxia-related alterations in vascular structure and function: a systematic review and meta-analysis of rodent data. *European Respiratory Journal* 2022 Mar 17;59(3):2100866. (IF: 24.9, Q1, top 5%)

3. Harki O, BouyonS, SalléM, Arco-HiervesA, LemariéE, DemoryA, ChiricaC, VilgrainI, PépinJL, FauryG, **Briançon-MarjolletA**. Inhibition of vascular endothelial cadherin cleavage prevents elastic fiber alterations and atherosclerosis induced by intermittent hypoxia in mouse aorta. *International Journal of Molecular Sciences*, 2022 Jun 24;23(13):7012. doi: 10.3390/ijms23137012. (IF 5.6, Q1, top 25%).

Requested domains of expertise (up to 5 keywords):

Vascular physiology, hypoxia, inflammation, cell biology.