

**Supervisor(s):**

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**Host laboratory:**

BioSanté, <https://biosante-lab.fr/en>

**Host group/team:**

MAB2: Mechanisms of Angiogenesis in Biological Barriers

**Title of the M2 research internship:**

Role of prokineticin receptor antagonist in long-term cerebrovascular dysfunction

**Project summary:**

Preeclampsia (PE) is a pregnancy complication characterized by proteinuria, hypertension and placenta hypoperfusion, leading to increased risk of adverse fetal, neonatal and maternal outcomes. Clinical studies demonstrated that few years after the preeclamptic incident; women are daily subjective to cognitive failures, affecting memory and concentration with white matter lesions and vascular dementia.

The cerebral endothelium is a complex and dynamic multicellular structure separating the central nervous system from the systemic circulation. Acute or chronic inflammation of the vascular unit is known to be implicated in the potential devastating effects of cerebral vascular breakdown that mediates cognitive functions. The prokineticin family, PROK1 and PROK2, have recently been reported to control vascular permeability in highly vascularized systems. PROKs act through specific G protein-coupled receptors, PROKR1 and PROKR2, to control multiple biological functions, including angiogenesis, neurogenesis of olfactory bulb, neuronal survival, and inflammation.

Preliminary data from our group demonstrated that treatment of a mouse model of PE with the PROKR antagonists attenuated PE symptoms, suggesting a potential direct effect of PROKs on PE cognitive-associated effects.

The proposed project aims at characterizing the impact of PROKs on the cerebrovascular barrier. First, the student will test the effect of the plasma collected from the genetic mouse model of PE or plasma collected from preeclamptic patients on brain blood barrier (BBB) integrity. This test will also be performed in the absence or presence of PROKR antagonists

Second, PROKs' involvement in neurological disorders of PE mice during gestation and several months after preeclamptic gestation will be evaluated in PE mice treated with PROKR antagonist. The samples are all available in the laboratory, the student will use the MRI test to analyze structural modifications of the brain, the neurological lesions and hemorrhage-ischemia events

The Master 2 candidate should have strong knowledge in cell biology.

**Keywords:**

cerebrovascular system, inflammation signaling, therapy for preeclampsia

**Relevant publications of the team:**

Reynaud D, Sergent F, Abi Nahed R, Traboulsi W, Collet C, Marquette C, Hoffmann P, Balboni G, Zhou QY, Murthi P, Benharouga M, Alfaidy N. Evidence-Based View of Safety and Effectiveness of Prokineticin Receptors Antagonists during Pregnancy. *Biomedicines*. 2021 Mar 17;9(3):309. doi:10.3390/biomedicines9030309. PMID: 33802771; PMCID:PMC8002561.

Sergent F, Hoffmann F, Brouillet S, Garnier V, Salomon A, Murthi P, Benharouga M, Feige JJ, Alfaidy N. Sustained Endocrine Gland-Derived Vascular Endothelial Growth Factor Levels Beyond the First Trimester of Pregnancy Display Phenotypic and Functional Changes Associated With the Pathogenesis of Pregnancy-Induced Hypertension ». *Hypertension*. 2016, 68(1):148-56. <https://doi.org/10.1161/HYPERTENSIONAHA.116.07442>.

Traboulsi W, Brouillet S, Sergent F, Boufettal H, Samouh N, Aboussaouira T, Hoffmann P, Feige JJ, Benharouga M, Alfaidy N. Prokineticins in Central and Peripheral Control of Human Reproduction. *Horm. Mol. Biol. Clin. Invest.* 2015;24(2):73-81. <https://doi.org/10.1515/hmbci-2015-0040>.

Alfaidy N, Hoffmann P, Boufettal H, Samouh N, Aboussaouira T, Benharouga M, Feige JJ, Brouillet S. The Multiple Roles of EG-VEGF/PROK1 in Normal and Pathological Placental Angiogenesis. *BioMed Res. Int.*, 2014, 451906. <https://doi.org/10.1155/2014/451906>.