

Thesis proposal for the autumn 2025 at CEA-Irig Grenoble reference: IRIG/BCI SL-DRF-25-0411

Characterisation of cerebrovascular changes during pre-eclampsia: what role in the development of long-term maternal dementia?

Thesis project: Pre-eclampsia is a specific complication of pregnancy associated with hypertension and hypoperfusion of the placenta, as well as an elevated concentration of circulating inflammatory factors secreted by the placenta, leading to an increased risk of adverse neonatal outcomes for the foetus and mother, as well as consequences for neurovascular function. However, preeclampsia is not confined to pregnancy and, more than 20 years later, women are still at increased risk of stroke and cognitive impairment. Clinical studies have shown that these patients have brain lesions on MRI. MAB2's work on a mouse model of preeclamptic pregnancy has demonstrated the direct involvement of these inflammatory factors, including prokineticins (PROKs) and their receptors. In a cellular model of the blood-brain barrier, we have shown that PROKs modify vascular permeability. Otherwise, our recent results demonstrate a direct link between the preeclamptic event and the development of late brain lesions and inflammation. In addition, recent metabolomics and proteomics results show strong perturbations in the genome-wide histone modification profile that could be involved in vascular alterations and the development of vascular and/or neurodegenerative dementia. The aim of the PhD project is to characterise the vascular changes that occur at the time of PE and their long-term consequences on cognitive function, and to identify potential therapeutic targets for preventive treatment. These objectives will be addressed by studies using the mouse model of preeclampsia. The studies will draw on the expertise of the team and on collaborations with experts in the blood-brain interface, MRI and behavioural tests, as well as in the analysis of histone modifications.

Relevant publications

Younes [...] and Marquette. « Effects of Prokineticins on Cerebral Cell Function and Blood–Brain Barrier Permeability. *IJMS*, 2023, **24** (20): 15428. <https://doi.org/10.3390/ijms242015428>.

Sergent [...] Marquette *et al.* Antagonisation of Prokineticin Receptor-2 Attenuates Preeclampsia Symptoms. *JCMM*, 2025, **29**(2): e70346. doi.org/10.1111/jcmm.70346.

Penaud *et al.* Connecting Metabolic and Epigenetic Dysregulations in Huntington's Disease. *JNNP*, 2024, **95**(suppl 1): A31-32. doi.org/10.1136/jnnp-2024-EHDN.76.

Doridot *et al.* Preeclampsia-like symptoms induced in mice by fetoplacental expression of STOX1 are reversed by aspirin treatment. *Hypertension*, 2013, **61**(3): 662. doi.org/10.1161/HYPERTENSIONAHA.111.202994.

Desirable: Experience in neuroscience, cellular biology, epigenetic, biochemistry, histology, will be appreciated; willingness to work in an interdisciplinary environment; structured and independent work.

Work environment: The thesis will be supervised by Dr. Christel Marquette (CEA in Grenoble, France). This interdisciplinary project will involve the student interacting with other teams and platforms in different institutes.

Application: The thesis is expected starting from october 2025. Applications including CV, available results of the Master graduation exams, motivation letter and coordinates of 2 references should be sent to: christel.marquette@cea.fr