

## GRAL MSc RESEARCH SCHOLARSHIP 2020-2021

### RESEARCH INTERNSHIP PROPOSAL

#### Institute / Group

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#### Research Project Title

Localization and role of Prokineticin receptors 1 and 2 in cerebral vascular endothelial cell

#### Description of the project

Preeclampsia (PE), a pregnancy-specific complication that presents with maternal hypertension and placenta hypoperfusion, is associated with increased risk of adverse fetal, neonatal, and maternal outcomes. The pathogenesis is related to proinflammatory environment that leads to widespread endothelial dysfunction. During PE syndrome, the brain is also affected and specially the vascular system at the blood–brain barrier (BBB) level. It is now well established that the BBB is a dynamic structure which modifications in the vascular permeability are associated with a multitude of acute and chronic CNS disorders, such as cognitive impairments and dementia. In dementia related pathologies, i.e. PE or Alzheimer’s disease (AD), several reports evidenced that inflammatory and angiogenic factors favors cognitive symptoms by interacting with the BBB. Therefore, we propose to explore in AD and PE, the effect of two inflammatory and angiogenic cytokines, the prokineticin 1 and 2, described as controlling endothelial permeability. Experiments will be performed both in vitro using a cellular model mimicking the BBB vascular unit and in vivo using APP/PSEN $\epsilon$ 9 mice models of AD, PROK1 & PROK2 knockout mouse model and the genetic PE mouse model (STOX1-PE). These animal models will be used i) to determine the expression status of the prokineticin family of proteins in vivo, ii) to test the development of AD in PROK1 and PROK2 knockout models and to evaluate the potential therapeutic effects of PROK receptor antagonists. These investigations will be carried out by immunohistology, Western Blot and RNA analyses. Recommended background: Neurosciences, Neurobiology, Angiogenesis

#### Keywords

Prokineticin, neurovascular, permeability, cognitive disorders, neuroinflammation

#### Relevant publications of the team

- Pansieri, J., Josserand, V., Lee, S. J., Rongier, A., Imbert, D., Sallanon, M. M., ... & Guidetti, M. (2019). Ultraviolet–visible–near-infrared optical properties of amyloid fibrils shed light on amyloidogenesis. *Nature Photonics*, 13(7), 473-479.
- Plissonneau, M., Pansieri, J., Heinrich-Balard, L., Morfin, J. F., Stransky-Heilkron, N., Rivory, P., ... & Tóth, É. (2016). Gd-nanoparticles functionalization with specific peptides for  $\beta$ -amyloid plaques targeting. *Journal of nanobiotechnology*, 14(1), 60.
- Podlovni, H., Ovadia, O., Kisliouk, T., Klipper, E., Zhou, Q. Y., Friedman, A., ... & Meidan, R. (2006). Differential expression of prokineticin receptors by endothelial cells derived from different vascular beds: a physiological basis for distinct endothelial function. *Cellular physiology and biochemistry*, 18(6), 315-326.
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