



MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2025-2026

(internship from January to June 2026)

Host laboratory:

CarMeN lab (Cardiovascular Metabolism Diabetology Nutrition) Inserm U1060 Université Claude Bernard Lyon 1 Groupement Hospitalier EST Bâtiment B13, IHU OPERA 59 boulevard Pinel 69500 BRON -FR

Host team :

IRIS team (Ischemia-reperfusion injury syndromes): http://carmen.univ-lyon1.fr/equipe-3-ischemia-reperfusion-syndromes/

Internship supervisors :

Marlène Wiart, PhD Directrice de recherche CNRS <u>marlene.wiart@univ-lyon1.fr</u>

Mélanie Paillard Chargée de recherche Inserm <u>melanie.paillard@univ-lyon1.fr</u>

Project title : Evaluating a new therapeutic target for ischemic stroke using multiparametric MRI in a murine model

Project summary :

Ischemic stroke is a frequent and disabling disease. Understanding the pathophysiological mechanisms involved in the formation of cerebral lesions following stroke has become a priority for developing new therapeutic strategies for neuroprotection. Experimental studies have shown that raising the intracellular concentration of cyclic adenosine monophosphate (cAMP) can moderate brain damage following stroke (Biomedicines 2021), notably through an immunomodulatory action. We have identified one of the main cAMP effector proteins. To our knowledge, the role of this protein in the pathogenesis of stroke has not yet been studied. Our preliminary results show that it could be a promising therapeutic target in stroke.

The aim of the internship is to evaluate the impact of modulating this protein of interest in the first week following stroke in mice. The experimental protocol has already been approved and is scheduled for the first half of 2026 as part of Paul Clottes' PhD thesis. The trainee's tasks will be as follows:





1/ Support for technical staff performing surgery and MRI, in particular for handling and monitoring animals (anesthesia, temperature, catheter placement, recovery);

2/ Neurofunctional assessments (Benderson neuroscore and pole test) for analysis;

3/ Terminal sampling (blood and brain after perfusion) and brain preparation;

4/ MRI analysis (lesions, neuroinflammation);

5/ Immunohistology (neuroinflammation).

Specifically, the trainee will evaluate the impact of treatment with our novel treatment on lesion size measured on MRI, neurofunctional tests, and neuroinflammation measured on MRI by USPIOs and immunohistology.

3-5 recent publications :

- Ong et al. Mitochondria dysfunction, a potential target for cytoprotection against ischaemia-reperfusion injury in a mouse stroke model. Neurotherapeutics 2025 doi: 10.1016/j.neurot.2025.e00549
- Gurler et al. Reduced Folate Carrier 1 (RFC1/Slc19a1) Suppression Exacerbates Blood-Brain Barrier Breakdown in Experimental Ischemic Stroke in Adult Mice. Pre-print BioRxiv 2024. doi 10.1101/2024.10.28.620539
- Dumot et al. Neurofunctional and neuroimaging readouts for designing a preclinical stem-cell therapy trial in experimental stroke. Sci Rep, 2022, 12(1): 4700 doi <u>10.1038/s41598-022-08713-z</u>
- Hubert et al. Multimodal imaging with NanoGd reveals spatiotemporal features of neuroinflammation after experimental stroke. Adv Science 2021, doi <u>10.1002/advs.202101433</u>
- 5. Basalay et al. Neuroprotection by remote ischemic conditioning in the setting of acute ischemic stroke: a preclinical two-centre study. Sci Rep 2020 Oct 9;10(1):16874 doi 10.1038/s41598-020-74046-4