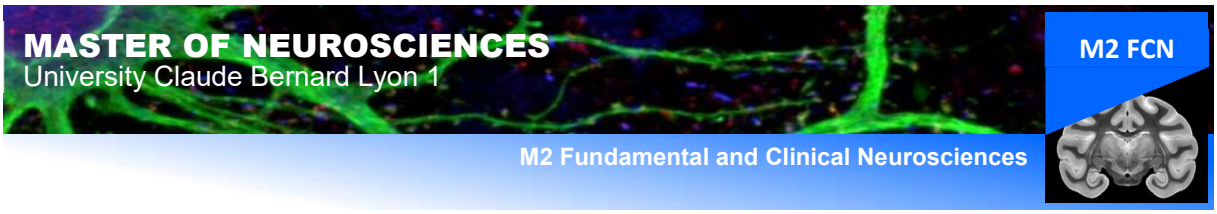

MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2023-2024

(internship from January to June 2024)

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
marlene.wiart@univ-lyon1.fr

Olivier Pascual, PhD
Directeur de recherche Inserm
olivier.pascual@inserm.fr

Project title :
Investigating the effects of phagocytosis modulators on microglial phagocytosis in an *in vitro* model of ischemic stroke

Project summary : *approx 10 lines*

Acute ischemic stroke (AIS) occurs in 140,000 persons in France each year and is a major public health issue. Microglial phagocytosis is emerging as a therapeutic target in AIS. The core objective of our project is to provide the proof-of-concept (POC) that microglial phagocytosis is a druggable target which modulation improves AIS outcome. Our hypothesis is that enhancing phagocytosis will result in better brain cleaning, dampened inflammation and thus prevent secondary brain damage and improve stroke outcome. We aim to test this hypothesis in an *in vitro* model of ischemic stroke. The first aim of the internship is to set-up the *in vitro* assay of apoptotic neurons phagocytosis from our international collaborator Amanda Sierra (Spain) described in (1), based on the primary culture of microglia mastered by the internship co-supervisor Olivier Pascual (2), in the context of oxygen and nutrients deprivation (OND) to mimick AIS. The second aim of the internship is to investigate the effects of drugs identified

by Amanda Sierra as phagocytosis modulators (inhibitors and agonists) in that model. The perspective is to test the best drug candidates in an *in vivo* murine model of AIS.

Reference:

1. Diaz-Aparicio I*, et al.* (2020) Microglia Actively Remodel Adult Hippocampal Neurogenesis through the Phagocytosis Secretome. *J Neurosci* 40(7):1453-1482.
2. Hubert V*, et al.* (2021) Multimodal Imaging with NanoGd Reveals Spatiotemporal Features of Neuroinflammation after Experimental Stroke. *Adv Sci (Weinh)*:e2101433.

3-5 recent publications :

1. Tavakoli C, Cuccione E, Dumot C, Balegamire J, Si-Mohamed S, Kim J, Crola-da-Silva- C, Chevalier Y, Berthezene Y, Boussel L, Douek P, Cormode D, Elleaume H, Brun E, **Wiart M.** High-resolution synchrotron K-edge subtraction CT allows tracking and quantifying therapeutic cells and their scaffold in a rat model of focal cerebral injury and can serve as a reference for spectral photon counting CT. NanoTheranostics. 2023 :16;7(2):176-186.
2. Dumot C, Po C, Capin L, Hubert V, Ong E, Chourrout M, Bolbos R, Amaz C, Auxenfans C, Canet-Soulas E, Rome C, Chauveau F, **Wiart M**. Neurofunctional and neuroimaging readouts for designing a preclinical stem-cell therapy trial in experimental stroke. Sci Rep, 2022, **12**(1): 4700. https://doi.org/10.21203/rs.3.rs-1019878/v1
3. Hubert V, Hristovska I, Karpati S, Benkeder S, Dey A, Dumot C, Amaz C, Chounlamountri N, Watrin C, Comte JC, Chauveau F, Brun E, Marche P, Lerouge F, Parola S, Berthezène Y, Vorup-Jensen T, **Pascual O**, and **Wiart M**. Multimodal imaging with NanoGd reveals spatiotemporal features of neuroinflammation after experimental stroke. Adv Science 2021, e2101433. https://onlinelibrary.wiley.com/doi/10.1002/advs.202101433
4. Karpati S, Hubert V, Hristovska I, Lerouge F, Chaput F, Bretonnière Y, Andraud C, Banyasz A, Micouin G, Monteil M, Lecouvey M, Mercey M, Dey A, Marche, Lindgren M, **Pascual O**, **Wiart M**, Parola S. Hybrid Multimodal Contrast Agent for Multiscale In Vivo Investigation of Neuroinflammation. Nanoscale, 2021, **13**, 3767-3781
https://doi.org/10.1039/D0NR07026B
5. Basalay MV*, **Wiart M***, Chauveau F, Dumot C, Leon C, Amaz C, Bolbos R, Cash D, Kim E, Mechtouff L, Cho TH, Nighoghossian N, Davidson SM, Ovize M, Yellon DM. 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. *co-first authors