

## **MASTER 2 Fundamental and Clinical Neurosciences**

### **Internship proposal 2023-2024**

*(internship from January to June 2024)*

**Host laboratory: Mechanisms in Integrated Life Sciences (MeLis) 8 avenue Rockefeller 69008 LYON**

**Host team :** *Synaptopathie et autoanticorps* <https://www.inmq.fr/honnorat/>

**Internship supervisors :** *Olivier Pascual CRCN* [olivier.pascual@inserm.fr](mailto:olivier.pascual@inserm.fr)

**Project title :** *Cognitive impairments mediated by microglia during chronic anesthesia*

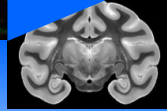
#### **Project summary :**

Cognitive impairment due to prolonged medically induced coma represents an enormous clinical and socioeconomic burden affecting millions of patients worldwide. The disruptive neurobiological, cognitive, and behavioral consequences of general anesthesia have been so far viewed mainly in connection with impaired neurogenesis and synaptic toxicity. Recent studies indicate that anesthesia lasting for more than 6 hours have wide consequences on synaptic pruning and cortical architecture in the adult mice. These deleterious aspects of anesthetics have been widely studied in vivo and in vitro focusing mainly on neuronal mechanisms. However, the potential involvement of glial cells has never been investigated in the context of cognitive impairments due to chronic anesthesia (CA). In this project, we propose to evaluate the contribution of microglial, the immune cells of the brain, in the spine density decrease. For this purpose, we will monitor spine density and spine phagocytosis by microglial cells following chronic anesthesia. Using immunohistochemistry and q-RTPCR, we will monitor phagocytosis and complement markers as well as internalization of synaptic component in microglial cells using high resolution imaging technics (STED). The presence of neuronal elements in microglial cells following chronic anesthesia will show for the first time that microglia are likely to be involved in the cognitive impairment following chronic anesthesia.

#### **3-5 recent publications :**

Cabirol MJ, Cardoit L, Courtand G, Mayeur ME, Simmers J, Pascual O, Thoby-Brisson M. *Microglia shape the embryonic development of mammalian respiratory networks*. Elife. 2022 Nov 2;11:e80352. PMID: 36321865.

Please send your proposal to [marion.richard@univ-lyon1.fr](mailto:marion.richard@univ-lyon1.fr) for publication on the Master of Neuroscience website.



Hristovska I, Robert M, Combet K, Honnorat J, Comte JC, Pascual O. *Sleep decreases neuronal activity control of microglial dynamics in mice*. Nat Commun. 2022 Oct 21;13(1):6273. doi: 10.1038/s41467-022-34035-9. PMID: 36271013; PMCID: PMC9586953.

Hubert V, Hristovska I, Karpatis 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\*, Wiart M\*. *Multimodal Imaging with NanoGd Reveals Spatiotemporal Features of Neuroinflammation after Experimental Stroke*. Adv Sci (Weinh). 2021 Sep;8(17):e2101433. PMID: 34197055.

Hristovska I, Verdonk F, Comte JC, Tsai ES, Desestret V, Honnorat J, Chrétien F, Pascual O. *Ketamine/xylazine and barbiturates modulate microglial morphology and motility differently in a mouse model*. PLoS One. 2020 Aug 6;15(8):e0236594. PMID: 32760073.

Takata-Tsuji F, Chounlamountri N, Do LD, Philippot C, Novion Ducassou J, Couté Y, Ben Achour S, Honnorat J, Place C, Pascual O. *Microglia modulate gliotransmission through the regulation of VAMP2 proteins in astrocytes*. Glia. 2021 Jan;69(1):61-72. PMID: 32633839.