



## MASTER 2 Fundamental and Clinical Neurosciences

### Internship proposal 2024-2025

*(internship from January to June 2025)*

**Host laboratory:** MeLis - CNRS UMR 5284 - INSERM U1314 Université Claude Bernard Lyon 1  
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**Host team :** SynatAc [https://inmq.fr/melis/fr/team\\_honorat.php](https://inmq.fr/melis/fr/team_honorat.php)

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**Project title :** Effect of blood brain opening on microglia activation and myelination

**Project summary :** *approx 10 lines*

Pathologies of the nervous system leading to motor disorders, including multiple sclerosis, are devastating disorders with limited available treatments, which mainly treat the symptoms of the disease. In this proposal, we offer to **explore ultrasound mediated blood brain barrier (BBB) opening as a positive enhancer of microglia function during demyelination/remyelination processes**. First, we will quantify the impact of BBB opening vs ultrasound alone on microglial activation and characterize their phenotypes and molecular signatures. Secondly, two protocols of BBB opening will be compared in physiological condition and in a cuprizone mediated demyelination model. Here, we will qualify and quantify the effect of repeated BBB opening on microglial activation and on myelination. This project will mainly rely on immunohistochemistry, western blotting and qRT-PCR technics. Mainly, we want to address if repeated opening of the BBB can help to slow down the loss of myelin via microglia protective activity. This would be a first translational approach for patients having a demyelinating episode, where acute treatment could be envisioned. Altogether, this project offers a disruptive approach to improve the care of patients suffering from multiple sclerosis.

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

1: 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. doi: 10.7554/eLife.80352.

2: Hristovska I, Robert M, Combet K, Honorat 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.

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, Wiart M. Multimodal Imaging with NanoGd Reveals Spatiotemporal Features of Neuroinflammation after Experimental Stroke. *Adv Sci (Weinh)*. 2021 Sep;8(17):e2101433. doi:10.1002/advs.202101433.

4: 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. doi: 10.1002/glia.23884.

5: Zakaria M, Ferent J, Hristovska I, Laouarem Y, Zahaf A, Kassoussi A, Mayeur ME, Pascual O, Charron F, Traiffort E. The Shh receptor Boc is important for myelin formation and repair. *Development*. 2019 May 2;146(9):dev172502. doi: 10.1242/dev.172502.