

MASTER 2 Neurosciences Fondamentales et Cliniques
UCB Lyon 1, Lyon, France

Internship proposal 2020-2021
(internship from January to end of May 2021)

Host laboratory:

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Host team :

Rejane RUA, PhD

Group leader 'Immunosurveillance of the Central Nervous System'

<http://www.ciml.univ-mrs.fr/science/lab-rejane-rua/immunosurveillance-central-nervous-system>

Internship supervisors :

Dr. Rejane Rua, Group leader, Inserm position
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Project title :

Unravelling the neuroprotective roles of macrophages at the brain surface

Project summary :

The surface of the Central Nervous System (CNS) is connected to the periphery by layers of highly vascularized membranes, the meninges. Although the brain has been considered immune-privileged for decades, it has been recently shown by our team and others that the meninges are populated by a myriad of resident immune sentinels. Unexpectedly, immune cells specifically located in the meninges play a role in neuronal function, tissue homeostasis as well as infectious, inflammatory and age-related neurodegenerative diseases. Due to their strategic location at the interface between the periphery and the brain, the **meninges thus function as a nurturing tissue enveloping the CNS and also represent its first line of protection**. A breach in this protective system can allow the spread of neuroinvasive pathogens (e.g. HIV, Zika, LCMV) and subsequent CNS

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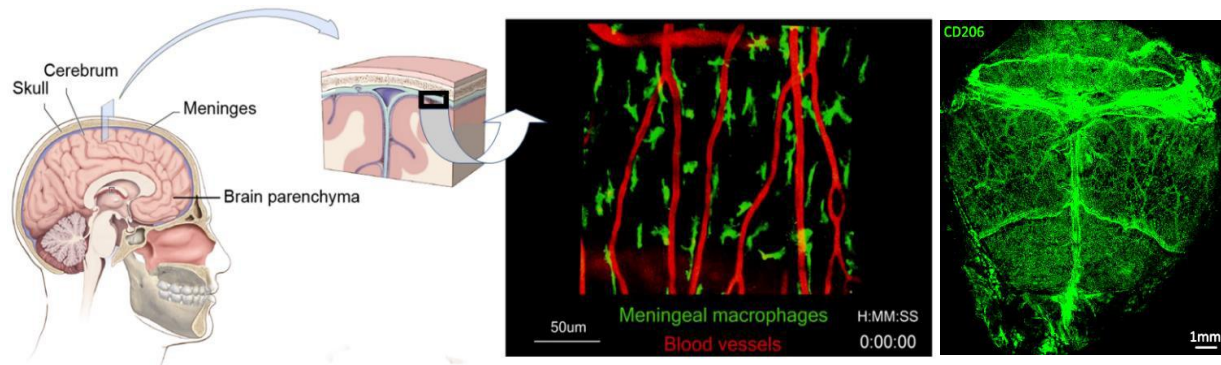


Figure 1. Location of the meninges at brain surface (left). Image extracted from an intravital movie of CX3CR1-GFP mouse showing a top-down view of meningeal macrophages (green) along the vasculature (red) (middle). Bone-in meningeal whole mounts showing the vast network of meningeal macrophages (identified by the mannose receptor CD206) covering the brain surface (right).

Meningeal macrophages are organized in a vast network that constantly monitor and scan the entire brain surface. **The objective of this project is to understand how macrophages at the brain surface maintain neuronal functions and prevent microbial spread into the CNS.**

We hypothesize that meningeal macrophages are heterogeneous and that distinct macrophage subpopulations differ in the magnitude and quality of their pro-neuronal versus antimicrobial response. To address these questions, we will combine multiparametric flow cytometry, state-of-the-art single-cell transcriptomics, CRISPR-Cas9 technology and intravital imaging approaches to analyze the heterogeneity and functions of meningeal macrophages in wild-type and transgenic mouse models.

3-5 recent publications :

1. **Rua R, et al.** *Infection drives meningeal engraftment by inflammatory monocytes that impairs CNS immunity.* **Nat Immunol.** 2019
2. **Manglani M, Rua R, et al.** *Method to quantify cytokines and chemokines in mouse brain tissue using Bio-Plex multiplex immunoassays.* **Methods.** 2019
3. **Rua R, McGavern DB.** *Advances in Meningeal Immunity.* **Cell Press Trends Mol Med.** 2018
4. **Kwong B*, Rua R* et al.** *T-bet-dependent NKp46+ innate lymphoid cells regulate the onset of TH17-induced neuroinflammation.* **Nat Immunol.** 2017
5. **Vermeire J, Roesch F, Sauter D, Rua R, et al.** *HIV Triggers a cGAS-Dependent, Vpu- and Vpr-Regulated Type I Interferon Response in CD4+ T Cells.* **Cell Rep.** 2016

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