Team: Immunosurveillance of the Central Nervous System
http://www.ciml.univ-mrs.fr/science/lab-rejane-rua/immunosurveillance-central-nervous-system.
Group leader: Rejane RUA
Internship supervisors: Narjess Haidar (PhD), Laure Salvon (PhD), Amnah Alsayyar (PhD) & Rejane RUA (PI)
Address: Centre d'Immunologie Marseille-Luminy, 163 av. Luminy, 13288 Marseille Cedex 9
Mail: haidar@ciml.univ-mrs.fr; salvon@ciml.univ-mrs.fr ; alsayyar@ciml.univ-mrs.fr

Neuroimmunology Internship proposal – 2nd semester of 2025

Exploring the impact of border macrophages on neurocognition in health and disease

The meninges represent a tissue enveloping the brain. Recent data, including from our team, revealed that surprisingly, they contain a large panel of resident immune cells, including meningeal macrophages, which completely revolutionized the scientific view on neuroimmune interactions by adding new players in the game.

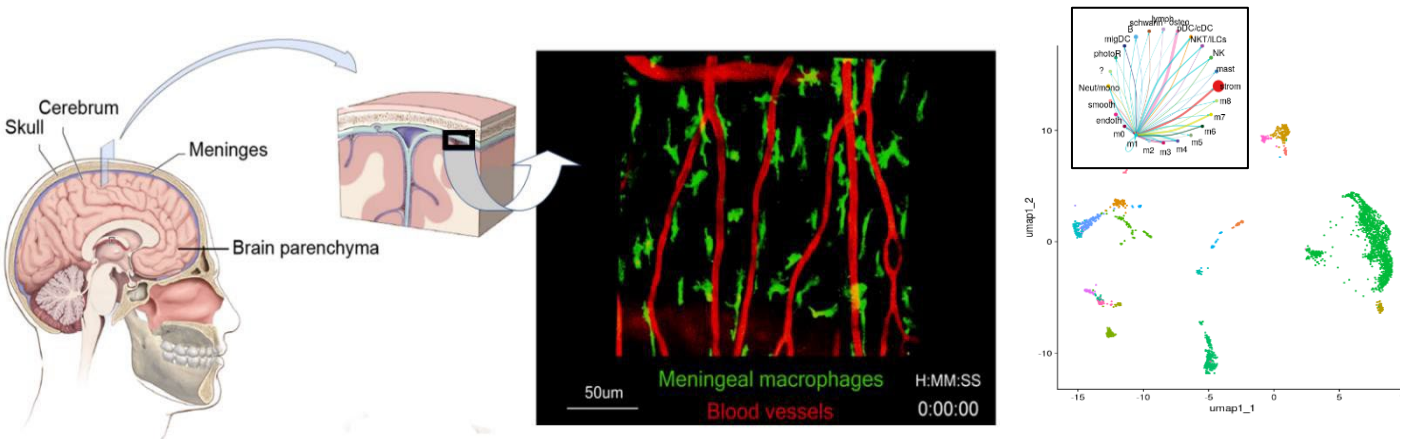

Figure 1. Location of the meninges at the surface of the brain (left). Image extracted from an intravital movie of CX3CR1-GFP mouse showing a top-down view of meningeal macrophages (green) along the vasculature (red) (middle). UMAP representation of immune and non-immune meningeal populations and CellChatDB prediction of macrophage interactions (right).

Meningeal immune cells can have a beneficial role in brain functions and promote social and cognitive behavior in the adult mice. Whether this positive action on the brain also occurs in early-life and whether it can help brain development and growth is unknown. Interestingly, the meninges and their resident immune cells (including macrophages) penetrate the brain parenchyma between substructures, including the cerebellum and also the hippocampus which is an important neurogenic niche. In this line, **the objective of this M2 project is to investigate whether meningeal macrophages could influence brain function in:**

1: physiological conditions, through the **release of specific factors**.

2: pathological conditions, as early-life inflammation correlates with an increased risk of developing neurological disorders, including autism, epilepsy, schizophrenia, ADHD, through deregulation of neuroimmune communication.

To address these questions, we are combining multiple chemical and genetic innovative models to manipulate and deplete macrophages, and analyze neurogenic and immunologic outputs on the hippocampus and cerebellum with RT-qPCR, Flow Cytometry, Immunohistochemistry and an original *in vitro* approaches of meningeal explant co-culture

with neurospheres developed in the team. Behavioral experiments are also done to assess the cognitive output on the mice.

The student will join a young and dynamic team (ERC laureate) consisting of 2 researchers, 1 post-doc, 1 engineer, 4 PhD students, and will be supervised by Laure Salvon (PhD), Narjess Haidar (PhD), Amnah Alsayyar (PhD) and Rejane Rua (PI). The CIML institute, located at the entrance of the Parc National des Calanques, stands as a leading immunology institute in France, with approximately 250 members and offering access to essential equipment, including state-of-the-art microscopes, cytometers, Histology and genomic facilities.

Selection of recent publications

Da Mesquita S, Rua R. Brain border-associated macrophages: common denominators in infection, aging, and Alzheimer's disease. Trends Immunol. (2024)

Eme-Scolan E, Arnaud-Paroutaud L, Haidar N, Roussel-Queval A & Rua R. Meningeal regulation of infections: A double-edged sword. European Journal of Immunology (2023).

Rebejac J, Eme-Scolan E, Arnaud-Paroutaud L, (…) and Rua, R. Meningeal macrophages protect against viral neuroinfection. Immunity (2022)

Rua R, Pujol N. IL-17: good fear no tears. Nat Immunol comments (2020)

Rua R, et al. Infection drives meningeal engraftment by inflammatory monocytes that impairs CNS immunity. Nature Immunology (2019)

Rua R, McGavern DB. Advances in Meningeal Immunity. Cell Press Trends Mol Med (2018)

Kwang and Rua, et al. T-bet-dependent NKp46 + innate lymphoid cells regulate the onset of T H 17-induced neuroinflammation, 2017, Nature Immunology