MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2022-2023

Host laboratory: CRNL Neurocampus Centre Hospitalier Le Vinatier, Bât. 462 – Neurocampus Michel Jouvet, 95, boulevard Pinel - 69675 Bron

Host team : Forgetting, https://crnl.univ-lyon1.fr/index.php/fr/Recherche/Equipes/23

Internship supervisors: Romain Marignier, MD PhD, professor of neurology at HCL, *marignierro@gmail.com* **and Paul Salin, DR CNRS, researcher,** *paul.salin@sommeil.univ-lyon1.fr*

Project title: Understanding the neurological mechanisms underlying memory impairments in neuromyelitis optica, an autoimmune disease.

Project summary : Neuromyelitis optica (NMO) is an autoimmune demyelinating disease, distinct from multiple sclerosis, which is characterized by alterations of the optic nerve, spinal cord and brain areas associated with the presence of pathogenic serum autoantibodies. It is the consequence of an "astrocytopathy" associated with anti-Aquaporin 4 (AQP4) auto-antibodies inducing oligodendrocyte damage secondary to astrocytic injury (1,2). Memory impairment has recently come to the forefront of this disease as it is frequently reported in patients with NMO, with a prevalence of up to 70%. These cognitive impairments are currently a poorly understood symptom and remain undertreated. Typical treatments such as immunosuppressive therapies remain inadequate to decrease cognitive impairments. The aim of the M2 project is to study the action of AQP4 on two forms of long-term synaptic plasticity, long-term potentiation (LTP) and long-term depression (LTD) in two cortical regions playing a key role in long-term memory: the hippocampus and prefrontal cortex. The LTP represents the best known cellular model of memory and the LTD is involved in pathological forms of forgetting such as those at work in Alzheimer's disease (3). A pilot in vitro pharmacological, electrophysiological and imaging study suggests that AQP4 induces LTD in the hippocampus through astrocyte damage. The aim of the internship will be to study whether there is an impairment of LTP by auto-antibodies and to test pharmacological tools that could restore it.

(1) Marignier R, Cobo Calvo A, Vukusic S. Neuromyelitis optica and neuromyelitis optica spectrum disorders. *Curr Opin Neurol*. (2017); 30: 208-215.
(2) Richard C, Ruiz A, Cavagna S, Bigotte M, Vukusic S, Masaki K, Suenaga T, Kira JI, Giraudon P, Marignier R. Connexins in neuromyelitis optica: a link between astrocytopathy and demyelination. *Brain*. (2020);143: 2721-2732.
(3) (3)Martin L, Bouvet P, Chounlamountri N, Watrin C, Besançon R, Pinatel D, Meyronet D, Honnorat J, Buisson A, Salin PA, Meissirel C. VEGF counteracts amyloid-β-induced synaptic dysfunction. *Cell Rep.* (2021) ;35(6):109121

Please send your proposal to marion.richard@univ-lyon1.fr for publication on the Master of Neuroscience website.