



POST-DOCTORAL POSITION IN NEUROBIOLOGY at LYON - FRANCE

Description

A post-doctoral position is available in Lyon, in the context of the recently awarded National Referral Center for Rare Inflammatory Disorders of the brain and the spinal cord (MIRCEM).

The landscape of inflammatory demyelinating disorders of the central nervous system has changed in the last few years, opening new challenges. Besides multiple sclerosis (MS), rare antibody-mediated demyelinating diseases, such as neuromyelitis optica spectrum disorder (NMOSD) have emerged. NMOSD is a severe condition, characterized by specific auto-antibody (Ab) directed against astrocyte-ependyma/aquaporin-4 protein. More recently, a new entity, delineated by the presence of Ab against the myelin/oligodendrocyte glycoprotein (MOG), has been characterized. Although MOG-Ab disease (MOGAD) shares clinical features with NMOSD, recent epidemiological and clinical data, as well as immunological and pathological studies, have clearly demonstrated that MOGAD is an independent entity, different from MS and NMOSD.

The Lyon referral center laboratory (located at the Lyon Neurocampus building of CRNL) is implicated in both: i) optimization of Ab detection methods for NMO, MOGAD and related disorders, at the national and international level; ii) deciphering the immunopathogenicity of autoantibodies directed against glial cells.

The project proposed here aims at assessing the pathogenic effect of human antibodies against MOG, using original models already available in the laboratory (see project description below). Our research team is seeking a highly qualified motivated neurobiologist to fill a Post-Doctoral Fellowship position in the area of antibody-mediated neuro-inflammation.

Mentoring and Environment

The project will combine *in vivo* (pre-clinical animal model) and *in vitro* (glial primary cultures, myelinating cultures) models of antibody-mediated neuro-inflammation, with proteomic analysis as well as immune characterization.

Materials: *in-vivo* surgery and *in-vivo* imaging, cell cultures, microscopy, FACS, cytology/histology

Qualification

- PhD or equivalent doctoral degree in neurobiology
- Excellent communication skills
- Willing to work in a rich clinical and multidisciplinary environment

The candidate will benefit from all facilities provided by the Lyon Neurosciences Research Center -CRNL (cell culture L2, microscopy, FACS, *in vivo* facilities), the Lyon Neurological Hospital (database, statistical support) and biobank (CSF, serum biosamples), and the clinical experience of expert neurologists.

He/She will be expected to develop translational studies in available pre-clinical models and develop ad-hoc *in vitro* experiments.



Application and contact

The position is open immediately (**15 OCT 2019**) for a starting date expected on January 2020.

This is a one-year renewable position with a gross salary between 2620€ - 3962€/months, according to previous experience.

Application file should include:

- CV
- Letter of intent
- Names and addresses of two references

For more information or to apply for the position (including an up-to-date CV and motivation letter), please contact: Dr Romain Marignier romain.marignier@chu-lyon.fr, and Anne Ruiz anne.ruiz@inserm.fr

PROJECT SYNOPSIS

Myelin oligodendrocyte glycoprotein (MOG) is a central nervous system (CNS) myelin component expressed on the outer lamella of the myelin sheath. While MOG has been controversially discussed as a putative autoantigen in autoimmune CNS demyelinating diseases for decades, it is a well-known antigenic target in the experimental autoimmune encephalomyelitis (EAE) model. Recent emergence of conformation-dependent assays for the detection of MOG-antibodies (Ab) has depicted a distinct phenotype of adults and children with CNS demyelination, presenting with a usually relapsing disease course.

Physiopathology of MOGAD is not yet fully understood, but there are accumulating evidences suggesting a direct pathogenic effect of MOG-Ab on myelin, leading to further neurological impairment.

Our study project aims at better understanding the pathogenic role of human MOG antibodies, per se, in absence of inflammatory environment. We have already used this paradigm in investigating AQP4-Ab mediated NMO/MS, and demonstrated that autoantibodies directed against membrane protein induce structural and functional change of the targeted cell.

The main objectives of the project are:

- 1) Choice and Purification of antibodies from different MOGAD patients (children vs adult, relapsing vs monophasic, severe vs mild course)
- 2) Evaluation of the binding capacities of MOG-Ab on murine tissue, and cell-based assays
- 3) Deciphering in vitro the Impact of MOG-Ab exposure on various glial cell cultures, including myelinating cultures
- 4) Deciphering in vivo the Effect of MOG-Ab exposure (intracerebral infusion) on rat model: multiparametric assessment (myelin/ neural/ ependymal histology, electrophysiology, motor behavior)