Postdoctoral position on Amyotrophic Lateral Sclerosis disease mechanisms and therapeutic modulation with a focus on the cerebral cortex

Project description :
A postdoctoral position is open in the INSERM Unit 1118 in Strasbourg, France.
The goal of the project is to shed light on the role of early cortical network alterations on the onset and progression of the neurodegenerative disease Amyotrophic Lateral Sclerosis (ALS, Lou Gehrig's disease, maladie de Charcot). ALS is clinically defined by the combined degeneration of two neuronal populations: the corticospinal neurons (CSN or upper motor neurons) located in the cerebral cortex and that extend axons to the brain stem and spinal cord, and the bulbar and spinal motor neurons (MN or lower motor neurons) located in the brain stem and spinal cord and that connect to the skeletal muscles.
Recent clinical and pathological studies suggest that ALS might start in the motor cortex and spread along the corticofugal axonal projections (including CSN), either via altered cortical excitability and subsequent excitotoxicity or via prion-like propagation of misfolded proteins. Using mouse genetics, we recently provided the first experimental arguments in favour of the corticofugal hypothesis, and ruled out the possibility of a corticofugal propagation by prion-like mechanisms. We now aim at testing the possibility that corticofugal propagation of ALS could rely on initial cortical hyperexcitability and altered corticofugal neurons activity.
Our goal is to develop an approach to efficiently and sustainably silence CFuPN in adult mice using the DREADD technology and to evaluate the consequences of CFuPN silencing on ALS onset and progression in a mouse models of the disease. The project will contribute to determine whether cortical network dysfunction should become the scope of future therapeutic developments for ALS.

Related publications :
- Scekic-Zahirovic J, Fischer M, Geoffrey Stuart-Lopez G, Burg T, Gilet J, Dirrig-Grosch S, Marques C, Birling MC, Kessler P & **Rouaux C**. Evidence that corticofugal propagation of ALS pathology is not mediated by prion-like mechanism (2020) ***Prog Neurobiol***, online ahead of print.
- Burg T. Bichara C, Scekic-Zahirovic J, Fischer M, Stuart-Lopez G, Brunet A, Lefebvre F, Cordero-Erausquin M & **Rouaux C**. Absence of subcerebral projection neurons is beneficial in a mouse model of ALS (2020) ***Ann Neurol***, 88(4):688-702.
- Marques C. Fischer M , Keime C, Burg T, Brunet A, Scekic-Zahirovic J, and **Rouaux C**. Early alterations of RNA metabolism and splicing from adult corticospinal neurons in an ALS mouse model (2019) ***bioRxiv***. doi:10.1101/gr.1239303.

Funding :
The project is currently funded by and ERC starting grant (CorticALS, #639737) and an ARSLA research grant.

Research environment :
Our INSERM Unit is dedicated to unravelling the mechanisms that trigger ALS and the related Fronto-temporal dementia (FTD), two terminal neurodegenerative diseases.
https://www.u1118.inserm.fr/
We recently moved to the newly delivered "Centre de Recherche en BioMédecine de Strasbourg (CRBS)" on the campus of the Faculty of Medicine of the University of Strasbourg.
https://www.unistra.fr/index.php?id=29901
Our lab is part to the broader Neuropôle federation that gather the whole neuroscience community of the University of Strasbourg.
https://neuropole.unistra.fr/
http://en.unistra.fr/index.php?id=21304

Candidate profile : We seek to hire a highly motivated and creative postdoctoral fellow. The postdoc candidate should have expertise in rodent neurosurgery and rodent motor behaviour. A background in DREADD and electrophysiology would be really appreciated.

Salary and benefits : between 24 and 30 k€/year depending on experience; full health and social coverage.

Expected start : 01/05/2021

Application process :
Candidates should apply by sending a CV, a motivation letter (current research, scientific interests and career goals), and the contact details of two academic references to caroline.rouaux@inserm.fr
Application deadline : 28/02/21