



## MASTER 2 Fundamental and Clinical Neurosciences

### Internship proposal 2024-2025

*(internship from January to June 2025)*

**Host laboratory:** Lyon Neuroscience Research Center CRNL. Inserm U1028 - CNRS UMR5292 - UCBL. Centre Hospitalier Le Vinatier - Bâtiment 462 - Neurocampus. 95 boulevard Pinel. 69675 Bron Cedex

**Host team :** TIGER; Website: <https://www.crnl.fr/en/equipe/tiger>;

**Internship supervisors :** Dr Vincent Magloire; group leader, chercheur INSERM;  
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**Project title:** Selectively targeting the claustrum with optogenetic tools to study and harness its inhibitory power in epilepsy.

**Project summary :** Our group is interested in how different cell types, and brain regions regulate brain excitability in physiological conditions and in paroxysmal disorders (<https://www.ibexlaboratory.com/>).

Here, we propose to study and harness the inhibitory power of the claustrum, a small elusive structure at the interface between the cortex and subcortical areas. The claustrum receives inputs from and projects to almost all cortical areas. Moreover, while claustrum-cortical projection neurons excite both excitatory pyramidal neurons and inhibitory Parvalbumin-positive and Neurogliaform (NGF) cells, the net effect of claustrum stimulation is a long-lasting inhibition of the neocortex that is mediated by synchronous activation of NGF cells across cortical layers. We will therefore hijack the claustrum to globally inhibit the cortex and see whether this can stop seizures.

To begin with, the project will involve developing and characterising the method to selectively target the claustrum with optogenetic and chemogenetic tools using stereotaxic viral injections and immunostaining. We will then express an optogenetic actuator in the claustrum and study whether optogenetic stimulation of claustral fibres in the different neocortical areas can stop or reduce seizure activity either in *ex vivo* or in *in vivo* animal models of epilepsy. This second part will involve extracellular electrophysiology and optogenetic stimulation.

This project could be the foundation of a PhD project and be further developed for *in vivo* investigations using a variety of electrophysiological methods (e.g. Neuropixels), closed-loop

optogenetic manipulation and imaging techniques (e.g. Miniscope, photometry, two-photon microscopy).

### Recent publications:

1. Jackson, J., Karnani, M.M., Zemelman, B.V., Burdakov, D., and Lee, A.K. (2018). Inhibitory Control of Prefrontal Cortex by the Claustrum. *Neuron* 99, 1029-1039.e4. 10.1016/j.neuron.2018.07.031.
2. Jackson, J., Smith, J.B., and Lee, A.K. (2020). The Anatomy and Physiology of Claustrum-Cortex Interactions. *Annual Review of Neuroscience* 43, 231–247. 10.1146/annurev-neuro-092519-101637.
3. Atilgan, H., Doody, M., Oliver, D.K., McGrath, T.M., Shelton, A.M., Echeverria-Altuna, I., Tracey, I., Vyazovskiy, V.V., Manohar, S.G., and Packer, A.M. (2022). Human lesions and animal studies links the claustrum to perception, salience, sleep, and pain. *Brain*, awac114. 10.1093/brain/awac114.
4. Marriott, B.A., Do, A.D., Zahacy, R., and Jackson, J. (2021). Topographic gradients define the projection patterns of the claustrum core and shell in mice. *Journal of Comparative Neurology* 529, 1607–1627. 10.1002/cne.25043.
5. Magloire, V., Cornford, J., Lieb, A., Kullmann, D.M., and Pavlov, I. (2019). KCC2 overexpression prevents the paradoxical seizure-promoting action of somatic inhibition. *Nat Commun* 10, 1225. 10.1038/s41467-019-08933-4.
6. Meletti, S., Giovannini, G., d’Orsi, G., Toran, L., Monti, G., Guha, R., Kirytopoulos, A., Pascarella, M.G., Martino, T., Alexopoulos, H., et al. (2017). New-Onset Refractory Status Epilepticus with Claustrum Damage: Definition of the Clinical and Neuroimaging Features. *Front Neurol* 8, 111. 10.3389/fneur.2017.00111.