



MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2023-2024

(internship from January to June 2024)

Host laboratory: Lyon's Neurosciences Research Center (U1028/UMR5292)

Host team : Translational Group in Epilepsy Research (TIGER)

Internship supervisors :

Pr Sylvain RHEIMS, team co-leader and Professor of Neurology at Lyon 1 University and Hospices Civils de Lyon. Sylvain.rheims@univ-lyon1.fr

Dr Hayet KOUCHI, post-doc. hayet_kouchi@yahoo.fr

Dr Jonathon SMITH, post-doc. smithjonathon1995@gmail.com

Project title : Temporal relation between epilepsy evolution and alteration of respiratory function in Dravet Syndrome (DS)

Project summary :

- This project is integrated within the framework of the Eranet-NEURON funded project AUTONOMIC (<https://www.neuron-eranet.eu/projects/AUTONOMIC/>)

- DS is a severe neurodevelopmental disease, characterized by infancy onset, severe cognitive deficit and drug-resistant seizures, and high risk of seizure-related death. Among the causes of premature deaths in patients with epilepsy, sudden and unexpected death in epilepsy (SUDEP) represents a major cause. Experimental and clinical data suggest that most SUDEP cases result from postictal brainstem dysfunction, including central respiratory arrest. Importantly, fatal post-ictal apnea could be facilitated by chronic alterations of respiratory functions. SUDEP in DS might therefore be the result of a seizure-induced fatal apnea in a patient who has developed epilepsy-related vulnerability to central respiratory dysfunction. However the temporal dynamic of the onset and evolution of the respiratory vulnerability in DS and the potential relation between repetition of seizures and evolution of inter-ictal respiratory function remains to be investigated.

- The objective of the project is to analyze the evolution of the inter-ictal respiratory function with repetition of seizure in Scn1a^{RH/+} mice, a mouse model of DS, and development of spontaneous seizures

- The internship will directly perform and analyze inter-ictal respiratory monitoring using repetitive plethysmography and EKG monitoring in wild type and Scn1a^{RH/+} mice. She/he will also be involved in correlation between respiratory data and alteration of brainstem serotonin network investigated with RTqPCR.

3-5 recent publications :

Kouchi H, Ogier M, Dieuset G, et al. Respiratory dysfunction in two rodent models of chronic epilepsy and acute seizures and its link with the brainstem serotonin system. *Scientific Reports* 2022;

Salgueiro-Pereira, A, Duprat, F, Pousinha, PA et al. A two-hit story: Seizures and genetic mutation interaction sets phenotype severity in SCN1A epilepsies. *Neurobiology of Disease* 2019; 125:31-44.

Ryvlin, P, Rheims, S, Lhatoo, SD. Risks and predictive biomarkers of sudden unexpected death in epilepsy patient. *Curr Opin Neurol* 2019; 32:205-212.

Rheims, S, Alvarez, BM, Alexandre, V et al. Hypoxemia following generalized convulsive seizures: Risk factors and effect of oxygen therapy. *Neurology* 2019; 92:e183-e193

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