

MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2022-2023

(internship from January to June 2023)

Host laboratory: French Agency for Food, Environmental and Occupational Health & Safety of Lyon, 31 avenue Tony Garnier, 69364, Lyon, Cedex 7, France.

Host team: Neurodegenerative disease Unit (Head unit: Thierry BARON (HDR))

<https://www.anses.fr/fr/portails/1807/content/150369>

Internship supervisors: Johann VULIN (PhD) Research project manager

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Project title: Development and use of super resolution confocal microscopy approach for study of synaptic microconnectivity in a transgenic mouse model of Parkinson disease.

Project summary : *approx 10 lines*

The research work of the unit is devoted to the study of human neurodegenerative diseases, in particular Parkinson's disease (PD). Using mouse models of PD, part of the work carried out aims at understanding how neuropathological lesions are propagated in the nervous system during the progression of the disease. A second focus is to better understand to which extent exposure to pesticides is a risk factor for this disease.

The proposed work will be carried out using transgenic mice (M83)(Giasson et al., 2002) exposed to a neurotoxic pesticide. M83 mice are expressing human alpha-synuclein mutated in A53T, which is associated with familial forms of PD.

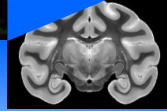
For further assessment of neurotoxic insults, we have adapted a recently published method for the analysis of synaptic microconnectivity (Sauerbeck et al. Neuron, 2020). This method is based on the use of super-resolution confocal microscopy which allows the localization of pre- and postsynaptic elements and thus to identify functional synapses.

In this project, the student will be in charge of analyzing the synaptic activity of the central nervous system of M83 mice exposed to pesticides. He/she will be in charge of preparing the samples (cryosections), performing the immuno-labeling (immuno-fluorescence), performing the image capture (confocal microscopy), processing and analyzing the images using computer and statistical tools (Imaris, Matlab) with the help of the PLATIM platform.

Depending on the student's progress on this method, he/she may consider participating in the realization and analysis of other methods (biochemical analysis, *in situ* labeling, neuron counting).

3-5 recent publications :

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



- Baron et al., Co-expression of APP/PS1 disrupts the distribution of brain lesions in a synucleinopathy transgenic mouse model (M83). *Acta Neuropathol.*, 2022.
- Arsac et al., Chronic Exposure to paraquat induces alpha-synuclein pathogenic modifications in *Drosophila*. *Int. J. Mol. Sci.*, 2021.
- Nicot et al., Seeded propagation of α -synuclein aggregation in mouse brain using protein misfolding cyclic amplification. *FASEB J.*, 2019.
- Sargent et al., 'Prion-like' propagation of the synucleinopathy of M83 transgenic mice depends on the mouse genotype and type of inoculum. *J Neurochem.*, 2017.