MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2026-2027

(internship from January to June 2027)

Host laboratory: ANSES - Laboratoire de Lyon. 31 avenue Tony Garnier 69364 Lyon cedex 07

Host team: Unité Maladies Neurodégénératives et du Neuro-développement (MN2D)
https://www.anses.fr/fr/content/unite-maladies-neurodegeneratives-du-laboratoire-de-lyon

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Project title: Characterization of the pathological human alpha-synuclein protein in a humanized transgenic mouse model with different forms of synucleinopathies

Project summary:

Multiple system atrophy (MSA) is a severe neuro-degenerative disease associated with the aggregation of the alpha-synuclein (a-syn) protein (synucleinopathy) characterized by intracytoplasmic deposits mainly in oligodendrocytes, in contrast with the mainly neuronal localisation of a-syn aggregates in Parkinson's disease. Our laboratory is working in a transgenic mouse model of synucleinopathy (M83) overexpressing a mutated (A53T) form of the human a-syn protein, in order to understand the molecular mechanisms of propagation of brain lesions (1, 2). In the last of these studies (2), in collaboration with the Institut des Maladies Neurodégénératives - Bordeaux (Dr F. Ichas), we described that a synthetic alpha-synuclein fibril (1B) mimicking the protein involved in MSA patients strikingly exacerbated the pathology of M83 mice and showed some a-syn deposits not only in neurons, but also in oligodendrocytes. Here we propose to set up some immunofluorescence or/and chemiluminescence studies to identify and characterize the presence of a-syn deposits in oligodendrocytes *versus* neurons of M83 mice in which the pathology has been accelerated by the intra-cerebral inoculation of an extract from a MSA brain patient (2) or by 1B fibers (3). The methods will use antibodies recognizing oligodendrocytes/neurons and a-syn phosphorylated at serine 129 (EP1536Y) or ligands recognizing amyloid proteins (thioflavin, ADlumin-1)(3) used as markers of the a-syn aggregation. The results will be compared to those in M83 mice in which the pathology has been accelerated by i.c. inoculations of a brain extract from sick M83 mice (1, 4).

Recent publications:

1 - 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. 143:126-135. doi: 10.1111/jnc.1413

2 - Burger et al., Synthetic α-synuclein fibrils replicate in mice causing MSA-like pathology. Nature, Nature, 2025. 648:409-417. doi: 10.1038/s41586-025-09698-1.
3 - Zhu et al., Highly sensitive chemiluminescence imaging of misfolded proteins in neurodegenerative models. Proc Natl Acad Sci USA, 2026. 123:e2513311123. doi: 10.1073/pnas.2513311123.
4 - Lau et al., α-synuclein strains target distinct brain regions and cell types. Nat Neurosci, 2020. 23:21-31. doi: 10.1038/s41593-019-0541-x.