

MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2026-2027

(internship from January to June 2027)

Host laboratory: *Institut NeuroMyogène, MeLiS laboratory. 8 avenue Rockefeller Lyon 1*

Host team : *Team SynatAc <https://melis-lyon.fr/equipe-honorat/>*

Internship supervisors :

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Project title: Characterizing antibodies pathogenicity in anti-IgLON5 disease using human neuronal culture derived from hiPSCs and super resolution microscopy

Project summary: Anti-IgLON5 disease is a rare autoimmune encephalitis with a broad clinical spectrum, which makes it difficult to diagnose. This disease is characterized by the presence of anti-IgLON5 antibodies, targeting IgLON5 protein at the surface of neurons. Most patients progressively develop a tauopathy associated with neurodegeneration, likely due to IgLON5 autoantibodies^{1,2}. However, **the mechanisms by which those antibodies contribute to neurodegeneration is not yet elucidated**. Recent results from the team have demonstrated that anti-IgLON5 antibodies from patient's cerebrospinal fluid (CSF) deregulate the neuronal surface distribution of IgLON5, which could then disrupt its interaction with protein partners and alter downstream signaling pathways. Anti-IgLON5 antibodies present in CSF and serum from patients are predominantly of the **IgG1 and IgG4 subclasses**, but their respective roles on IgLON5 pathophysiology are not clearly elucidated^{1,3,4}.

The objective of this master 2 internship project is to characterize the specific impact of anti-IgLON5 antibodies subtypes on IgLON5 cell surface reorganization.

To this end, the intern will purify IgG1 and IgG4 antibodies from serum of IgLON5 patients using **biochemical** assays. The impact of each antibody subtype on IgLON5 surface distribution and its interacting protein partners will be investigated using **human neuronal cultures** derived from human induced pluripotent stem cells and **super resolution STED microscopy**. In addition, the intern will be trained in image analysis with specialized softwares (Icy, Imaris), as well as in data analysis and statistics using R.



1. Gelpi, E. *et al.* Neuropathological spectrum of anti-IgLON5 disease and stages of brainstem tau pathology: updated neuropathological research criteria of the disease-related tauopathy. *Acta Neuropathol. (Berl.)* **148**, 53 (2024).
2. Graus, F. *et al.* Anti-IgLON5 Disease 10 Years Later: What We Know and What We Do Not Know. *Neurol. Neuroimmunol. Neuroinflammation* **12**, e200353 (2025).
3. Sabater, L., Planagumà, J., Dalmau, J. & Graus, F. Cellular investigations with human antibodies associated with the anti-IgLON5 syndrome. *J. Neuroinflammation* **13**, 226 (2016).
4. Askin, B. *et al.* Autoimmune antibody-induced neuronal hyperactivity triggers pathological Tau in IgLON5 disease. Preprint at <https://doi.org/10.1101/2024.03.10.584272> (2024).