

**Master 2 internship project  
Year 2023-2024**

**Laboratory/Institute:** Grenoble Institut Neurosciences - GIN

**Director:** E. Barbier

**Team:** Neurocytoskeleton dynamics and structure

**Head of the team:** I. Arnal

**Name and status of the scientist in charge of the project:** Julien Aureille (Research fellow)

**HDR:** yes  no

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**Program of the Master's degree in Biology:**

- Microbiology, Infectious Diseases and Immunology       Structural Biology of Pathogens  
 Physiology, Epigenetics, Differentiation, Cancer       Neurosciences and Neurobiology

**Title of the project:**

**Investigating the microtubule dynamics control of KANK1 in human iPSC-derived neurons**

**Objectives (up to 3 lines):**

The main objective of this project is to understand how the protein KANK1 controls the microtubule dynamics in human iPSC-derived neurons. To this end, the student will combine several approaches including live microscopy imaging, micropatterning and biochemistry on cortical neurons derived from human iPSC.

**Abstract (up to 10 lines):**

Amyotrophic lateral sclerosis (ALS) represents a rapidly progressing neurodegenerative disease and is characterized by a degeneration of the motor neurons. A recent study which combined machine learning approach with data from induced pluripotent stem cells-derived motor neurons from patient with ALS, revealed that KANK1 was associated with the highest number of ALS-associated genetic variants. However, the role of KANK1 in neurons still remains to elucidate. KANK1 is a protein known to link microtubule tips with the major component of integrin-mediated focal adhesion, talin. Our hypothesis is that KANK1 interaction with microtubules in the vicinity of integrin adhesions is critical and an impairment of these interactions can affect the balance between stable and dynamic microtubules, found altered in ALS. By combining a broad range of approaches, the student will (i) characterize the integrin-mediated adhesions of iPSC-derived neurons and (ii) will address in this context, the role of KANK1 in the microtubule dynamics.

**Methods (up to 3 lines):**

Cell culture and iPSCs differentiation, Live microscopy imaging (TIRF, FRAP, Confocal imaging,) Immunofluorescence, Micropatterning, Biochemistry (Western Blot, Pull-down), Data analysis (FIJI).

**Up to 3 relevant publications of the team:**

- Aureille J. *et al.* (2023) Focal adhesions are controlled by microtubules through local contractility regulation. biorxiv
- Peris *et al.* (2022) Tubulin tyrosination regulates synaptic function and is disrupted in Alzheimer's disease. Brain
- Rafiq NBM *et al.* (2019) A mechano-signalling network linking microtubules, myosin IIA filaments and integrin-based adhesions Nat. Material

**Requested domains of expertise (up to 5 keywords):**