Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2026-2027

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:
Virginie Stoppin-Mellet, MCF UGA **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: Study of the pathological functions of mutant Tau proteins

Objectives (up to 3 lines):

The main objectives of this project are 1) to determine how mutations on Tau proteins affect its interactions with microtubules, 2) to evaluate how such pathological variants of Tau alter the physiological functions of WT non-mutated Tau.

Abstract (up to 10 lines):

In neurons, microtubules are involved in key cellular functions such as axonal transport and synaptic plasticity. Tau is a major neuronal microtubule-associated protein that also interacts with actin and regulates microtubule–actin crosstalk. In many neurodegenerative disorders collectively known as tauopathies, Tau undergoes abnormal modifications that lead to cytoskeletal defects. A major challenge in understanding tau toxicity is elucidating the molecular mechanisms by which pathological forms of Tau disrupt cytoskeletal organization. In this context, the aim of this internship is to determine how Tau mutations alter its ability to regulate microtubules and whether pathological Tau variants affect the physiological functions of wild-type (WT) Tau. To address these questions, biomimetic assays and single-molecule approaches will be used to reconstitute cytoskeletal networks from purified proteins. This "Learning-by-Building" approach will enable us to decipher the molecular mechanisms underlying the cytoskeletal defects induced by pathological Tau variants in neuronal cells.

Methods (up to 3 lines): Protein expression (bacteria) and purification (chromatography, affinity), co-sedimentation assays, SDS-PAGE. Bio-mimetic assays. Imaging (video-microscopy, TIRF) and image analysis (ImageJ).

Up to 3 relevant publications of the team:

* Prezel et al. (2018) Tau can switch microtubule network organizations: from random networks to dynamic and stable bundles. Molecular Biology of the Cell 29(2):154–165. doi: 10.1091/mbc.E17-06-0429.
* Stoppin-Mellet et al. (2020) Studying Tau-Microtubule interaction using single-molecule TIRF microscopy. Methods Mol Biol 2101:77-91
* Fourest-Lieuvin et al. (2023) Controlled Tau cleavage in cells reveals abnormal localizations of Tau fragments. Neuroscience 518:162-177.

Requested domains of expertise (up to 5 keywords):

Cytoskeleton ; Protein biochemistry ; Fluorescence microscopy ; Data analysis