UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2024-2025

Laboratory/Institute: Grenoble Institut Neurosciences - GIN **Director:** E. Barbier
Team: Neurocytoskeleton Dynamics and Structure
Head of the team: I. Arnal / A. Andrieux

Name and status of the scientist in charge of the project: Virginie Stoppin-Mellet, MCF
HDR: yes ☐ **no** ☒
Address: Bâtiment Edmond J. Safra, chemin Fortuné Ferrini, 38700 La Tronche, France
Phone: +33 (0)4 56 52 06 89 **e-mail:** virginie.stoppin-mellet@univ-grenoble-alpes.fr

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: Regulation of microtubule/actin interplay by Tau

Objectives (up to 3 lines):

The main objectives of this project are 1) to reconstitute in a cell-free environment, the co-assembly of microtubule and actin cytoskeletons, 2) to determine how Tau control the interplay between microtubule and actin, 3) to evaluate how pathological variants of Tau affect microtubule/actin interactions.

Abstract (up to 10 lines):

The cytoskeleton regulates major biological functions such as cell differentiation, cell migration and cell division. Importantly, actin microfilaments and microtubules interact with each other, and this interaction seems key for some cellular functions in eukaryotic cells. Yet, the mechanisms underlying actin/microtubule crosstalk are still unclear. We recently found that Tau, a major microtubule regulator in neurons, is also able to bind actin filaments. Strikingly in many brain diseases, Tau is abnormally modified and induces cytoskeleton defects. Moreover Tau modifications are also associated with bad prognosis in some cancers. In this context, the aim of this internship is to determine the **how Tau regulates microtubule/actin interplay** using biomimetic assays that reconstitute cytoskeleton networks from purified proteins. This Learning-By-Building approach will enable us to decipher the molecular mechanisms underlying the cytoskeleton defects induced by pathological variants of Tau.

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:

* Elie *et al*. (2015) Tau co-organizes dynamic microtubule and actin networks. Sci Rep 5:9964
* 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