UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Internship project Master 2
Year 2021-2022

Laboratory/Institute: Grenoble Institute of Neuroscience **Director:** Frédéric Saudou
Team: Neurocytoskeleton Dynamics and Structure
Head of the team: Isabelle Arnal & Annie Andrieux
Name and status of the scientist in charge of the project:
Anne Fourest-Lieuvin, PhD, Researcher, CEA **HDR:** yes ☒ no ☐
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Program of the Master's degree in Biology:

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

Title of the project: Truncation of tau and cytoskeleton alteration in neurons

Objectives (up to 3 lines):

Truncated forms of tau are present in neurons during brain disorders like Alzheimer's disease. These truncated proteins may exhibit toxic gain of functions, leading to cytoskeleton changes and neuronal impairments. The main objective is to investigate how tau fragments affect neuronal cytoskeleton properties.

Abstract (up to 10 lines):

Tau is a cytoskeleton-associated protein involved in microtubule and actin regulation, which contributes to the proper functions of neurons. Since the identification of tau as a major component of the neurofibrillary tangles characterizing Alzheimer's disease, much attention has been given to tau aggregative properties. However, recent studies have proposed that soluble truncated forms of tau exhibit toxic gain of functions, leading to cytoskeleton changes and neuronal impairments. Yet, the mechanisms by which these truncated forms alter microtubule and actin networks are still unknown. The student will explore the cytoskeleton-regulative properties of tau fragments in cultured primary hippocampal neurons transduced with each fragment by the mean of lentiviral vectors, already available in the laboratory. Using expansion protocols and super-resolution microscopy, the student will determine the effects of tau fragments on microtubule and actin arrays present in neuronal processes.

Methods (up to 3 lines):

Mouse brain dissection, cell culture (primary hippocampal neurons), transduction with lentiviral vectors, expansion methods, immunofluorescence, Airyscan confocal microscopy.

Up to 3 relevant publications of the team:

Ramirez-Rios, S., E. Denarier, A. Vinit, E. Prezel, V. Stoppin-Mellet, L. Peris, A. Andrieux, L. Serre, A. Fourest-Lieuvin, and I. Arnal. 2016. Tau antagonizes EB tracking at microtubule ends through a phosphorylation-dependent mechanism. *Mol biol cell*. 27:2924-34.

Osseni, A., M. Sébastien, O. Sarrault, M. Baudet, Y. Couté, J. Fauré, A. Fourest-Lieuvin*, and I. Marty*. 2016. Triadin and CLIMP-63 form a link betwen triads and microtubules in muscle cells. *J Cell Sci*. 129:3744-55.*co-senior

Elie, A., E. Prezel, C. Guerin, E. Denarier, S. Ramirez-Rios, L. Serre, A. Andrieux, A. Fourest-Lieuvin, L. Blanchoin, and I. Arnal. 2015. Tau co-organizes dynamic microtubule and actin networks. *Scientific reports*. 5:9964.

Requested domains of expertise (up to 5 keywords):

Cellular and molecular biology, optical microscopy, English.