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: Neuropathologies and Synaptic Dysfunctions **Head of the team:** A. Buisson

Name and status of the scientists in charge of the project:
Leticia Peris, CR Inserm, **HDR**, and Martina Aleman, Phd student

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Program of the Master's degree in Biology:

☐ Microbiology, Infectious Diseases and Immunology ☐ Biochemistry & Structure
☐ Physiology, Epigenetics, Differentiation, Cancer ☒ **Neurosciences and Neurobiology**

Title of the project:

Convergent Aβ and Tau toxicity on the synaptic cytoskeleton in Alzheimer's disease

Objectives (up to 3 lines):

This project aims to determine how Aβ and tau cooperate to disrupt the synaptic cytoskeleton and drive synapse loss in Alzheimer's disease. The student will investigate the impact of individual and combined Aβ and tau pathology on microtubule and actin dynamics and assess whether restoring tyrosinated microtubules protects synapses using advanced microscope imaging and transgenic neuron models.

Abstract (up to 10 lines):

Alzheimer's disease, the leading cause of dementia, is characterized by early synaptic failure underlying memory and cognitive decline. Amyloid-β (Aβ) and tau converge at synapses, where they disrupt the neuronal cytoskeleton, including microtubules (MTs) and actin networks, which are essential for synaptic structure and function. We showed that Aβ induces excessive MT stabilization, leading to dendritic spine weakening, actin loss, and synaptic dysfunction, while also promoting pathogenic tau changes that amplify toxicity. Tau further disrupts actin dynamics, exacerbating spine instability and loss. Importantly, restoring a dynamic, tyrosinated MT state protects dendritic spines and counteracts Aβ-induced damage. However, how Aβ and tau mechanistically cooperate at the synaptic cytoskeleton remains unclear. The Master 2 student will investigate the individual and combined toxicity of Aβ and tau in neuronal models and test whether enhancing MT tyrosination can protect neurons from their synergistic effects. Using advanced imaging, cellular approaches and biochemical approaches, the project aims to uncover mechanisms of synaptic degeneration and identify cytoskeletal-based strategies to preserve neuronal connectivity in Alzheimer's disease.

Methods (up to 3 lines):

Techniques used will include cellular biology (primary neuronal cultures, virus infection, immunofluorescence and confocal microscopy), molecular biology (DNA purification, PCR) and biochemistry (brain dissection, subcellular fractionation, western-blot analysis).

Up to 3 relevant publications of the team:

Peris L, Parato J, Qu X, Soleilhac JM, Lanté F, Kumar A, Pero ME, Martínez-Hernández J, Corrao C, Falivelli G, Payet F, Gory-Fauré S, Bosc C, Blanca Ramirez M, Sproul A, Brocard J, Di Cara B, Delagrange P, Buisson A, Goldberg Y, Moutin MJ, Bartolini F, Andrieux A. Tubulin tyrosination regulates synaptic function and is disrupted in Alzheimer's disease. Brain. 2022 Jul 29;145(7):2486-2506.

Zorgniotti A, Sharma A, Ramirez-Rios S, Sanyal C, Aleman M, Ditamo Y, Moutin MJ, Bisig CG, Peris L. L-Dopa-modified microtubules lead to synapse instability in cultured neurons: possible implications in Parkinson's disease therapy. NPJ Parkinsons Dis. 2025 Oct 17;11(1):298.

Martínez-Hernández J, Parato J, Sharma A, Soleilhac JM, Qu X, Tein E, Sproul A, Andrieux A, Goldberg Y, Moutin MJ, Bartolini F, Peris L. Crosstalk between acetylation and the tyrosination/detyrosination cycle of α-tubulin in Alzheimer's disease. Front Cell Dev Biol. 2022;10:926914.

Requested domains of expertise (up to 5 keywords):

Neuroscience, synaptic biology, cytoskeleton dynamics, cell culture, fluorescence microscopy.