Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2025-2026

Laboratory/Institute: Grenoble Institut Neurosciences **Director:** Dr E. Barbier
Team: Neuropathologies and Synaptic Dysfunctions **Head of the team:** Pr A. Buisson
Name and status of the scientist in charge of the project: Mireille Albrieux, Professor UGA
HDR: yes ☑ no ☐
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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: Early glutamate dyshomeostasis in the pathogenesis of Alzheimer's disease

Objectives (up to 3 lines):

Astrocyte-neuron interplay is crucial to modulate and regulate synapse function and we highlighted its key role at the onset of Alzheimer's disease (AD). We will assess in detail astrocytic functions related to disturbance of synaptic transmission, such as glutamate uptake and homeostasis regulation.

Abstract (up to 10 lines):

Despite recent advances, the recurrent failure of therapeutic strategies for Alzheimer's disease is partly due to their focus on advanced stages of the disease. We uncovered a promising new early neuroprotective target, the TRPA1 channel, which has shown efficacy in treating AD in a transgenic mouse model (Paumier et al., 2022). This astrocytic channel becomes activated by the amyloid-β peptide, resulting in increased calcium activity within these cells (Bosson et al., 2017). Subsequently, this leads to neuronal hyperactivity in neighboring cells, which will ultimately contribute to irreversible neurodegeneration. Our recent findings demonstrate that prolonged treatment with a TRPA1 inhibitor (HC030031) normalizes both astrocytic and neuronal activities in an AD transgenic mouse model. This normalization preserved the structural integrity of synapses from irreversible damage and forestalled characteristic mnesic decline (Paumier et al., 2022). The aim of this project is to elucidate the mechanisms by which the amyloid β peptide affects the TRPA1 channel and the subsequent functional repercussions of this activation focusing on TRPA1-dependent synaptic dysregulation. To achieve this goal, we will employ a multidisciplinary approach encompassing neurophysiology, cellular biology and brain imaging.

Methods (up to 3 lines):

Biological material: transgenic mice model of AD; acute brain slices ; hippocampal neuron-astrocyte co-cultures. Patch-clamp: functional recording of astrocytic glutamate transport current. Cellular biology: Glutamate transporter trafficking (diffusion, endocytosis). *In vivo* imaging: GluCEST MRI.

Up to 3 relevant publications of the team:

Bosson, A., Paumier, A., Boisseau, S., Jacquier-Sarlin, M., Buisson, A., Albrieux, M. (2017). TRPA1 channels promote astrocytic Ca2+ hyperactivity and synaptic dysfunction mediated by oligomeric forms of amyloid-β peptide. *Molecular Neurodegeneration* 12 (1) : 53.

Paumier A., Boisseau S., Jacquier-Sarlin M., Pernet-Gallay K., Buisson A., Albrieux M. (2022). Astrocyte-neuron interplay is critical for Alzheimer's disease pathogenesis and is rescued by TRPA1 channel blockade. *Brain* 145 (1):388-405.

Requested domains of expertise (up to 5 keywords):

Neurobiology, neurophysiology, astrocyte physiology, electrophysiology.
Animal experimentation (diploma offered in early January).