UFR de Chimie et de Biologie
UNIVERSITÉ Grenoble Alpes

Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2023-2024

Laboratory/Institute: Grenoble Institut Neurosciences - GIN **Director:** E. Barbier
Team: Neuropathology and synaptic dysfunctions **Head of the team:** A. Buisson

Name and status of the scientist in charge of the project: Alain Buisson, PU 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 X Neurosciences and Neurobiology

Title of the project:

Objectives (up to 3 lines): The objective of the M2 internship project is to gain insights into the mechanisms leading to synaptotoxicity in Alzheimer's disease and to develop an innovative therapeutic approach.

Abstract (up to 10 lines):
Alzheimer's disease (AD) is known to be the leading cause of dementia worldwide, which affects over 50 million people globally. Not only is dementia now considered the 7th source of mortality, but this number is expected to increase over the years, touching up to 78 million people in 2030. While most patients are diagnosed after 65 years old with sporadic AD (SAD), about 1-2% are diagnosed with familial AD (FAD), systematically with an early-onset, generally considered more severe. The similarities between the two forms of AD and the easier access to transgenic models for FAD through point mutations, led to the active use of APP mutations as insight on the pathogenesis of the more common sporadic form of AD. Several mutations on the transmembrane protein APP have been discovered over the last decade, one of them, named the Swedish mutation, has been proved to worsen the effect of AD through increased synaptic toxicity. More recently, a mutation named Icelandic has been characterized as a protective.

Our group investigated the potential protective properties of the Icelandic mutation Aβ1-42 A2T peptide. We identified a potential role of this mutation on neuronal synaptic density through live-imaging and confirmed that its addition in the extracellular space protects the synapses from the effect of pathological Aβ1-42 overexpression observed in this FAD model. This project will focuse on the mechanism responsible for this protection and whether these properties only apply to this specific form of Aβ is yet to be determined.

Methods (up to 3 lines): primary cortical neurons cultures, molecular biology techniques, live cell imaging, Animal models of Alzheimer's disease.

Up to 3 relevant publications of the team:

Long term worsening of amyloid pathology, cerebral function, and cognition after a single inoculation of beta-amyloid seeds with Osaka mutation (2023) Celestine, M ; Jacquier-Sarlin, M ; Borel, E ; Petit, F ; Perot, JB ; Herard, AS ; Bousset, L; Buisson, A ; Dhenain, M (2023) Acta Neuropathol. Com., Vol 11,

Astrocyte-neuron interplay is critical for Alzheimer's disease pathogenesis and is rescued by TRPA1 channel blockade, Paumier, Adrien [1] Boisseau, Sylvie [1] Jacquier-Sarlin Muriel) [1] Pernet-Gallay, Karin [1] ; Buisson, Alain Albrieux, Mireille Mar 29 2022 | Jul 2021 (Early Access) | BRAIN 145 (1) , pp.388-405

Effect of Ab Oligomers on Neuronal APP Triggers a Vicious Cycle Leading to the Propagation of Synaptic Plasticity Alterations to Healthy Neurons. Marta Rolland, Rebecca Powell, Muriel Jacquier-Sarlin, Sylvie Boisseau, Robin Reynaud-Dulaurier, Jose Martinez-Hernandez, Louise André, Eve Borel, Alain Buisson, and Fabien Lanté, The Journal of Neuroscience, July 1, 2020 • 40(27):5161–5176 • 5161

Requested domains of expertise (up to 5 keywords):
Neuronal cultures, biochemistry, molecular biology approaches, Alzheimer's diseases, synaptotoxicity