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: Brain aging and repair **Head of the team:** M.Decressac

Name and status of the scientist in charge of the project: M.Decressac, CRCN Inserm
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 ☒ Neurosciences and Neurobiology

Title of the project: Investigating the protective effect of a variant of human alpha-synuclein

Objectives (up to 3 lines):

The main objective of this project is to use complementary method to determine if a natural variant of alpha-synuclein is less toxic than the common sequence. This will support the idea that some individuals might be genetically protected against Parkinson's disease.

Abstract:

Parkinson's disease is a neurodegenerative condition characterized by the progressive loss of dopamine neurons in the substantia nigra and the accumulation intracellular inclusions enriched in alpha-synuclein aggregates. Hence, this protein plays a key role in the pathogenic mechanisms underlying Parkinson's disease. However, most of our knowledge on alpha-synuclein is based on its toxic gain of function. Using a phylogenic approach, we identified a sequence that abolishes the toxicity of this protein and we determined the residues responsible for this effect. Interestingly, genomic databases indicate that individuals naturally carry these residues. Therefore, we formulate the hypothesis that this polymorphism of human alpha-synuclein may represent the first protective variant against Parkinson's disease. To address this question, we will use in vitro (cell lines, primary neurons, IPS cells) and in vivo systems (mice) in combination with various readouts (microscopy, biochemistry…).

Methods:

The student will use/discover several techniques such as: in vitro and in vivo genome editing, brain surgery, induced pluripotent stem cells, cell lines, biochemistry, mass spectrometry.

Up to 3 relevant publications of the team:

- Buisson et al. (2019) Movement disorders
- Decressac et al. (2012) Neurobiology of disease
- Tamurrino et al (2015) Acta Neuropathologica Communications

Requested domains of expertise (up to 5 keywords):

Parkinson's disease, genetics, in vitro and in vivo models