

**Master 2 internship project
Year 2024-2025**

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: **HDR:** yes no
Address: Bâtiment Edmond J. Safra, chemin Fortuné Ferrini, 38700 La Tronche, France
Phone: 04.56.52.05.43 **e-mail:** Michael.decressac@inserm.fr

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: Study of a rare variant of human alpha-synuclein

Objectives:

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 phylogenetic 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
Tamburrino et al., 2015; Acta Neurophologica Communications

Requested domains of expertise (up to 5 keywords):

Genetics, molecular biology, cell culture.