

**Master 2 internship project
Year 2023-2024**

Laboratory/Institute: Grenoble Institut Neurosciences - GIN
Team: Intracellular dynamics and neurodegeneration

Director: E. Barbier
Head of the team: F. Saudou

Name and status of the scientist in charge of the project:

Frédéric Saudou (PUPH UGA) / Sophie Lenoir (chercheuse UGA)

HDR: yes no

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Program 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:

Restoring Huntingtin function in axonal transport to treat Huntington's disease

Objectives (up to 3 lines):

The objectives of the project are to restore the function of the huntingtin protein in the regulation of intracellular dynamics in neurons and investigate the effects in vitro and in vivo in mouse models

Abstract (up to 10 lines):

Huntington's disease (HD) is caused by the abnormal polyglutamine expansion in the N-ter part of huntingtin (HTT), a large protein of 350kDa. Over the past years, we proposed that HTT acts a scaffold for the molecular motors and through this function, regulates the efficiency of vesicular transport along microtubules in neurons. Here we propose to manipulate HTT protein genetically with the objective to restore its function in axonal transport and through the use of genetic therapy approaches to investigate the beneficial effects in vivo in HD mouse models.

Methods (up to 3 lines):

Techniques used will include molecular biology, biochemistry, primary cultures, state of the art live-imaging microscopy and the development and use of new microfluidic devices to study intracellular dynamics as well as viral transduction approaches in vivo and the study of behavior and pathology in mice

Up to 3 relevant publications of the team:

Vitet H et al. Huntingtin recruits KIF1A to transport synaptic vesicle precursors along the mouse axon to support synaptic transmission and motor skill learning **Elife** 2023, Jul 11;12:e81011.doi: 10.7554/eLife.81011.

Scaramuzzino C, Cuoc EC, Pla P, Humbert S, **Saudou F**. Calcineurin and huntingtin form a calcium-sensing machinery that directs neurotrophic signals to the nucleus. **Science Adv.** 2022 Jan 7;8(1):eabj8812.

Virlogeux A, et al. (2018) Reconstituting Corticostriatal Network On-a-Chip Reveals the Contribution of the Presynaptic Compartment to Huntington's Disease. **Cell Reports**, Jan 2;22(1):110-122. doi: 10.1016/j.celrep.2017.12.013.

Requested domains of expertise (up to 5 keywords):

Cell biology, neurobiology, imaging techniques, mouse, microfluidics