

**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) / Anthony Procès (postdoctorant 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:

Energy metabolism as a regulator of axonal transport in health and Huntington's disease

Objectives (up to 3 lines):

The objectives of the project are to understand the role of the huntingtin protein in the regulation of intracellular dynamics in neurons and its relation to energy metabolism

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. Huntingtin also scaffolds glycolytic enzymes that provide energy for axonal transport. Here we propose to study the sources of energy for axonal transport in response to neuronal activity and the role of HTT in this mechanism in both normal and Huntington's disease conditions.

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 in connected neuronal networks.

Up to 3 relevant publications of the team:

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.

Hinckelmann MV, et al., (2016) Self-propelling vesicles define glycolysis as the minimal energy machinery for neuronal transport **Nature Communications**, 7:13233. doi: 10.1038/ncomms13233.

Requested domains of expertise (up to 5 keywords):

Cell biology, neurobiology, imaging techniques, microscopy, microfluidics