

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

Laboratory/Institute: Grenoble Institut Neurosciences - GIN

Director: E. Barbier

Team: Central Nervous system

Head of the team: H. Nawabi

Name and status of the scientist in charge of the project: M. Barnat, CRCN Inserm

HDR: yes no

Address: Bâtiment Edmond J. Safra, chemin Fortuné Ferrini, 38700 La Tronche, France

Phone: 04 56 52 06 21

e-mail: monia.barnat@univ-grenoble-alpes.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: Understanding the developmental mechanisms regulating the formation of the cerebral cortex

Objectives:

The project aims to characterize the molecular and cellular mechanisms regulating the brain development during mammalian and human embryogenesis. More specifically, we focus on the development of the cerebral cortex to shed light on the etiology of neurodevelopmental disorders.

Abstract:

The cerebral cortex is a six-layered brain structure that ensures higher motor, sensory and cognitive functions. Its laminar organization reflects the fine regulation of developmental processes which, if altered, can lead to malformations of cortical development. These malformations are associated with clinical manifestations combining intellectual and/or motor deficits. Therefore, understanding how the cortex develops *in utero* is a sine qua non condition for deciphering neurodevelopmental disorders and their associated pathophysiological mechanisms. The cortical layers, holding a well-defined number and subtype of excitatory neurons, arise the sequential differentiation of progenitors into neurons that subsequently migrate to reach their final location. Using a combination of multi-scale approaches, we aim to study the developmental mechanisms that regulate the acquisition of neuronal identity and the orderly build-up of cortex with a special focus on crosstalk between the different cell types populating the developing cortex.

Methods:

Murine lines (crossing, genotyping), in utero electroporation, microscopy and videomicroscopy, primary culture (embryonic brain slices, cortical neuroprogenitor cells), histology (embryonic and post-natal brain sections), immunohistochemistry and immunocytochemistry, molecular biology techniques.

Up to 3 relevant publications of the team:

Wennagel D, Braz BY, Capizzi M, Barnat M, Humbert S. *Huntingtin coordinates dendritic spine morphology and function through cofilin-mediated control of the actin cytoskeleton*. **Cell Rep.** (2022). 40(9):111261.

Barnat M, Capizzi M, Aparicio E, Boluda S, Wennagel D, Kacher R, Kassem R, Lenoir S, Agasse F, Braz BY, Liu JP, Ighil J, Tessier A, Zeitlin SO, Duyckaerts C, Dommergues M, Durr A, Humbert S. *Huntington's disease alters human neurodevelopment*. **Science** (2020). 369(6505):787-793.

Barnat M, Le Friec J, Benstaali C and Humbert S. *Huntingtin-mediated multipolar-bipolar transition of newborn cortical neurons is critical for their postnatal neuronal morphology*. **Neuron** (2017). 93(1):99-114.

Requested domains of expertise:

Neurobiology, Cortical development, Cellular biology, Cell adhesion and dynamics, Molecular biology