

Institute for Advanced Biosciences - Grenoble

Master 2 internship project – 2024

LKB1 signaling to connect metabolism and epigenetics

Laboratory/Institute: Institute for Advanced Biosciences

Director: Pierre Hainaut

Address: site Santé, Allée des Alpes, Grenoble 38700 La Tronche

Co-supervision with:

Guillermo Orsi, CRCN INSERM

Team: Epigenetics of Regeneration and Cancer

Phone: 06 85 11 72 45

Chantal Thibert, CRCN CNRS

Group: LKB1 & p53 balance in development and diseases

Phone: 07 70 5 28 59

HDR: yes no

Head of the team: Guillermo Orsi

e-mail: guillermo.orsi@univ-grenoble-alpes.fr

HDR: yes no

Head of the team: P. Hainaut

e-mail: chantal.thibert@univ-grenoble-alpes.fr

Funding: 6-months internship

Title of the project:

LKB1 signaling to connect metabolism and epigenetics during cell fate choices

Objectives: The Master2 project aims at unravelling the molecular mechanisms by which the metabolic regulator and master kinase LKB1 bridges together metabolism, epigenomics and cell fate during neural crest stem cell (NCCs) formation.

Abstract: Cell fate choices, such as self-renewal or differentiation, rely on precisely defined gene expression programs, tightly controlled by chromatin remodeling complexes. Metabolic changes have recently been uncovered to drive chromatin dynamics and control gene expressions governing cell differentiation. However, the connection between signaling pathways and chromatin-modifying metabolites is still underexplored especially during stem cell fate choices. The project relies on unique genetically engineered mouse models generated by C. Thibert's team to spatiotemporally inactivate *Lkb1* in NCCs, as well as a NCC line which can be cultivated as progenitors or differentiated into several neural crest derivatives. G. Orsi's lab is expert in chromatin dynamics using cutting-edge approaches in high-resolution

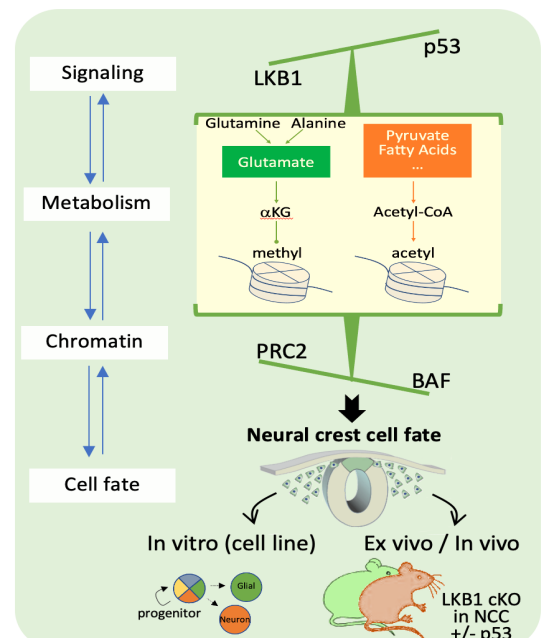


Fig1. Connecting metabolism to chromatin through signaling during neural crest cell fate

epigenomic profiling (Cut&Run technology) and microscopy.

Using these models, the master student will characterize epigenomic and transcriptional profiles depending on LKB1 activity in progenitors or differentiated NCCs both *in vitro* and *ex vivo*.

This master project is part of a collaborative project between the two teams of IAB and the team of L. Le Cam (IRCM, Montpellier) with ongoing funding applications.

Requested domains of expertise: Chromatin dynamics, Cell signaling, Cell biology, Development, Metabolism, Bioinformatics.

Methods: Handling of a neural crest stem cell line (cultures of progenitors, neurons and glial cells); NCCs sorting by FACS from embryos; Chromatin dynamics by Cut&Run-qPCR and Cut&Run-seq; Gene expression analysis by RT-qPCR and RNA-seq; Western blot; Immunofluorescence and confocal microscopy; Bioinformatic analyses of sequencing data.

Relevant publications of the team:

- * Torres-Campana D, Horard B, Denaud S, Benoit G, Loppin B, Orsi GA. Three classes of epigenomic regulators converge to hyperactivate the essential maternal gene deadhead within a heterochromatin mini-domain. *PLoS Genet.* **2022**;18(1):e1009615.
- * Orsi GA, Kasinathan S, Hughes KT, Saminadin-Peter S, Henikoff S, Ahmad K. High-resolution mapping defines the cooperative architecture of Polycomb response elements. *Genome Res.* **2014**;24(5):809-820.
- * Radu AG, Torch S, Fauvelle F, Pernet-Gallay K, Blervaque R, Lucas A, Delmas V, Schlattner U, Tricaud N, Lafenechère L, Hainaut P, Tricaud N, Pingault V, Bondurand N, Bardeesy N, Larue L, Thibert C and Billaud M. LKB1 specifies neural crest cell lineages through pyruvate-alanine cycling. *Science Advances* **2019**, eaau5106.
- * Thibert C, Lucas A, Billaud M, Torch S, Mével-Aliset M, Allard J. Functions of LKB1 in neural crest development: the story unfolds. *Developmental Dynamics.* **2023** dvyd.581.

Candidates: application should be sent to Guillermo Orsi and Chantal Thibert with a motivation letter, a CV, L3 & M1 grades and recommendation letters.

The job offer is also available through the Euraxess website: <https://euraxess.ec.europa.eu/jobs/110903>