Master's degree in Biology – Chemistry-Biology Department

Master 2 internship project
Year 2024-2025

Laboratory/Institute: IAB
Director: Pierre Hainaut
Team: Translational Epigenetics
Head of the team: Jérôme Govin

Name and status of the scientist in charge of the project:
Sylvain Carras and Anouk Emadali **HDR: yes** ☒ **no** ☐
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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:

How EHHADH reactivation can reprogram lymphoma metabolism and epigenome?

Objectives (up to 3 lines):

The identification of a predictive signature involving the liver-specific metabolic enzyme EHHADH in DLBCL suggests that a poor-prognosis lymphoma subclass could display a hepatocyte-like fatty acid metabolism. We postulate that this metabolic shift in DLBCL cells towards a liver-specific program could be responsible for generalized metabolic alterations and destabilization of the epigenomic landscape. Here, we propose to explore how DLBCL reprogramming through EHHADH reactivation can impact their lipid and energy metabolism as well as epigenome and gene expression program driving disease aggressivity and treatment resistance.

Abstract (up to 10 lines):
We have recently identified an 8 tissue-specific gene signature whose reactivation in lymphomas is associated with poor prognosis. This signature could help identify the 30 to 40% of patients who do not respond to treatment and also guide the development of new therapeutic strategies. Among these genes, the enzyme EHHADH plays a central role in liver-specific metabolic functions. Moreover, it is now clear that metabolic disturbances can impact the epigenetic regulation of gene expression through the availability of small molecules involved in histone modifications. These dysregulations may contribute to provide selective advantages to tumor cells, enabling cancer to develop and escape treatment. In this project, we propose to characterize the impact of EHHADH protein reactivation on the metabolism and epigenetics of lymphomas to better understand how it can contribute, through cellular reprogramming, to the acquisition of traits associated with tumor aggressiveness. Thus, this project is expected to have both a fundamental impact, by characterizing a new mechanism involved in lymphoma progression, and a clinical impact, by identifying patients who will not respond to treatment and therapeutic vulnerabilities to define new targeted treatments.

Methods (up to 3 lines): cell culture, gene editing, flow cytometry (evaluation of cell death and proliferation) epigenomics (Cut&Run, performed in collaboration with Epinomics platform), sample preparation for metabolomics analyses (performed in collaboration with GEMELI platform)

Up to 3 relevant publications of the team:
Bouroumeau et al, Hemasphere, 2021, PMID: 34131636
Bussot et al, Br J Haematol., 2021, PMID: 34155628
Carras, J Exp Med, 2021, PMID: 34043588

Requested domains of expertise (up to 5 keywords):

Epigenetics, lipid and energy metabolism, lymphoid cancers