**Lab**: CRCI2NA

**Team**: Team #11 reMove-B

**Name and position of the supervisor:** Antonin Papin MCU, David Chiron DR

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**Candidate:** Elyne Roux

**Title of the internship:** Impact of epigenetic alterations in the activation of resistance pathways in mantle cell B lymphoma

**Summary of the internship proposal:** Despite advances in molecular tumor profiling and characterization of malignant ecosystems, therapeutic resistance remains a major challenge in aggressive lymphomas. Epigenetic deregulation, such as histone methylation, is emerging as a key factor driving resistance in various cancers, but its functional consequences remain poorly understood. In this project, we will use mantle cell lymphoma (MCL)—an aggressive and incurable B-cell lymphoma—as a model to explore how these epigenetic modifications contribute to resistance pathway overactivation such as NFkB. Our aim is to uncover new insights into the molecular and functional impacts of epigenetic alterations, particularly involving NSD2, which is frequently deregulated in MCL. This project seeks to deepen our fundamental understanding of resistance mechanisms and identify novel therapeutic targets to improve treatment strategies for cancer patients.

Using datasets from high-throughput technologies (Cut&Run, RNA-seq) this project aims to:

1. Investigate the differential accessibility of NFκB subunit binding sites in tumor versus normal B cells.

2. Assess the impact of histone methylation alterations on NFκB pathway overactivation, focusing on a gain-of-function NSD2 model.

In addition to omics, the project will leverage established cellular models—including CRISPR/Cas9-engineered isogenic lines and *ex vivo* cultures of primary MCL cells from a local cohort of MCL patients.

Option(s) linked to the project:

Hematology  Oncology

Immunology-Cancerology  Nuclear Medicine

Option(s) linked to the profile:

Clinical Research Profile  Data Analyst Profile

Experimental Biology Profile