Internship proposition
One page max
M2 I3/0HNU 2024-25

**Lab:** CRCI2NA

**Team:** Team 11 (reMoVE-B)

**Name and position of the supervisor:** Dr Antonin PAPIN (Assistant Professor) and Pr Agnès Aubry (Professor)

**Email of the supervisor**: antonin.papin@univ-nantes.fr and agnes.aubry@univ-nantes.fr

**Candidate:** Camille GLEMAREC

**Title of the internship:** Role of NSD2 alterations in mature B cell malignancies

**Summary of the internship proposal:** Mature B cell malignancies such as mantle cell lymphoma (MCL) and multiple myeloma (MM) are often incurable for patients who fail chemotherapy. Among the genetic alterations in these pathologies, the NSD2 gene is often affected. Indeed, 20% of MCL patients harbor NSD2 gain-of-function mutations, and 15% of MM patients present a translocation t(4;14) that places NSD2 expression under the control of the immunoglobulin heavy chain promotor. In both hemopathies, these patients have poor overall survival, and strategies to overcome resistance or treat NSD2-altered patients are an unmet medical need. NSD2 is a methyltransferase that catalyzes the H3K36me2 chromatin mark involved in transcription activation. Although NSD2 is altered, we still do not know the mechanisms of action and the biological effects of NSD2 mutations in MCL, and little is known concerning NSD2 overexpression in MM. Specifically, we hypothesize that NSD2 alterations mediate dramatic epigenetic changes that trigger new transcription programs driving proliferation, survival, and chemoresistance of tumor cells. Based on this rationale, our research project will define the molecular and biological impact of NSD2 alterations in MCL and MM to identify NSD2 alteration-induced vulnerabilities and develop new therapeutic strategies.
The objectives of the internship will be (1) to optimize the ongoing development of MCL and MM cell line models, such as isogenic cell lines for NSD2 alterations (MCL) and NSD2 over/downregulation methods (MM), (2) to assess the NSD2-mediated resistance to treatment by drug testing using the optimized cell lines, and (3) to initiate the molecular exploration of the observed NSD2-mediated resistance by comparing and contrasting the different NSD2 alterations in the different models.
This project will utilize molecular biology techniques such as CRISPR-Cas9 technologies, gene over/downregulation systems, and cellular biology techniques such as cell culture and drug testing, among others.

Option(s) linked to the project:
☐ Clinical Research Profile
☐ Data Analyst Profile
x **Experimental Biology Profile**