Internship Proposition
(one page max)

Master 2 GP Immunology & ImmunoIntervention (I^3)
2025-2026

Lab: CR2TI

Team: 4

Name and position of the supervisor: Nataliya Yeremenko, Research Engineer

Email of the supervisor: Nataliya.Yeremenko@univ-nantes.fr

Candidate (if internship filled):

Title of the internship: Metabolic and Phenotypic Remodelling in B-cell Differentiation: Unveiling Novel Vulnerabilities through BOB1 Inhibition

Summary of the internship proposal:

B-cell cancers, often driven by dysregulated B-cell development within lymphoid organs, present a significant challenge in oncology. The transcriptional co-activator BOB1 (POU2AF1), in partnership with OCT2 (POU2F2), plays a central role in normal B-cell differentiation and, crucially, acts as a key driver in the pathogenesis of B-cell lymphomas. Its distinctive expression profile – highly restricted in healthy tissues but often overexpressed and essential for lymphoma cell survival – makes BOB1 a compelling therapeutic target.
Our team has developed innovative small-molecule inhibitors designed to interfere with the critical BOB1-OCT2 protein-protein interaction. In vitro studies, combining a human primary B-cell differentiation model with high-resolution single-cell RNA sequencing data, have shown that BOB1 inhibition significantly impacts metabolic and amino acid synthesis pathways, leading to varied cellular outcomes across different B-cell populations. We observed a range of responses to the treatment, from strong anti-proliferative effects and suppression of immunoglobulin class switching in activated precursors to the blockade of plasmablast development and notable functional impairments in differentiated plasmablasts. Interestingly, preliminary data indicated that resting memory and naive B-cell subsets were less impaired. This Master's project offers a unique opportunity to deepen our understanding of how BOB1 inhibition affects B-cell biology. Particular emphasis will be placed on uncovering the precise mechanisms of cell death (or survival) and the associated metabolic shifts across various B-cell subsets, including naive, memory, and plasma cells. The successful candidate will utilise a suite of advanced cellular and molecular techniques, such as high-parameter flow cytometry for detailed phenotypic and cell death analyses (e. g., Annexin V/PI, cleaved Caspase-3 detection), alongside cutting- edge metabolic assays (e. g., ATP production, oxygen consumption rate, MitoSOX for mitochondrial reactive oxygen species). This interdisciplinary project aims to dissect the complex relationship between BOB1 activity, metabolic reprogramming, and cell fate decisions in B-cells, ultimately revealing novel metabolic vulnerabilities for targeted therapy development against B-cell cancers. We seek a highly motivated and skilled student, passionate about translational research at the intersection of immunology, metabolism, and cancer biology.

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Option(s) linked to the project:

☐ Clinical Research Profile (Recherche Clinique)
☐ Data Analyst Profile (Recherche et Analyse de Données Omiques)
☐ Experimental Biology Profile (Recherche Expérimentale)

Form to be sent by email to : gpi3@univ-nantes.fr