Internship Proposition
(one page max)
Master 2 GP Immunology & ImmunoIntervention (I^3)
2026-2027

Lab: CR2TI

Team: 4

Name and position of the supervisor: Nataliya Yeremenko / Nicolas Degauque

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Candidate (if internship filled):

Title of the internship: Targeting the BOB1-OCT Axis to Decipher Metabolic Control of B-cell Differentiation

Scientific Context. The Germinal Center (GC) reaction serves as the engine of adaptive immunity, providing a specialized microenvironment for B-cell proliferation, somatic hypermutation, and affinity maturation. The transition from a GC B cell to a secretory plasma cell necessitates a massive metabolic expansion to support accelerated protein synthesis and organelle remodeling. Dysregulation of these high-energy developmental states is a primary driver of autoimmune diseases and B-cell malignancies, such as B-cell lymphomas and multiple myeloma. In these pathological contexts, cells hijack physiological metabolic pathways to fuel uncontrolled proliferation and survival. Central to this developmental program is the transcriptional co-activator BOB1, which, in complex with its partner OCT2, acts as a master regulator of B-cell fate. Our team has developed innovative small-molecule BOB1 inhibitors (BOB1i) that disrupt this interaction, effectively halting plasma cell differentiation and isotype switching while inducing selective apoptosis in mature B-cell cancer lines. We hypothesize that the BOB1-OCT2 axis functions as a metabolic gatekeeper whose inhibition disrupts the bioenergetic framework required for effector function and malignant survival.

Objectives. The primary goal of this internship is to characterize how the BOB1-OCT2 axis controls the metabolic programs essential for plasma cell differentiation and the survival of malignant B cells. The project will follow three specific aims. First, we will characterize the bioenergetic signatures of primary B cells during in vitro plasma cell differentiation compared to mature B-cell cancer lines. Second, we will evaluate the impact of BOB1i by quantifying how BOB1 inhibition disrupts these metabolic profiles and whether it triggers cell cycle arrest or programmed cell death. Finally, the project will test whether stressors, such as glucose deprivation or inhibition of the pentose phosphate pathway, synergize with BOB1 inhibitors to eliminate malignant B cells.

Methods. Isolation and culture of human B cells from peripheral blood, maintenance of mature B-cell cancer lines. Multi-parametric flow cytometry to assess cellular phenotypes and cytokine expression and functional metabolic assays to quantify glucose uptake, reactive oxygen species (ROS) levels, and mitochondrial activity. Pharmacological modulation to perturb both the BOB1-OCT2 axis and specific metabolic pathways to observe functional consequences on cell fate.

Expected Outcomes. This project will clarify how the BOB1-OCT2 axis sustains the high metabolic demands of plasma cell differentiation and B-cell cancer survival. It will provide a robust mechanistic basis for utilizing BOB1 inhibitors as a novel therapeutic strategy for treating B-cell malignancies and antibody-mediated autoimmune diseases.☐ Clinical Research Profile (Recherche Clinique)
☐ Data Analyst Profile (Recherche et Analyse de Données Biologiques)
☒ Experimental Biology Profile (Recherche Expérimentale)

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