



Internship proposition  
One page max  
M2 I3/OHNU 2024-25



Lab: CRCI²NA/INSERM U1307/ CNRS UMR6075/UN

team: Team 6: "Signaling in Oncogenesis, Angiogenesis, and Permeability"

Name and position of the supervisor: Nicolas BIDERE, DR2 INSERM

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Candidate:

Title of the internship: Deciphering novel Regulators of Lymphocyte Activation and Lymphomagenesis

Summary of the internship proposal:

Diffuse large B-cell lymphoma (DLBCL) represents the most prevalent form of lymphoma in humans. The aggressive Activated B-cell-like (ABC) subtype of DLBCL pirates a signaling complex of CARMA1 BCL10, and MALT1 (CBM complex), that couples signals from antigen receptors in B and T lymphocytes to NF- $\kappa$ B. In addition to its scaffolding properties within the CBM, MALT1 display a paracaspase activity essential for the optimal activation of lymphocytes. Moreover, MALT1 emerges as a promising therapeutical target for ABC DLBCL, as its pharmacological inhibition is toxic. However, the precise mechanisms governing the assembly and regulation of the CBM complex remain elusive.

This project aims to integrate data mining approaches with unbiased omic screens, molecular biology techniques, and biochemistry assays, along with *in vitro* and *in vivo* experiments, to uncover novel factors involving lymphocyte activation and lymphomagenesis. This work will identify potential therapeutical targets to rewire the aberrant NF- $\kappa$ B signaling in ABC DLBCL.

- Renaud CCN, (...), Bidère N. The centrosomal protein 131 participates in the regulation of mitochondrial apoptosis. **Commun Biol.** **2023** Dec 15;6(1):1271. PMID: 38102401.

- Thys A, (...), Bidère N. Serine 165 phosphorylation of SHARPIN regulates the activation of NF- $\kappa$ B. **iScience.** **2020** Dec 13;24(1):101939. PMID: 33392484.

- Douanne T, (...), Bidère N. CYLD Regulates Centriolar Satellites Proteostasis by Counteracting the E3 Ligase MIB1. **Cell Reports.** **2019** May 7;27(6):1657-1665.e4. PMID: 31067453.

- Dubois SM, (...), Bidère N. A catalytic-independent role for the LUBAC in NF- $\kappa$ B activation upon antigen receptor engagement and in lymphoma cells. **Blood.** **2014** Apr 3;123(14):2199-203. PMID: 24497531.

- Alexia C, (...), Bidère N. The endoplasmic reticulum acts as a platform for ubiquitylated components of nuclear factor  $\kappa$ B signaling. **Science Signaling.** **2013** Sep 3;6(291):ra79. PMID: 24003256.

- Bidère N, (...), Lenardo MJ. Casein kinase 1alpha governs antigen-receptor-induced NF- $\kappa$ B activation and human lymphoma cell survival. **Nature.** **2009** Mar 5;458(7234):92-6. PMID: 19118383.

Option(s) linked to the project:

- Clinical Research Profile
- Data Analyst Profile
- Experimental Biology Profile