BOB-HOP : Bridging the gap to in vivo efficacy and potency through scaffold hopping of BOB1-OCT2 small-molecules inhibitors

The BOB1-OCT2 transcriptional complex is a lineage-restricted master regulator of the germinal centre B-cell program, driving both autoimmune pathology and aggressive B-cell malignancies. Its selective expression profile provides an exceptional therapeutic window; however, systemic exposure to first-generation inhibitors remains limited by suboptimal pharmacokinetic properties despite strong mechanistic proof-of-concept. BOB-HOP brings together an interdisciplinary consortium uniting immunology (CR2TI), medicinal chemistry (CEISAM), and translational onco-haematology (CRCI2NA) to overcome this bottleneck. The consortium will implement a rational chemical optimisation strategy to generate optimised, nanomolar-potency derivatives. These optimised inhibitors will be evaluated across two high-unmet-need contexts: (i) autoimmunity, using Collagen-Induced Arthritis models to quantify suppression of pathogenic antibody responses, and (ii) oncology, assessing selective apoptosis and efficacy in Mantle Cell Lymphoma and Multiple Myeloma models. A co-supervised PhD student will ensure continuous chemistry-immunology integration, accelerating iterative optimisation. Supported by key research networks, BOB-HOP aims to deliver a proprietary series of potent BOB1–OCT2 inhibitors and establish a clinically actionable therapeutic path within the Nantes Université ecosystem.