Laboratory: UMR1227 LBAI (B Lymphocytes, Autoimmunity, and Immunotherapies)

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Internship Title: Impact of the PD-1/PD-L1 Pathway on the Functional Orientation of B Cells

Summary of the Proposed Project:

B cells play a crucial role in the immune response by secreting antibodies and cytokines, as well as presenting antigens to T cells. Depending on the context, they can exert pro-inflammatory or regulatory effects. Regulatory B lymphocytes (Bregs) are essential in maintaining immune tolerance and preventing autoimmunity. One of the key mechanisms involved in regulating this tolerance is the programmed cell death receptor PD-1. Although PD-1 is expressed by B cells, its role in the functional orientation of B cells remains unknown.

Studies have shown that PD-1+ B cells are present in tumor tissues and are associated with poor clinical outcomes, suggesting a potential pro-tumorigenic role of these cells. Using *in vitro* models, it has been demonstrated that PD-1+ B cells acquire regulatory functions, such as suppressing T cell proliferation. In contrast, in autoimmune conditions, PD-1+ B cells present in the synovial tissue of patients with rheumatoid arthritis express activation markers and cytokines like TNF-α and IL-6, suggesting a pro-inflammatory role.

Our preliminary data show an increase in IL-10 expression in stimulated PD-1+ B cells compared to PD-1- B cells, while also observing IL-6 expression, suggesting a dual role for PD-1+ B cells.

This internship project will focus on studying the impact of the PD-1/PD-L1 pathway on the functional polarization of B cells using *in vitro* models. The first phase of the internship will consist of analyzing the cytokine profile of stimulated PD-1+ B cells *in vitro*, using intracellular staining by flow cytometry and multiplex immunoassays. The PD-1/PD-L1 pathway will be modulated using therapeutic antibodies. The second phase will investigate the role of the PD-1/PD-L1 pathway in the acquisition of immunosuppressive functions, using a co-culture model of B cells and autologous T cells to generate B cells with an immunoregulatory profile. T cell proliferation will be quantified by flow cytometry, as well as the production of pro- and anti-inflammatory cytokines.

This internship will provide hands-on training in the *in vitro* culture of human B and T cells, cell isolation, spectral flow cytometry, and multiplex immunoassays. It may also include the use of bioinformatics tools for analyzing multiparametric flow cytometry data.