

## Master Project Proposal

**Title: Unveiling the role of SAMHD1 in the differentiation of follicular helper T cells and its relation to HIV susceptibility**

### **Synopsis:**

Follicular helper T cells (Tfh), specialized CD4 T cells that promote B cell maturation to mount antibody (Ab) responses, have been shown to be key human immunodeficiency virus (HIV)-1 reservoirs. Although various studies have addressed the role of Tfh in HIV/ acquired immune deficiency syndrome (AIDS), there are important gaps concerning the impact of HIV-1 infection on Tfh phenotype, function and differentiation.

Tfh are characterized by the expression of ICOS, PD-1, CXCR5, interleukin-21 (IL-21) and master transcription factor Bcl6. Bcl6 has been reported to impact cellular susceptibility of Tfh to HIV infection, related to HIV transcription and modulation of HIV restriction factors expression such as SAMHD1. In agreement SAMHD1 levels are very low in Tfh in germinal centres possibly playing a role in their HIV susceptibility. There are no data on the levels of SAMHD1 during Tfh differentiation and on its possible contribution of the reported high ability of pre-Tfh cells to support viral infection.

We will evaluate the SAMHD1 expression, at both protein and transcriptional level using flow cytometry, throughout in-vitro Tfh differentiation, as well as in tonsillar CD4 T cell populations in different stages of Tfh maturation. We will manipulate SAMHD1 expression or function to further evaluate its impact in the process of Tfh differentiation.

This proposal will provide a better understanding on the viral-host interaction during Tfh differentiation and its relevance in HIV pathogenesis.

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