Expansion of Tfh and atypical B-Cell subsets associated with long-term immunity to the *Plasmodium vivax* DBPII antigen

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Duffy Binding Protein region II (DBPII) is a leading *P. vivax* (Pv) blood-stage vaccine candidate. Polymorphisms within B-cell epitopes limit its efficacy by inducing strain-specific immunity. The engineered DEKnull-2 induces broadly inhibitory IgG antibodies that block *Pv*. A 15-years follow-up study in the Brazilian Amazon allowed to identify persistent responders with strain-transcending DBPII antibody response (PR). Here, we hypothesized that the interaction between follicular T helper cells (Tfh) and B-cells is more efficient in PR driving strain-transcending DBPII antibody response. In this study, characterization of Tfh and B-cell subsets was performed to identify immune signatures associated with PR phenotype. For that, PBMC samples were isolated over 15-Year follow-up study from DBPII responders (PR) and non-responders (NR). PBMC were stimulated with DBPII and DEKnull-2 (6 days at 37˚C), followed by multiparametric flow cytometry analysis to identify Tfh /B cells subsets. Supervised analysis revealed significant expansion of Tfh cells with Th1-like and Th2/Th17-like phenotypes in PR. In addition, increased frequencies of Tbet+ and CXCR3+ atypical B cells subsets were observed in PR following stimulation with both DBPII and DEKnull-2, suggesting an association with long-term antibody response. Further, unsupervised clustering analysis confirmed the expansion of $CXCR5^+$ cells within both memory $CD4^+$ T cells and B-cells. Taken together, these findings highlight the relevant contribution of these Tfh and B cells subsets for maintenance of persistent and broadly DBPII antibody response, providing critical insights for vaccine design. Finally, the results reinforce the potential of DEKnull-2 as a key component of a multivalent vaccine against *Pv* malaria. (**Support by** CNPq, CAPES, FAPEMIG, NIH, Fiocruz/ReTMavi)