

T-CELL IMMUNE RESPONSE TO *PLASMODIUM FALCIPARUM* CHIMERIC VACCINE CANDIDATE GMZ2.6C AND ITS EPITOPES IN INDIVIDUALS EXPOSED TO MALARIA LIVING IN THE BRAZILIAN AMAZON

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Introduction: The GMZ2.6c malaria vaccine candidate is a multi-stage *Plasmodium falciparum* chimeric protein that contains a fragment of the sexual-stage Pfs48/45-6C protein genetically fused to GMZ2, an asexual-stage construction consisting of Glutamate-rich Protein (GLURP) and Merozoite Surface Protein-3 (MSP-3). Our group previously showed that GMZ2.6c is widely recognized by antibodies from Brazilian-exposed individuals and that anti-GMZ2.6c levels appear to increase with exposure to malaria infection and may contribute to parasite immunity. **Objective:** Evaluate the cellular immune response against GMZ2.6c and its components, and identify T-cell epitopes in individuals naturally exposed to malaria in the Brazilian Amazon. **Methods:** This study was carried out using PBMCs from individuals from Cruzeiro do Sul and Mâncio Lima, Acre state, and Guajará, Amazonas state. PBMCs were stimulated with GMZ2.6c, MSP-3, GLURP, and Pfs48/45, and central (CM) and effector (EM) memory CD4⁺ and CD8⁺T cells, as well as cell activation markers, were analyzed by flow cytometer. The levels of cytokines in supernatant cultures were measured using BD CBA Human Th1/Th2/Th17 kit. The relative number of IFN- γ -secreting T cells against pools of synthetic peptides for MSP-3 (Mpp I), GLURP (Gpp I), and Pfs48/45 (Ppp I and Ppp II) predicted by Immune Epitope DataBase (IEDB) was performed by ELISpot. **Results:** The results showed that individuals living in Brazilian endemic areas present cellular immune responses against GLURP, MSP-3, and Pfs48/45 able to recall CD4⁺T cell response after stimulation with GMZ2.6c. However, *P. falciparum* infection might modulate the immune response by reducing CD4⁺T_{EM} cells and inducing a prominent pro-inflammatory Th1 response. In the absence of the parasite, higher percentages of CD4⁺T_{EM} cells and the balance between Th1 and Th2 cytokine production suggest a booster of antigen-specific T cells with pro-inflammatory and regulatory profiles that may enhance the anti-parasite effector mechanism. The four pools containing T-cell epitopes induced IFN- γ T-cell response in a naturally exposed population of the Brazilian Amazon, validating the prediction of T-cell epitopes. **Conclusion:** The GMZ2.c protein is widely recognized by CD4⁺T cells from individuals living in

malaria-endemic areas in Brazil. Also, we identified multiple T-cell epitopes derived from GLURP, MSP-3, and *Pfs48/45*, highlighting the importance of GMZ2.6c as a multi-stage vaccine candidate.