Naturally acquired antibodies to *Plasmodium vivax* Pv_LISP-2, a potential liver stage vaccine antigen

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Abstract

Introduction: *Plasmodium vivax* is responsible for most malaria cases in Latin America and Southeast Asia and can cause severe manifestations. Prevention strategies such as vaccines, have been hampered by the complexity of the parasite's life cycle, especially in the liver stages. The *P.vivax*-Liver-Specific Protein 2 (Pv_LISP-2) has been described as essential for intrahepatic development, but its antigenicity has not yet been explored. **Objective:** Thus, in this study we evaluate the naturally acquired humoral response against two regions of Pv_LISP-2 in populations from the Brazilian Amazon exposed to *P. vivax* infection. **Methods:** Plasma samples were collected from infected individuals in Manaus (Amazonas state) and Boa Vista (Roraima state). Two structural regions of Pv_LISP-2 (Pv_L.seq1 and Pv_L.seq2) were expressed in *E. coli*, purified, and applied in ELISA assays to detect total IgM, IgG, and IgG subclasses antibodies. Furthermore, longitudinal follow-up was conducted for up to 180 days in part of the Manaus cohort. **Results:** Pv_LISP-2 fragments were recognized by antibodies of *P. vivax*-infected individuals. During the acute phase, the response was characterized by high levels of IgM, followed by the induction of IgG, especially against Pv_L.seq1. The cytophilic subclasses IgG1 and IgG3 were the predominant subclasses. IgM responses correlated with parasitemia and days of symptoms but showed a negative association with hematological parameters (hemoglobin, hematocrit, and erythrocytes). **Conclusion:** This is the first study to evaluate naturally acquired antibodies against this liver-stage antigen of *P.vivax*, we showed that Pv_LISP-2 is naturally antigenic in individuals exposed to vivax malaria. While the functional implications of these responses remain to be fully elucidated, our findings support further investigation of Pv_LISP-2 as a potential vaccine candidate targeting the liver stage of *P. vivax*.