COMPARATIVE INVESTIGATION OF *PLASMODIUM VIVAX* IN BONE MARROW AND PERIPHERAL BLOOD SAMPLES FROM INDIVIDUALS NATURALLY EXPOSED TO MALARIA VIVAX IN BRAZILIAN AMAZON

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Background: *Plasmodium vivax* (*Pv*) has a unique tropism to invade immature reticulocytes. Recent studies revealed significant enrichment of parasite biomass in the bone marrow (BM) and spleen when compared to the peripheral blood (PB). The effects behind this cell tropism in disease progression are poorly understood, hindering progress in understanding Pv immunopathogenesis. **Objective**: The present study hypothesizes phenotypic and functional differences between parasite populations developing in the BM versus those in the PB. **Methods**: To test this hypothesis, we aim to integrate transcriptome data analyzes and functional assays performed *ex-vivo* with *Pv* isolated from from BM vs. PB reticulocytes. BM aspirates and PB matched samples were collected from uncomplicated *Pv* cases admitted at FMT-HVD (Manaus-AM). **Results:** To date, 26 patients have consented to the collection of matched BM and PB samples. Whole blood, plasma, and mononuclear cells were isolated and cryopreserved. Analysis of BM and blood smears showed no differences in total parasitemia (% of infected red blood cells) and stage distribution between BM and PB. However, analysis of transcriptomic signatures by bulk-RNA-seq, indicated enrichment of sexually committed schizonts (AP2-G+ parasites), rings and immature gametocytes in the BM, compared to blood, during *P. vivax* infection. Upregulation of genes associated with different metabolic pathways, including PC biosynthesis and reticulocyte invasion in BM parasites were also observed. Additionally, functional analysis of rosette formation in 9 patients demonstrated a higher density in BM samples when compared to PB, particularly in those collected during malaria recurrence episode. **Conclusion:** These findings represent a pioneering study to better understand the unique adaptation of *P. vivax* in the BM niche, with implications to malaria diagnosis and treatment as well as strategies towards the malaria elimination agenda.

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