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, BM aspirates and PB matched samples were collected from *Pv* cases admitted at FMT-HVD (Manaus-AM) aiming to integrate *ex-vivo* transcriptome data analysis and functional assays performed with *Pv-infected* reticulocytes.
Results: The first paired *ex vivo* BM–PB single-cellRNA-seq dataset, recapitulated canonical developmental clustering of assexual and sexual trajectories and enabled pseudotime reconstruction of a continuous asexual maturation path with stage-aligned metabolic, chromatin, lipid, and ApiAP2 regulatory dynamics. In parallel, the bulk RNA-seq revealed compartmentalized gametocytogenesis, with BM parasites showing increased sexual commitment (AP2-G upregulation) consistent with early/immature gametocytes, whereas PB parasites were enriched for transcripts compatible with mature, transmission-ready sexual stages. In ageement, MFA assays showed higher oocyst burdens in *Anopheles* spp. fed with PB-derived parasites, indicating greater infectivity of circulating gametocytes compared to BM. Finally, rosetting was detected in both compartments but occurred more frequently in the BM, particularly in recurrent infections, supporting niche-associated adhesive phenotypes.
Conclusions: The data highlight the compartment-specific features of *Pv* infection corroborating that the BM acts as a key hematopoietic reservoir. Ongoing and future work will expand the number of samples and analysis to test differential signatures to clarify persistence and transmission mechanisms within BM niches.

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