

Evolutionary inferences of *P. vivax* Duffy Binding Protein II (Pvdbp-II): The Indian setting

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The requirement of an efficient *P. vivax* vaccine is crucial as evidenced from reports of drug resistance globally. PvDBPII, a leading vaccine candidate for *P. vivax*, has cleared Phase I clinical trial and is reported to be highly polymorphic, which might be a major obstacle on the way of attaining a successful vaccine. India, a significant contributor to *P. vivax* malaria burden in the WHO-SEAR, exhibits varying *P. vivax* endemicity. Hence, understanding the pattern of diversity and selection in Pvdbp in India would be vital for developing a DBP-based vaccine.

Genetic diversity and natural selection of PvDBP-II was investigated in 73 *P. vivax* isolates collected from different parts of India. Out of a total of 57 SNPs identified, 18 were non-synonymous and 3 were synonymous mutations. The overall nucleotide diversity of 73 PvDBP-II isolates was 0.00609 with 22 haplotypes ($H_d=0.87$) identified. The high ratio of non-synonymous to synonymous mutations suggests that PvDBPII had evolved under positive selection.

Polymorphisms of PvDBP-II shows that isolates from India were genetically diverse. Also, findings from this study further confirmed that mutations and natural selection might increase and sustain evasion of host immunity. These results expand our understanding of *P. vivax* evolution in India and, more crucially, solidify the rationale for the development of a blood-stage *P. vivax* malaria vaccine.

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Malaria, India, *P. vivax*, PvDBPII, genetic diversity, natural selection

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