PhD abstract

Name of scholar	:	Surendra Kumar Prajapati
Name of supervisor	:	Dr. Moshahid A. Rizvi
Name of co-supervisor	:	Dr. Hema Joshi
Department	:	Biosciences
Title of Thesis	:	Molecular studies on housekeeping genes of *Plasmodium vivax*

Malaria is an ancient human infectious disease, tolls around 350-500 million clinical episodes annually, and caused by five species of *Plasmodium* parasites. The parasite *P. falciparum* is the most severe form causing malignant malaria, while *P. vivax* is the most widespread species out side the Africa and causes widespread morbidity but little mortality. Geographical sub division played an important role in genetic structuring and speciation of the organism. *Plasmodium vivax* had been categorized into two distinct lineages, Old World (Asia, Asia Pacific) and New World (South and Central America), distinguishable by gene conversion in the *S-type 18S SSU rRNA* gene, polymorphisms in an open reading frame (*orf470*) of the apicoplast genome, mosquito transmission. Based on the above features, New World and Old World were proposed as two sub-species or separate species. We have investigated this hypothesis by typing *S type 18S SSU rRNA* variations (*S type-1*: Old world, *S type-2*: New world) and their further characterization using a panel of genetic markers namely drug resistance (2), antigen (7), housekeeping genes (10), minisatellite (10) and microsatellite (8) markers to determine drug resistance potential, antigen repertoires and pattern of selection, genetic diversity, phylogenetic relation, and evolutionary histories of these two proposed lineages. Geographic mapping of *S-type 18S SSU rRNA* variations in 390 *P. vivax* isolates (n = 354) revealed presence of both sub-types in Indian sub-continent, which suggests lack of geographical sub-division between them. Further, our panel of genetic markers consistently revealed similar patterns for drug resistance potential, antigen repertoires and positive selection, genetic diversity, and evolutionary histories between Old and New world *P. vivax* parasites, providing no evidence for the hypothesis that New world is a sub-species or separate species of *P. vivax*. Coalescence analysis of the Time to the Most Recent Common Ancestor

(TMRCA) estimate using SNPs in selectively putative housekeeping genes revealed MRCA of *P. vivax* was present in India about 232,000-304,000 years ago. For the first time we reported that nuclear neutral marker (putative housekeeping genes) displayed a similar evolutionary history of *P. vivax* as it was inferred with mitochondrial genome diversity. In conclusion, our findings revealed Indian *P. vivax* isolates are highly diverse, represent global genetic variations, have ancient evolutionary history in Indian subcontinent, and support Asian origin theory of *P. vivax*. The fixation of *S type-1* and *S type-2* isolates in Melanesia and America respectively does not represent two sub species or separate species of *P. vivax* rather it represent two alleles. Global distribution of *S-type 18S SSU rRNA* variants, genetic diversity of parasite, and human migration events strongly suggest that both *S-type 18S SSU rRNA* variants of *P. vivax* could have originated in Indian sub continent and *S type-1* spread towards Melanesia and *S type-2* towards American continent. In addition, study revealed footprint of connection between human migration in the ancient time and spread of infectious diseases.