

Publication

The origins of malaria artemisinin resistance defined by a genetic and transcriptomic background

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Author(s) Zhu, Lei; Tripathi, Jaishree; Rocamora, Frances Maureen; Miotto, Olivo; van der Pluijm, Rob; Voss, Till S.; Mok, Sachel; Kwiatkowski, Dominic P.; Nosten, François; Day, Nicholas P. J.; White, Nicholas J.; Dondorp, Arjen M.; Bozdech, Zbynek

Author(s) at UniBasel [Voss, Till](#) ;

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The predisposition of parasites acquiring artemisinin resistance still remains unclear beyond the mutations in Pfk13 gene and modulation of the unfolded protein response pathway. To explore the chain of casualty underlying artemisinin resistance, we reanalyze 773 *P. falciparum* isolates from TRACI-study integrating TWAS, GWAS, and eQTL analyses. We find the majority of *P. falciparum* parasites are transcriptomically converged within each geographic site with two broader physiological profiles across the Greater Mekong Subregion (GMS). We report 8720 SNP-expression linkages in the eastern GMS parasites and 4537 in the western. The minimal overlap between them suggests differential gene regulatory networks facilitating parasite adaptations to their unique host environments. Finally, we identify two genetic and physiological backgrounds associating with artemisinin resistance in the GMS, together with a farnesyltransferase protein and a thioredoxin-like protein which may act as vital intermediators linking the Pfk13 C580Y mutation to the prolonged parasite clearance time.

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