Xeno-monitoring of molecular drivers of artemisinin and partner drug resistance in *P. falciparum* populations in malaria vectors across Cameroon

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Background: Monitoring of drug resistance in *Plasmodium* populations is crucial for malaria control. This has primarily been performed in humans and rarely in mosquitoes where parasites genetic recombination occurs. Here, we characterized the *Plasmodium* spp populations in wild *Anopheles* vectors by analyzing the genetic diversity of the *P. falciparum* kelch13 and *mdr1* gene fragments implicated in artemisinin and partner drug resistance across Cameroon in three major malaria vectors.

Methods: *Anopheles* mosquitoes were collected across nine localities in Cameroon and dissected into the head/thorax (H/T) and abdomen (Abd) after species identification. A TaqMan assay was performed to detect *Plasmodium* infection. Fragments of the Kelch 13 and *mdr1* genes were amplified in *P. falciparum* positive samples and directly sequenced to assess their drug resistance polymorphisms and genetic diversity profile.

Results: The study revealed a high *P. falciparum* sporozoite rate alongside epidemiological signatures of significant *P. malariae* circulation in the major malaria vectors. Low genetic diversity with six- and eight-point mutations were observed in the *k13* and *mdr1* backbones respectively. Remarkably, the R575I *k13* and Y184F *mdr1* mutations were the predominant variants in the *P. falciparum* populations.

Conclusion: The emerging signal of the R575I polymorphism in the *Pfk13* propeller backbone entails the regular surveillance of molecular markers to inform evidence-based policy decisions. Moreover, the high frequency of the $^{86}N^{184}F$ allele highlights concerns on the plausible decline in efficacy of artemisinin-combination therapies (ACTs); further implying that parasite genotyping from mosquitoes can provide a more relevant scale for quantifying resistance epidemiology in the field.