

Table S1. Primers of the promoter region of *CYP6M2* and *CYP6P4*

Primer name	Sequence 5'-3'	Product size	Annealing T°C
6M2p3i-Fw	5'-AGTACTTCACAGCGCCCAAC-3'	1 020bp	58°C
6M2pr3-Rv	5'-CACCACGATCCTGCCAGTAG-3'		
6M2full-Fw	5'-GTCGGTGGACAGTCAAATTCA-3'	1 600bp	56°C
6M2full-Rv	5'-CTAAATCTTATCCACCTTCAA-3'		
CYP6P4.pr1-Fw	5'-GACACCGTACACGTTTCTGC-3'	835bp	65°C
CYP6P4.pr1-Rv	5'-ATGTACGATGCGTGCTTGGA-3'		
CYP6P4.ful1-Fw	5'-GCGCATGAAAGCTAGGGAT-3'	1 600bp	67°C
CYP6P4.ful2-Rv	5'-ACAGTACACTTACAATTCCTTCGG-3'		

Fw, primers forward, **Rv**, primers reverse.

Table S2. Specific primers of *CYP6M2* and *CYP6P4* diagnostic assays

Mutation	PCR type	Primers/enzymes name and sequence	Annealing T°C	Products size
A/G in <i>CYP6M2</i> promoter	RFLP-PCR	6M2p _{fw} : GAAGCCGATGCTTGAGATAAGA 6M2p _{rv} : CGTGTGTGTCAGGATGAGTT BsrDI: GCAATGNN (incubation, 65°C)	58	D/D: Deletion carriers at 545bp (undigested) I/I: Insertion carriers 2 band 382bp and 167bp
A392S- <i>CYP6M2</i>	AS-PCR	6M2f _w : TGATGAGCAAAGACGGAGAGAAGT 6M2r _v : CATAACGAATCGCAGCCCAAC A392f _w : CGGTACGAAATCCGTCCTGGtGG 392S _r v: GGATCATGACGGCTGTACCcGA	50	392S/S at 527bp A/A392 at 202bp A392S-RS, two bands
A/T in <i>CYP6P4</i> promoter	RFLP-PCR	6p4p1f _w : TCGATCCGAAATCGTTCATACTC 6p4p1r _v : CCGCGTTTACTTGATGGTGTGAG PvuII: CAGCTG (incubation, 37°C)	58	D+/D+ (T/T): Deletion carriers at 548bp (undigested) D-/D-: Insertion carriers 2 band 374bp and 168bp
c/t in in <i>CYP6P4</i> -gene at codon 144	RFLP-PCR	6p4-ful1f _w : GCGCATGAAAGCTAGGGAT 6p4-ful1r _v : GCCAGCTCGTTCATCGTCAG EagI: CGGTCTG (incubation, 37°C)	61,5	t/t at 600bp (undigested) c/c, two bands at 357bp and 269bp
C168S- <i>CYP6P4</i>	AS-PCR	6p4-ful1f _w : GCGCATGAAAGCTAGGGAT 6p4-ful1r _v : GCCAGCTCGTTCATCGTCAG 502A _r v: CCTTCATCTCAATCTCGCGGTGcCT 502Tf _w : CTTGAAGTATATGAACGAGCtCT	57	A168A at 614bp T168T at 426bp A168T-RS, two bands

fw, forward primer; rv, reverse primer; D, Deletion; I, insertion; S, Serine; A, Alanine; C, Cysteine; S, Serine; t, thymine; a, adenine; c, cytosine;

Table S3. Genotype and allele frequencies of 1014F *ldr* mutations in *An. gambiae* and *An. coluzzii* populations

Population	Genotype			N	2N	Allele	
	RR	RS	SS			f(R)	f(S)
<i>An. gambiae</i>							
F ₀	30	0	0	30	60	1.00	0.00
HR F ₄	40	18	0	58	116	0.84	0.16
HS F ₄	1	15	37	53	106	0.16	0.84
<i>An. coluzzii</i>							
F ₀	26	4	0	30	60	0.93	0.07
HR F ₄	18	12	0	30	60	0.80	0.20
HS F ₄	0	4	26	30	60	0.07	0.93

RR, homozygous resistant, **RS**, heterozygous resistant, **SS**, homozygous susceptible.

Table S4. Frequency of key mutations found and genetic variability parameters of *CYP6M2* per allele in *An. gambiae*

Pop.	Region	Position	Sample	Ref. seq.	Mut. Seq.	Aa change	Type of mut.	Mutation freq. (%)	n/N
<i>An. gambiae</i>	upstream	Indel [#]	Kisumu	T(ins.)	C(del.)	n.a	n.a	0.00	0/3
			HS (F4)	T(ins.)	C(del.)	n.a	n.a	0.83	1/6
			HR (F4)	T(ins.)	C(del.)	n.a	n.a	0.88	1/8
	Full-gene	1 252 (codon 392)	Kisumu	GCC	TCC	A/S	NSyn	0.00	0/7
			HS (F ₄)	GCC	TCC	A/S	NSyn	0.57	4/7
			HR (F ₄)	GCC	TCC	A/S	NSyn	0.71	5/7
<i>CYP6M2</i>		Allele	2n	S	H	Hd	π	D	D*
		392S	18	25	11	0.889	0.0059	1.028	1.572
		392A	24	33	9	0.899	0.0089	2.074*	1.668**
		All	42	51	20	0.948	0.0124	2.124*	1.929**

2n, number of sequences (2n* = Sequences were unphased because of the observed heterozygosity); D, Tajima's statistics; D*, Fu and Li's statistics; H, number of haplotypes; Hd, haplotype diversity; Syn, Synonymous mutations; Nsyn, Non-synonymous mutations; π , nucleotide diversity; S, number of polymorphic sites; pKa: Synonymous polymorphism per site; pKs: non-Synonymous polymorphism per site; * = $P < 0.05$; ** = $P < 0.02$; n=number of samples containing mutant allele; N= total number of successfully sequenced samples; n.a, non-available; #, associated to a point mutation at 322 position.

Table S5. Frequency of key mutations found and genetic variability parameters of intergenic region between *CYP6P4* and *CYP6P5* per allele in *An. gambiae*

Pop.	Region	Position	Sample	Ref. seq.	Mut. Seq.	Mutation freq. (%)	n/N
<i>An. gambiae</i>	promoter	Indel [#]	Kisumu	A	T	0.14	1.5/8
			HS (F ₄)	A	T	0.44	4/9
			HR (F ₄)	A	T	1.00	6/6
<i>CYP6P4pr</i>	Allele	2n	S	H(Hd)	π	D	D*
	273-T	21	5	5(0.595)	0.0013	-0.618	1.339
	273-A	23	19	7(0.834)	0.0094	2.108*	1.374**
	All	44	19	11(0.838)	0.0083	2.047*	1.655**

pr, promoter; 2n, 2n, number of sequences (2n* = Sequences were unphased because of the observed heterozygosity); S, number of polymorphic sites; H, number of haplotypes; Hd, haplotype diversity; π, nucleotide diversity; D, Tajima's statistics; D *, Fu and Li's statistics; * = P < 0.05; ** = P < 0.02; n=number of samples containing mutant allele; N = total number of successfully sequenced samples; #, associated to a point mutation at 273 position.

Table S6. Frequency of key mutations found and genetic variability parameters of the upstream region of mutation per allele in *An. gambiae*

Pop.	Region	Position	Sample	Ref. seq.	Mut. Seq.	Aa change	Type of mut.	Mutation freq. (%)	n/N
<i>An. gambiae</i>	Full-gene	432	Kisumu	GGC	GGT	G/G	Syn	0.20	2/10
		(codon 144)	HS (F ₄)	GGC	GGT	G/G	Syn	0.28	4.5/9
			HR (F ₄)	GGC	GGT	G/G	Syn	0.95	9.5/10
		502	Kisumu	TGC	AGC	C/S	NSyn	0.15	1.5/10
		(codon 168)	HS (F ₄)	TGC	AGC	C/S	NSyn	0.27	2.5/9
			HR (F ₄)	TGC	AGC	C/S	NSyn	0.70	7/10
		Alleles	2n	S	H	Hd	π	D	D*
<i>CYP6P4</i>	144-T	32	17	19	0.920	0.005	0.665	1.365	
	144-C	26	13	15	0.950	0.005	1.854	1.330	
	168S	22	12	11	0.861	0.0033	1.096	1,470	
	168C	36	14	22	0.968	0.0053	2.128*	1,441**	
	All	58	17	33	0.970	0.0062	2.385*	1.632**	

2n, number of sequences (2n* = Sequences were unphased because of the observed heterozygosity); D, Tajima's statistics; D *, Fu and Li's statistics; H, number of haplotypes; Hd, haplotype diversity; Syn, Synonymous mutations; NSyn, Non-synonymous mutations; π , nucleotide diversity; S, number of polymorphic sites; pKa: Synonymous polymorphism per site; pKs: non-Synonymous polymorphism per site; * = $P < 0.05$; ** = $P < 0.02$; n=number of samples containing mutant allele; N = total number of successfully sequenced samples.