

Table S1: List of primers used in the study

	Forward primer	Reverse primer	Expected size (bp)
<b>qRT-PCR primers</b>			
<i>GSTe2</i>	GTTTGAAGCAGTTGCCATACTACGAGG	TCAAGCTTTAGCATTTCCTCCTTTTTGG C	101
<i>CYP6P9a</i>	CAGCGCGTACACCAGATTGTGTAA	TCA CAA TTT TTC CAC CTT CAA GTA ATT ACC CGC	92
<i>CYP6P9b</i>	CAGCGCGTACACCAGATTGTGTAA	TTA CAC CTT TTC TAC CTT CAA GTA ATT ACC CGC	97
<i>CYP9J11</i>	CAAATTTAAAGAGTGCGCTAGG	GTAGATGGTGCCAAGGATGG	115
<i>Actin</i>	TTAAACCCAAAAGCCAATCG	ACCGGATGCATACAGTGACA	111
<i>RSP7</i>	GTGTTTCGGTTCCAAGGTGAT	TCCGAGTTCATTTCAGCTC	98
<b>Primers for functional analysis</b>			
<i>GSTe2</i>	<b>AGATCT</b> ATGACCAAGCTAGTTCTGTAC ACGCT GAATTC <b>CATATG</b> ACCAAGCTAGTTCTG TACACGCT	<b>TCTAGA</b> TCAAGCTTTAGCATTTCCTCCT TTTTGGC CCG <b>CTCGAG</b> TCAAGCTTTAGCATTTC TCCTTTTTGGC	
<i>CYP9J11</i>			
<i>CYP9J11Full</i>	ATG GAG ATC GAT TTG ATG GTT CT	TTA CAT ACT AAC TTC GTT ATC TTT CTT TCT AGG	
<i>ompA+2F</i>	<b>GGAATTC</b> <b>CATATG</b> AAAAAAGACAGCTA TCGCG		
<i>ompA+2CYP9J11_F</i>	AACCATCAAATCGATCTCCATCGGAGC GGCCTGCGCTACGGTAGCGAA		
<i>ompA+2CYP9J11_R</i>		<b>TCTAGATCTAGATTACATACTAACTTCGTTATCTT</b> TC	
<b>Primers used for amplification for polymorphism analysis</b>			
<i>CYP6P9a</i>	ATCCCTAACTATTTAAAGGCAAT	TCACAATTTTTCCACCTTCAAGTAATTACCCGC	2.2
<i>CYP6P9b</i>	CATACTATAATACTAGACGCG	TTACACTTTTCTACCTTCAAGTAATTACCCGC	1.8

In red is restriction site for *Bgl*III; in green is for *Xba*I; blue is for *Nde*I; purple is for *Xho*I; *Eco*RI is dark brown.

**Table S2: Detoxification genes commonly up-regulated only in two countries between Uganda (UG), Malawi (MAL) and Benin (BN)**

Probe Name			UG	MAL	BN	Description
CUST_13921_PI426302897	Afun013921	AGAP006709-PA	49.5		27.4	chymotrypsin 1
CUST_11037_PI426302897	Afun011037	AGAP003581-PA	8.0		13.1	alcohol dehydrogenase
CUST_12461_PI426302897	Afun012461	AGAP000288-PA	6.8		10.5	alcohol dehydrogenase
CUST_6368_PI426302897	Afun006368	AGAP003785-PB	6.4		3.2	glucose dehydrogenase
CUST_15244_PI426302897	Afun015244	AGAP000820-PA	5.9		4.1	cuticular protein rr-1 family
CUST_13481_PI426302897	Afun013481 (GSTe1)	AGAP009195-PA	5.6		2.3	glutathione-s-transferase gst
CUST_8354_PI426302897	Afun008354 (GSTD3)	AGAP004382-PA	5.1		4.3	glutathione transferase
CUST_3731_PI406199772	CD577517.1		4.7		2.1	cuticle protein
CUST_1088_PI406199772	EE590086.1		4.5		2.6	d7-related 1 protein
CUST_15331_PI426302897	Afun015331	AGAP001039-PB	3.9		29.4	cytochrome p450 307a1
CUST_3736_PI406199772	CD577515.1		3.8		3.3	cuticle protein
CUST_12666_PI426302897	Afun012666	AGAP002429-PA	3.7		3.8	cytochrome p450
CUST_7722_PI426302897	Afun007722	AGAP009850-PA	3.6		2.8	abc transporter
CUST_5005_PI406199798	AGAP003680-RA	AGAP003680-RA	3.5		3.4	abc transporter
CUST_574_PI406199772	EE589639.1		3.2		5.4	d7-related 1 protein
CUST_4392_PI426302897	Afun004392	AGAP008213-PA	2.7		2.6	cytochrome p450
CUST_143_PI426302897	Afun000143	AGAP000818-PA	2.4		2.7	cytochrome p450 cyp9k1
CUST_13218_PI426302897	Afun013218	AGAP000284-PA	2.3		2.3	cytochrome p450
CUST_10836_PI426302897	Afun010836	AGAP006228-PA	2.3		3.7	esterase b1
CUST_45_PI426302897	Afun000045 (GSTe2)	AGAP009194-PA	2.1		12.2	glutathione-s-transferase gst
CUST_13870_PI426302897	Afun013870	AGAP012697-PA	14.8	7.5		sulfotransferase
CUST_12777_PI426302897	Afun012777	AGAP009246-PA	10.3	2.1		cytochrome p450
CUST_9_PI426302915	CYP6M4.seq		9.2	5.3		cytochrome p450
CUST_9492_PI426302897	Afun009492	AGAP001722-PA	8.8	5.9		carboxylesterase
CUST_15523_PI426302897	Afun015523	AGAP010581-PA	5.7	3.1		abc transporter

CUST_979_PI426302897	Afun000979	AGAP006711-PA	4.5	3.7	chymotrypsin 1
CUST_1149_PI406199772	EE590022.1		4.4	2.4	d7-related 1 protein
CUST_3836_PI406199772	CD577459.1		4.3	3.6	cuticle protein
CUST_13272_PI406199769	combined_c6791		4.2	4.8	cytochrome p450
CUST_3830_PI406199772	CD577462.1		4.2	2.7	cuticle protein
CUST_11963_PI426302897	Afun011963	AGAP006220-PA	4.0	2.8	aldehyde oxidase
CUST_4920_PI406199772	BU038983.1		3.8	2.6	cuticle protein
CUST_1150_PI406199772	EE590022.1		3.7	2.3	d7-related 1 protein
CUST_13273_PI406199769	combined_c6791		3.6	4.2	cytochrome p450
CUST_7_PI426302915	CYP6M3.seq		2.9	10.1	cytochrome p450
CUST_1687_PI406199772	EE589439.1		2.9	5.7	d7-related 1 protein
CUST_7127_PI426302897	Afun007127	AGAP009241-PA	2.6	2.4	cytochrome p450
CUST_7008_PI426302897	Afun007008	AGAP012156-PA	2.6	2.2	ABC transporter
CUST_5935_PI406199769	combined_c3002		2.4	2.7	superoxide dismutase
CUST_7482_PI426302897	Afun007482	AGAP002693-PA	2.4	2.3	ABC transporter
CUST_12478_PI426302897	Afun012478	AGAP005757-PA	2.2	3.1	carboxylesterase
CUST_7696_PI406199798	AGAP008141- RA__3R	AGAP008141- RA	2.2	8.5	argininosuccinate lyase
CUST_3394_PI426302897	Afun003394	AGAP000284-PA	2.1	2.4	cytochrome p450
CUST_7499_PI426302897	Afun007499 (GSTD1-5)	AGAP004164-PA	2.1	2.9	glutathione transferase
CUST_27_PI406199775	CYP6P9a		39.4	4.3	cytochrome p450
CUST_30_PI406199775	CYP6P9b		24.0	4.1	cytochrome p450
CUST_25_PI406199775	CYP6P9a		16.3	3.4	cytochrome p450
CUST_1096_PI406199769	combined_c557		11.8	3.8	trypsin
CUST_26_PI406199775	CYP6P9a		9.8	2.7	cytochrome p450
CUST_13614_PI426302897	Afun013614	AGAP003446-PA	8.3	4.0	zinc finger protein 616
CUST_13328_PI426302897	Afun013328	AGAP000384-PA	8.0	2.2	zinc finger protein 650
CUST_8241_PI406199769	combined_c4173		4.8	3.7	glycoprotein 93

CUST_200_P1426302897	Afun000200	AGAP004038-PA	3.5	2.2	chorion peroxidase
CUST_1823_P1406199769	combined_c920		3.4	9.4	glutathione-s-transferase
CUST_431_P1406199788	gb-CYP6M3		2.9	2.6	cytochrome p450
CUST_10614_P1426302897	Afun010614	AGAP006380-PA	2.5	3.0	ABC transporter
CUST_1182_P1406199772	EE589982.1		2.3	2.4	d7-related 1 protein
CUST_7646_P1426302897	Afun007646	AGAP006225-PA	2.0	4.0	aldehyde oxidase

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**Table S3:** Summary statistics for polymorphism of *CYP6P9a* and *CYP6P9b* between the FANG susceptible and the resistant strains from Malawi and Mozambique

Samples	N	S	h	Syn	Nonsyn	$\pi$ (k)	D (Tajima)	D* (Fu and Li)
<i>CYP6P9a</i>								
Uganda Alive	14	41	7	26	8	0.008 (16.05)	1.07 <sup>ns</sup>	1.4 <sup>*</sup>
Uganda dead	12	15	8	8	6	0.0024 (4.8)	-0.14 <sup>ns</sup>	-0.44 <sup>ns</sup>
All Uganda	26	50	15	30	14	0.0061 (12.1)	-0.35 <sup>ns</sup>	0.88 <sup>ns</sup>
Malawi	20	13	5	4	2	0.001(1.98)	-1.65 <sup>ns</sup>	-1.98 <sup>ns</sup>
Total	46	61	20	33	16	0.01(20.1)	1.4 <sup>ns</sup>	0.05 <sup>ns</sup>
<i>CYP6P9b</i>								
Uganda Alive	16	42	2	22	7	0.003(5.25)	-2.45 <sup>***</sup>	-3.5 <sup>**</sup>
Uganda dead	14	43	3	23	7	0.0029 (6.26)	-2.34 <sup>***</sup>	-3.1 <sup>**</sup>
All Uganda	30	45	4	25	7	0.003 (5.5)	-1.89 <sup>*</sup>	1.19 <sup>ns</sup>
Malawi	20	12	2	6	3	0.0007(1.2)	-2.3 <sup>**</sup>	-3.5 <sup>**</sup>
Total	50	73	6	44	12	0.012(21.43)	0.98 <sup>ns</sup>	1.09 <sup>ns</sup>

N= number of sequences (n); S, number of polymorphic sites; Syn, Synonymous mutations; Nonsyn, Non-synonymous mutations;  $\pi$ , nucleotide diversity (k= mean number of nucleotide differences); Tajima's D and Fu and Li's D statistics, ns, not significant.