

Table S1. Mean EC₅₀ values (nanomolar) with 95% confidence intervals (CIs) for lumefantrine (LUM), halofantrine (HLF), mefloquine (MEF), and chloroquine (CQ). Color represents presence of the 803 (green) or GB4 (yellow) *pfmdr1* allele.

Clone	LUM			HLF			MEF			CQ		
	EC ₅₀	95% CI	n	EC ₅₀	95% CI	n	EC ₅₀	95% CI	n	EC ₅₀	95% CI	n
803	3.21	2.80 -- 3.66	6	1.48	1.35 -- 1.61	4	31.67	29.0 -- 34.6	7	147.9	143.7 -- 152.3	5
GB4	0.55	0.46 -- 0.67	5	0.32	0.29 -- 0.35	7	10.84	10.5 -- 11.2	6	74.0	68.2 -- 80.3	3
11C2	0.78	0.67 -- 0.91	3	0.83	0.53 -- 1.28	3	7.99	6.4 -- 10.0	3	67.9	61.2 -- 75.4	3
24G11	1.49	1.36 -- 1.64	3	2.38	2.09 -- 2.61	3	8.85	8.1 -- 9.6	3	152.8	151.5 -- 154.1	3
36D5	1.83	1.73 -- 1.93	4	1.52	1.42 -- 1.64	3	22.95	20.6 -- 25.7	4	132.3	127.8 -- 137.0	3
36E5	2.94	2.54 -- 3.39	4	2.11	1.94 -- 2.29	4	31.11	25.4 -- 39.0	5	92.0	88.2 -- 96.1	3
36F11	0.76	0.68 -- 0.85	3	1.48	1.34 -- 1.63	3	7.82	6.4 -- 9.5	3	89.3	86.7 -- 92.0	3
36H9	1.51	1.15 -- 1.89	4	0.41	0.34 -- 0.48	3	18.25	7.6 -- 34.0	3	50.0	45.5 -- 55.0	3
37D9	1.13	0.93 -- 1.36	3	0.68	0.61 -- 0.75	3	14.94	10.9 -- 20.7	4	112.2	108.5 -- 116.0	3
38G5	2.69	2.35 -- 3.09	3	2.64	2.55 -- 2.74	3	28.72	24.8 -- 33.4	3	99.1	96.1 -- 102.2	3
39C3	0.76	0.67 -- 0.85	3	0.49	0.45 -- 0.54	3	7.76	6.0 -- 10.1	3	47.1	44.6 -- 49.7	3
39C5	4.19	3.80 -- 4.64	3	3.78	2.99 -- 4.85	3	29.89	28.9 -- 30.9	3	60.0	44.5 -- 80.7	3
39H5	2.73	2.37 -- 3.15	3	0.95	0.86 -- 1.04	4	21.91	19.3 -- 24.9	5	52.8	40.3 -- 69.2	4
40E7	3.07	2.39 -- 3.99	4	1.99	1.80 -- 2.21	3	33.88	26.1 -- 45.6	4	93.3	84.6 -- 102.8	4
43A6	0.76	0.67 -- 0.85	4	0.53	0.48 -- 0.58	3	9.03	7.6 -- 10.7	4	133.3	115.6 -- 153.6	3
43E5	3.30	3.05 -- 3.57	4	3.10	2.86 -- 3.38	3	41.13	35.6 -- 47.7	4	42.2	36.9 -- 48.1	3
44D4	1.24	1.19 -- 1.29	4	1.03	0.91 -- 1.15	4	8.90	6.8 -- 11.7	5	111.4	108.8 -- 114.0	4
44F6	0.82	0.71 -- 0.94	3	0.59	0.54 -- 0.64	3	11.05	9.0 -- 13.6	5	62.2	60.7 -- 63.8	4
46G9	0.76	0.70 -- 0.82	4	0.42	0.40 -- 0.46	3	10.44	8.5 -- 12.8	4	70.5	68.4 -- 72.7	3
48C1	0.69	0.60 -- 0.80	4	0.32	0.29 -- 0.35	5	9.31	5.7 -- 14.5	5	88.8	87.0 -- 90.6	3
61D3	0.97	0.87 -- 1.08	4	1.96	1.75 -- 2.19	3	11.23	8.4 -- 14.9	4	49.5	47.2 -- 51.8	4
76H10	0.97	0.88 -- 1.07	3	0.87	0.79 -- 0.96	3	10.83	9.0 -- 13.0	3	147.1	137.2 -- 157.7	3
85G7	5.21	4.72 -- 5.77	4	3.30	2.84 -- 3.60	4	47.08	39.3 -- 57.4	4	78.2	72.3 -- 84.6	3
87E7	2.79	2.49 -- 3.13	3	1.38	0.99 -- 2.04	3	19.64	16.6 -- 23.4	3	69.7	60.3 -- 80.7	3

Table S2. Mean DTR values (days) and 95% confidence intervals from lumefantrine (LUM) assays of the 803×GB4 parasites. Color indicates inheritance of the 803 (green) or GB4 (yellow) *pfmdr1* allele.

Clone	LUM		
	DTR	95% CI	n
803	3.8	2.8 -- 4.8	5
GB4	17.0	15.0 -- 16.6	5
11C2	19.2	16.7 -- 21.7	5
24G11	14.0	2.0 -- 13.8	5
36D5	10.3	6.4 -- 11.3	3
36E5	8.0	1.1 -- 13.9	4
36F11	15.8	12.5 -- 17.5	4
36H9	7.0	4.2 -- 7.1	2
37D9	14.0	11.4 -- 16.6	4
38G5	5.7	3.5 -- 7.6	3
39C3	18.3	15.5 -- 21.0	4
39C5	5.5	2.4 -- 7.1	4
39H5	8.8	6.9 -- 9.8	6
40E7	7.5	0.2 -- 12.9	2
43A6	14.0	10.3 -- 17.7	4
43E5	4.8	2.3 -- 6.3	4
44D4	19.0	16.5 -- 21.5	3
44F6	14.0	10.6 -- 17.4	4
46G9	21.3	16.2 -- 26.5	3
48C1	18.0	13.7 -- 22.3	3
61D3	12.4	8.9 -- 11.8	5
76H10	15.0	11.4 -- 16.6	3
85G7	4.3	16.1 -- 17.9	4
87E7	8.3	5.1 -- 10.9	3

Table S3. List of 117 predicted genes within a ~500 kb region of the *Plasmodium falciparum* chromosome 5 region linked to EC₅₀ and DTR measures of lumefantrine (LUM) response. The *pfmdr1* gene, located near the maximal LOD at 966,290 is indicated in bold font. The locations and descriptions of the genes are from PlasmoDB.

[Gene ID]	[Genomic Location]	[Product Description]
PF3D7_0516800	700,120 - 707,256	AP2 domain transcription factor AP2-O2, putative
PF3D7_0516900	712,762 - 713,772	60S ribosomal protein L2
PF3D7_0517000	715,765 - 716,675	60S ribosomal protein L12, putative
PF3D7_0517100	718,425 - 719,855	conserved protein, unknown function
PF3D7_0517200	720,743 - 722,641	conserved Plasmodium protein, unknown function
PF3D7_0517300	724,681 - 725,751	serine/arginine-rich splicing factor 1
PF3D7_0517400	731,407 - 735,162	FACT complex subunit SPT16, putative
PF3D7_0517500	735,887 - 738,400	UTP--glucose-1-phosphate uridylyltransferase, putative
PF3D7_0517600	740,156 - 741,034	F-actin-capping protein subunit beta, putative
PF3D7_0517700	743,179 - 745,329	eukaryotic translation initiation factor 3 subunit B, putative
PF3D7_0517800	745,798 - 746,634	apicortin, putative
PF3D7_0517900	747,795 - 749,677	zinc finger protein, putative
PF3D7_0518000	750,661 - 752,435	NOSIP domain-containing protein, putative
PF3D7_0518100	753,298 - 757,544	protein AMR2
PF3D7_0518200	758,503 - 758,898	SWIB/MDM2 domain-containing protein
PF3D7_0518300	759,831 - 760,998	proteasome subunit beta type-1, putative
PF3D7_0518400	762,103 - 762,792	cyclin, putative
PF3D7_0518500	763,532 - 766,903	ATP-dependent RNA helicase DDX23, putative
PF3D7_0518600	769,310 - 773,140	WD repeat-containing protein 26, putative
PF3D7_0518700	774,075 - 780,438	mRNA-binding protein PUF1
PF3D7_0518800	783,638 - 784,991	secreted ookinete protein, putative
PF3D7_0518900	785,664 - 786,565	conserved protein, unknown function
PF3D7_0519000	788,599 - 789,480	histone RNA hairpin-binding protein, putative
PF3D7_0519100	790,399 - 790,773	50S ribosomal protein L14, mitochondrial, putative
PF3D7_0519200	791,719 - 792,936	V-type proton ATPase 16 kDa proteolipid subunit
PF3D7_0519300	795,527 - 797,473	protoheme IX farnesyltransferase, putative

PF3D7_0519400	798,036 - 798,775	40S ribosomal protein S24
PF3D7_0519500	801,450 - 809,127	CCR4 domain-containing protein 1, putative
PF3D7_0519600	812,648 - 814,915	zinc finger protein, putative
PF3D7_0519700	817,066 - 819,139	FoP domain-containing protein, putative
PF3D7_0519800	820,719 - 822,908	EELM2 domain-containing protein, putative
PF3D7_0519900	825,835 - 827,412	conserved protein, unknown function
PF3D7_0520000	828,953 - 829,883	40S ribosomal protein S9, putative
PF3D7_0520100	831,617 - 834,343	protein phosphatase PPM9, putative
PF3D7_0520200	835,314 - 837,407	mediator of RNA polymerase II transcription subunit 17, putative
PF3D7_0520300	838,428 - 839,083	U6 snRNA-associated Sm-like protein LSm2, putative
PF3D7_0520400	839,655 - 840,560	single-stranded DNA-binding protein, putative
PF3D7_0520500	841,723 - 842,655	phosphomethylpyrimidine kinase, putative
PF3D7_0520600	843,586 - 844,817	bis(5'-nucleosyl)-tetraphosphatase [asymmetrical]
PF3D7_0520700	845,843 - 848,767	CDC73 domain-containing protein, putative
PF3D7_0520800	849,862 - 856,026	conserved protein, unknown function
PF3D7_0520900	857,038 - 858,477	Adenosylhomocysteinase
PF3D7_0521000	859,373 - 861,063	conserved Plasmodium protein, unknown function
PF3D7_0521100	861,930 - 867,583	conserved Plasmodium protein, unknown function
PF3D7_0521200	868,892 - 869,878	conserved protein, unknown function
PF3D7_0521300	870,184 - 874,570	zinc finger protein, putative
PF3D7_0521400	875,873 - 877,561	conserved protein, unknown function
PF3D7_0521500	878,068 - 879,762	ribosomal large subunit pseudouridylate synthase, putative
PF3D7_0521600	880,065 - 880,355	conserved Plasmodium protein, unknown function
PF3D7_0521700	882,376 - 884,901	ATP-dependent RNA helicase DDX1, putative
PF3D7_0521800	885,714 - 888,232	AFG1-like ATPase, putative
PF3D7_0521900	888,657 - 895,144	conserved Plasmodium protein, unknown function
PF3D7_0522000	896,018 - 896,940	conserved Plasmodium protein, unknown function
PF3D7_0522100	897,465 - 899,756	conserved Plasmodium protein, unknown function
PF3D7_0522200	901,414 - 902,173	transcription initiation factor TFIID subunit 10, putative
PF3D7_0522300	902,613 - 904,844	18S rRNA (guanine-N(7))-methyltransferase, putative
PF3D7_0522400	907,837 - 936,315	conserved Plasmodium protein, unknown function

PF3D7_0522500	937,231 - 938,037	50S ribosomal protein L17, apicoplast, putative
PF3D7_0522600	940,249 - 941,700	inner membrane complex protein
PF3D7_0522700	942,767 - 943,873	iron-sulfur assembly protein
PF3D7_0522800	944,184 - 944,931	pre-mRNA-splicing factor BUD31, putative
PF3D7_0522900	948,951 - 953,609	zinc finger protein, putative
PF3D7_0523000	957,890 - 962,149	multidrug resistance protein 1
PF3D7_0523100	963,227 - 965,044	mitochondrial-processing peptidase subunit alpha, putative
PF3D7_0523200	966,123 - 969,737	heptatricopeptide repeat-containing protein, putative
PF3D7_0523300	970,266 - 970,962	cytochrome c oxidase subunit ApiCOX18, putative
PF3D7_0523400	973,518 - 975,876	DnaJ protein, putative
PF3D7_0523500	976,690 - 977,815	dynein light chain Tctex-type, putative
PF3D7_0523600	978,665 - 979,870	conserved protein, unknown function
PF3D7_0523700	980,754 - 985,354	conserved Plasmodium membrane protein, unknown function
PF3D7_0523800	990,005 - 992,059	divalent metal transporter, putative
PF3D7_0523900	993,433 - 994,607	MerC domain-containing protein, putative
PF3D7_0524000	998,753 - 1,002,124	karyopherin beta
PF3D7_0524100	1,004,237 - 1,008,108	conserved Plasmodium protein, unknown function
PF3D7_0524200	1,008,636 - 1,009,404	conserved Plasmodium membrane protein, unknown function
PF3D7_0524300	1,010,951 - 1,012,171	conserved Plasmodium protein, unknown function
PF3D7_0524400	1,013,453 - 1,014,550	ribosome-interacting GTPase 1, putative
PF3D7_0524500	1,016,198 - 1,016,569	conserved Plasmodium protein, unknown function
PF3D7_0524600	1,017,809 - 1,018,582	50S ribosomal protein L12, apicoplast, putative
PF3D7_0524700	1,019,585 - 1,019,902	mitochondrial import receptor subunit TOM22, putative
PF3D7_0524800	1,021,408 - 1,024,307	ubiquitin fusion degradation protein 1, putative
PF3D7_0524900	1,027,396 - 1,030,362	S-adenosyl-L-methionine-dependent tRNA 4-demethylwyosine synthase
PF3D7_0525000	1,036,229 - 1,038,343	zinc finger protein, putative
PF3D7_0525100	1,041,745 - 1,043,766	acyl-CoA synthetase
PF3D7_0525200	1,045,462 - 1,051,253	structural maintenance of chromosomes protein 6, putative
PF3D7_0525300	1,052,468 - 1,053,913	conserved protein, unknown function
PF3D7_0525400	1,057,651 - 1,059,054	7-helix-1 protein
PF3D7_0525500	1,059,918 - 1,065,509	WD repeat-containing protein, putative

PF3D7_0525600	1,066,526 - 1,067,712	RNA methyltransferase, putative
PF3D7_0525700	1,068,516 - 1,069,285	conserved protein, unknown function
PF3D7_0525800	1,071,247 - 1,072,149	inner membrane complex protein 1g, putative
PF3D7_0525900	1,073,646 - 1,075,644	NIMA related kinase 2
PF3D7_0526000	1,075,913 - 1,078,333	RAP protein, putative
PF3D7_0526100	1,079,779 - 1,081,008	conserved Plasmodium membrane protein, unknown function
PF3D7_0526200	1,081,558 - 1,083,816	ADP-ribosylation factor GTPase-activating protein, putative
PF3D7_0526200	1,081,558 - 1,083,816	ADP-ribosylation factor GTPase-activating protein, putative
PF3D7_0526300	1,085,623 - 1,086,594	WD repeat-containing protein 55, putative
PF3D7_0526400	1,088,423 - 1,089,508	conserved Plasmodium protein, unknown function
PF3D7_0526500	1,090,930 - 1,095,084	conserved Plasmodium protein, unknown function
PF3D7_0526600	1,101,203 - 1,114,777	conserved Plasmodium protein, unknown function
PF3D7_0526700	1,117,261 - 1,119,651	conserved protein, unknown function
PF3D7_0526800	1,120,704 - 1,121,810	conserved Plasmodium protein, unknown function
PF3D7_0526900	1,123,610 - 1,124,595	transmembrane emp24 domain-containing protein, putative
PF3D7_0527000	1,125,099 - 1,128,146	DNA replication licensing factor MCM3, putative
PF3D7_0527100	1,129,959 - 1,130,754	ubiquitin-conjugating enzyme E2 N, putative
PF3D7_0527200	1,132,937 - 1,134,854	ubiquitin carboxyl-terminal hydrolase 14
PF3D7_0527300	1,135,976 - 1,137,870	methionine aminopeptidase 1a, putative
PF3D7_0527400	1,140,627 - 1,141,154	conserved Plasmodium protein, unknown function
PF3D7_0527500	1,143,618 - 1,145,359	Hsc70-interacting protein
PF3D7_0527600	1,145,857 - 1,148,810	conserved Plasmodium protein, unknown function
PF3D7_0527700	1,150,234 - 1,150,306	tRNA Glutamic acid
PF3D7_0527800	1,151,227 - 1,151,309	tRNA Leucine
PF3D7_0527900	1,153,676 - 1,155,673	ATP-dependent RNA helicase DDX41, putative
PF3D7_0528000	1,156,205 - 1,156,579	proteasome maturation factor UMP1, putative
PF3D7_0528100	1,157,840 - 1,161,553	AP-1 complex subunit beta, putative
PF3D7_0528200	1,163,408 - 1,165,072	eukaryotic translation initiation factor 3 subunit E, putative
PF3D7_0528300	1,166,520 - 1,168,010	conserved protein, unknown function

Table S4. Results of *pfmdr1* copy number analysis* of *Plasmodium falciparum* lines 3D7, Dd2, 76H10, GB4 and 803.

Clone	Ct-FAM	Ct-Cy5	dCt	IndivCopy	Spread	dCT	Max CT	Mean CTs	Comment	OVERALL MEAN	Calibrator 1 Copy No.	Calibrator 2 Copy No.	Calibrator 3 Copy No.
3D7 3/1/2013	31.99	31.37	0.62	0.42	0.18	32.04	31.64	Ok	0.79	1.00	0.40	0.98	
	32.04	31.39	0.65	0.41									
	31.93	31.13	0.8	0.37									
DD2 3/1/2013	30.68	31.34	-0.66	2.55	0.16	31.34	30.93	Ok	1.99	2.50	1.00	2.46	
	30.54	31.24	-0.7	2.62									
	30.63	31.17	-0.54	2.35									
76H10	29.86	29.23	0.63	1.04	0.11	30.37	29.86	Ok	0.81	1.02	0.41	1.00	
	30.36	29.73	0.63	1.04									
	30.37	29.63	0.74	0.97									
GB4	30.39	29.68	0.71	0.99	0.03	30.39	29.94	Ok	0.79	0.99	0.40	0.98	
	30.23	29.52	0.71	0.99									
	30.24	29.56	0.68	1.01									
CP803 control	31.73	31.05	0.68	1.01	0.30	34.16	32.72	Ok	0.73	0.92	0.37	0.90	
	33.5	32.72	0.78	0.94									
	34.16	33.18	0.98	0.82									
CP803 60nM	29.99	29.3	0.69	1.00	0.04	30.15	29.67	Ok	0.79	0.99	0.40	0.97	
	29.93	29.2	0.73	0.97									
	30.15	29.45	0.7	0.99									

* Copy number determinations were performed using the using the oligonucleotide primers and methods of Price *et al.* (2004, Mefloquine resistance in *Plasmodium falciparum* and increased *pfmdr1* gene copy number. *Lancet* 364, 438-447).