Supplementary Information Contents

Supplementary Tables

Country	Institute	Ethics approving institution	Ethics committee	local ID(s)
Gambia	MRC Laboratories	MRC Gambia	MRC Ethics Committee	SCC 1029v2 SCC670/630
Mali	University of Bamako	University of Bamako, FMPOS, MRTC	FMPOS REC	No/18/FMPOS No/06-18bis/FMPOS
Burkina Faso	Centre National de Recherche et de Formation sur le Paludisme	Ministry of Health & Ministry of Science and Education	Health Research Ethics Committee	No 2007-048
Ghana (Navrongo)	Navrongo Memorial Institute for Medical Research with Navrongo Health Research Centre	Navrongo	Navrongo IRB	NMIMR-IRB CPN 016/01-02 NMIMR-IRB CPN 029/05-06
Ghana (Kumasi)	Kwame Nkrumah University of Science and Technology	Ghana Health Service	GHS ERC	GHS-ERC-03/9/06
		School Medical Sciences, KNUST	Committee on Human Research Publication and Ethics	CHRPF/07/01/06 CHRPE SMS UST dated 24-05-2007
Nigeria	University of Ibadan (UI)	Institute of Child Health, College of Medicine, University of Ibadan	UI/UCH Ethics committee	UI/IRC/06/0034
Cameroon	University of Buea	University of Buea	IRB	University of Buea ethical clearance 07-12-2005
		Govt of Cameroon	Provincial Delegate for Public Health	D7.1.A/MPH/SWP/PDPH /PS.CH/2340/811
Kenya	KEMRI-Wellcome Research Programme	KEMRI, Kilifi	KEMRI REC	SCC1192
Tanzania	Joint Malaria Programme, Kilimanjaro Christian Medical Centre	London School Hygiene and Tropical Medicine	LSHTM ERC	4093
		NIMR	NIMR Research Coordinating Committee	NIMR/HQ/R.8a/Vol. IX/513
Malawi	Blantyre Malaria Project with Malawi-Liverpool-Wellcome Programme	University of Malawi, College of Medicine	CoM REC	P.05/06/442
Viet Nam	Oxford University Clinical Research Unit	Hospital Tropical Diseases	REC	SECHTD dated 20/04/2006
Papua New Guinea	Papua New Guinea Institute for Medical Research	Govt PNG	PNG Medical Research Advisory Committee	MRAC No:06.21
		PNG IMR	PNG IMR IRB	IMR IRB 0603
UK	Oxford University	Oxford University	OXTREC	OXTREC 020-06

Supplementary Table 1: Partner sites. Partner sites for MalariaGEN Consortial Project 1 (Genetic Determinants of Resistance to Malaria) with details of the partner institution and local approving bodies. Supplementary Figure 5 shows a map of these Partner sites (http://www.malariagen.net/projects/cp1).

Country	Study Design
Gambia	**Unmatched Case-Control study.** **2801 cases** - recruited from hospitals in/near Banjul. **4527 controls** - cord blood samples were collected from labour wards of various hospitals primarily in western division of the country. Other samples were sampled from Gambian Biobank blood donors.
Mali	**Matched Case-Control study.** **510 cases** - recruited from a hospital in Bamako. **389 controls** - recruited from community, individually matched to cases by age, ethnicity, place of residence & duration of residence
Burkina Faso	**Unmatched Case-Control study.** **983 cases** - recruited from hospitals in Ouagadougou. **816 controls** - recruited from rural villages near Ouagoadougou
Ghana (Navrongo/Noguchi)	**Matched Case-control study.** **2459 cases** - recruited from hospitals in Kassena-Nankana District. **2129 controls** - selected from demographic surveillance system in same district, some frequency & some individually matched to cases by age, gender, location & ethnicity
Ghana (Kumasi)	**Unmatched Case-Control study.** **1923 cases** recruited from hospitals in Kumasi. **2326 controls** are cord bloods recruited from labour wards in Kumasi.
Nigeria	**Unmatched Case-Control study.** **114 cases** - recruited from hospitals in Ibadan. **88 controls** - recruited from communities in areas surrounding hospitals from which cases recruited
Cameroon	**Unmatched Case-Control study.** **914 cases** - recruited from hospitals/health centres in South-West, Litteral & Central Regions. **914 controls** - recruited from schools in South-West Region and blood bank in Central Region
Kenya	**Unmatched Case-Control study.** **2741 cases** - recruited from Kilifi District Hospital. **4183 controls** - recruited from demographic surveillance system representative of area in which cases reside
Tanzania	**Matched Case-Control study.** **501 cases** - recruited from a hospital in Muheza. **504 controls** - recruited from community, individually matched to cases by ethnicity of at least one parent, electorial ward of residence & age
Malawi	**Unmatched Case-Control study.** **1815 cases** - recruited from a hospital in Blantyre. **3272 controls** - cord blood samples taken from same hospital as cases
Viet Nam	**Case-control study.** **1014 cases** - recruited from a hospital in Ho Chi Minh City & provincial hospitals in Southern Vietnam. **2791 controls** - recruited from community, individually matched to cases by age, gender, ethnicity & location, & cord blood samples taken from a hospital in Ho Chi Minh City and a hospital in Dong Thap province
PNG	**Matched Case-Control study.** **658 cases** - recruited from main hospital in Madang province. **553 controls** - recruited from community, individually matched to cases by ethnicity, age, gender & residence, & from children with chronic minor skin infections presenting to clinics near residence of case, individually matched to cases by age, gender and ethnicity where possible
Total	**16433 cases** **22492 controls**

Supplementary Table 2: Summary study design descriptions of contributing partner studies to MalariaGEN Consortial Project 1 (CP1). Data incudes total numbers of cases and controls collected at each site preceding the filtering process as described in the Methods section. Further information for each site and study can be found on the MalariaGEN web site (see URLs)

	Cases			Controls		
Study site	**Number**	**% Males**	**Age in Years Median(IQR)**	**Number**	**% Males**	**Age in Years Median(IQR)**
Gambia	2425	52	3.8(2.2-4.3)	3342	50	0(0-0)
Mali	453	56	3(1.7-3.7)	344	51	3.1(2-3.8)
Burkina Faso	865	57	3.7(2-4.4)	729	52	3(2-2.7)
Ghana (Kumasi)	682	57	1.3(0.9-1.6)	489	56	1.2(0.8-1.4)
Ghana (Navrongo)	1496	54	2(1-2.8)	2042	52	0(0-0)
Nigeria	77	61	2.9(1.6-3.3)	40	45	2.6(1.2-3.1)
Cameroon	621	54	2.1(1.2-3.1)	578	72	21(7.6-19.2)
Kenya	2268	52	2.2(1.2-2.7)	3949	50	0.5(0.4-0.6)
Tanzania	429	53	1.7(1.1-2)	453	45	2.8(2.1-3.1)
Malawi	1388	51	2.8(1.8-3.3)	2697	52	0(0-0)
Viet Nam	794	73	29(22-32.2)	2538	54	0(0-5.1)
Papua New Guinea	392	56	3(2.1-3.4)	240	52	3.3(2.2-3.7)
Total	**11890**	**55**	**2.8(1.5-5.2)**	**17441**	**52**	**0(0-1.9)**

Supplementary Table 3: Descriptive Statistics. Features of severe malaria cases and controls after quality control filtering, as described in the Methods section. IQR, interquartile range.

Study site		Gender: %	Age in years: %	Ethnicity (%)
		M / F / missing	<5 / 5-15 / >15 / missing	
Gambia	Cases	51 / 46 / 3	71 / 29 / 0 / 0.4	Mandinka (32), Jola (15), Fula (13), Wollof (12), Other (28), Not recorded (0.4)
	Controls	44 / 51 / 4	84 / 0.4 / 5 / 11	Mandinka (30), Jola (12), Fula (18), Wollof (13), Other (20), Not recorded (8)
Mali	Cases	55 / 43 / 2	78 / 22 / 0 / 0	Bambara (42), Bambara mixed (9), Malinke (12), Peulh (6), Sarakole (7), Other (25)
	Controls	47 / 48 / 5	77 / 23 / 0 / 0.5	Bambara (46), Bambara mixed (5), Malinke (12), Peulh (6), Sarakole (5), Other (26)
Burkina Faso	Cases	54 / 42 / 4	72 / 28 / 0 / 1	Mossi (100)
	Controls	50 / 48 / 2	99 / 1 / 0 / 0	Mossi (100)
Ghana (Kumasi)	Cases	50 / 44 / 7	84 / 15 / 0 / 0.2	Akans (Ashanti/Eastern) (54), Frafra/Nankana/Grushie/Kusasu (8), Other (36)
	Controls	50 / 46 / 4	100 / 0 / 0 / 0	Akans (Ashanti/Eastern) (66), Frafra/Nankana/Grushie/Kusasu (5), Other (30)
Ghana (Noguchi/ Navrongo)	Cases	55 / 42 / 3	100 / 0 / 0 / 0	Kasem (58), Nankam (29), Other (14), Not recorded (0.2)
	Controls	52 / 43 / 5	60 / 0 / 0 / 20	Kasem (55), Nankam (33), Other (12)
Nigeria	Cases	57 / 38 / 5	87 / 13 / 0 / 0	Yoruba (97), Other (3)
	Controls	49 / 41 / 10	75 / 25 / 0 / 0	Yoruba (98), Other (2)
Cameroon	Cases	47 / 43 / 10	74 / 15 / 0.1 / 11	Bantu (38), Semi-Bantu (42), Other (11), Not recorded (9)
	Controls	65 / 33 / 2	7 / 43 / 41 / 9	Bantu (41), Semi-Bantu (40), Other (5), Not recorded (11)
Kenya	Cases	49 / 45 / 7	83 / 11 / 0.04 / 6	Chonyi (23), Giriama (59), Kauma (7), Other (10), Not recorded (0.2)
	Controls	49 / 48 / 3	100 / 0 / 0 / 0	Chonyi (36), Giriama (46), Kauma (11), Other (7)
Tanzania	Cases	51 / 45 / 4	96 / 4 / 0 / 0	Mzigua(26), Mzigua mixed (7), Wasambaa (20), Wasambaa mixed (11), Wabondei (11), Wabondei mixed (7), Other (18)
	Controls	44 / 53 / 3	92 / 8 / 0 / 0	Mzigua (28), Mzigua mixed (5), Wasambaa (20), Wasambaa mixed (10), Wabondei (12), Wabondei (6), Other (18)
Malawi	Cases	50 / 46 / 4	82 / 18 / 0 / 0.5	Malawi (100)
	Controls	47 / 42 / 12	100 / 0 / 0 / 0	Malawi (100)
Viet Nam	Cases	71 / 29 / 1	5 / 6 / 89 / 0	Kinh (88), Other (10), Not recorded (3)
	Controls	51 / 45 / 4	82 / 5 / 13 / 0.3	Kinh (94), Other (6), Not recorded (0.4)
PNG	Cases	55 / 44 / 1	82 / 18 / 0 / 0.2	Madang (67), Madang mixed (6), Sepik (8), Other (9), Not recorded (10)
	Controls	38 / 33 / 30	81 / 18 / 0 / 2	Madang (63), Madang mixed (5), Sepik (7), Other (8), Not recorded (16)
Total	Cases	52 / 43 / 4	78 / 15 / 6 / 2	
	Controls	49 / 46 / 5	88 / 4 / 4 / 5	

Supplementary Table 4: Gender, age and ethnicity of cases and controls collected by each contributing partner study to MalariaGEN Consortial Project 1 (CP1). These data represent the proportions included for analysis following the filtering process (as described in the Methods section). Ethnic groups representing <5% of the site sample set are grouped together as 'Other'.

Gene	Chr	SNP Ref	Alternative Name	Location	Ancestral Allele[a]	Derived Allele	Single Letter code	Mean Frequency (min - max)	References
ATP2B4	1	rs55868763		203652140	C	G	S	0.73(0.62-1)	
ATP2B4	1	rs1541255		203652141	A	G	D	0.27(0-0.38)	
ATP2B4	1	rs10900585		203654024	G	T	K	0.71(0.57-0.98)	1,2
ATP2B4	1	rs4951074		203660781	G	A	R	0.26(0-0.37)	
ATP2B4	1	rs3753036		203677250	G	A	R	0.04(0-0.17)	
CR1	1	rs17047660	McC (McCoy)	207782856	A	G	R	0.26(0.16-0.37)	3-8,9
CR1	1	rs17047661	SI (Swain-Lagley)	207782889	A	G	R	0.72(0.67-0.8)	
DARC	1	rs2814778	Duffy – FyA/FyB	159174683	T	C	Y	0.83 (0.83-1)	10-12
IL10	1	rs3024500		206940831	G	A	R	0.39(0.06-0.55)	13,14
IL10	1	rs1800896		206946897	T	C	Y	0.29(0.06-0.4)	
IL10	1	rs1800890		206949365	A	T	W	0.19(0.04-0.34)	
IL1A	2	rs17561	IL1A G4845T	113537223	C	A	M	0.16(0.05-0.23)	15-17
IL1B	2	rs1143634	IL1B A2	113590390	G	A	R	0.1(0.01-0.24)	
TLR9	3	rs187084		52261031	G	A	R	0.70(0.50-0.77)	18-20
TLR1	4	rs4833095		38799710	C	T	Y	0.15(0.07-0.47)	21
TLR6	4	rs5743810		38830350	G	A	R	0.01(0.01-0.02)	21
TLR6	4	rs5743809		38830514	A	G	R	0.04(0.01-0.08)	
C6	5	rs1801033		41199959	T	G	K	0.48 (0.42-0.60)	22-24
IL13	5	rs20541		131995964	G	A	R	0.23(0.09-0.42)	25
IL4	5	rs2243250	IL-4-589	132009154	C	T	Y	0.76(0.45-0.83)	17,25-27
IRF1	5	rs2706384		131826880	G	T	K	0.44(0.38-0.78)	28
LTA	6	rs2239704	LTA +77	31540141	C	A	M	0.26(0.12-0.46)	17,29-43
LTA	6	rs909253	LTA NCO1	31540313	A	G	R	0.47(0.12-0.56)	
TNF	6	rs1799964	TNFa -1031	31542308	T	C	Y	0.2(0.12-0.41)	31,32,37,40,44-49
TNF	6	rs1800750	TNF-376	31542963	G	A	R	0.04(0.01-0.42)	
TNF	6	rs1800629	TNF -308	31543031	G	A	R	0.11(0.07-0.14)	
TNF	6	rs361525	TNF -238	31543101	G	A	R	0.05(0.01-0.09)	
TNF	6	rs3093662	TNF +851	31544189	A	G	R	0.08(0.01-0.12)	
CD36	7	rs3211938	CD36 T1264G	80300449	T	G	K	0.09(0.02-0.27)	50-56
CD36	7	G1439C[b]	CD36 G1439C	80302110	G	C	S	0.02(0.01-0.06)	
ABO	9	rs8176746		136131322	G	T	K	0.17(0.13-0.26)	57-59
ABO	9	rs8176719		136132909	C (INS)	- (DEL)	I	0.69(0.59-0.78)	
TLR4	9	rs4986791		120475602	C	T	Y	0.01(0.01-0.02)	18,19,60-64
TLR4	9	rs4986790		120475302	A	G	R	0.06(0.01-0.11)	
HBB	11	rs33950507	HbE	5248173	G (INS)	- (DEL)	I	0.01(0.01-0.04)	65-68
HBB	11	rs334	HbS	5248232	T	A	W	0.07(0.03-0.11)	69-72 73
HBB	11	rs33930165	HbC	5248233	G	A	R	0.03(0.01-0.15)	73-77
IL22	12	rs2227507	IL22+4583	68642647	T	C	Y	0.04(0.01-0.04)	
IL22	12	rs1012356	IL22+2611	68644618	A	T	W	0.51(0.04-0.58)	
IL22	12	rs2227491	IL22+708	68646521	T	C	Y	0.63(0.05-0.71)	78
IL22	12	rs2227485	IL22-485	68647713	G	A	R	0.47(0.05-0.58)	
IL22	12	rs2227478	IL22-1394	68648622	G	A	R	0.67(0.28-0.85)	
SPTB	14	rs229587		65263300	T	C	Y	0.35(0.22-0.61)	79
ADORA2B	17	rs2535611		15861332	C	T	Y	0.07(0.01-0.14)	80
NOS2	17	rs2297518		26096597	G	A	R	0.12(0.05-0.16)	81-86
NOS2	17	rs1800482	NOS2A -954/969	26128509	C	G	S	0.09(0.06-0.12)	
NOS2	17	rs9282799	NOS2A -1173	26128728	G	A	R	0.05(0.03-0.08)	
NOS2	17	rs8078340	NOS2A -1659	26129212	G	A	R	0.2(0.02-0.28)	
ICAM1	19	rs1799969	ICAM1 codon241	10394792	G	A	R	0(0-0)	55,56,87,88
ICAM1	19	rs5498	ICAM1 codon469	10395683	A	G	R	0.14(0.11-0.54)	
GNAS	20	rs8386		57485812	C	T	Y	0.16(0.12-0.27)	89,90
CD40LG	23	rs3092945	CD40LG -727	135729609	T	C	Y	0.27(0.03-0.47)	91-93
CD40LG	23	rs1126535	CD40LG +220	135730555	T	C	Y	0.14(0.08-0.4)	
G6PD	X	rs1050829	G6PD +376	153763492	T	C	Y	0.39 (0.32-0.52)	94-98
G6PD	X	rs1050828	G6PD +202	153764217	C	T	Y	0.15(003-0.29)	

Supplementary Table 5: Summary of 55 SNPs selected for analysis due to a known association with malaria and successfully genotyped. Details of SNPs include an alternate name, ancestral or reference allele, the single letter nucleotide code, the mean frequency of the derived allele in controls (with range by ethnicity) plus selected references. All SNPs are referenced to GRCh37, dbSNP137 and Ensembl build 73.

Chr, Chromosome.

[a]Ancestral allele is assigned from dbSNP137 or, where not available, from human reference sequence Ensembl build 73.

[b]No rs designation.

Gene	Chr	SNP Ref	Alternative Name	Location	Ancestral Allele[a,b]	Derived Allele[b]	Single Letter code	Mean Frequency (min - max)	References
GBP7	1	rs1803632		89582690	G	C	S	0.51(0.28-0.75)	25
IL17RD	3	rs6780995		57138419	G	A	R	0.51(0.15-0.61)	99
IL17RE	3	rs708567		9960070	C	T	Y	0.43(0.11-0.71)	99
CTL4	6	rs2242665		31839309	C	T	Y	0.70(0.62-0.82)	
IL20RA	6	rs1555498		137325847	C	T	Y	0.53(0.39-1)	100,101
CFTR	7	rs17140229		117230283	T	C	Y	0.36(0.29-0.45)	102,103
NOD1	7	rs2075820		30492237	C	T	Y	0.38(0.15-0.45)	104,105
RTN3	11	rs542998		63487386	T	C	Y	0.49(0.34-0.98)	
TRIM5	11	rs7935564		5718517	G	A	R	0.42(0.17-0.52)	106
ADCY9	16	rs2230739		4033436	T	C	Y	0.15(0.07-0.39)	80,107
ADCY9	16	rs10775349		4079823	C	G	S	0.30(0.11-0.99)	
IL4R	16	rs1805015		27374180	T	C	Y	0.39(0.11-0.49)	108,109
EMR1	19	rs373533		6919624	C	A	M	0.43(0.31-0.67)	110
EMR1	19	rs461645		6919753	A	G	R	0.57(0.34-0.69)	
DERL3	22	rs1128127		24179132	G	A	R	0.47(0.01-0.60)	
AMELX/AMELY	X	None assigned	Amelogenin_SNP1	11313735	G	A	R	NA	
AMELX/AMELY	X	None assigned	Amelogenin_SNP2	11316106	T	C	Y	NA	
AMELX/AMELY	X	None assigned	Amelogenin_SNP6	11316650	C	A	M	NA	

Supplementary Table 6: Additional genes and SNPs selected for analysis and successfully genotyped. Summary of 18 additional SNPs genotyped, 15 of which were selected due to a non genetic association with severe malaria and 3 of which (in the AMELX/AMELY genes) were selected for gender typing. Details of SNPs include an alternate name, ancestral or reference allele, the single letter nucleotide code, the mean frequency of the derived allele in controls (with range by ethnicity) plus selected references. All SNPs are referenced to GRCh37, dbSNP137 and Ensembl build 73.
Chr, Chromosome.
[a]Ancestral allele is assigned from dbSNP137 or, where not available, from human reference sequence Ensembl build 73.
[b]For AMELX/AMELY SNPs, ancestral allele column shows X chromosome allele and derived allele column shows Y chromosome allele.

Gene	Chr	SNP Ref	Alternative Name	Location	Ancestral Allele[a,b]	Derived Allele[b]	Single Letter code	References
FCGR2a	1	rs1801274	FCGR2a-H131R	161479745	A	G	R	111,112
RGS2	1	rs2179652		192769826	T	C	Y	80,113
TLR10	4	rs11096957		38776491	T	G	K	114
TLR1	4	rs5743611		38800214	C	G	S	21
CD36	7	None assigned	CD36_I1444D	80302115	I	D	I	50-56
ABO	9	rs8176747		136131315	C	G	S	57-59
ABO	9	rs8176743		136131415	C	T	Y	57-59
CASP5	11	rs523104		104869708	G	C	S	
SPTB	14	rs77806		65253232	C	T	Y	79
RAGE	14	rs2236493		102695693	C	T	Y	115
MARVELD3	16	rs2334880		71653637	A	G	R	2
ICAM1	19	rs5491	ICAM-1codon29	10385540	A	T	W	55,56,87,88
CEACAM1	19	rs8110904		43031369	A	G	R	116
APOE	19	rs7412	APOE_ Arg176Cys	45412079	C	T	Y	117-120
GNAS	20	rs2057291		57472043	G	A	R	89
AMELX/AMELY	X	None assigned	Amelogenin_SNP3	11316131	A	G	R	

Supplementary Table 7: Genes and SNPs selected for genotyping and analyses dropped due to poor genotyping quality. List of 16 additional SNPs, including 1 (in the AMELX/AMELY gene) selected for gender typing, which were dropped as a consequence of poor genotyping quality. Details of SNPs include an alternate name, ancestral or reference allele, the single letter nucleotide code, the mean frequency of the derived allele in controls (with range by ethnicity) plus selected references. All SNPs are referenced to GRCh37, dbSNP137 and Ensembl build 73.
Chr, Chromosome.
[a]Ancestral allele is assigned from dbSNP137 or, where not available, from human reference sequence Ensembl build 73.
[b]For AMELX/AMELY SNPs, ancestral allele column shows X chromosome allele and derived allele column shows Y chromosome allele.

Gene	Chromosome	SNP Ref	Sample	Best Model[a]	Best Model OR(95% CI)	Best Model *P*	Heterozygote OR(95% CI)	Derived Homozygote OR(95% CI)	Genotypic *P*	Frequency (Derived Homozygote/ Heterozygote/Ancestal Homozygote) Cases	Controls	Alleles An	De
ABO	9	rs8176746	All	D	1.25(1.19-1.32)	2.01×10^{-17}	1.24(1.18-1.31)	1.37(1.2-1.56)	8.19×10^{-17}	0.2(7512/3817/507)	0.17(11943/4852/565)	C	A
ABO	9	rs8176719	All	R	0.74(0.7-0.78)	4.99×10^{-33}	0.88(0.81-0.96)	0.67(0.62-0.73)	1.01×10^{-33}	0.64(1506/5533/4750)	0.69(1700/7215/8238)	I	D
ADCY9	16	rs2230739	All	H	0.94(0.89-1)	0.05	0.94(0.88-1)	0.99(0.85-1.16)	0.15	0.13(9115/2463/290)	0.15(12706/4094/604)	A	G
ADCY9	16	rs10775349	All	R	1.09(0.96-1.24)	0.18	1(0.94-1.06)	1.09(0.96-1.24)	0.4	0.26(7270/3134/1461)	0.3(9884/4518/3000)	C	G
ADORA2B	17	rs2535611	All	A	1.01(0.95-1.08)	0.69	1.01(0.94-1.09)	1.03(0.78-1.36)	0.92	0.08(10044/1629/98)	0.07(14377/2198/130)	T	C
ATP2B4	1	rs55868763	All	D	1.33(1.21-1.47)	9.52×10^{-09}	1.31(1.19-1.46)	1.34(1.21-1.49)	5.91×10^{-08}	0.71(742/3935/4554)	0.68(1428/5690/6229)	C	G
ATP2B4	1	rs1541255	All	R	0.75(0.68-0.83)	4.87×10^{-09}	0.98(0.92-1.04)	0.74(0.67-0.82)	3.10×10^{-08}	0.29(4558/3922/743)	0.32(6241/5667/1439)	A	G
ATP2B4	1	rs10900585	All	D	1.32(1.21-1.45)	1.69×10^{-09}	1.32(1.2-1.46)	1.33(1.2-1.46)	1.37×10^{-08}	0.68(868/4056/4203)	0.66(1644/5722/5737)	G	T
ATP2B4	1	rs4951074	All	R	0.77(0.7-0.86)	7.64×10^{-07}	0.98(0.92-1.04)	0.76(0.69-0.85)	4.13×10^{-06}	0.29(4365/3605/658)	0.31(6115/5392/1284)	G	A
ATP2B4	1	rs3753036	All	H	0.98(0.87-1.09)	0.67	0.98(0.87-1.09)	0.99(0.64-1.54)	0.91	0.03(9900/540/28)	0.04(14787/1253/81)	G	A
C6	5	rs1801033	All	R	0.99(0.94-1.06)	0.87	1(0.94-1.06)	0.99(0.93-1.07)	0.98	0.46(3418/5885/2531)	0.48(4757/8591/4003)	A	C
CD36	7	G1439C	All	H	0.67(0.54-0.84)	4.19×10^{-04}	0.67(0.54-0.84)	1.74(0.49-6.15)	1.36×10^{-03}	0.01(6374/138/6)	0.02(7252/236/5)	G	C
CD36	7	rs3211938	All	H	0.9(0.83-0.97)	6.17×10^{-03}	0.9(0.84-0.97)	1.08(0.86-1.35)	0.02	0.09(8904/1590/173)	0.09(12291/2178/174)	T	G
CD40LG	X	rs3092945	M	M	0.9(0.83-0.98)	1.04×10^{-02}	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.28(4487/0/1737)	0.27(6449/0/2348)	T	C
CD40LG	X	rs3092945	F	R	0.78(0.69-0.88)	8.93×10^{-05}	1.03(0.95-1.12)	0.79(0.7-0.9)	3.63×10^{-04}	0.3(2636/2035/513)	0.27(4581/2621/849)	T	C
CD40LG	X	rs3092945	All	R	0.85(0.79-0.91)	1.11×10^{-06}	1.11(1.02-1.2)	0.86(0.81-0.92)	2.40×10^{-07}	0.29(7123/2035/2250)	0.27(11030/2621/3197)	T	C
CD40LG	X	rs1126535	M	M	1(0.91-1.1)	0.99	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.15(5527/0/948)	0.14(7793/0/1290)	T	C
CD40LG	X	rs1126535	F	R	0.94(0.74-1.19)	0.58	1(0.92-1.1)	0.94(0.74-1.19)	0.86	0.14(3967/1283/126)	0.14(6206/1904/193)	T	C
CD40LG	X	rs1126535	All	R	0.98(0.89-1.07)	0.59	1.03(0.95-1.12)	0.98(0.89-1.07)	0.67	0.14(9494/1283/1074)	0.14(13999/1904/1483)	T	C
CFTR	7	rs17140229	All	H	0.98(0.92-1.04)	0.49	0.98(0.92-1.05)	1.02(0.93-1.12)	0.72	0.38(3314/3963/1234)	0.36(5182/5816/1632)	T	C
CR1	1	rs17047660	All	R	1.05(0.95-1.16)	0.32	1(0.94-1.06)	1.05(0.95-1.16)	0.61	0.27(5669/4132/856)	0.26(8059/5508/1048)	A	G
CR1	1	rs17047661	All	H	1.02(0.96-1.07)	0.56	1.02(0.92-1.13)	1(0.9-1.11)	0.84	0.73(783/4181/5701)	0.72(1159/5820/7633)	A	G
CTL4	6	rs2242665	All	D	0.92(0.85-1)	0.06	0.92(0.84-1.01)	0.92(0.85-1.01)	0.16	0.7(1163/4804/5816)	0.7(1670/7134/8465)	G	A
DARC	1	rs2814778	All	D	4.91(0.4-60.95)	0.2	4.27(0.35-52.71)	4.08(0.32-52.06)	0.5	0.89(1171/44/9691)	0.83(2751/59/13799)	A	G
DERL3	22	rs1128127	All	H	0.98(0.93-1.03)	0.41	0.97(0.91-1.03)	0.98(0.92-1.06)	0.66	0.49(3314/5323/3159)	0.47(5327/7634/4290)	G	A
EMR1	19	rs373533	All	D	1.03(0.98-1.09)	0.28	1.03(0.98-1.09)	1.02(0.95-1.09)	0.51	0.45(3612/5755/2376)	0.43(5667/8256/3280)	G	T
EMR1	19	rs461645	All	R	0.97(0.92-1.02)	0.2	1.02(0.95-1.09)	0.98(0.91-1.05)	0.38	0.55(2413/5784/3650)	0.57(3357/8303/5726)	T	C
G6PD	X	rs1050829	M	M	1.08(1.01-1.17)	0.04	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.4(3396/0/2228)	0.38(4679/0/2869)	T	C
G6PD	X	rs1050829	F	H	0.93(0.86-1)	0.06	0.92(0.85-1)	0.98(0.87-1.1)	0.17	0.38(1921/2285/762)	0.39(2606/3356/1062)	T	C
G6PD	X	rs1050829	All	R	1.06(1-1.13)	0.05	0.94(0.87-1.02)	1.05(0.99-1.12)	0.05	0.39(5317/2285/2990)	0.38(7285/3356/3931)	T	C
G6PD	X	rs1050828	M	M	1.1(0.99-1.22)	0.07	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.15(4811/0/866)	0.15(6483/0/1105)	C	T
G6PD	X	rs1050828	F	H	0.9(0.82-0.99)	0.02	0.9(0.82-0.99)	1.11(0.87-1.42)	0.06	0.14(3705/1152/134)	0.15(5069/1770/174)	C	T
G6PD	X	rs1050828	All	A	1.02(0.97-1.06)	0.15	0.9(0.82-0.98)	1.1(1-1.21)	6.35×10^{-03}	0.15(8516/1152/1000)	0.15(11552/1770/1279)	C	T
GBP7	1	rs1803632	All	A	1.03(0.99-1.07)	0.11	1.03(0.97-1.09)	1.06(0.99-1.14)	0.27	0.49(3170/5725/2965)	0.51(4369/8259/4777)	G	C
GNAS	20	rs8386	All	H	0.96(0.9-1.02)	0.16	0.96(0.9-1.02)	1.04(0.89-1.22)	0.33	0.16(7505/2863/318)	0.16(10246/3995/398)	C	T
HBB	11	rs33950507	All	H	0.99(0.67-1.45)	0.94	1.01(0.68-1.48)	1.4(0.55-3.58)	0.78	0.01(4029/39/8)	0.01(6447/127/27)	G	A
HBB	11	rs334	All	H	0.14(0.12-0.16)	1.62×10^{-225}	0.14(0.12-0.16)	1.4(1.02-1.92)	7.92×10^{-225}	0.02(10388/213/84)	0.07(12773/1791/77)	A	T
HBB	11	rs33930165	All	A	0.71(0.63-0.8)	6.87×10^{-09}	0.71(0.61-0.82)	0.5(0.34-0.73)	5.13×10^{-08}	0.04(6866/445/46)	0.03(9341/515/74)	G	A
ICAM1	19	rs1799969	All	ADH*	0.94(0.45-1.96)	0.86	n.c.[§]	n.c.[§]	n.c.[§]	0(5459/11/0)	0(9294/27/0)	G	A

ICAM1	19	rs5498	All	D	1.04(0.98-1.1)	0.18	1.04(0.98-1.1)	1.03(0.87-1.21)	0.4	0.15(8560/2900/334)	0.14(12716/4164/411)	A	G
IL10	1	rs3024500	All	H	0.98(0.93-1.03)	0.39	0.98(0.92-1.03)	0.99(0.92-1.07)	0.69	0.41(4274/5380/2197)	0.39(6859/7440/3080)	A	G
IL10	1	rs1800896	All	R	0.94(0.87-1.02)	0.15	1.02(0.97-1.08)	0.95(0.87-1.04)	0.27	0.3(5800/4869/1168)	0.29(8946/6734/1723)	T	C
IL10	1	rs1800890	All	R	0.88(0.78-0.99)	0.04	0.98(0.92-1.03)	0.87(0.77-0.99)	0.08	0.19(7740/3647/486)	0.19(11441/5183/784)	A	T
IL13	5	rs20541	All	A	0.99(0.95-1.04)	0.77	0.99(0.93-1.06)	0.98(0.87-1.12)	0.96	0.21(6031/2955/492)	0.23(8778/4974/938)	C	T
IL17RD	3	rs6780995	All	H	1.03(0.98-1.08)	0.29	1.04(0.97-1.11)	1.02(0.95-1.09)	0.51	0.53(2739/5616/3486)	0.51(4680/7806/4890)	G	A
IL17RE	3	rs708567	All	D	1.05(0.99-1.11)	0.08	1.06(1-1.12)	1.04(0.97-1.12)	0.19	0.47(3416/5579/2750)	0.43(5820/7587/3555)	G	A
IL1A	2	rs17561	All	H	1.07(1.02-1.13)	0.01	1.07(1.02-1.14)	1.02(0.88-1.18)	0.04	0.17(8141/3377/361)	0.16(12491/4439/479)	G	T
IL1B	2	rs1143634	All	A	1.05(1-1.11)	0.07	1.05(0.98-1.12)	1.14(0.93-1.4)	0.18	0.12(9216/2457/188)	0.1(13962/3178/215)	C	T
IL20RA	6	rs1555498	All	A	1.02(0.99-1.06)	0.23	1.02(0.96-1.08)	1.05(0.97-1.13)	0.49	0.49(3368/5336/3162)	0.53(4600/7179/5633)	C	T
IL22	12	rs2227507	All	A	0.98(0.89-1.08)	0.65	0.96(0.87-1.06)	1.42(0.74-2.72)	0.41	0.03(9960/708/19)	0.04(13593/1033/20)	T	C
IL22	12	rs1012356	All	D	1.06(1-1.13)	0.04	1.06(1-1.13)	1.06(0.99-1.14)	0.13	0.5(3017/5757/3091)	0.51(4254/8493/4643)	A	T
IL22	12	rs2227491	All	D	1.07(0.99-1.15)	0.1	1.06(0.98-1.14)	1.08(0.99-1.16)	0.21	0.64(1717/5075/4986)	0.63(2505/7684/7080)	T	C
IL22	12	rs2227485	All	H	1.04(0.99-1.09)	0.11	1.05(0.99-1.11)	1.02(0.95-1.09)	0.24	0.46(3495/5705/2627)	0.47(4979/8362/4021)	G	A
IL22	12	rs2227478	All	H	1.04(0.99-1.09)	0.15	1.04(0.96-1.13)	1(0.92-1.09)	0.35	0.65(1562/5209/5089)	0.67(2059/7268/8059)	G	A
IL4	5	rs2243250	All	H	1.06(1.01-1.12)	0.03	1.1(0.99-1.23)	1.04(0.94-1.16)	0.07	0.75(754/4284/6566)	0.76(1101/6094/10066)	C	T
IL4R	16	rs1805015	All	H	0.98(0.93-1.03)	0.48	0.99(0.93-1.05)	1.01(0.94-1.09)	0.73	0.41(4375/5288/2172)	0.39(6872/7570/2912)	T	C
IRF1	5	rs2706384	All	A	0.94(0.91-0.98)	1.35×10^{-03}	0.94(0.89-1)	0.89(0.83-0.96)	0.01	0.42(3964/5423/2137)	0.44(5462/8154/3434)	C	A
LTA	6	rs2239704	All	D	1.04(0.98-1.09)	0.18	1.04(0.98-1.09)	1.04(0.95-1.14)	0.4	0.28(6129/4502/1088)	0.26(9604/6224/1411)	G	T
LTA	6	rs909253	All	A	0.97(0.94-1)	0.08	0.97(0.92-1.03)	0.94(0.87-1.01)	0.21	0.45(3676/5627/2464)	0.47(4997/8355/3853)	T	C
NOD1	7	rs2075820	All	H	1.03(0.98-1.08)	0.21	1.03(0.97-1.08)	0.99(0.92-1.06)	0.43	0.38(4526/5577/1732)	0.38(6692/8105/2597)	G	A
NOS2	17	rs2297518	All	A	0.96(0.91-1.02)	0.17	0.97(0.91-1.03)	0.89(0.73-1.09)	0.35	0.11(9380/2301/159)	0.12(13373/3691/298)	G	A
NOS2	17	rs1800482	All	H	0.97(0.9-1.04)	0.38	0.97(0.9-1.04)	1(0.75-1.34)	0.68	0.09(8916/1644/86)	0.09(12169/2320/120)	G	C
NOS2	17	rs9282799	All	A	1.1(1.02-1.19)	0.02	1.08(0.99-1.18)	1.49(0.98-2.27)	0.03	0.06(9443/1196/51)	0.05(13124/1476/45)	C	T
NOS2	17	rs8078340	All	R	0.92(0.82-1.03)	0.14	1.02(0.96-1.07)	0.92(0.82-1.04)	0.3	0.21(7302/4000/544)	0.2(11224/5365/808)	C	T
RTN3	11	rs542998	All	H	0.97(0.92-1.02)	0.28	0.97(0.91-1.03)	0.99(0.92-1.07)	0.54	0.45(3897/5109/2775)	0.49(5203/7090/4964)	T	C
SPTB	14	rs229587	All	R	1.04(0.96-1.12)	0.34	0.98(0.93-1.04)	1.03(0.95-1.12)	0.52	0.33(5027/4720/1359)	0.35(7361/7416/2348)	T	C
TLR1	4	rs4833095	All	R	1.1(0.94-1.28)	0.23	0.98(0.92-1.04)	1.09(0.93-1.27)	0.36	0.13(9042/2422/314)	0.15(12637/3942/681)	C	T
TLR4	9	rs4986791	All	H	1.12(0.92-1.37)	0.25	1.12(0.92-1.37)	0.29(0.03-2.9)	0.27	0.01(11657/195/1)	0.01(17141/248/3)	C	T
TLR4	9	rs4986790	All	R	0.78(0.58-1.07)	0.12	1.04(0.96-1.12)	0.79(0.58-1.07)	0.18	0.07(10234/1525/75)	0.06(15371/1879/112)	A	G
TLR6	4	rs5743810	All	H	1.09(0.88-1.34)	0.43	1.09(0.88-1.34)	0.87(0.09-8.7)	0.73	0.01(11243/166/1)	0.01(16903/227/3)	C	T
TLR6	4	rs5743809	All	D	1.05(0.95-1.15)	0.33	1.05(0.95-1.15)	1.03(0.63-1.66)	0.62	0.04(10384/922/30)	0.04(15698/1279/43)	T	C
TLR9	3	rs187084	All	R	1.04(0.98-1.09)	0.2	0.99(0.9-1.09)	1.02(0.93-1.13)	0.42	0.71(960/4335/5625)	0.7(1455/6473/7909)	C	T
TNF	6	rs1799964	All	D	1.04(0.98-1.09)	0.18	1.04(0.98-1.09)	1.04(0.92-1.18)	0.41	0.2(7689/3638/506)	0.2(11148/5452/767)	T	C
TNF	6	rs1800629	All	D	1.01(0.95-1.07)	0.76	1.01(0.95-1.07)	1.01(0.82-1.25)	0.95	0.11(9373/2282/172)	0.11(13921/3273/222)	G	A
TNF	6	rs361525	All	H	1.08(0.99-1.17)	0.09	1.07(0.99-1.17)	0.87(0.55-1.37)	0.2	0.05(10704/1125/31)	0.05(15732/1647/55)	G	A
TNF	6	rs3093662	All	H	1.04(0.97-1.12)	0.24	1.04(0.97-1.12)	0.91(0.69-1.21)	0.41	0.08(9954/1798/87)	0.08(14652/2591/143)	A	G
TRIM5	11	rs7935564	All	H	0.98(0.93-1.03)	0.37	0.98(0.93-1.04)	1.01(0.94-1.08)	0.65	0.46(3564/5681/2514)	0.42(5881/8072/3205)	G	A

Supplementary Table 8: All severe malaria association signals. Summary of association signals at all SNPs for *all-severe-malaria* across the 12 contributing Consortial Project 1 study sites. Odds ratios (OR), 95% confidence intervals (95% CI) and p-values (*P*) are presented for the best model (for autosomal SNPs and for females at X chromosome SNPs this is the model (selected from additive, recessive, dominant or heterozygote advantage) that has the most significant association; for males at X chromosome, this is the male hemizygote model and; for all individuals combined at X chromosome SNPs this is the model (selected from additive, recessive or dominant) that has the most significant association. Heterozygote and homozygote ORs from a genotypic model are also presented. Results are adjusted for HbS (except rs334), gender and ethnicity. Sites at which a SNP was found to be monomorphic were excluded from the analysis. An, ancestral; De, derived; n.c., not calculated. [a]Models are A, additive; D, dominant; H, heterozygote advantage; M, male hemizygote; R, recessive. [§] Genotype counts too small for accurate calculation. [¶]Not applicable to male hemizygotes. *Models are equivalent due to zero genotype class.

Gene	Chromosome	SNP Ref	Sample	Best Model[a]	Best Model OR(95% CI)	Best Model *P*	Heterozygote OR(95% CI)	Derived Homozygote OR(95% CI)	Genotypic *P*	Frequency (Derived Homozygote/ Heterozygote/Ancestal Homozygote) Cases	Frequency (Derived Homozygote/ Heterozygote/Ancestal Homozygote) Controls	Alleles An	Alleles De
ABO	9	rs8176746	All	A	1.27(1.18-1.36)	2.00×10^{-11}	1.29(1.19-1.4)	1.53(1.25-1.88)	1.38×10^{-10}	0.2(2148/1049/138)	0.17(11943/4852/565)	C	A
ABO	9	rs8176719	All	R	0.73(0.67-0.79)	8.85×10^{-16}	0.84(0.74-0.96)	0.63(0.56-0.72)	2.95×10^{-16}	0.64(415/1537/1373)	0.69(1700/7215/8238)	I	D
ADCY9	16	rs2230739	All	A	0.95(0.87-1.03)	0.23	0.95(0.86-1.05)	0.91(0.7-1.19)	0.49	0.12(2593/675/69)	0.15(12706/4094/604)	A	G
ADCY9	16	rs10775349	All	A	0.97(0.9-1.04)	0.35	0.98(0.9-1.07)	0.9(0.73-1.11)	0.58	0.24(2065/944/327)	0.3(9884/4518/3000)	C	G
ADORA2B	17	rs2535611	All	H	1.09(0.98-1.22)	0.13	1.09(0.98-1.21)	0.94(0.61-1.45)	0.30	0.09(2779/524/27)	0.07(14377/2198/130)	T	C
ATP2B4	1	rs55868763	All	D	1.41(1.21-1.66)	9.35×10^{-06}	1.43(1.17-1.77)	1.53(1.25-1.89)	1.48×10^{-04}	0.71(137/791/929)	0.68(1428/5690/6229)	C	G
ATP2B4	1	rs1541255	All	R	0.7(0.59-0.82)	4.03×10^{-06}	0.93(0.83-1.04)	0.65(0.53-0.79)	1.02×10^{-04}	0.29(932/788/137)	0.32(6241/5667/1439)	A	G
ATP2B4	1	rs10900585	All	D	1.35(1.17-1.57)	3.06×10^{-05}	1.49(1.22-1.81)	1.58(1.3-1.92)	1.34×10^{-05}	0.69(159/816/851)	0.66(1644/5722/5737)	G	T
ATP2B4	1	rs4951074	All	R	0.75(0.64-0.88)	3.66×10^{-04}	1(0.89-1.12)	0.64(0.51-0.79)	6.97×10^{-05}	0.28(890/762/121)	0.31(6115/5392/1284)	G	A
ATP2B4	1	rs3753036	All	H	0.92(0.76-1.11)	0.38	1.22(0.93-1.59)	1.34(0.3-5.94)	0.36	0.02(1946/72/2)	0.04(14787/1253/81)	G	A
C6	5	rs1801033	All	R	0.99(0.9-1.09)	0.89	1(0.92-1.1)	1(0.89-1.11)	0.99	0.47(942/1667/720)	0.48(4757/8591/4003)	A	C
CD36	7	G1439C	All	H	0.71(0.49-1.02)	0.06	0.71(0.49-1.02)	4.09(0.86-19.43)	0.04	0.02(1228/37/3)	0.02(7252/236/5)	G	C
CD36	7	rs3211938	All	R	1.35(0.94-1.94)	0.12	0.96(0.85-1.08)	1.33(0.93-1.92)	0.23	0.08(2621/412/42)	0.09(12291/2178/174)	T	G
CD40LG	X	rs3092945	M	M	0.85(0.75-0.97)	1.35×10^{-02}	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.25(1289/0/439)	0.27(6449/0/2348)	T	C
CD40LG	X	rs3092945	F	R	0.9(0.74-1.09)	0.27	1.02(0.9-1.16)	0.91(0.74-1.11)	0.52	0.29(813/576/157)	0.27(4581/2621/849)	T	C
CD40LG	X	rs3092945	All	R	0.85(0.76-0.94)	0	1.07(0.95-1.2)	0.86(0.77-0.95)	4.74×10^{-03}	0.27(2102/576/596)	0.27(11030/2621/3197)	T	C
CD40LG	X	rs1126535	M	M	1.02(0.88-1.19)	0.76	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.15(1495/0/266)	0.14(7793/0/1290)	T	C
CD40LG	X	rs1126535	F	R	0.72(0.48-1.07)	0.09	1.01(0.89-1.15)	0.72(0.48-1.08)	0.24	0.15(1141/396/30)	0.14(6206/1904/193)	T	C
CD40LG	X	rs1126535	All	R	0.96(0.83-1.1)	0.57	1.05(0.93-1.2)	0.96(0.84-1.11)	0.62	0.15(2636/396/296)	0.14(13999/1904/1483)	T	C
CFTR	7	rs17140229	All	D	0.95(0.86-1.05)	0.35	0.95(0.86-1.06)	0.97(0.83-1.13)	0.64	0.35(871/916/255)	0.36(5182/5816/1632)	T	C
CR1	1	rs17047660	All	A	1.09(1.02-1.17)	7.56×10^{-03}	1.09(1-1.19)	1.19(1.02-1.4)	0.03	0.27(1647/1185/248)	0.26(8059/5508/1048)	A	G
CR1	1	rs17047661	All	H	1.03(0.95-1.12)	0.41	1.02(0.88-1.2)	0.99(0.85-1.15)	0.71	0.71(246/1266/1566)	0.72(1159/5820/7633)	A	G
CTL4	6	rs2242665	All	A	0.97(0.92-1.03)	0.39	0.96(0.84-1.11)	0.94(0.82-1.08)	0.68	0.7(319/1375/1624)	0.7(1670/7134/8465)	G	A
DARC	1	rs2814778	All	H	0.72(0.37-1.38)	0.3	n.c.[§]	n.c.[§]	n.c[§].	0.92(250/11/2960)	0.83(2751/59/13799)	A	G
DERL3	22	rs1128127	All	A	0.99(0.94-1.05)	0.76	0.99(0.9-1.09)	0.98(0.88-1.1)	0.95	0.49(911/1539/865)	0.47(5327/7634/4290)	G	A
EMR1	19	rs373533	All	H	1.07(0.99-1.16)	0.08	1.09(1-1.19)	1.05(0.94-1.17)	0.16	0.46(971/1665/681)	0.43(5667/8256/3280)	G	T
EMR1	19	rs461645	All	H	1.08(1-1.17)	0.05	1.07(0.96-1.18)	0.98(0.87-1.09)	0.12	0.55(675/1675/984)	0.57(3357/8303/5726)	T	C
G6PD	X	rs1050829	M	M	0.92(0.82-1.03)	0.16	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.35(1009/0/553)	0.38(4679/0/2869)	T	C
G6PD	X	rs1050829	F	A	0.93(0.86-1.02)	0.12	0.94(0.83-1.07)	0.87(0.72-1.04)	0.29	0.36(601/703/195)	0.39(2606/3356/1062)	T	C
G6PD	X	rs1050829	All	A	0.95(0.9-1)	0.03	0.95(0.84-1.06)	0.9(0.82-0.99)	0.11	0.36(1610/703/748)	0.38(7285/3356/3931)	T	C
G6PD	X	rs1050828	M	M	0.81(0.68-0.96)	1.39×10^{-02}	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.12(1384/0/191)	0.15(6483/0/1105)	C	T
G6PD	X	rs1050828	F	H	0.87(0.76-1.01)	0.06	0.87(0.76-1.01)	1.04(0.72-1.51)	0.16	0.14(1129/338/39)	0.15(5069/1770/174)	C	T
G6PD	X	rs1050828	All	A	0.91(0.85-0.97)	6.08×10^{-03}	0.86(0.75-0.99)	0.85(0.72-0.99)	0.02	0.13(2513/338/230)	0.15(11552/1770/1279)	C	T
GBP7	1	rs1803632	All	D	1.08(0.98-1.18)	0.11	1.07(0.98-1.18)	1.08(0.97-1.21)	0.28	0.5(835/1640/856)	0.51(4369/8259/4777)	G	C
GNAS	20	rs8386	All	R	1.21(0.95-1.55)	0.13	0.96(0.87-1.05)	1.2(0.94-1.54)	0.22	0.15(2225/773/85)	0.16(10246/3995/398)	C	T
HBB	11	rs33950507	All	H	1.1(0.56-2.15)	0.79	1.11(0.57-2.19)	1.74(0.16-19.46)	0.88	0.01(1091/10/1)	0.01(6447/127/27)	G	A
HBB	11	rs334	All	H	0.11(0.08-0.15)	4.67×10^{-88}	0.11(0.08-0.15)	0.3(0.12-0.74)	9.16×10^{-89}	0.01(3041/42/5)	0.07(12773/1791/77)	A	T
HBB	11	rs33930165	All	A	0.72(0.56-0.94)	1.07×10^{-02}	0.73(0.54-0.99)	0.5(0.2-1.25)	0.04	0.02(1412/56/5)	0.03(9341/515/74)	G	A
ICAM1	19	rs1799969	All	ADH*	0.59(0.14-2.54)	0.44	n.c.[§]	n.c.[§]	n.c[§].	0(1982/2/0)	0(9294/27/0)	G	A
ICAM1	19	rs5498	All	A	1.07(0.99-1.15)	0.11	1.07(0.97-1.17)	1.13(0.87-1.47)	0.27	0.14(2435/801/80)	0.14(12716/4164/411)	A	G

IL10	1	rs3024500	All	D	0.94(0.86-1.03)	0.17	0.94(0.86-1.02)	0.96(0.85-1.07)	0.36	0.42(1177/1501/655)	0.39(6859/7440/3080)	A	G
IL10	1	rs1800896	All	R	0.95(0.83-1.07)	0.38	0.98(0.91-1.07)	0.94(0.82-1.07)	0.64	0.32(1586/1377/358)	0.29(8946/6734/1723)	T	C
IL10	1	rs1800890	All	A	0.96(0.89-1.02)	0.2	0.97(0.89-1.05)	0.89(0.74-1.07)	0.39	0.2(2128/1058/148)	0.19(11441/5183/784)	A	T
IL13	5	rs20541	All	H	0.97(0.88-1.07)	0.52	0.97(0.88-1.07)	1(0.82-1.23)	0.81	0.21(1570/773/133)	0.23(8778/4974/938)	C	T
IL17RD	3	rs6780995	All	R	0.94(0.86-1.02)	0.16	1(0.91-1.11)	0.94(0.84-1.05)	0.37	0.54(753/1575/999)	0.51(4680/7806/4890)	G	A
IL17RE	3	rs708567	All	A	1.03(0.97-1.09)	0.33	1.03(0.94-1.13)	1.06(0.95-1.18)	0.61	0.47(988/1566/759)	0.43(5820/7587/3555)	G	A
IL1A	2	rs17561	All	H	1.09(1-1.19)	0.06	1.09(1-1.19)	1(0.8-1.26)	0.16	0.18(2264/976/99)	0.16(12491/4439/479)	G	T
IL1B	2	rs1143634	All	H	1.03(0.93-1.13)	0.56	1.03(0.93-1.13)	0.99(0.7-1.39)	0.84	0.11(2614/681/43)	0.1(13962/3178/215)	C	T
IL20RA	6	rs1555498	All	H	0.97(0.9-1.06)	0.52	0.98(0.9-1.08)	1.02(0.91-1.14)	0.76	0.5(924/1500/912)	0.53(4600/7179/5633)	C	T
IL22	12	rs2227507	All	A	1(0.86-1.16)	0.99	1.01(0.87-1.18)	0.75(0.25-2.22)	0.85	0.04(2742/217/4)	0.04(12811/980/20)	T	C
IL22	12	rs1012356	All	R	1.02(0.94-1.12)	0.6	1.01(0.91-1.11)	1.03(0.92-1.15)	0.86	0.5(835/1632/868)	0.51(4254/8493/4643)	A	T
IL22	12	rs2227491	All	D	1.08(0.96-1.21)	0.21	1.07(0.95-1.21)	1.08(0.96-1.23)	0.44	0.64(453/1488/1369)	0.63(2505/7684/7080)	T	C
IL22	12	rs2227485	All	H	1.07(0.99-1.15)	0.1	1.06(0.96-1.16)	0.97(0.87-1.09)	0.22	0.45(995/1651/684)	0.47(4979/8362/4021)	G	A
IL22	12	rs2227478	All	R	0.92(0.85-1)	0.04	1.04(0.92-1.18)	0.95(0.84-1.08)	0.10	0.64(433/1524/1380)	0.67(2059/7268/8059)	G	A
IL4	5	rs2243250	All	R	0.89(0.82-0.96)	3.61×10^{-03}	1.07(0.9-1.26)	0.94(0.8-1.11)	0.01	0.74(204/1222/1762)	0.76(1101/6094/10066)	C	T
IL4R	16	rs1805015	All	R	1.06(0.96-1.18)	0.23	1(0.92-1.1)	1.07(0.95-1.19)	0.48	0.42(1184/1523/624)	0.39(6872/7570/2912)	T	C
IRF1	5	rs2706384	All	D	0.92(0.85-1)	0.04	0.92(0.85-1.01)	0.9(0.8-1.01)	0.11	0.4(1189/1509/550)	0.44(5462/8154/3434)	C	A
LTA	6	rs2239704	All	A	1.06(1-1.14)	0.06	1.07(0.99-1.17)	1.12(0.96-1.3)	0.16	0.26(1852/1186/268)	0.26(9604/6224/1411)	G	T
LTA	6	rs909253	All	A	0.96(0.91-1.01)	0.13	0.95(0.87-1.04)	0.92(0.82-1.03)	0.31	0.45(1024/1602/693)	0.47(4997/8355/3853)	T	C
NOD1	7	rs2075820	All	H	1.08(1-1.16)	0.06	1.07(0.98-1.16)	0.97(0.86-1.09)	0.16	0.39(1230/1609/486)	0.38(6692/8105/2597)	G	A
NOS2	17	rs2297518	All	R	0.76(0.55-1.05)	0.08	0.97(0.89-1.07)	0.75(0.54-1.04)	0.20	0.12(2569/709/47)	0.12(13341/3684/298)	G	A
NOS2	17	rs1800482	All	A	0.89(0.8-0.99)	0.03	0.91(0.81-1.02)	0.59(0.33-1.05)	0.05	0.08(2613/442/13)	0.09(12169/2320/120)	G	C
NOS2	17	rs9282799	All	A	1.12(0.99-1.27)	0.07	1.1(0.97-1.26)	1.59(0.84-3.03)	0.14	0.06(2741/332/13)	0.05(13124/1476/45)	C	T
NOS2	17	rs8078340	All	R	0.84(0.69-1.01)	0.06	1.04(0.95-1.13)	0.85(0.7-1.03)	0.11	0.22(2012/1168/145)	0.2(11224/5365/808)	C	T
RTN3	11	rs542998	All	H	0.96(0.88-1.04)	0.3	0.96(0.87-1.05)	0.99(0.88-1.12)	0.58	0.45(1112/1448/759)	0.49(5203/7090/4964)	T	C
SPTB	14	rs229587	All	R	1.01(0.9-1.15)	0.82	1(0.92-1.09)	1.01(0.89-1.16)	0.97	0.33(1512/1390/368)	0.35(7361/7416/2348)	T	C
TLR1	4	rs4833095	All	R	1.15(0.89-1.48)	0.29	1.01(0.91-1.12)	1.15(0.89-1.5)	0.56	0.12(2580/662/82)	0.15(12637/3942/681)	C	T
TLR4	9	rs4986791	All	H	0.98(0.7-1.38)	0.93	n.c.[§]	n.c.[§]	n.c[§].	0.01(828/12/0)	0.01(4187/74/3)	C	T
TLR4	9	rs4986790	All	R	0.63(0.35-1.13)	0.1	1.01(0.9-1.15)	0.62(0.35-1.12)	0.24	0.07(2687/378/13)	0.07(12626/1852/112)	A	G
TLR6	4	rs5743810	All	H	1.01(0.73-1.41)	0.93	n.c.[§]	n.c.[§]	n.c[§].	0.01(1693/33/0)	0.01(7539/184/3)	C	T
TLR6	4	rs5743809	All	H	1.13(0.99-1.3)	0.08	1.13(0.99-1.29)	0.5(0.19-1.27)	0.06	0.05(2932/311/5)	0.04(15698/1279/43)	T	C
TLR9	3	rs187084	All	R	1.07(0.99-1.17)	0.1	1.01(0.86-1.19)	1.08(0.93-1.27)	0.25	0.72(228/1087/1477)	0.7(1455/6473/7909)	C	T
TNF	6	rs1799964	All	H	1.06(0.97-1.15)	0.18	1.06(0.97-1.15)	0.97(0.8-1.18)	0.39	0.21(2080/1107/141)	0.2(11148/5452/767)	T	C
TNF	6	rs1800629	All	R	1.12(0.81-1.53)	0.49	0.97(0.88-1.07)	1.11(0.81-1.52)	0.65	0.11(2584/629/51)	0.11(13681/3273/222)	G	A
TNF	6	rs361525	All	H	1.05(0.93-1.19)	0.43	1.05(0.93-1.19)	0.81(0.41-1.61)	0.61	0.06(2947/378/10)	0.05(15732/1647/55)	G	A
TNF	6	rs3093662	All	R	0.76(0.49-1.16)	0.19	1.01(0.91-1.12)	0.76(0.49-1.17)	0.42	0.1(2670/588/26)	0.08(14381/2583/143)	A	G
TRIM5	11	rs7935564	All	D	0.93(0.85-1.01)	0.09	0.94(0.85-1.02)	0.92(0.82-1.02)	0.23	0.44(1042/1608/673)	0.42(5881/8072/3205)	G	A

Supplementary Table 9: Cerebral malaria only association signals. Summary of association signals for all SNPs for *cerebral malaria only* across the 12 contributing Consortial Project 1 study sites. Odds ratios (OR), 95% confidence intervals (95% CI) and p-values (*P*) are presented for the best model (for autosomal SNPs and for females at X chromosome SNPs this is the model (selected from additive, recessive, dominant or heterozygote advantage) that has the most significant association; for males at X chromosome, this is the male hemizygote model and; for all individuals combined at X chromosome SNPs this is the model (selected from additive, recessive or dominant) that has the most significant association. Heterozygote and homozygote ORs from a genotypic model are also presented. Results are adjusted for HbS (except rs334), gender and ethnicity. Sites at which a SNP was found to be monomorphic were excluded from the analysis. An, ancestral; De, derived; n.c., not calculated. [a]Models are A, additive; D, dominant; H, heterozygote advantage; M, male hemizygote; R, recessive. [§] Genotype counts too small for accurate calculation. [¶]Not applicable to male hemizygotes. *Models are equivalent due to zero genotype class.

Gene	Chromosome	SNP Ref	Sample	Best Model[a]	Best Model OR(95% CI)	Best Model *P*	Heterozygote OR(95% CI)	Derived Homozygote OR(95% CI)	Genotypic *P*	Frequency (Derived Homozygote/ Heterozygote/Ancestal Homozygote) Cases	Controls	Alleles An	De
ABO	9	rs8176746	All	D	1.28(1.16-1.42)	1.71×10^{-06}	1.28(1.15-1.42)	1.34(1.04-1.71)	1.01×10^{-05}	0.22(1342/746/97)	0.17(11943/4852/565)	C	A
ABO	9	rs8176719	All	R	0.68(0.62-0.76)	7.97×10^{-14}	0.9(0.77-1.05)	0.63(0.54-0.74)	3.10×10^{-13}	0.62(302/1054/816)	0.69(1700/7215/8238)	I	D
ADCY9	16	rs2230739	All	R	0.9(0.62-1.31)	0.59	0.98(0.87-1.11)	0.9(0.62-1.3)	0.84	0.12(1701/453/39)	0.15(12706/4094/604)	A	G
ADCY9	16	rs10775349	All	R	1.18(0.9-1.54)	0.25	1.02(0.91-1.14)	1.18(0.9-1.56)	0.48	0.23(1396/581/214)	0.3(9884/4518/3000)	C	G
ADORA2B	17	rs2535611	All	A	0.95(0.83-1.08)	0.43	0.95(0.82-1.1)	0.9(0.53-1.54)	0.73	0.07(1865/280/19)	0.07(14377/2198/130)	T	C
ATP2B4	1	rs55868763	All	D	1.48(1.22-1.81)	5.39×10^{-05}	1.43(1.17-1.77)	1.53(1.25-1.89)	0.00	0.71(137/791/929)	0.68(1428/5690/6229)	C	G
ATP2B4	1	rs1541255	All	R	0.67(0.55-0.82)	3.96×10^{-05}	0.93(0.83-1.04)	0.65(0.53-0.79)	0.00	0.29(932/788/137)	0.32(6241/5667/1439)	A	G
ATP2B4	1	rs10900585	All	D	1.53(1.27-1.84)	3.68×10^{-06}	1.49(1.22-1.81)	1.58(1.3-1.92)	1.34×10^{-05}	0.69(159/816/851)	0.66(1644/5722/5737)	G	T
ATP2B4	1	rs4951074	All	R	0.64(0.51-0.79)	1.22×10^{-05}	1(0.89-1.12)	0.64(0.51-0.79)	6.97×10^{-05}	0.28(890/762/121)	0.31(6115/5392/1284)	G	A
ATP2B4	1	rs3753036	All	A	1.21(0.94-1.56)	0.15	1.22(0.93-1.59)	1.34(0.3-5.94)	0.36	0.02(1946/72/2)	0.04(14787/1253/81)	G	A
C6	5	rs1801033	All	D	0.94(0.84-1.04)	0.24	0.94(0.84-1.05)	0.95(0.82-1.09)	0.49	0.45(675/1069/445)	0.48(4757/8591/4003)	A	C
CD36	7	G1439C	All	H	0.9(0.64-1.27)	0.56	n.c.[§]	n.c.[§]	n.c[§].	0.03(596/44/0)	0.03(3470/199/5)	G	C
CD36	7	rs3211938	All	A	0.88(0.77-1)	0.05	0.88(0.76-1.03)	0.73(0.44-1.22)	0.14	0.08(1730/287/22)	0.09(12291/2178/174)	T	G
CD40LG	X	rs3092945	M	M	0.87(0.75-1.01)	0.07	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.31(773/0/349)	0.27(6449/0/2348)	T	C
CD40LG	X	rs3092945	F	R	0.71(0.56-0.9)	3.49×10^{-03}	1.13(0.96-1.32)	0.75(0.58-0.97)	4.89×10^{-03}	0.33(424/411/103)	0.27(4581/2621/849)	T	C
CD40LG	X	rs3092945	All	R	0.82(0.73-0.94)	2.97×10^{-03}	1.15(0.98-1.34)	0.84(0.74-0.96)	2.11×10^{-03}	0.32(1197/411/452)	0.27(11030/2621/3197)	T	C
CD40LG	X	rs1126535	M	M	1.05(0.86-1.27)	0.65	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.15(1012/0/178)	0.14(7793/0/1290)	T	C
CD40LG	X	rs1126535	F	R	1.31(0.86-1.99)	0.22	0.96(0.81-1.15)	1.29(0.85-1.97)	0.43	0.15(738/230/34)	0.14(6206/1904/193)	T	C
CD40LG	X	rs1126535	All	R	1.08(0.91-1.27)	0.37	0.96(0.8-1.14)	1.08(0.91-1.27)	0.61	0.15(1750/230/212)	0.14(13999/1904/1483)	T	C
CFTR	7	rs17140229	All	H	0.94(0.84-1.05)	0.27	0.94(0.83-1.06)	0.99(0.84-1.17)	0.54	0.38(694/807/265)	0.36(5182/5816/1632)	T	C
CR1	1	rs17047660	All	D	0.91(0.82-1.01)	0.07	0.91(0.82-1.01)	0.91(0.75-1.11)	0.19	0.28(1065/803/163)	0.26(8059/5508/1048)	A	G
CR1	1	rs17047661	All	D	1.1(0.9-1.35)	0.35	1.1(0.89-1.35)	1.1(0.9-1.36)	0.64	0.75(135/767/1140)	0.72(1159/5820/7633)	A	G
CTL4	6	rs2242665	All	H	0.89(0.81-0.99)	0.03	0.8(0.67-0.95)	0.87(0.74-1.03)	0.03	0.71(214/821/1141)	0.7(1670/7134/8465)	G	A
DARC	1	rs2814778	All	H	1.75(0.83-3.68)	0.16	13.95(0.23-835.58)	8.65(0.13-557.62)	0.22	0.93(150/9/1981)	0.83(2751/59/13799)	A	G
DERL3	22	rs1128127	All	D	0.93(0.82-1.05)	0.23	0.93(0.81-1.05)	0.93(0.81-1.07)	0.48	0.51(588/978/615)	0.47(5327/7634/4290)	G	A
EMR1	19	rs373533	All	R	0.98(0.87-1.11)	0.78	1(0.89-1.11)	0.98(0.85-1.13)	0.96	0.45(667/1057/443)	0.43(5667/8256/3280)	G	T
EMR1	19	rs461645	All	H	1.02(0.92-1.12)	0.75	1.02(0.9-1.16)	1.01(0.88-1.16)	0.94	0.55(449/1065/675)	0.57(3357/8303/5726)	T	C
G6PD	X	rs1050829	M	M	1.23(1.07-1.41)	4.55×10^{-03}	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.42(634/0/468)	0.38(4679/0/2869)	T	C
G6PD	X	rs1050829	F	R	1.23(1.01-1.5)	0.04	1.01(0.86-1.2)	1.24(1-1.54)	0.12	0.41(325/426/167)	0.39(2606/3356/1062)	T	C
G6PD	X	rs1050829	All	R	1.23(1.1-1.38)	4.08×10^{-04}	0.99(0.85-1.16)	1.23(1.09-1.38)	2.11×10^{-03}	0.42(959/426/635)	0.38(7285/3356/3931)	T	C
G6PD	X	rs1050828	M	M	1.49(1.24-1.79)	3.55×10^{-05}	n.c.[¶]	n.c.[¶]	n.c.[¶]	0.2(894/0/222)	0.15(6483/0/1105)	C	T
G6PD	X	rs1050828	F	R	1.94(1.3-2.89)	1.92×10^{-03}	0.96(0.8-1.16)	1.92(1.28-2.87)	7.51×10^{-03}	0.16(669/215/41)	0.15(5069/1770/174)	C	T
G6PD	X	rs1050828	All	A	1.19(1.1-1.28)	2.62×10^{-05}	0.93(0.78-1.12)	1.55(1.31-1.83)	1.66×10^{-06}	0.18(1563/215/263)	0.15(11552/1770/1279)	C	T
GBP7	1	rs1803632	All	A	1.05(0.98-1.12)	0.19	1.04(0.92-1.16)	1.1(0.96-1.26)	0.41	0.47(623/1066/503)	0.51(4369/8259/4777)	G	C
GNAS	20	rs8386	All	H	0.98(0.88-1.1)	0.76	0.98(0.88-1.1)	0.99(0.73-1.34)	0.95	0.17(1413/571/61)	0.16(10246/3995/398)	C	T
HBB	11	rs33950507	All	H	1.12(0.31-4.02)	0.87	n.c.[§]	n.c.[§]	n.c[§].	0.05(28/3/0)	0.04(2383/124/27)	G	A
HBB	11	rs334	All	H	0.11(0.07-0.15)	9.25×10^{-65}	0.11(0.08-0.16)	3.91(2.61-5.88)	1.18×10^{-71}	0.03(1965/31/45)	0.07(12773/1791/77)	A	T
HBB	11	rs33930165	All	A	0.74(0.6-0.9)	2.11×10^{-03}	0.73(0.57-0.92)	0.57(0.28-1.14)	8.73×10^{-03}	0.04(1465/116/10)	0.03(9341/515/74)	G	A
ICAM1	19	rs1799969	All	ADH*	1.33(0.37-4.81)	0.67	n.c.[§]	n.c.[§]	n.c[§].	0(977/3/0)	0(9294/27/0)	G	A
ICAM1	19	rs5498	All	A	1.07(0.97-1.18)	0.2	1.05(0.94-1.18)	1.2(0.89-1.63)	0.40	0.16(1555/555/78)	0.14(12716/4164/411)	A	G

IL10	1	rs3024500	All	D	0.98(0.88-1.09)	0.72	0.98(0.88-1.09)	0.99(0.85-1.14)	0.93	0.41(769/1031/391)	0.39(6859/7440/3080)	A	G
IL10	1	rs1800896	All	R	0.95(0.8-1.11)	0.5	1(0.9-1.11)	0.94(0.8-1.12)	0.79	0.3(1082/896/209)	0.29(8946/6734/1723)	T	C
IL10	1	rs1800890	All	A	0.95(0.87-1.03)	0.23	0.97(0.87-1.08)	0.85(0.67-1.09)	0.41	0.19(1442/666/85)	0.19(11441/5183/784)	A	T
IL13	5	rs20541	All	D	1.13(1-1.26)	0.04	1.12(0.99-1.26)	1.18(0.91-1.52)	0.12	0.21(1200/582/96)	0.23(8778/4974/938)	C	T
IL17RD	3	rs6780995	All	A	0.98(0.92-1.05)	0.65	0.99(0.87-1.12)	0.97(0.84-1.11)	0.90	0.53(493/1064/634)	0.51(4680/7806/4890)	G	A
IL17RE	3	rs708567	All	H	1.02(0.92-1.12)	0.7	1.02(0.9-1.15)	1(0.87-1.15)	0.93	0.5(568/1044/550)	0.43(5820/7587/3555)	G	A
IL1A	2	rs17561	All	R	1.06(0.81-1.38)	0.67	1(0.89-1.11)	1.06(0.81-1.39)	0.91	0.17(1520/601/74)	0.16(12491/4439/479)	G	T
IL1B	2	rs1143634	All	A	1.02(0.92-1.13)	0.72	1.01(0.9-1.14)	1.08(0.72-1.6)	0.92	0.12(1695/461/33)	0.1(13962/3178/215)	C	T
IL20RA	6	rs1555498	All	A	1.1(1.02-1.18)	0.01	1.06(0.95-1.19)	1.21(1.05-1.39)	0.03	0.47(635/1042/518)	0.53(4600/7179/5633)	C	T
IL22	12	rs2227507	All	A	0.96(0.79-1.17)	0.72	0.92(0.75-1.13)	2.35(0.76-7.32)	0.29	0.04(1551/110/4)	0.04(12811/980/20)	T	C
IL22	12	rs1012356	All	A	1.06(0.99-1.14)	0.09	1.04(0.92-1.18)	1.13(0.98-1.3)	0.21	0.5(595/1017/582)	0.51(4254/8493/4643)	A	T
IL22	12	rs2227491	All	A	1.07(0.99-1.15)	0.08	1.07(0.91-1.26)	1.14(0.97-1.35)	0.21	0.65(326/883/972)	0.63(2505/7684/7080)	T	C
IL22	12	rs2227485	All	R	1.06(0.94-1.19)	0.36	0.97(0.86-1.09)	1.04(0.9-1.19)	0.59	0.46(679/1004/501)	0.47(4979/8362/4021)	G	A
IL22	12	rs2227478	All	H	1.05(0.95-1.16)	0.33	1.05(0.9-1.23)	1.01(0.86-1.18)	0.62	0.64(303/984/904)	0.67(2059/7268/8059)	G	A
IL4	5	rs2243250	All	D	1.17(0.96-1.42)	0.12	1.19(0.97-1.46)	1.15(0.94-1.4)	0.23	0.74(150/830/1195)	0.76(1101/6094/10066)	C	T
IL4R	16	rs1805015	All	R	1.01(0.89-1.14)	0.88	1(0.89-1.12)	1.01(0.87-1.16)	0.99	0.42(763/1000/422)	0.39(6872/7570/2912)	T	C
IRF1	5	rs2706384	All	R	0.88(0.77-1)	0.05	1(0.89-1.12)	0.88(0.76-1.02)	0.15	0.44(683/1028/408)	0.44(5462/8154/3434)	C	A
LTA	6	rs2239704	All	D	0.93(0.84-1.04)	0.19	0.93(0.83-1.03)	0.96(0.81-1.14)	0.39	0.31(1059/854/237)	0.26(9604/6224/1411)	G	T
LTA	6	rs909253	All	R	1.07(0.95-1.2)	0.29	1.01(0.9-1.14)	1.07(0.93-1.24)	0.56	0.46(680/999/493)	0.47(4997/8355/3853)	T	C
NOD1	7	rs2075820	All	A	0.93(0.87-1)	0.05	0.92(0.82-1.02)	0.87(0.75-1.02)	0.13	0.36(893/997/299)	0.38(6692/8105/2597)	G	A
NOS2	17	rs2297518	All	R	0.81(0.5-1.31)	0.38	1.02(0.9-1.16)	0.81(0.5-1.32)	0.64	0.1(1751/404/21)	0.12(13341/3684/298)	G	A
NOS2	17	rs1800482	All	A	1.07(0.95-1.21)	0.29	1.06(0.92-1.21)	1.23(0.75-2.01)	0.54	0.09(1678/342/21)	0.09(12169/2320/120)	G	C
NOS2	17	rs9282799	All	A	1.13(0.98-1.3)	0.11	1.12(0.96-1.31)	1.4(0.65-3.01)	0.27	0.07(1781/251/9)	0.05(13124/1476/45)	C	T
NOS2	17	rs8078340	All	A	0.97(0.89-1.05)	0.45	0.98(0.88-1.09)	0.92(0.73-1.15)	0.72	0.22(1322/765/103)	0.2(11224/5365/808)	C	T
RTN3	11	rs542998	All	D	0.98(0.89-1.09)	0.74	0.98(0.88-1.1)	0.99(0.85-1.15)	0.94	0.42(770/985/426)	0.49(5203/7090/4964)	T	C
SPTB	14	rs229587	All	D	0.93(0.84-1.03)	0.16	0.92(0.83-1.03)	0.95(0.79-1.13)	0.37	0.31(925/800/207)	0.35(7361/7416/2348)	T	C
TLR1	4	rs4833095	All	H	0.87(0.77-0.99)	0.04	0.88(0.77-1)	1.06(0.72-1.56)	0.11	0.11(1734/393/37)	0.15(12637/3942/681)	C	T
TLR4	9	rs4986791	All	H	1.27(0.89-1.8)	0.19	n.c.[§]	n.c.[§]	n.c[§].	0.01(867/18/0)	0.01(4187/74/3)	C	T
TLR4	9	rs4986790	All	R	0.63(0.35-1.13)	0.1	1.02(0.89-1.18)	0.63(0.35-1.13)	0.25	0.09(1694/323/16)	0.07(12626/1852/112)	A	G
TLR6	4	rs5743810	All	H	1.04(0.67-1.62)	0.85	1.05(0.67-1.62)	7.29(0.67-79.55)	0.38	0.01(785/14/1)	0.01(7539/184/3)	C	T
TLR6	4	rs5743809	All	A	1.03(0.86-1.23)	0.75	1.02(0.85-1.24)	1.14(0.42-3.1)	0.94	0.04(1892/163/5)	0.04(15698/1279/43)	T	C
TLR9	3	rs187084	All	D	0.87(0.74-1.03)	0.12	0.87(0.73-1.04)	0.87(0.73-1.04)	0.30	0.7(216/852/1091)	0.7(1455/6473/7909)	C	T
TNF	6	rs1799964	All	A	1.06(0.97-1.16)	0.23	1.05(0.94-1.17)	1.14(0.88-1.48)	0.48	0.18(1487/614/87)	0.2(11148/5452/767)	T	C
TNF	6	rs1800629	All	R	0.8(0.52-1.24)	0.31	1.03(0.91-1.17)	0.81(0.52-1.25)	0.54	0.12(1606/435/28)	0.11(13681/3273/222)	G	A
TNF	6	rs361525	All	H	1.12(0.94-1.34)	0.21	1.12(0.94-1.34)	0.86(0.33-2.25)	0.43	0.04(2019/171/5)	0.05(15732/1647/55)	G	A
TNF	6	rs3093662	All	R	1.26(0.75-2.12)	0.4	1.01(0.87-1.16)	1.26(0.75-2.13)	0.69	0.07(1770/270/18)	0.08(14381/2583/143)	A	G
TRIM5	11	rs7935564	All	A	1.01(0.95-1.09)	0.69	1.01(0.9-1.14)	1.03(0.89-1.18)	0.92	0.48(589/1078/487)	0.42(5881/8072/3205)	G	A

Supplementary Table 10: Severe malarial anaemia only association signals. Summary of association signals for all SNPs for *severe malarial anaemia only* across the 12 contributing Consortial Project 1 study sites. Odds ratios (OR), 95% confidence intervals (95% CI) and p-values (*P*) are presented for the best model (for autosomal SNPs and for females at X chromosome SNPs this is the model (selected from additive, recessive, dominant or heterozygote advantage) that has the most significant association; for males at X chromosome, this is the male hemizygote model and; for all individuals combined at X chromosome SNPs this is the model (selected from additive, recessive or dominant) that has the most significant association. Heterozygote and homozygote ORs from a genotypic model are also presented. Results are adjusted for HbS (except rs334), gender and ethnicity. Sites at which a SNP was found to be monomorphic were excluded from the analysis. An, ancestral; De, derived; n.c., not calculated. [a]Models are A, additive; D, dominant; H, heterozygote advantage; M, male hemizygote; R, recessive. [§] Genotype counts too small for accurate calculation. [¶]Not applicable to male hemizygotes. *Models are equivalent due to zero genotype class.

Sickle Cell Trait Phenotype Site	Heterozygote Frequency (Heterozygote/Total) Cases	Controls	OR (95% CI)	*P*
Males and Females – Heterozygote Advantage Model				
Severe malaria				
Gambia	0.01 (32/2415)	0.14 (460/3332)	0.09(0.06-0.12)	2.80×10^{-74}
Mali	0.01 (4/453)	0.08 (28/344)	0.09(0.03-0.27)	4.08×10^{-08}
Burkina Faso	0.02 (21/865)	0.1 (73/729)	0.22(0.14-0.37)	6.94×10^{-11}
Ghana (Navrongo)	0.03 (19/682)	0.1 (50/489)	0.25(0.14-0.43)	7.99×10^{-08}
Ghana (Kumasi)	0.02 (32/1495)	0.13 (271/2042)	0.13(0.09-0.2)	4.83×10^{-35}
Nigeria	0.12 (9/77)	0.22 (9/40)	0.46(0.16-1.28)	0.14
Cameroon	0.05 (32/621)	0.17 (99/576)	0.26(0.17-0.4)	3.17×10^{-11}
Kenya	0.03 (57/2261)	0.15 (594/3941)	0.15(0.12-0.2)	6.33×10^{-60}
Tanzania	0.01 (5/428)	0.17 (75/452)	0.06(0.02-0.15)	5.31×10^{-18}
Malawi	0 (2/1388)	0.05 (132/2696)	0.03(0.01-0.11)	1.64×10^{-22}
All	0.02 (213/10685)	0.12 (1791/14641)	0.14(0.12-0.16)	1.62×10^{-225}
Cerebral malaria only				
Gambia	0.01 (9/783)	0.14 (460/3332)	0.07(0.04-0.14)	1.10×10^{-32}
Mali	0 (0/86)	0.08 (28/344)	n.c.[§]	n.c.[§]
Burkina Faso	0 (0/107)	0.1 (73/729)	n.c.[§]	n.c.[§]
Ghana (Navrongo)	0.05 (1/22)	0.1 (50/489)	0.42(0.06-3.21)	0.34
Ghana (Kumasi)	0.01 (3/230)	0.13 (271/2042)	0.1(0.03-0.31)	3.33×10^{-09}
Nigeria	0 (0/6)	0.22 (9/40)	n.c.[§]	n.c.[§]
Cameroon	0.05 (2/39)	0.17 (99/576)	0.26(0.06-1.08)	0.02
Kenya	0.03 (25/908)	0.15 (594/3941)	0.17(0.11-0.26)	6.79×10^{-28}
Tanzania	0 (0/34)	0.17 (75/452)	0(0-Inf)	7.73×10^{-04}
Malawi	0 (2/873)	0.05 (132/2696)	0.04(0.01-0.18)	7.84×10^{-15}
All	0.01 (42/3088)	0.12 (1791/14641)	0.11(0.08-0.15)	4.67×10^{-88}
Severe malarial anaemia only				
Gambia	0.01 (3/456)	0.14 (460/3332)	0.04(0.01-0.13)	5.48×10^{-24}
Mali	0.01 (1/185)	0.08 (28/344)	0.06(0.01-0.41)	9.55×10^{-06}
Burkina Faso	0 (0/39)	0.1 (73/729)	n.c.[§]	n.c.[§]
Ghana (Navrongo)	0.02 (5/248)	0.1 (50/489)	0.18(0.07-0.45)	8.22×10^{-06}
Ghana (Kumasi)	0.02 (11/551)	0.13 (271/2042)	0.14(0.07-0.27)	1.07×10^{-15}
Nigeria	0.38 (3/8)	0.22 (9/40)	1.98(0.39-10.11)	0.42
Cameroon	0.04 (3/82)	0.17 (99/576)	0.18(0.06-0.59)	3.23×10^{-04}
Kenya	0.02 (3/158)	0.15 (594/3941)	0.11(0.04-0.36)	5.18×10^{-08}
Tanzania	0.01 (2/182)	0.17 (75/452)	0.06(0.01-0.24)	6.83×10^{-10}
Malawi	0 (0/132)	0.05 (132/2696)	n.c.[§]	n.c.[§]
All	0.02 (31/2041)	0.12 (1791/14641)	0.11(0.07-0.15)	9.25×10^{-65}

Supplementary Table 11: HbS All Heterozygous Model. Frequency of cases and controls heterozygous for sickle-cell haemoglobin (HbS) derived from rs334. Odds Ratios (OR), 95% Confidence Intervals (95% CI) and p-values (*P*) for association of HbS heterozygotes with severe malaria, cerebral malaria only and severe malarial anaemia only for all individuals at each study site and at all study sites combined. Results are adjusted for gender and ethnicity. Sites at which HbS is not present (Vietnam and Papua New Guinea) were excluded from this analysis. Het, Heterozygotes; n.c., not calculated. [§] sample size too small for accurate calculation**.**

Blood Group O Phenotype Site	Derived Homozygote Frequency (Derived Homozygote/Total) Cases	Controls	OR (95% CI)	*P*
Males and Females – Recessive Model				
All severe malaria				
Gambia	0.39 (945/2418)	0.46 (1551/3337)	0.75(0.67-0.84)	3.08×10^{-07}
Mali	0.29 (131/450)	0.43 (146/340)	0.57(0.42-0.78)	3.15×10^{-04}
Burkina Faso	0.37 (321/859)	0.44 (320/721)	0.75(0.61-0.92)	6.30×10^{-03}
Ghana (Navrongo)	0.39 (260/666)	0.4 (193/484)	0.93(0.73-1.19)	0.58
Ghana (Kumasi)	0.37 (547/1478)	0.5 (984/1978)	0.61(0.52-0.7)	1.66×10^{-11}
Nigeria	0.35 (27/77)	0.62 (24/39)	0.31(0.14-0.71)	4.68×10^{-03}
Cameroon	0.44 (267/603)	0.54 (310/570)	0.69(0.54-0.88)	2.46×10^{-03}
Kenya	0.47 (1055/2256)	0.55 (2126/3888)	0.74(0.66-0.82)	2.64×10^{-08}
Tanzania	0.44 (188/424)	0.48 (219/452)	0.85(0.64-1.12)	0.25
Malawi	0.43 (600/1385)	0.5 (1297/2603)	0.76(0.66-0.87)	4.05×10^{-05}
Vietnam	0.34 (271/789)	0.4 (993/2506)	0.78(0.66-0.93)	4.62×10^{-03}
Papua New Guinea	0.36 (138/384)	0.32 (75/235)	1.22(0.86-1.72)	0.27
All	0.4 (4750/11789)	0.48 (8238/17153)	0.74(0.7-0.78)	4.99×10^{-33}
Cerebral malaria only				
Gambia	0.4 (311/783)	0.46 (1551/3337)	0.77(0.66-0.91)	1.86×10^{-03}
Mali	0.28 (24/86)	0.43 (146/340)	0.55(0.32-0.94)	0.03
Burkina Faso	0.34 (36/106)	0.44 (320/721)	0.66(0.43-1.01)	5.32×10^{-02}
Ghana (Navrongo)	0.35 (7/20)	0.4 (193/484)	0.73(0.28-1.89)	0.51
Ghana (Kumasi)	0.4 (89/225)	0.5 (984/1978)	0.64(0.47-0.87)	4.02×10^{-03}
Nigeria	0.17 (1/6)	0.62 (24/39)	0.1(0.01-1.06)	0.03
Cameroon	0.43 (16/37)	0.54 (310/570)	0.65(0.33-1.28)	0.21
Kenya	0.48 (437/903)	0.55 (2126/3888)	0.79(0.69-0.92)	2.35×10^{-03}
Tanzania	0.26 (9/34)	0.48 (219/452)	0.35(0.16-0.77)	6.13×10^{-03}
Malawi	0.42 (369/872)	0.5 (1297/2603)	0.73(0.62-0.85)	5.93×10^{-05}
Vietnam	0.29 (61/210)	0.4 (993/2506)	0.6(0.44-0.82)	1.00×10^{-03}
Papua New Guinea	0.3 (13/43)	0.32 (75/235)	0.87(0.41-1.81)	0.70
All	0.41 (1373/3325)	0.48 (8238/17153)	0.73(0.67-0.79)	8.85×10^{-16}
Severe malarial anaemia only				
Gambia	0.36 (165/457)	0.46 (1551/3337)	0.65(0.53-0.8)	3.74×10^{-05}
Mali	0.3 (55/184)	0.43 (146/340)	0.61(0.41-0.9)	1.12×10^{-02}
Burkina Faso	0.39 (15/38)	0.44 (320/721)	0.84(0.43-1.64)	0.61
Ghana (Navrongo)	0.4 (96/242)	0.4 (193/484)	0.93(0.68-1.29)	0.68
Ghana (Kumasi)	0.36 (195/549)	0.5 (984/1978)	0.55(0.45-0.69)	5.19×10^{-08}
Nigeria	0.5 (4/8)	0.62 (24/39)	0.67(0.14-3.18)	0.61
Cameroon	0.38 (30/78)	0.54 (310/570)	0.55(0.33-0.92)	2.09×10^{-02}
Kenya	0.42 (68/160)	0.55 (2126/3888)	0.62(0.45-0.85)	3.18×10^{-03}
Tanzania	0.42 (74/178)	0.48 (219/452)	0.76(0.53-1.11)	0.15
Malawi	0.48 (63/130)	0.5 (1297/2603)	0.93(0.65-1.33)	0.69
Vietnam	0.38 (11/29)	0.4 (993/2506)	1(0.47-2.15)	1.00
Papua New Guinea	0.34 (40/119)	0.32 (75/235)	1.05(0.65-1.7)	0.85
All	0.38 (816/2172)	0.48 (8238/17153)	0.68(0.62-0.76)	7.97×10^{-14}

Supplementary Table 12: Blood Group O All Individuals Recessive Model. Frequency of cases and controls homozygous for the derived allele at rs8176719. Odds Ratios (OR), 95% Confidence Intervals (95% CI) and p-values (*P*) for association of Blood Group O with severe malaria, cerebral malaria only and severe malarial anaemia only for all individuals at each study site and at all study sites combined. Results are adjusted for gender, sickle-cell haemoglobin and ethnicity.

G6PD+202 Phenotype Site	Derived-Allele Frequency (Derived Homozygote/ Heterozygote/Ancestal Homozygote) Cases	Controls	OR (95% CI)	*P*
Males and Females – Additive Model				
Severe malaria				
Gambia	0.02 (2341/45/32)	0.03 (3202/83/51)	0.9(0.74-1.1)	0.32
Mali	0.17 (345/58/50)	0.17 (263/47/34)	0.99(0.8-1.23)	0.92
Burkina Faso	0.17 (661/116/85)	0.14 (576/91/58)	1.12(0.95-1.32)	0.18
Ghana (Navrongo)	0.21 (490/92/99)	0.19 (353/81/54)	1.08(0.92-1.28)	0.35
Ghana (Kumasi)	0.2 (1093/214/187)	0.18 (1510/299/216)	1.06(0.96-1.18)	0.26
Nigeria	0.14 (63/7/7)	0.28 (22/12/5)	0.53(0.29-0.97)	0.04
Cameroon	0.11 (523/48/47)	0.11 (502/25/51)	1.09(0.89-1.34)	0.41
Kenya	0.19 (1673/311/270)	0.19 (2863/639/438)	1.01(0.93-1.09)	0.85
Tanzania	0.16 (334/49/45)	0.2 (319/85/49)	0.83(0.67-1.03)	0.09
Malawi	0.21 (993/212/178)	0.2 (1942/408/323)	1.03(0.94-1.13)	0.52
All	0.15 (8516/1152/1000)	0.15 (11552/1770/1279)	1.02(0.97-1.06)	0.45
Cerebral malaria only				
Gambia	0.02 (766/9/9)	0.03 (3202/83/51)	0.75(0.53-1.06)	0.10
Mali	0.08 (75/8/3)	0.17 (263/47/34)	0.58(0.35-0.94)	0.03
Burkina Faso	0.16 (78/21/6)	0.14 (576/91/58)	1.05(0.77-1.43)	0.76
Ghana (Navrongo)	0.14 (18/2/2)	0.19 (353/81/54)	0.75(0.34-1.65)	0.47
Ghana (Kumasi)	0.15 (182/28/20)	0.18 (1510/299/216)	0.86(0.68-1.09)	0.21
Nigeria	0.08 (5/1/0)	0.28 (22/12/5)	0.32(0.07-1.36)	0.12
Cameroon	0.06 (36/1/2)	0.11 (502/25/51)	0.71(0.3-1.66)	0.43
Kenya	0.17 (682/135/89)	0.19 (2863/639/438)	0.94(0.84-1.05)	0.26
Tanzania	0.19 (25/5/4)	0.2 (319/85/49)	0.95(0.55-1.63)	0.85
Malawi	0.18 (646/128/95)	0.2 (1942/408/323)	0.94(0.84-1.05)	0.27
All	0.13 (2513/338/230)	0.15 (11552/1770/1279)	0.91(0.85-0.97)	6.08×10^{-03}
Severe malarial anaemia only				
Gambia	0.03 (437/11/9)	0.03 (3202/83/51)	1.11(0.8-1.53)	0.53
Mali	0.22 (133/24/28)	0.17 (263/47/34)	1.18(0.91-1.53)	0.21
Burkina Faso	0.22 (28/5/6)	0.14 (576/91/58)	1.36(0.85-2.18)	0.20
Ghana (Navrongo)	0.24 (174/26/47)	0.19 (353/81/54)	1.22(0.98-1.51)	0.07
Ghana (Kumasi)	0.23 (383/83/85)	0.18 (1510/299/216)	1.19(1.03-1.38)	0.02
Nigeria	0.31 (5/1/2)	0.28 (22/12/5)	1.34(0.39-4.6)	0.65
Cameroon	0.17 (63/8/10)	0.11 (502/25/51)	1.54(1.06-2.22)	0.02
Kenya	0.26 (108/20/32)	0.19 (2863/639/438)	1.32(1.07-1.63)	1.08×10^{-02}
Tanzania	0.15 (147/13/21)	0.2 (319/85/49)	0.81(0.61-1.08)	0.16
Malawi	0.27 (85/24/23)	0.2 (1942/408/323)	1.28(1.02-1.61)	0.03
All	0.18 (1563/215/263)	0.15 (11552/1770/1279)	1.19(1.1-1.28)	2.62×10^{-05}

Supplementary Table 13: G6PD+202 Males and Females Additive Model. Frequency of the derived-allele at G6PD+202 (rs1050828) in all cases and controls. Odds ratios (OR), 95% confidence intervals (95% CI) and p-values are presented for association of the derived-allele with all severe malaria, cerebral malaria only and severe malarial anaemia only for all individuals at each study site and at all study sites combined. Results are adjusted for sickle-cell trait and ethnicity. Sites where rs1050828 is not present (Vietnam and Papua New Guinea) were excluded from this analysis.

G6PD+202 Phenotype Site	Derived-Allele Frequency (Derived Hemizygote/Total) Cases	Controls	OR (95% CI)	*P*
Males – Hemizygote Model				
All severe malaria				
Gambia	0.02 (29/1265)	0.03 (49/1684)	0.81(0.5-1.31)	0.39
Mali	0.18 (47/255)	0.18 (31/174)	0.94(0.56-1.58)	0.82
Burkina Faso	0.15 (75/488)	0.14 (51/375)	1.15(0.78-1.69)	0.49
Ghana (Navrongo)	0.22 (86/386)	0.18 (49/272)	1.29(0.87-1.92)	0.21
Ghana (Kumasi)	0.2 (160/799)	0.18 (184/1051)	1.12(0.87-1.44)	0.38
Nigeria	0.09 (4/47)	0.17 (3/18)	0.32(0.06-1.71)	0.20
Cameroon	0.13 (44/336)	0.11 (48/419)	1.31(0.83-2.07)	0.25
Kenya	0.2 (232/1167)	0.19 (376/1989)	1.13(0.93-1.36)	0.22
Tanzania	0.15 (34/227)	0.19 (39/205)	0.75(0.44-1.27)	0.29
Malawi	0.22 (155/707)	0.2 (275/1401)	1.13(0.91-1.41)	0.28
All	0.15 (866/5677)	0.15 (1105/7588)	1.1(0.99-1.22)	0.07
Cerebral malaria only				
Gambia	0.02 (9/398)	0.03 (49/1684)	0.78(0.37-1.62)	0.49
Mali	0.06 (3/51)	0.18 (31/174)	0.25(0.07-0.92)	0.02
Burkina Faso	0.07 (4/57)	0.14 (51/375)	0.46(0.16-1.33)	0.12
Ghana (Navrongo)	0.08 (1/12)	0.18 (49/272)	0.39(0.05-3.15)	0.32
Ghana (Kumasi)	0.16 (18/116)	0.18 (184/1051)	0.82(0.47-1.44)	0.48
Nigeria	0 (0/4)	0.17 (3/18)	0(0-Inf)	0.16
Cameroon	0.1 (2/20)	0.11 (48/419)	0.94(0.21-4.2)	0.93
Kenya	0.15 (71/465)	0.19 (376/1989)	0.82(0.62-1.08)	0.16
Tanzania	0.18 (3/17)	0.19 (39/205)	1.01(0.26-3.92)	0.99
Malawi	0.18 (80/435)	0.2 (275/1401)	0.91(0.69-1.2)	0.49
All	0.12 (191/1575)	0.15 (1105/7588)	0.81(0.68-0.96)	0.01
Severe malarial anaemia only				
Gambia	0.03 (8/240)	0.03 (49/1684)	1.15(0.53-2.48)	0.73
Mali	0.24 (25/105)	0.18 (31/174)	1.32(0.71-2.47)	0.38
Burkina Faso	0.21 (4/19)	0.14 (51/375)	1.63(0.52-5.12)	0.42
Ghana (Navrongo)	0.25 (38/155)	0.18 (49/272)	1.48(0.9-2.41)	0.12
Ghana (Kumasi)	0.25 (72/289)	0.18 (184/1051)	1.4(0.99-1.97)	0.06
Nigeria	0.25 (1/4)	0.17 (3/18)	1.5(0.1-23.07)	0.77
Cameroon	0.2 (8/40)	0.11 (48/419)	2.58(1.09-6.12)	0.04
Kenya	0.33 (29/89)	0.19 (376/1989)	2.2(1.39-3.5)	1.41×10^{-03}
Tanzania	0.16 (17/108)	0.19 (39/205)	0.9(0.47-1.74)	0.76
Malawi	0.3 (20/67)	0.2 (275/1401)	1.72(1-2.94)	0.06
All	0.2 (222/1116)	0.15 (1105/7588)	1.49(1.24-1.79)	3.55×10^{-05}

Supplementary Table 14: G6PD+202 Males Hemizygote Model. Frequency of the derived-allele at G6PD+202 (rs1050828) in male cases and controls Odds ratios (OR), 95% confidence intervals (95% CI) and p-values (*P*) are presented for association of the derived-allele with severe malaria, cerebral malaria only and severe malarial anaemia only for males at each study site and at all study sites combined. Results are adjusted for sickle-cell trait and ethnicity. Sites where rs1050828 is not present (Vietnam and Papua New Guinea) were excluded from this analysis.

G6PD+202 Phenotype Site	Derived Homozygote Frequency (Derived Homozgote/Total) Cases	Controls	OR (95% CI)	*P*
Females – Recessive Model				
Severe malaria				
Gambia	0 (3/1153)	0 (2/1652)	n.c.[§]	n.c.[§]
Mali	0.02 (3/198)	0.02 (3/170)	n.c.[§]	n.c.[§]
Burkina Faso	0.03 (10/374)	0.02 (7/350)	1.36(0.5-3.65)	0.54
Ghana (Navrongo)	0.04 (13/295)	0.02 (5/216)	2.39(0.79-7.19)	0.10
Ghana (Kumasi)	0.04 (27/695)	0.03 (32/974)	1.11(0.63-1.95)	0.71
Nigeria	0.1 (3/30)	0.1 (2/21)	n.c.[§]	n.c.[§]
Cameroon	0.01 (3/282)	0.02 (3/159)	n.c.[§]	n.c.[§]
Kenya	0.03 (38/1087)	0.03 (62/1951)	1.16(0.76-1.78)	0.50
Tanzania	0.05 (11/201)	0.04 (10/248)	1.66(0.63-4.34)	0.30
Malawi	0.03 (23/676)	0.04 (48/1272)	0.89(0.53-1.48)	0.65
All	0.03 (134/4991)	0.02 (174/7013)	1.15(0.9-1.46)	0.27
Cerebral malaria only				
Gambia	0 (0/386)	0 (2/1652)	n.c.[§]	n.c.[§]
Mali	0 (0/35)	0.02 (3/170)	n.c.[§]	n.c.[§]
Burkina Faso	0.04 (2/48)	0.02 (7/350)	n.c.[§]	n.c.[§]
Ghana (Navrongo)	0.1 (1/10)	0.02 (5/216)	n.c.[§]	n.c.[§]
Ghana (Kumasi)	0.02 (2/114)	0.03 (32/974)	n.c.[§]	n.c.[§]
Nigeria	0 (0/2)	0.1 (2/21)	n.c.[§]	n.c.[§]
Cameroon	0 (0/19)	0.02 (3/159)	n.c.[§]	n.c.[§]
Kenya	0.04 (18/441)	0.03 (62/1951)	1.4(0.81-2.44)	0.24
Tanzania	0.06 (1/17)	0.04 (10/248)	n.c.[§]	n.c.[§]
Malawi	0.03 (15/434)	0.04 (48/1272)	0.9(0.5-1.63)	0.73
All	0.03 (39/1506)	0.02 (174/7013)	1.09(0.76-1.57)	0.65
Severe malarial anaemia only				
Gambia	0 (1/217)	0 (2/1652)	n.c.[§]	n.c.[§]
Mali	0.04 (3/80)	0.02 (3/170)	n.c.[§]	n.c.[§]
Burkina Faso	0.1 (2/20)	0.02 (7/350)	n.c.[§]	n.c.[§]
Ghana (Navrongo)	0.1 (9/92)	0.02 (5/216)	7.37(2.04-26.67)	1.15×10^{-03}
Ghana (Kumasi)	0.05 (13/262)	0.03 (32/974)	1.31(0.6-2.85)	0.50
Nigeria	0.25 (1/4)	0.1 (2/21)	n.c.[§]	n.c.[§]
Cameroon	0.05 (2/41)	0.02 (3/159)	n.c.[§]	n.c.[§]
Kenya	0.04 (3/71)	0.03 (62/1951)	n.c.[§]	n.c.[§]
Tanzania	0.05 (4/73)	0.04 (10/248)	n.c.[§]	n.c.[§]
Malawi	0.05 (3/65)	0.04 (48/1272)	n.c.[§]	n.c.[§]
All	0.04 (41/925)	0.02 (174/7013)	1.94(1.3-2.89)	1.92×10^{-03}

Supplementary Table 15: G6PD+202 Females Recessive Model. Frequency of female cases and controls homozygous for the derived-allele at G6PD+202 (rs1050828). Odds ratios (OR), 95% confidence intervals (95% CI) and p-values are presented for association of derived homozygotes with severe malaria, cerebral malaria only and severe malarial anaemia only for females at each study site and at all study sites combined. Results are adjusted for sickle-cell trait and ethnicity. Sites where rs1050828 is not present (Vietnam and Papua New Guinea) were excluded from this analysis. n.c. not calculated. [§] Genotype counts too small for accurate calculation.

G6PD+202 Phenotype Site	Heterozygote Frequency (Heterozgote/Total) Cases	Controls	OR (95% CI)	*P*
Females – Heterozygote Advantage Model				
Severe malaria				
Gambia	0.04 (45/1153)	0.05 (83/1652)	0.82(0.56-1.21)	0.32
Mali	0.29 (58/198)	0.28 (47/170)	1.02(0.64-1.63)	0.93
Burkina Faso	0.31 (116/374)	0.26 (91/350)	1.23(0.88-1.7)	0.22
Ghana (Navrongo)	0.31 (92/295)	0.38 (81/216)	0.75(0.52-1.09)	0.14
Ghana (Kumasi)	0.31 (214/695)	0.31 (299/974)	1.06(0.85-1.33)	0.62
Nigeria	0.23 (7/30)	0.57 (12/21)	0.23(0.07-0.77)	0.01
Cameroon	0.17 (48/282)	0.16 (25/159)	0.9(0.52-1.56)	0.72
Kenya	0.29 (311/1087)	0.33 (639/1951)	0.82(0.7-0.97)	0.02
Tanzania	0.24 (49/201)	0.34 (85/248)	0.54(0.35-0.85)	6.34×10^{-03}
Malawi	0.31 (212/676)	0.32 (408/1272)	0.98(0.8-1.2)	0.85
All	0.23 (1152/4991)	0.25 (1770/7013)	0.9(0.82-0.99)	0.02
Cerebral malaria only				
Gambia	0.02 (9/386)	0.05 (83/1652)	0.48(0.24-0.98)	0.03
Mali	0.23 (8/35)	0.28 (47/170)	0.79(0.33-1.92)	0.60
Burkina Faso	0.44 (21/48)	0.26 (91/350)	2.08(1.12-3.87)	0.02
Ghana (Navrongo)	0.2 (2/10)	0.38 (81/216)	0.4(0.08-1.94)	0.22
Ghana (Kumasi)	0.25 (28/114)	0.31 (299/974)	0.78(0.48-1.27)	0.31
Nigeria	0.5 (1/2)	0.57 (12/21)	0.89(0.05-16.66)	0.94
Cameroon	0.05 (1/19)	0.16 (25/159)	0.24(0.03-1.93)	0.11
Kenya	0.31 (135/441)	0.33 (639/1951)	0.89(0.71-1.13)	0.34
Tanzania	0.29 (5/17)	0.34 (85/248)	0.69(0.23-2.07)	0.50
Malawi	0.29 (128/434)	0.32 (408/1272)	0.9(0.71-1.14)	0.38
All	0.22 (338/1506)	0.25 (1770/7013)	0.87(0.76-1.01)	0.06
Severe malarial anaemia only				
Gambia	0.05 (11/217)	0.05 (83/1652)	1.06(0.55-2.04)	0.87
Mali	0.3 (24/80)	0.28 (47/170)	1.12(0.61-2.03)	0.72
Burkina Faso	0.25 (5/20)	0.26 (91/350)	0.89(0.31-2.53)	0.83
Ghana (Navrongo)	0.28 (26/92)	0.38 (81/216)	0.66(0.39-1.13)	0.13
Ghana (Kumasi)	0.32 (83/262)	0.31 (299/974)	1.22(0.88-1.68)	0.23
Nigeria	0.25 (1/4)	0.57 (12/21)	0.17(0.01-2.77)	0.17
Cameroon	0.2 (8/41)	0.16 (25/159)	1.14(0.46-2.84)	0.77
Kenya	0.28 (20/71)	0.33 (639/1951)	0.77(0.45-1.33)	0.34
Tanzania	0.18 (13/73)	0.34 (85/248)	0.34(0.17-0.67)	9.81×10^{-04}
Malawi	0.37 (24/65)	0.32 (408/1272)	1.26(0.75-2.11)	0.39
All	0.23 (215/925)	0.25 (1770/7013)	0.93(0.77-1.11)	0.42

Supplementary Table 16: G6PD+202 Females Heterozygote Advantage Model. Frequency of female cases and controls heterozygous for the the derived-allele at G6PD+202 (rs1050828). Odds ratios (OR), 95% confidence intervals (95% CI) and p-values are presented for association of heterozygotes with severe malaria, cerebral malaria and severe malarial anaemia for females at each study site and at all study sites combined. Results are adjusted for sickle-cell trait and ethnicity. Sites where rs1050828 is not present (Vietnam and Papua New Guinea) were excluded from this analysis.

G6PD+202	Model Allele Counts			
Phenotype	**Cases**	**Controls**	**OR (95% CI)**	***P***
Females – All Sites – Heterozygote vs. Homozygous for Ancestral Allele				
All severe malaria	1152/3705	1770/5069	0.9(0.82-0.99)	0.03
Cerebral malaria only	338/1129	1770/5069	0.87(0.76-1.01)	0.06
Severe malarial anaemia only	215/669	01770/5069	0.96(0.8-1.16)	0.68
Females – All Sites – Heterozygote vs. Homozygous for Derived-Allele				
All severe malaria	1152/134	1770/174	0.8(0.62-1.03)	0.09
Cerebral malaria only	338/39	01770/174	0.84(0.57-1.23)	0.38
Severe malarial anaemia only	0.84 (215/41)	1770/174	0.49(0.32-0.75)	1.51×10^{-03}
Females – All Sites – Homozygous for Derived vs. Homozygous for Ancestral Allele				
All severe malaria	134/3705	174/5069	1.1(0.87-1.41)	0.43
Cerebral malaria only	39/1129	174/5069	1.05(0.73-1.52)	0.80
Severe malarial anaemia only	41/669	174/5069	1.88(1.25-2.83)	3.54×10^{-03}

Supplementary Table 17: G6PD+202 Female Various Models. Counts of cases and controls in given model categories at G6PD+202 (rs1050828). Odds ratios (OR), 95% Confidence Intervals (95% CI) and p-values (*P*) are presented for association of G6PD+202 with severe malaria, cerebral malaria only and severe malarial anaemia only in females for various models at all study sites combined. Results are adjusted for sickle-cell trait and ethnicity. Sites where rs1050828 is not present (Vietnam and Papua New Guinea) were excluded from this analysis.

ATP2B4	Derived-Allele Frequency (Derived Homozygote/ Heterozygote/Ancestal Homozygote)			
Phenotype Site	**Cases**	**Controls**	**OR (95% CI)**	***P***
Males and Females – Dominant Model				
Severe malaria				
Gambia	0.91 (204/1021/1161)	0.87 (426/1369/1485)	1.61(1.34-1.93)	1.64×10^{-07}
Mali	0.92 (35/164/228)	0.92 (25/141/156)	0.97(0.56-1.68)	0.92
Burkina Faso	0.91 (78/377/388)	0.91 (63/292/365)	0.94(0.66-1.34)	0.75
Ghana (Navrongo)	0.94 (34/246/334)	0.97 (5/74/86)	0.52(0.19-1.39)	0.16
Ghana (Kumasi)	0.87 (102/365/294)	0.81 (240/586/405)	1.54(1.16-2.03)	2.32×10^{-03}
Nigeria	0.84 (12/39/25)	0.88 (4/15/15)	0.77(0.22-2.68)	0.68
Cameroon	0.87 (80/264/253)	0.83 (96/240/240)	1.24(0.89-1.74)	0.20
Kenya	0.91 (150/786/688)	0.89 (429/1689/1644)	1.29(1.06-1.58)	1.14×10^{-02}
Tanzania	0.89 (48/199/178)	0.87 (58/211/182)	1.18(0.77-1.81)	0.44
Malawi	0.91 (125/595/654)	0.88 (298/1105/1159)	1.27(1.01-1.58)	0.04
Vietnam	1 (0/33/746)	1 (0/89/2367)	n.c.[§]	n.c.[§]
All	0.9 (868/4056/4203)	0.87 (1644/5722/5737)	1.32(1.21-1.45)	1.69×10^{-09}
Cerebral malaria only				
Gambia	0.92 (65/330/380)	0.87 (426/1369/1485)	1.67(1.27-2.21)	1.48×10^{-04}
Mali	0.91 (7/35/39)	0.92 (25/141/156)	0.89(0.35-2.26)	0.81
Burkina Faso	0.93 (8/46/53)	0.91 (63/292/365)	1.16(0.54-2.51)	0.70
Ghana (Navrongo)	1 (0/10/9)	0.97 (5/74/86)	n.c.[§]	n.c.[§]
Ghana (Kumasi)	0.86 (16/58/43)	0.81 (240/586/405)	1.43(0.77-2.63)	0.24
Nigeria	0.67 (2/3/1)	0.88 (4/15/15)	0.34(0.04-3.03)	0.35
Cameroon	0.87 (5/14/20)	0.83 (96/240/240)	1.31(0.5-3.47)	0.58
Kenya	0.9 (59/285/266)	0.89 (429/1689/1644)	1.23(0.92-1.65)	0.15
Tanzania	0.88 (4/17/12)	0.87 (58/211/182)	1.2(0.4-3.62)	0.74
Malawi	0.91 (79/370/413)	0.88 (298/1105/1159)	1.26(0.97-1.64)	0.08
Vietnam	1 (0/13/195)	1 (0/89/2367)	n.c.[§]	n.c.[§]
All	0.91 (245/1168/1236)	0.87 (1644/5722/5737)	1.35(1.17-1.57)	3.06×10^{-05}
Severe malarial anaemia only				
Gambia	0.93 (33/197/219)	0.87 (426/1369/1485)	1.92(1.32-2.78)	2.25×10^{-04}
Mali	0.93 (12/68/95)	0.92 (25/141/156)	1.14(0.55-2.38)	0.73
Burkina Faso	0.89 (4/17/16)	0.91 (63/292/365)	0.79(0.27-2.32)	0.68
Ghana (Navrongo)	0.95 (11/92/122)	0.97 (5/74/86)	0.53(0.16-1.69)	0.27
Ghana (Kumasi)	0.88 (45/189/155)	0.81 (240/586/405)	1.94(1.31-2.86)	4.81×10^{-04}
Nigeria	0.5 (4/3/1)	0.88 (4/15/15)	0.12(0.02-0.74)	0.02
Cameroon	0.85 (12/33/34)	0.83 (96/240/240)	1.11(0.56-2.22)	0.76
Kenya	0.92 (12/75/68)	0.89 (429/1689/1644)	1.67(0.9-3.13)	0.08
Tanzania	0.92 (15/84/81)	0.87 (58/211/182)	1.46(0.79-2.72)	0.22
Malawi	0.91 (11/58/60)	0.88 (298/1105/1159)	1.36(0.72-2.55)	0.33
Vietnam	1 (0/1/29)	1 (0/89/2367)	n.c.[§]	n.c.[§]
All	0.91 (159/816/851)	0.87 (1644/5722/5737)	1.53(1.27-1.84)	3.68×10^{-06}

Supplementary Table 18: ATP2B4 Males and Females Dominant Model. Frequency of the derived allele at ATP2B4 (rs10900585) in all cases and controls. Odds ratios (OR), 95% confidence intervals (95% CI) and p-values (*P*) are presented for association of the derived-allele with all severe malaria, cerebral malaria only and severe malarial anaemia only for all individuals at each study site and at all study sites combined. Results are adjusted for sickle-cell trait and ethnicity. Sites at which rs10900585 is monomorphic (Papua New Guinea) were excluded from this analysis. n.c., not calculated. [§] sample size too small for accurate calculation.

CD40LG	Derived Homozygote Frequency (Derived Homozygote/Total)			
Phenotype **Site**	**Cases**	**Controls**	**OR (95% CI)**	***P***
Males and Females – Recessive Model				
All severe malaria				
Gambia	0.24 (586/2406)	0.36 (1159/3204)	0.54(0.48-0.61)	2.30×10^{-22}
Mali	0.25 (114/449)	0.24 (82/335)	0.99(0.7-1.41)	0.96
Burkina Faso	0.24 (205/862)	0.22 (156/720)	1.02(0.79-1.31)	0.89
Ghana (Navrongo)	0.25 (168/675)	0.25 (116/458)	0.93(0.7-1.25)	0.63
Ghana (Kumasi)	0.25 (366/1483)	0.25 (491/1937)	0.92(0.78-1.1)	0.37
Nigeria	0.21 (16/77)	0.31 (12/39)	0.5(0.19-1.35)	0.17
Cameroon	0.2 (120/610)	0.21 (120/576)	1.14(0.84-1.55)	0.39
Kenya	0.18 (406/2258)	0.13 (521/3927)	1.42(1.22-1.65)	7.57×10^{-06}
Tanzania	0.15 (63/426)	0.12 (54/444)	1.08(0.71-1.65)	0.73
Malawi	0.15 (206/1372)	0.15 (406/2683)	1.01(0.84-1.22)	0.91
Vietnam	0 (0/790)	0.03 (80/2525)	n.c.[§]	n.c.[§]
All	0.2 (2250/11408)	0.19 (3197/16848)	0.85(0.79-0.91)	1.11×10^{-06}
Cerebral malaria only				
Gambia	0.26 (200/780)	0.36 (1159/3204)	0.6(0.5-0.72)	3.54×10^{-08}
Mali	0.29 (25/85)	0.24 (82/335)	1.18(0.68-2.05)	0.56
Burkina Faso	0.21 (22/107)	0.22 (156/720)	0.82(0.48-1.4)	0.47
Ghana (Navrongo)	0.18 (4/22)	0.25 (116/458)	0.64(0.19-2.12)	0.47
Ghana (Kumasi)	0.25 (57/226)	0.25 (491/1937)	0.99(0.69-1.42)	0.96
Nigeria	0.33 (2/6)	0.31 (12/39)	0.8(0.06-11.21)	0.87
Cameroon	0.11 (4/38)	0.21 (120/576)	0.54(0.19-1.59)	0.27
Kenya	0.17 (158/906)	0.13 (521/3927)	1.36(1.1-1.68)	4.19×10^{-03}
Tanzania	0.18 (6/34)	0.12 (54/444)	1.58(0.62-4.05)	0.34
Malawi	0.14 (118/861)	0.15 (406/2683)	0.92(0.73-1.15)	0.46
Vietnam	0 (0/209)	0.03 (80/2525)	n.c.[§]	n.c.[§]
All	0.18 (596/3274)	0.19 (3197/16848)	0.85(0.76-0.94)	2.45×10^{-03}
Severe malarial anaemia only				
Gambia	0.25 (114/457)	0.36 (1159/3204)	0.56(0.45-0.71)	1.01×10^{-06}
Mali	0.23 (42/183)	0.24 (82/335)	0.86(0.55-1.34)	0.51
Burkina Faso	0.23 (9/39)	0.22 (156/720)	1.06(0.48-2.34)	0.89
Ghana (Navrongo)	0.24 (59/245)	0.25 (116/458)	0.79(0.54-1.15)	0.22
Ghana (Kumasi)	0.22 (122/549)	0.25 (491/1937)	0.78(0.6-1.01)	0.06
Nigeria	0.5 (4/8)	0.31 (12/39)	2.36(0.24-23.12)	0.46
Cameroon	0.14 (11/80)	0.21 (120/576)	0.8(0.39-1.62)	0.53
Kenya	0.25 (40/157)	0.13 (521/3927)	2.29(1.51-3.46)	8.64×10^{-05}
Tanzania	0.14 (26/181)	0.12 (54/444)	0.9(0.52-1.56)	0.70
Malawi	0.19 (25/130)	0.15 (406/2683)	1.4(0.88-2.22)	0.15
Vietnam	0 (0/31)	0.03 (80/2525)	n.c.[§]	n.c.[§]
All	0.22 (452/2060)	0.19 (3197/16848)	0.82(0.73-0.94)	2.97×10^{-03}

Supplementary Table 19: CD40LG Females Recessive Model. Frequency of female cases and controls homozygous for the derived allele at CD40LG (rs3092945). Odds ratios (OR), 95% confidence intervals (95% CI) and p-values are presented for association of derived homozygotes with severe malaria, cerebral malaria only and severe malarial anaemia only for females at each study site and at all study sites combined. Results are adjusted for sickle-cell trait and ethnicity. Sites where rs3092945 is not present (Papua New Guinea) were excluded from this analysis. n.c. not calculated. [§] Genotype counts too small for accurate calculation.

Gene 1	Gene 2	SNP 1	SNP 2	Best Model 1[a]	Best Model 2[a]	Phenotype	Sample	Genotype Test of Interaction P-value	Best Model Test of Interaction P-value
ATP2B4	HbS	rs1541255	rs334	R	H	SM	F	3.95×10^{-02}	1.01×10^{-01}
ATP2B4	HbC	rs1541255	rs33930165	R	A	SM	M	3.86×10^{-02}	3.35×10^{-03}
ATP2B4	HbC	rs1541255	rs33930165	R	A	SM	All	4.11×10^{-03}	1.34×10^{-03}
ATP2B4	G6PD	rs1541255	rs1050828	R	A	SM	F	1.92×10^{-01}	4.23×10^{-02}
ATP2B4	ABO	rs10900585	rs8176746	D	D	SM	All	4.61×10^{-02}	6.47×10^{-01}
ATP2B4	HbS	rs10900585	rs334	D	H	SM	F	1.12×10^{-02}	3.07×10^{-01}
ATP2B4	HbC	rs10900585	rs33930165	D	A	SM	M	6.82×10^{-02}	3.34×10^{-03}
ATP2B4	HbC	rs10900585	rs33930165	D	A	SM	All	1.77×10^{-02}	1.27×10^{-03}
ATP2B4	G6PD	rs10900585	rs1050828	D	A	SM	F	2.91×10^{-01}	3.20×10^{-02}
ABO	CD40LG	rs8176746	rs3092945	D	R	SM	F	6.73×10^{-02}	3.26×10^{-02}
ABO	G6PD	rs8176746	rs1050828	D	A	SM	All	1.04×10^{-01}	3.28×10^{-02}
HBB	CD40LG	rs33930165	rs3092945	A	R	SM	M	8.07×10^{-02}	2.70×10^{-02}
HBB	CD40LG	rs33930165	rs3092945	A	R	SM	All	2.21×10^{-02}	3.75×10^{-02}
CD40LG	G6PD	rs3092945	rs1050828	R	A	SM	M	2.54×10^{-02}	2.17×10^{-02}
CD40LG	G6PD	rs3092945	rs1050828	R	A	SM	All	2.30×10^{-02}	2.26×10^{-03}
ATP2B4	HbS	rs10900585	rs334	D	H	CM	F	4.48×10^{-02}	1.06×10^{-01}
ATP2B4	HbC	rs10900585	rs33930165	D	A	CM	All	3.67×10^{-02}	8.48×10^{-02}
ABO	HbS	rs8176746	rs334	D	H	CM	M	4.13×10^{-02}	6.48×10^{-01}
ABO	HbS	rs8176719	rs334	R	H	CM	M	4.07×10^{-02}	8.19×10^{-01}
ATP2B4	ABO	rs1541255	rs8176719	R	R	SMA	F	3.16×10^{-03}	6.80×10^{-01}
ATP2B4	ABO	rs1541255	rs8176719	R	R	SMA	All	2.07×10^{-02}	3.00×10^{-01}
ATP2B4	HbS	rs1541255	rs334	R	H	SMA	All	2.32×10^{-01}	4.82×10^{-02}
ATP2B4	HbC	rs1541255	rs33930165	R	A	SMA	F	1.29×10^{-01}	3.23×10^{-02}
ATP2B4	ABO	rs10900585	rs8176719	D	R	SMA	F	4.27×10^{-03}	6.25×10^{-01}
ATP2B4	ABO	rs10900585	rs8176719	D	R	SMA	All	3.69×10^{-03}	8.60×10^{-01}
CD40LG	G6PD	rs3092945	rs1050828	R	A	SMA	All	5.52×10^{-02}	4.60×10^{-02}
ATP2B4	ABO	rs1541255	rs8176719	R	R	SMA	F	3.16×10^{-03}	6.80×10^{-01}

Supplementary Table 20: Gene-Gene Interaction. Summary of gene-gene interaction signals of association at all pairs of SNPs with $P < 0.05$ in either the "Genotype" test of interaction or the "Best Model" test of interaction for association with severe malaria (SM), cerebral malaria (CM) and severe malarial anaemia (SMA) in males, females and all individuals combined. Results are adjusted for gender and ethnicity. Study sites at which a SNP was monomorphic were excluded from the analysis. Best model for each SNP is selected according to its association with SM for all individuals across all sites in a fixed effect model adjusted for ethnicity and gender.

[a]Models are A, Additive; D, Dominant; H, Heterozygote Advantage; R ,Recessive.

Cerebral Malaria (CM)	Severe Malarial Anaemia (SMA)	CM OR SMA*	CM AND SMA	CM NOT SMA	SMA NOT CM	NEITHER CM NOR SMA	Not Determined
0	0	0	0	0	0	1	0
0	1	1	0	0	1	0	0
0	n.d.	n.d.	0	0	n.d.	n.d.	1
1	0	1	0	1	0	0	0
1	1	1	1	0	0	0	0
1	n.d.	1	n.d.	n.d.	0	0	1
n.d.	0	n.d.	0	n.d.	0	n.d.	1
n.d.	1	1	n.d.	0	n.d.	0	1
n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	1

Supplementary Table 21: Logic table used to combine the cerebral malaria (CM) and severe malaria anaemia (SMA) phenotypes. Where sufficient data were available to make a NO/YES classification a 0 or 1 was assigned respectively, otherwise not determined (n.d.) was assigned. The resulting classifications for CM and SMA were then combined according to the logic terms; OR, AND, NOT, NOR. Combinations not resulting in a positive classification from the AND, NOT, NOR operations were then classified as 'Not Determined'. This latter group includes all individuals with other severe malaria subtypes and those who may have cerebral malaria or severe malaria anaemia but lack information to classify them.

Header	description
multiplex_code	multiplex number
Assay type	sequenom assay type
rsnumber	rsnumber where assigned
alternate_name	common name for SNP used in the literature
SNP sequence	SNP definition with 15 flanking bases
gene_symbol	HGNC gene name
chromosome	chromosome
position	chromosomal position
stand	chromosome strand with respect to reference genome
1st-PCRP	first round PCR primer sequence
2nd-PCRP	first round PCR primer sequence
AMP_LEN	amplicon length for first-round PCR
UEP_DIR	universal extension primer direction with respect to SNP sequence
UEP_SEQ	universal extension primer sequence
UEP_MASS	universal extension primer mass (Da)
EXT1_SEQ	allele 1 primer extension product
EXT1_CALL	allele 1 genotype call
EXT1_MASS	allele 1 primer extension product mass (Da)
EXT2_SEQ	allele 2 primer extension product
EXT2_CALL	allele 2 genotype call
EXT2_MASS	allele 2 primer extension product mass (Da)
EXT3_SEQ	allele 3 primer extension product
EXT3_CALL	allele 3 genotype call
EXT3_MASS	allele 3 primer extension product mass (Da)

Supplementary Table 22: Header Dictionary for Supplementary Tables 23 and 24. These headers describe the column information some of which are typically found in a Sequenom Assay Design File. Further details may be found in the Spectrodesigner® assay design software manual (Sequenom® [see URLs]).

multiplex_code	Assay type	rsnumber	alternate_name	SNP_sequence	gene_symbol	chromosome	position	stand	1st-PCRP	2nd-PCRP	AMP_LEN	UEP_DIR	UEP_SEQ	UEP_MASS	EXT1_SEQ	EXT1_CALL	EXT1_MASS	EXT2_SEQ	EXT2_CALL	EXT2_MASS
W1	iPLEX	rs2227478	IL22-1394	GCAAGGTGCCACTGC[A/G]AAGGGTCGGAACCAC	IL22	12	68648622	1	ACGTTGGATGTCTGGCCACCTTCACAAATG	ACGTTGGATGTGAGATGGCACAGACCTAAG	104	R	GTGGTTCCGACCCTT	4534.9	GTGGTTCCGACCCTTC	G	4782.1	GTGGTTCCGACCCTTT	A	4862
W1	iPLEX	rs361525	TNF-238	ACCCCCCTMRGAATC[A/G]GAGCAGGGAGGATGG	TNF	6	31543101	1	ACGTTGGATGAAGCATCAAGGATACCCCTC	ACGTTGGATGCAGGGTCCTACACACAAATC	115	R	CCCATCCTCCCTGCTC	4689	CCCATCCTCCCTGCTCC	G	4936.2	CCCATCCTCCCTGCTCT	A	5016.1
W1	iPLEX	rs5498	ICAM-1codon469	GGGGAGGTCACCCGC[A/G]AGGTGACCGTGAATG	ICAM1	19	10395683	1	ACGTTGGATGACTCACAGAGCACATTCACG	ACGTTGGATGTGTCACTCGAGATCTTGAGG	115	R	ACATTCACGGTCACCT	4801.1	ACATTCACGGTCACCTC	G	5048.3	ACATTCACGGTCACCTT	A	5128.2
W1	iPLEX	rs1800890	IL-10-3533	TACTGATTTTAAATG[A/T]ATTTTTCCAGTGGGG	IL10	1	206949365	1	ACGTTGGATGCTGATTTCCCAGTACATCCC	ACGTTGGATGCAAGCCCAGATGCATAGTAG	110	R	CCCCCACTGGAAAAAT	4819.2	CCCCCACTGGAAAAATA	T	5090.4	CCCCCACTGGAAAAATT	A	5146.3
W1	iPLEX	rs1800896	IL-10-1082	TATCCCTACTTCCCC[C/T]TCCCAAAGAAGCCTT	IL10	1	206946897	1	ACGTTGGATGATTCCATGGAGGCTGGATAG	ACGTTGGATGCCAAGACAACACTACTAAGG	111	F	CCTATCCCTACTTCCCC	4977.2	CCTATCCCTACTTCCCCC	C	5224.4	CCTATCCCTACTTCCCCT	T	5304.3
W1	iPLEX	none assigned	amelogenin_XY_SNP6	CAATGGTAAACCTGC[A/C]TCTCTGTTTCTCACC	AMELX	X	11316650	1	ACGTTGGATGGCTTCTCTGGTTGGAGTCAC	ACGTTGGATGGGGCTCGTAACCATAGGAAG	103	F	GCCAATGGTAAACCTGC	5179.4	GCCAATGGTAAACCTGCC	C	5426.6	GCCAATGGTAAACCTGCA	A	5450.6
W1	iPLEX	rs8386		TGTGGACACTGAGAA[C/T]ATCCGCCGTGTGTTC	GNAS	20	57485812	1	ACGTTGGATGTGCATGCGCTGAATGATGTC	ACGTTGGATGTCATTTCACCTGCGCTGTGG	98	R	gTGAACACACGGCGGAT	5244.4	gTGAACACACGGCGGATA	T	5515.6	gTGAACACACGGCGGATG	C	5531.6
W1	iPLEX	rs17561	IL1A G4845T	ATCAAGCCTAGGTCA[G/T]CACCTTTTAGCTTCC	IL1A	2	113537223	-1	ACGTTGGATGATCTGCACTTGTGATCATGG	ACGTTGGATGTTTCACATTGCTCAGGAAGC	96	F	ATCATCAAGCCTAGGTCA	5467.6	ATCATCAAGCCTAGGTCAG	G	5754.8	ATCATCAAGCCTAGGTCAT	T	5794.7
W1	iPLEX	rs8176719		GGATGTCCTCGTGGT[-/G]ACCCCTTGGCTGGCT	ABO	9	136132909	-1	ACGTTGGATGCATGTGCAGTAGGAAGGATG	ACGTTGGATGTGTCGATGTTGAATGTGCCC	99	F	GAAGGATGTCCTCGTGGT	5570.6	GAAGGATGTCCTCGTGGTA	D	5841.8	GAAGGATGTCCTCGTGGTG	I	5857.8
W1	iPLEX	rs9282799	NOS2-1173	AGCAAAGTGTTGGGA[C/T]GGTGAGATCAAGGGT	NOS2	17	26128728	-1	ACGTTGGATGTTAGGGAGAAGTTGAGAAGC	ACGTTGGATGTGGACAGTGGTAGCAAAGTG	98	R	ttTCACCCTTGATCTCACC	5649.7	ttTCACCCTTGATCTCACCA	T	5920.9	ttTCACCCTTGATCTCACCG	C	5936.9
W1	iPLEX	rs334	HbS	TGCACCTGACTCCTR[A/T]GGAGAAGTCTGCCGT	HBB	11	5248232	-1	ACGTTGGATGCAACTTCATCCACGTTCACC	ACGTTGGATGTCAAACAGACACCATGGTGC	106	R	ctTAACGGCAGACTTCTCC	5723.7	ctTAACGGCAGACTTCTCCA	T	5994.9	ctTAACGGCAGACTTCTCCT	A	6050.8
W1	iPLEX	rs1800750	TNF-376	GCATCCTGTCTGGAA[A/G]TTAGAAGGAAACAGA	TNF	6	31542963	1	ACGTTGGATGCCAGGTCTGTGGTCTGTTTC	ACGTTGGATGCTCCCAGTTCTAGTTCTATC	91	R	GTGGTCTGTTTCCTTCTAA	5775.8	GTGGTCTGTTTCCTTCTAAC	G	6022.9	GTGGTCTGTTTCCTTCTAAT	A	6102.9
W1	iPLEX	rs229587		AGGCGCTGGTTTTCA[C/T]TGAGCCAGGTCTCTC	SPTB	14	65263300	1	ACGTTGGATGCAAAGCATGTCCCTCATTAC	ACGTTGGATGAAGGCCGCAATGAGAGAGAC	94	F	CACGAGGCGCTGGTTTTCA	5819.8	CACGAGGCGCTGGTTTTCAC	C	6067	CACGAGGCGCTGGTTTTCAT	T	6146.9
W1	iPLEX	rs1050829	G6PD_plus376	CCAGGTGGRGGGCAT[C/T]CATGTGGCTGTTGAG	G6PD	X	153763492	1	ACGTTGGATGAGTACGATGATGCAGCCTCC	ACGTTGGATGTAGAAGAGGCGGTTGGCCTG	105	R	ccctCCTCAACAGCCACATG	5966.9	ccctCCTCAACAGCCACATGA	T	6238.1	ccctCCTCAACAGCCACATGG	C	6254.1
W1	iPLEX	rs3024500		CTCTCTCCTGGGGGT[A/G]GGGGGTAGCTGGCTT	IL10	1	206940831	1	ACGTTGGATGGAGTGGGTGAATGAATTCTG	ACGTTGGATGTCTCTGATCAGGTTTGGAGC	111	R	ccctGAAGCCAGCTACCCCC	5967.9	ccctGAAGCCAGCTACCCCCC	G	6215.1	ccctGAAGCCAGCTACCCCCT	A	6295
W1	iPLEX	rs2227485	IL22-485	TGATCTNCTATAGTG[A/G]CTGAGTAAGCATTTT	IL22	12	68647713	1	ACGTTGGATGCTGGTAGGAAAATGAGTCCG	ACGTTGGATGGTTTTGTCTTAGTAGAGTTC	116	R	TGACCAAAATGCTTACTCAG	6085	TGACCAAAATGCTTACTCAGC	G	6332.2	TGACCAAAATGCTTACTCAGT	A	6412.1
W1	iPLEX	rs909253	LTA NcoI	GGGAACAGAGAGGAA[C/T]CATGGCAGAAACAGA	LTA	6	31540313	-1	ACGTTGGATGTCTCTGTCACACATTCTCTG	ACGTTGGATGGTCAGAGAAACCCCAAGGTG	115	R	cCATTCTCTGTTTCTGCCATG	6314.1	cCATTCTCTGTTTCTGCCATGA	T	6585.3	cCATTCTCTGTTTCTGCCATGG	C	6601.3
W1	iPLEX	rs3211938	CD36_T1264G	AAATTGTACATCATA[G/T]GGTGTGCTAGACATC	CD36	7	80300449	1	ACGTTGGATGTTGCATTTGCTGATGTCTAG	ACGTTGGATGCTCCAGTTGAAAACCCAGAC	117	R	gtttCTGATGTCTAGCACACC	6372.2	gtttCTGATGTCTAGCACACCC	G	6619.3	gtttCTGATGTCTAGCACACCA	T	6643.4
W1	iPLEX	rs1799969	ICAM-1codon241	GTCTGTTCCCTGGAC[A/G]GGCTGTTCCCAGTCT	ICAM1	19	10394792	1	ACGTTGGATGTCCTAGAGGTGGACACGCAG	ACGTTGGATGAACCTCTGGTCCCCAGTGC	120	F	ccaGTGGTCTGTTCCCTGGAC	6389.1	ccaGTGGTCTGTTCCCTGGACA	A	6660.3	ccaGTGGTCTGTTCCCTGGACG	G	6676.4
W1	iPLEX	rs2227491	IL22+708	GACGGCACACGGCCC[C/T]GTTCGTCACAACTGT	IL22	12	68646521	1	ACGTTGGATGATCACCACCACCCCAAGTAC	ACGTTGGATGTTCCACGGAGTCAGTGTAAG	98	F	gggcTGGACGGCACACGGCCC	6458.2	gggcTGGACGGCACACGGCCCC	C	6705.4	gggcTGGACGGCACACGGCCCT	T	6785.3
W1	iPLEX	rs3093662	TNF +851	GGAAGGTGAATACAC[A/G]GATGAATGGAGAGAG	TNF	6	31544189	1	ACGTTGGATGGTGTCTGGTTTTCTCTCTCC	ACGTTGGATGGGAAAGAGCTGTTGAATGCC	84	R	ttGTTTTCTCTCTCCATTCATC	6568.31	ttGTTTTCTCTCTCCATTCATCC	G	6815.5	ttGTTTTCTCTCTCCATTCATCT	A	6895.4
W1	iPLEX	rs17047661	SI (Swain-Lagley)	GTTGAAAATGCAATT[A/G]GAGTACCAGGAAACA	CR1	1	207782889	1	ACGTTGGATGCCCGGGCTGACATCTAAATC	ACGTTGGATGATGCACAGCTCCAGAAGTTG	117	R	aaacCTCCTGTTTCCTGGTACTC	6925.5	aaacCTCCTGTTTCCTGGTACTCC	G	7172.7	aaacCTCCTGTTTCCTGGTACTCT	A	7252.6
W1	iPLEX	rs1050828	G6PD_plus202	AACGGGCATRGCCCA[C/T]GATGAWGGTGTTTTC	G6PD	X	153764217	1	ACGTTGGATGATGGCCTTCTGCCCGAAAAC	ACGTTGGATGTCACTCTGTTTGCGGATGTC	102	R	ttcgGCCCGAAAACACCTTCATC	6928.5	ttcgGCCCGAAAACACCTTCATCA	T	7199.7	ttcgGCCCGAAAACACCTTCATCG	C	7215.7
W1	iPLEX	none assigned	CD36_G1439C	TTCACTTTACAATTT[C/G]CAANNCGGCTGCAGG	CD36	7	80302110	1	ACGTTGGATGGTTCTCTTTTTAGATAACTGG	ACGTTGGATGTGACCAATAGGTTGACCTGC	88	F	TAACTGGATTCACTTTACAATTT	6987.6	TAACTGGATTCACTTTACAATTTC	C	7234.8	TAACTGGATTCACTTTACAATTTG	G	7274.8
W1	iPLEX	rs4986791		GTGATTTTGGGACAA[C/T]CAGCCTAAAGTATTT	TLR4	9	120475602	1	ACGTTGGATGAGGTTGCTGTTCTCAAAGTG	ACGTTGGATGGGTAATAACACCATTGAAGC	96	F	TTCTCAAAGTGATTTTGGGACAA	7077.6	TTCTCAAAGTGATTTTGGGACAAC	C	7324.8	TTCTCAAAGTGATTTTGGGACAAT	T	7404.7
W1	iPLEX	rs1555498		ACACGGTAATAGATA[C/T]GGGCAAAACATACCA	IL20RA	6	137325847	1	ACGTTGGATGGATGGAATAGCCCATCACAG	ACGTTGGATGCAATCATCAGAGTTCAAGGC	113	F	AAAAAGAAACACGGTAATAGATA	7130.7	AAAAAGAAACACGGTAATAGATAC	C	7377.9	AAAAAGAAACACGGTAATAGATAT	T	7457.8
W1	iPLEX	rs1799964	TNF-1031	GAGAAGCTGAGAAGA[C/T]GAAGGAAAAGTCAGG	TNF	6	31542308	1	ACGTTGGATGTACATGTGGCCATATCTCCC	ACGTTGGATGGGGAAGCAAAGGAGAAGCTG	112	R	CCTCCAGACCCTGACTTTTCCTTC	7150.6	CCTCCAGACCCTGACTTTTCCTTCA	T	7421.9	CCTCCAGACCCTGACTTTTCCTTCG	C	7437.9
W1	iPLEX	rs2239704	LTA +77	AGGGCAGGACACTGC[G/T]GGGCGGTAGTCCAAA	LTA	6	31540141	-1	ACGTTGGATGGTGCTTCGTGCTTTGGACTA	ACGTTGGATGAGGTGCAGGAGGGACCGAG	91	R	gctgCGTGCTTTGGACTACCGCCC	7296.7	gctgCGTGCTTTGGACTACCGCCCC	G	7543.9	gctgCGTGCTTTGGACTACCGCCCA	T	7567.9
W1	iPLEX	rs2297518		TTCAGCATGAAGAGC[A/G]ATTTCTTCAGTTTCT	NOS2	17	26096597	1	ACGTTGGATGTTGAGAACTCTGTCATTCCC	ACGTTGGATGTTGTTGTTGAGCTCTTTCAG	95	R	gCTCTTTCTAGAAACTGAAGAAAT	7359.8	gCTCTTTCTAGAAACTGAAGAAATC	G	7607	gCTCTTTCTAGAAACTGAAGAAATT	A	7686.9
W1	iPLEX	rs1012356	IL22+2611	GACTTCCATTTAACT[A/T]TAATAAATCTCTTAC	IL22	12	68644618	1	ACGTTGGATGGCTTACCAATTCAGACTTCC	ACGTTGGATGCCCCGATCTCTTTTATACAG	107	F	tcCCAATTCAGACTTCCATTTAACT	7510.9	tcCCAATTCAGACTTCCATTTAACTA	A	7782.1	tcCCAATTCAGACTTCCATTTAACTT	T	7838
W1	iPLEX	rs187084		AAAGATCACTGCCCT[C/T]AAGAAGCTGACATTC	TLR9	3	52261031	-1	ACGTTGGATGTGCTGGGCACTGTACTGGAT	ACGTTGGATGTATTCCCCTGCTGGAATGTC	100	F	GATGCAGATAAAAGATCACTGCCCT	7659	GATGCAGATAAAAGATCACTGCCCTC	C	7906.2	GATGCAGATAAAAGATCACTGCCCTT	T	7986.1
W1	iPLEX	rs2230739		CTCCACACAGGTCAT[A/G]AAGAACTCCCCCGTG	ADCY9	16	4033436	-1	ACGTTGGATGTCCCAGTCATTCTGCTCCAC	ACGTTGGATGGAAGGTGGGACTAGCAAACG	100	F	ctaCACTCCTGCTCCACACAGGTCAT	7811.1	ctaCACTCCTGCTCCACACAGGTCATA	A	8082.3	ctaCACTCCTGCTCCACACAGGTCATG	G	8098.3
W1	iPLEX	rs2814778	Duffy – FyA/FyB	GCCTGTGCTTCCAAG[A/G]TAAGAGCCAAGGACT	DARC	1	159174683	-1	ACGTTGGATGAACCTGATGGCCCTCATTAG	ACGTTGGATGAGACAGAAGGGCTGGGACG	97	R	TGGCCCTCATTAGTCCTTGGCTCTTA	7879.1	TGGCCCTCATTAGTCCTTGGCTCTTAC	G	8126.3	TGGCCCTCATTAGTCCTTGGCTCTTAT	A	8206.2
W1	iPLEX	rs2535611		TGTCAGGTACACTTC[C/T]TTTTTTTTTTTTTTT	ADORA2B	17	15861332	1	ACGTTGGATGCGACATTGTAGAACCAGGAC	ACGTTGGATGGAGTGAAACTCTGTCTCAAG	92	F	ggcCCAGGACCTGTCAGGTACACTTC	7932.1	ggcCCAGGACCTGTCAGGTACACTTCC	C	8179.3	ggcCCAGGACCTGTCAGGTACACTTCT	T	8259.2
W1	iPLEX	rs4986790		ACTACTACCTCGATG[A/G]TATTATTGACTTATT	TLR4	9	120475302	1	ACGTTGGATGCACCAGGGAAAATGAAGAAAC	ACGTTGGATGAGCATACTTAGACTACTACC	99	R	GTCAAACAATTAAATAAGTCAATAATA	8291.5	GTCAAACAATTAAATAAGTCAATAATAC	G	8538.7	GTCAAACAATTAAATAAGTCAATAATAT	A	8618.6
W1	iPLEX	rs1805015		CGCAGCTTCAGCAAC[C/T]CCCTGAGCCAGTCAC	IL4R	16	27374180	1	ACGTTGGATGACCTGACTTGCACAGAGACG	ACGTTGGATGTCTCTGGGACACGGTGACTG	114	F	CAACCCTGCTTACCGCAGCTTCAGCAAC	8438.5	CAACCCTGCTTACCGCAGCTTCAGCAACC	C	8685.7	CAACCCTGCTTACCGCAGCTTCAGCAACT	T	8765.6
W2	iPLEX	rs33930165	HBC	GTGCACCTGACTCCT[A/G]WGGAGAAGTCTGCCG	HBB	11	5248233	1	ACGTTGGATGTCAAACAGACACCATGGTGC	ACGTTGGATGTTCATCCACGTTCACCTTGC	102	F	GTGCACCTGACTCCT	4503.9	GTGCACCTGACTCCTA	A	4775.1	GTGCACCTGACTCCTG	G	4791.1
W2	iPLEX	rs1800629	TNF-308	GTTTTGAGGGGCATG[A/G]GGACGGGGTTCAGCC	TNF	6	31543031	1	ACGTTGGATGCTGATTTGTGTGTAGGACCC	ACGTTGGATGGGAGGCAATAGGTTTTGAGG	86	R	GGCTGAACCCCGTCC	4513.9	GGCTGAACCCCGTCCC	G	4761.1	GGCTGAACCCCGTCCT	A	4841
W2	iPLEX	rs2075820		CCAGAGCGGGACCCC[A/G]AGGAGGTGTTTGCCT	NOD1	7	30492237	-1	ACGTTGGATGACCTGCTCTTCAAGCACTAC	ACGTTGGATGAAGCGCAGCAGGAAGGCAAAC	90	F	aCCAGAGCGGGACCCC	4861.2	aCCAGAGCGGGACCCCA	A	5132.4	aCCAGAGCGGGACCCCG	G	5148.4
W2	iPLEX	rs2242665		TTTCCATGGACCAAC[A/G]TTACTCCACCGGCGC	CTL4	6	31839309	-1	ACGTTGGATGTGGTGGTGTCATTGGTGATC	ACGTTGGATGGGCTCTCCCTTCCAGCTCT	107	R	AGCGCCGGTGGAGTAA	4971.2	AGCGCCGGTGGAGTAAC	G	5218.4	AGCGCCGGTGGAGTAAT	A	5298.3
W2	iPLEX	none assigned	amelogenin_XY_SNP1	CAAGCTTNCACNCNT[A/G]CCTCCTCTCTTCCTC	AMELX	X	11313735	1	ACGTTGGATGCTTGGTTTTGTGGGTGAGAG	ACGTTGGATGTGATACAACCAGAAGCCAGC	89	R	AGAGGAAGAGAGGAGG	5093.3	AGAGGAAGAGAGGAGGC	G	5340.5	AGAGGAAGAGAGGAGGT	A	5420.4
W2	iPLEX	rs352140		ATTCACGGAGCTACC[A/G]CGACTGGAGGCCCTG	TLR9	3	52231737	-1	ACGTTGGATGATAAGCTGGACCTCTACCAC	ACGTTGGATGTGGCTGTTGTAGCTGAGGTC	99	R	cCATTCACGGAGCTACC	5115.3	cCATTCACGGAGCTACCA	T	5386.5	cCATTCACGGAGCTACCG	C	5402.5
W2	iPLEX	rs1800482	NOS2-954	AGCTTCAGAGTTCGA[C/G]ACCAGCATGGACAAC	NOS2	17	26128509	-1	ACGTTGGATGCCACCACACCCAGCTAATAT	ACGTTGGATGGGGCAGATCACTTGAGCTTC	119	R	tTGTTGTCCATGCTGGT	5198.4	tTGTTGTCCATGCTGGTC	G	5445.6	tTGTTGTCCATGCTGGTG	C	5485.6
W2	iPLEX	rs6780995		AGGAGGCAGCTGGTC[A/G]TCTCTGTAGTTTGCT	IL17RD	3	57138419	1	ACGTTGGATGGTTCTTTGGTCTGTTGCAGG	ACGTTGGATGTCCCCTGGAGAAACATTTTG	92	R	GGAGCAAACTACAGAGA	5261.5	GGAGCAAACTACAGAGAC	G	5508.6	GGAGCAAACTACAGAGAT	A	5588.6
W2	iPLEX	rs542998		CCACAGTGAAAGTGG[C/T]TTTACCTGATGACCA	RTN3	11	63487386	1	ACGTTGGATGCTCTGCCAGTCCATTTCATC	ACGTTGGATGACTCTTTGGGTTCTGGAGTG	99	R	GGTGGTCATCAGGTAAA	5274.4	GGTGGTCATCAGGTAAAA	T	5545.7	GGTGGTCATCAGGTAAAG	C	5561.7
W2	iPLEX	rs33950507	HbE	GATGAAGTTGGTGGT[A/G/T]AGGCCCTGGGCAG	HBB	11	5248173	-1	ACGTTGGATGGTCTCCTTAAACCTGTCTTG	ACGTTGGATGCAAGGTGAACGTGGATGAAG	98	F	gGGATGAAGTTGGTGGT	5361.5	gGGATGAAGTTGGTGGTA	A	5632.7	gGGATGAAGTTGGTGGTG	G	5648.7
W2	iPLEX	rs17047660	McC (McCoy)	TGTATTTCTACTAAT[A/G]AATGCACAGCTCCAG	CR1	1	207782856	1	ACGTTGGATGGCATTTTCAACTTCTGGAGC	ACGTTGGATGATCAAGTTGGTGTTTGGAGC	99	R	cccCTGGAGCTGTGCATT	5466.6	cccCTGGAGCTGTGCATTC	G	5713.7	cccCTGGAGCTGTGCATTT	A	5793.6
W2	iPLEX	rs461645		CTTCACAAACCTGAA[C/T]GTTCTCCAGAGTGTA	EMR1	19	6919753	-1	ACGTTGGATGAAAGACGGCTTCTCAGATCC	ACGTTGGATGGTTCCCAACAGGTAGACAAG	115	R	ATCTACACTCTGGAGAAC	5467.6	ATCTACACTCTGGAGAACA	T	5738.8	ATCTACACTCTGGAGAACG	C	5754.8
W2	iPLEX	rs8078340	NOS2-1659	TGAACAAGGCAGAAC[C/T]AGCTACATCAGCACC	NOS2	17	26129212	-1	ACGTTGGATGGTGTCCTCTCCCTTGTAAAC	ACGTTGGATGTCTGTAGTGATGGAGGGATG	101	F	aCTTGAACAAGGCAGAAC	5525.6	aCTTGAACAAGGCAGAACC	C	5772.8	aCTTGAACAAGGCAGAACT	T	5852.7
W2	iPLEX	rs1803632		GAGGCCCATTGACTG[C/G]AATGCCACCTGRAAG	GBP7	1	89582690	1	ACGTTGGATGTAGAGAGAGTGACTCACGAG	ACGTTGGATGTCCTCAGCCATTCCAATGTC	94	F	gCACGAGGCCCATTGACTG	5813.8	gCACGAGGCCCATTGACTGC	C	6061	gCACGAGGCCCATTGACTGG	G	6101
W2	iPLEX	rs2243250	IL-4-589	TTGGGAGAACATTGT[C/T]CCCCAGTGCTGGGGT	IL4	5	132009154	1	ACGTTGGATGTGATACGACCTGTCCTTCTC	ACGTTGGATGTAACAGGCAGACTCTCCTAC	102	F	gAACTTGGGAGAACATTGT	5891.9	gAACTTGGGAGAACATTGTC	C	6139	gAACTTGGGAGAACATTGTT	T	6218.9
W2	iPLEX	none assigned	amelogenin_XY_SNP2	AAAAAGTGAGAGTAA[C/T]AATACTTGCCTCCTA	AMELX	X	11316106	1	ACGTTGGATGCTTATATGCTAGGAGGCA	ACGTTGGATGCAGTCAAGTTAATGAATCTC	103	R	gTGCTAGGAGGCAAGTATT	5907.9	gTGCTAGGAGGCAAGTATTA	T	6179.1	gTGCTAGGAGGCAAGTATTG	C	6195.1
W2	iPLEX	rs2706384		AGTGCCCGGGCGATC[A/C]CCTCGCCTGCGTTCG	IRF1	5	131826880	-1	ACGTTGGATGGAGATTCGGCCCAGTGTTC	ACGTTGGATGGGTATATCTCCCGAACGCAG	99	F	attCAAGTGCCCGGGCGATC	6118	attCAAGTGCCCGGGCGATCC	C	6365.2	attCAAGTGCCCGGGCGATCA	A	6389.2
W2	iPLEX	rs1801033		GACAGCCATGCACTG[A/C]GCCTCTGGTAGCCTT	C6	5	41199959	-1	ACGTTGGATGGTTAGATCTGTCTTGCGTCC	ACGTTGGATGGGAATGCATGGTTGAAAGGC	100	F	tgtGGGACAGCCATGCACTG	6158	tgtGGGACAGCCATGCACTGC	C	6405.2	tgtGGGACAGCCATGCACTGA	A	6429.2
W2	iPLEX	rs708567		GGCTCCTCCACCCCT[A/G]AGTCAGCTGCTCCTC	IL17RE	3	9960070	-1	ACGTTGGATGGAGGAAAAGTTTGGAGGAGC	ACGTTGGATGGTTCTCCTCACCATTCCTAG	83	R	aggTGGAGGAGCAGCTGACT	6247.1	aggTGGAGGAGCAGCTGACTC	G	6494.2	aggTGGAGGAGCAGCTGACTT	A	6574.2
W2	iPLEX	rs7935564		AGGCTGATAAAGGAG[A/G]ATCAAGAGGCTGAGA	TRIM5	11	5718517	1	ACGTTGGATGTTCCAGGCGGTTCTCTCTTG	ACGTTGGATGACAGGAAAAGCTGCAGGTAG	119	R	cccGCTTCTCAGCCTCTTGAT	6284.1	cccGCTTCTCAGCCTCTTGATC	G	6531.3	cccGCTTCTCAGCCTCTTGATT	A	6611.2
W2	iPLEX	rs1143634	IL1B A2	AGAACCTATCTTCTT[C/T]GACACATGGGATAAC	IL1B	2	113590390	-1	ACGTTGGATGGTGCTCCACATTTCAGAACC	ACGTTGGATGCAGTTCAGTGATCGTACAGG	106	F	CATTTCAGAACCTATCTTCTT	6306.1	CATTTCAGAACCTATCTTCTTC	C	6553.3	CATTTCAGAACCTATCTTCTTT	T	6633.2
W2	iPLEX	rs1126535	CD40LG +220	TATCTTCATAGAAGG[C/T]TGGACAAGGTAAGAT	CD40LG	X	135730555	1	ACGTTGGATGATCACCCAGATGATTGGGTC	ACGTTGGATGGGCTTGTGGTTCATCTTACC	99	F	GCTGTGTATCTTCATAGAAGG	6476.2	GCTGTGTATCTTCATAGAAGGC	C	6723.4	GCTGTGTATCTTCATAGAAGGT	T	6803.3
W2	iPLEX	rs8176746		GGCGATTTCTACTAC[A/C]TGGGGGSGTTCTTCG	ABO	9	136131322	-1	ACGTTGGATGCCCAGTCCCAGGCCTACAT	ACGTTGGATGTTGCACCGACCCCCCGAAGAA	97	F	ccACGAGGGCGATTTCTACTAC	6695.4	ccACGAGGGCGATTTCTACTACC	C	6942.5	ccACGAGGGCGATTTCTACTACA	A	6966.6
W2	iPLEX	rs17140229		TTGAGAATAGTGTTA[C/T]TTCAGTGAATCGATG	CFTR	7	117230283	1	ACGTTGGATGAAGTGCTACTTCTGCACCAC	ACGTTGGATGACAATATGGTCACCACATCG	88	F	ACCACTTTTGAGAATAGTGTTA	6748.4	ACCACTTTTGAGAATAGTGTTAC	C	6995.6	ACCACTTTTGAGAATAGTGTTAT	T	7075.5
W2	iPLEX	rs1128127		GGGTCTTCTGCAGGG[A/G]CATCCAGGAGCAGCT	DERL3	22	24179132	1	ACGTTGGATGTGTGCTGGCCTGTGCTCAAC	ACGTTGGATGGGCAGGTAATTGGGGTCTTC	103	R	aACAGAAAGCTGCTCCTGGATG	6768.4	aACAGAAAGCTGCTCCTGGATGC	G	7015.6	aACAGAAAGCTGCTCCTGGATGT	A	7095.5
W2	iPLEX	rs373533		GAGCCTGGTGGTCTT[G/T]GAAGAAGCGCTCATT	EMR1	19	6919624	-1	ACGTTGGATGTGATCTCAGAGGTGGTCAAG	ACGTTGGATGTCCTTTGTGGGCATGGAATC	99	F	ggCAAGGGAGCCTGGTGGTCTT	6847.4	ggCAAGGGAGCCTGGTGGTCTTG	G	7134.6	ggCAAGGGAGCCTGGTGGTCTTT	T	7174.5
W2	iPLEX	rs2227507	IL22+4583	CTTTGATCTCTCCAC[C/T]CTCTCCAAGCTGTGA	IL22	12	68642647	1	ACGTTGGATGGAAAACATGGCATAAATGCTC	ACGTTGGATGAACAGCAAATCCAGTTCTCC	119	R	aCTTATTTTCACAGCTTGGAGAG	7053.6	aCTTATTTTCACAGCTTGGAGAGA	T	7324.8	aCTTATTTTCACAGCTTGGAGAGG	C	7340.8
W2	iPLEX	rs5743810		GAACTCACCAGAGGT[C/T]CAACCTTACTGAATT	TLR6	4	38830350	-1	ACGTTGGATGAGGCATTTCCAAGTCGTTTC	ACGTTGGATGATTTTTATCAGAACTCACC	98	R	GAGGGTAAAATTCAGTAAGGTTG	7191.7	GAGGGTAAAATTCAGTAAGGTTGA	T	7462.9	GAGGGTAAAATTCAGTAAGGTTGG	C	7478.9
W2	iPLEX	rs20541	IL-13_46457	AAGTTTCAGTTGAAC[C/T]GTCCCTCGCGAAAAA	IL13	5	131995964	-1	ACGTTGGATGTGATGCTTTCGAAGTTTCAG	ACGTTGGATGCCAGTTTGTAAAGGACCTGC	100	F	cgGCTTTCGAAGTTTCAGTTGAAC	7358.8	cgGCTTTCGAAGTTTCAGTTGAACC	C	7606	cgGCTTTCGAAGTTTCAGTTGAACT	T	7685.9
W2	iPLEX	rs10775349		TGCCTGTTCAGCTTT[C/G]TTACACATTTTTCTA	ADCY9	16	4079823	-1	ACGTTGGATGAAAACCAGACCACTCAGTAG	ACGTTGGATGGTTGGCTCTTCAGTGAAGTG	86	R	ACCACTCAGTAGAAAAATGTGTAA	7377.8	ACCACTCAGTAGAAAAATGTGTAAC	G	7625	ACCACTCAGTAGAAAAATGTGTAAG	C	7665.1
W2	iPLEX	rs3092945	CD40LG -727	ACTGTTACAWCAGCA[C/T]CAACAATTATCTAAT	CD40LG	X	135729609	1	ACGTTGGATGCTGTGTACACTGTTCCAATC	ACGTTGGATGCAGATCTCTTAACTGCAGCC	109	R	GTTCCAATCCATTAGATAATTGTTG	7646	GTTCCAATCCATTAGATAATTGTTGA	T	7917.2	GTTCCAATCCATTAGATAATTGTTGG	C	7933.2
W2	iPLEX	rs5743809		AAAGTCTACAAATTC[C/T]GAATGCAAAAACCCT	TLR6	4	38830514	-1	ACGTTGGATGAATGAGACAGAAAGTCTAC	ACGTTGGATGGCGAATAAACTAGTTGGGTG	94	F	gATGAGACAGAAAGTCTACAAATTC	7707.1	gATGAGACAGAAAGTCTACAAATTCC	C	7954.2	gATGAGACAGAAAGTCTACAAATTCT	T	8034.1
W2	iPLEX	rs4833095		TTGTTTAAGGTAAGA[C/T]TTGATAACTTTGGAT	TLR1	4	38799710	1	ACGTTGGATGCCAAGTTGTTTCAATGTTGT	ACGTTGGATGACTTCCTAAGTATTCTGGCG	100	F	TGTTTCAATGTTGTTTAAGGTAAGA	7741.1	TGTTTCAATGTTGTTTAAGGTAAGAC	C	7988.2	TGTTTCAATGTTGTTTAAGGTAAGAT	T	8068.2
W2	iPLEX	rs5743611		TAATTTCTCATAATA[C/G]AATCCAGTATCTTGA	TLR1	4	38800214	-1	ACGTTGGATGCACTGTCAAAACTGAGGATT	ACGTTGGATGGGTTGAATTTGAAAACACTG	98	F	TGAGGATTTTGATAATTTCTCATAATA	8302.4	TGAGGATTTTGATAATTTCTCATAATAC	C	8549.6	TGAGGATTTTGATAATTTCTCATAATAG	G	8589.6

Supplementary Table 23: Sequenom Assay designs for the SNPs used in this study (Supplementary Tables 5-7). Header descriptions can be found in Supplementary Table 22. The assays are split into 2 multiplexes (assay groups) defined by the field called 'Multiplex_Code'. The SNP, gene and co-ordinates are taken from GRCh37, Ensembl build 73 and dbSNP137. Further details may be found in the Spectrodesigner® assay design software manual (Sequenom® [see URLs]).

multiplex_code	Assay type	rsnumber	alternate_name	SNP_sequence	gene_symbol	chromosome	position	stand	1st-PCRP	2nd-PCRP	AMP_LEN	UEP_DIR	UEP_SEQ	UEP_MASS	EXT1_SEQ	EXT1_CALL	EXT1_MASS	EXT2_SEQ	EXT2_CALL	EXT2_MASS	EXT3_SEQ	EXT3_CALL	EXT3_MASS
N/A	iPLEX	rs55868763		CTGCCAGACTTCATA[C/G]DGAAGAAAGGATCTA	ATP2B4	1	203652140	1	ACGTTGGATGTTCCACTCAGTTCCCCCATC	ACGTTGGATGTAGCCGTCCGAAGTCTAGAT	101	F	CTCGCTGCCAGACTTCATA	5723.7	CTCGCTGCCAGACTTCATAC	C	5970.9	CTCGCTGCCAGACTTCATAG	G	6010.9			
N/A	iPLEX	rs1541255		TGCYAGACTTCATAS[A/G/T]GAAGAAAGGATCT	ATP2B4	1	203652141	1	ACGTTGGATGTTCCACTCAGTTCCCCCATC	ACGTTGGATGTAGCCGTCCGAAGTCTAGAT	101	R	CCGTCCGAAGTCTAGATCCTTTCTTCC	7848.1	CCGTCCGAAGTCTAGATCCTTTCTTCC	G	8095.3	CCGTCCGAAGTCTAGATCCTTTCTTCA	T	8119.3	CCGTCCGAAGTCTAGATCCTTTCTTCT	A	8175.2
N/A	iPLEX	rs10900585		AGGAGTCTCACTCTT[G/T]TTGCCCAGGCAGGCT	ATP2B4	1	203654024	1	ACGTTGGATGTTTGTTTTGAGAAGGAGTC	ACGTTGGATGCCAAGATTGCACCATTGCAC	86	F	AGAAGGAGTCTCACTCTT	5498.6	AGAAGGAGTCTCACTCTTG	G	5785.8	AGAAGGAGTCTCACTCTTT	T	5825.7			
N/A	iPLEX	rs4951074		CTGTGACCTTRAATC[A/G]ACTGCTTTATCTCTA	ATP2B4	1	203660781	1	ACGTTGGATGTTGCTCCCTATCTGCTAGAC	ACGTTGGATGCAAGTTCATCATCCTCTGGC	100	R	CTCCTAGAGATAAAGCAGT	5820.8	CTCCTAGAGATAAAGCAGTC	G	6068	CTCCTAGAGATAAAGCAGTT	A	6147.9			
N/A	iPLEX	rs3753036		AAGCATTTCCTTTGC[A/G]TAGACACTTAGAGTG	ATP2B4	1	203677250	1	ACGTTGGATGTTCCAACCACCCACTCTAAG	ACGTTGGATGTGGACCTCATTGTCAATGGC	120	R	aaACCCACTCTAAGTGTCTA	6045	aaACCCACTCTAAGTGTCTAC	G	6292.1	aaACCCACTCTAAGTGTCTAT	A	6372.1			

Supplementary Table 24: Sequenom Assay designs for the ATP2B4 SNPs used in this study (Supplementary Tables 5-7). Header descriptions can be found in Supplementary Table 22. The assays are split into 2 multiplexes (assay groups) defined by the field called 'Multiplex_Code'. The SNP, gene and co-ordinates are taken from GRCh37, Ensembl build 73 and dbSNP137. Further details may be found in the Spectrodesigner® assay design software manual (Sequenom® [see URLs]).

MODEL	Ancestral Homozygotes	Heterozygotes	Derived Homozygotes
	Autosomal chromosomes and female X chromosomes		
GENOTYPE	**AA**	**AB**	**BB**
General	0	1	2
Additive or Additive	0	1	2
Dominant	0	1	1
Recessive	0	0	1
Heterozygote	0	1	0
Het vs Ancestral Hom	0	1	Omitted
Het vs Derived Hom	Omitted	1	0
Ancestral Hom vs Derived Hom	0	Omitted	1
	Males X chromosomes		
GENOTYPE	**A**		**B**
General	0		2
Additive or Additive	0		2
Dominant	0		1
Recessive	0		1
Heterozygote	n.a.		n.a.
Het vs Ancestral Hom	n.a.		n.a.
Het vs Derived Hom	n.a.		n.a.
Ancestral Hom vs Derived Hom	0		1

Supplementary Table 25: Coding of Alleles for logistic regression analysis with respect to the derived allele. In the general and additive models ancestral-allele homozygotes were coded as 0 for all chromosomes (autosomes and sex chromosomes), heterozygotes were coded as 1 and derived-allele homozygotes were coded as 2 (including the male derived-allele homozygotes so that they are treated equivalent to the female X chromosome derived-allele homozygotes in the analysis). For all other models the genotypes were coded as 0 or 1 depending on the model grouping requirements having 1 with respect to the model and derived allele.

n.a., not applicable to males because heterozygotes are not present.

Supplementary Note:

MalariaGEN Sample Handling Procedures

Sample Archiving:

Sample Collection:

Blood was collected from individuals typically by venupuncture into a non-heparin anti-coagulant (typically EDTA); volumes varied between <1ml to 10ml depending on clinical circumstances and ethical permissions.

DNA extraction:

The blood was processed locally to extract DNA using the local method of choice; either Nucleon™ BACC Genomic DNA Extraction Kits (Gen-Probe Life Sciences Ltd, Tepnel Research Products & Services, Manchester, UK [see URLs]), or Qiagen DNeasy Blood kits (Qiagen, Crawley, UK [see URLs]). Extractions were carried out according manufacturers' instructions although some local changes may have been made to the protocols to suit local conditions.

Sample Processing:

DNA was shipped frozen to Oxford. After arrival, the sample manifest was confirmed and all samples were relabeled and recoded with new sample_codes according to a standard format bearing no relationship to the original coding. Sample volumes were recorded and the DNA concentrations were measured using the PicoGreen® reagent (Invitrogen, Paisley, UK [see URLs]). An aliquot from each sample was diluted to 20ng/ul where possible to provide a 'working' sample allowing the remaining stock sample to be stored with little disturbance; an aliquot from samples below 20ng/ul was taken and used 'as is'. All DNAs were stored at -80^{o}C in screw-cap tubes with rubber 'O' ring seals (Greiner Bio-One, Stonehouse, UK; 0.5ml skirted tubes #693201-1, lids #366380-1 and 9x9 format boxes #TR81N [see URLs]).

Primer-extension Amplification (PEP):

PEP reaction:

Samples underwent a whole-genome amplification step using Primer-Extension Pre-Amplification as previously described[121]. gDNA was diluted to 1ng/ul in 96-well plates (Thermo-Fast® 96-skirted, Thermo Fisher Scientific, UK), leaving 2 to 3 empty wells for water controls.

A PCR reagent mixture of 45ul comprising;

2.2ul of 1:10 diluted N15 primers (Genetix Ltd, UK [see URLs]),
1.25ul 8mM pooled dNTP's (Sigma-Aldrich,UK [see URLs]),
2.5ul 50mM $MgCl_2$ (Bioline, UK [see URLs]),
5ul of 10X BioTaq buffer (Bioline, UK [see URLs]),
0.5ul 5U/ul Biotaq polymerase (Bioline [see URLs]),
33.55ul MilliQ water (Sigma-Aldrich,UK [see URLs]).

were added to each well of a 96-well skirted PCR plate (Thermo Fisher Scientific). Five microlitres of gDNA (1ng/ul) was added to the PEP PCR mixture and the plates were sealed with Flat-Cap Strips (Thermo fisher Scientific) before thermocycling using a MJ Tetrad (Bio-Rad, UK) with the following programme:

94°C for 3 min;
50 cycles of: 94 °C for 1min,
37 °C for 2 min
Ramp to 55°C at 0.1/sec
55 °C for 4 min

and a final extension of 72°C for 5 min,
maintain at 4°C

PEP DNA was stored neat at -20°C until used.

PEP testing:

Twelve samples were selected at random from the plate of PEP reactions prepared above. PCR reactions were prepared as described below for Sequenom genotyping except that the final reaction volume was 20ul; 1ul of neat PEP was used and a single primer pair designed from an existing iPLEX assay design was used:

forward primer: ACGTTGGATGTCTGTAGTGATGGAGGGATG

reverse primer: ACGTTGGATGGTGTCCTCTCCCTTGTAAAC

Samples were run on 2% Agarose gels to check band intensity and fidelity.

Genotyping:

Platform:

The genotyping methodology chosen was SEQUENOM® iPLEX® Gold which allowed up to 40 SNPs to be designed into a single reaction (multiplex) and for up to 384 samples to be processed on one chip (see URLs). All reagents specific for this process were purchased from SEQUENOM®. Other reagents used were purchased as described below.

SNP sets:

Genotyping was undertaken for all samples upon receipt in Oxford for a set of SNPs designed as part of the QC process or with relevance to malaria.

Our primary SNP set is shown in Supplementary Tables 5, 6 and 7. These were identified from literature searches in publications showing associations of SNPs with malaria infection/disease severity. To these were added assays designed to determine gender by comparing the Amelogenin gene between the X and Y chromosomes[122]. Other SNPs from research being undertaken in the laboratory at the time were added to complete the multiplex design process.

iPLEX design:

Polymorphism sequence information was downloaded from Ensembl (see URLs) and reformatted for the SEQUENOM® assay design process (see URLs). The SEQUENOM® RealSNP™ Assay Database (see URLs) tools ProxSNP and PreEXTEND were used to identify proximal SNPs in the region of the target SNPs and to mask and design first–round PCR primers (Amplicon Design). Multiplex design for the iPLEX methodology was then

undertaken using the MassARRAY® Assay Design v3.1 Software. Common settings for assay design included the addition of a universal 10 base 5' sequences and then at least 20 bases of sequence-specific bases. All first round reactions were designed for an average of amplicon of 100-bases pairs and ranging between 80 and 120 bases. Universal extension primers were designed with a mass range of 4500Da to 10,000Da (~15-mer to ~29-mer oligos).

For reasons of economy and processing time, we decided to focus on 2 multiplexes only. These multiplexes were then tested using a panel of CEPH and YRI HapMap DNAs. Poorly performing assays or poor concordance assays were removed from the multiplex.

Details of the final 2 multiplexes are provided in Supplementary Table 23 and additional markers typed for ATP2B4 are provided in Supplementary Table 24 as these were typed separately from the 2 primary multiplexes.

Sample preparation:

PEP DNA samples were diluted 1:10 using a phenol red solution (0.01mg/ml) to aid tracking into 384-well plates (yellow/red to purple colour change); 22.5ul of phenol red solution plated into each well of a 384-well plate and 2.5ul of neat PEP was added. An aliquot of diluted PEP was then immediately used for the first-round PCR reactions as described below. Unused diluted PEP was frozen at -20°C. NB: Diluted PEP kept at 4°C for more than 2 days or freeze-thawed more than twice was discarded as this was found too degraded for genotyping .

iPLEX primers:

All primers were purchased lyophilised from Metabion International AG (Martinsried, Germany [see URLs]).

First-round primers were hydrated at 100 uM and extension primers were hydrated at 300 uM. All primers were stored at -20°C.

First-Round reaction master-mix:

A master-mix comprising the following was prepared for each 384-well plate allowing some extra volume;

3.3 ul of each first-round primer (100mM),
214.5 ul $MgCl_2$ (50mM),
66 ul dNTPs (25mM pooled),
412.5 ul 10X HotStar Taq buffer (Qiagen),
132 ul HotStar Taq (5U/ul) (Qiagen) and
milliQ water to make a final volume of 1980ul.

First-Round Reaction:

PCR master mix (4.5 ul per well) was plated into a 384-well PCR plate (Thermo Fisher Scientific) and 3 ul of 1:10 diluted PEP DNA were added per well. Plates were sealed with Microseal 'A' lids (Bio-Rad) and cycled on an MJ Tetrad with the following conditions:

94 °C for 15 min,
44 cycles of; 94 °C for 20 sec,
56 °C for 30 sec,
72 °C for 1 min,
and 72°C for 3 min
maintain at 4°C

A 1ul sample from each well of a single row was run on a 2% agarose gel to confirm the PCR had worked prior to further processing.

Shrimp-alkaline Phosphatase treatment:

Unincorporated dNTP's were destroyed by adding 2ul of iPLEX shrimp-alkaline phosphatase (SAP) mixture to 5ul of first-round PCR reaction mixture and incubating at 37 °C for 40 min followed by a denaturation step at 85 °C for 5 min and then cooling to 15°C for 15 min.

Primer-Extension Reaction:

Extension-primer final reaction concentrations were dependent on their molecular mass based on SEQUENOM® protocol guidelines;

< 5800Da 0.84 uM,
5800 to 7000Da 1.04 uM,
7000 to 10,000 Da 1.25 uM,
>10,000Da 1.5uM.

Primer extension was carried out in the sample plate by adding 2 ul per well of a mixture containing;

0.2ul iPLEX termination mixture,
0.041ul extension Taq,
0.2ul extension buffer,
Primers (300mM);
- 0.025ul per primer up to 5800Da,
- 0.0312 ul per primer 5800 to 7000Da,
- 0.0375 ul per primer 7000 to 10,000 Da
- 0.045 ul per primer >10,000 Da

and water to 2ul.

The final extension reaction volume was 9 ul (5ul first-round reaction, 2ul SAP and 2ul of extension mixture).

Extension cycling was undertaken on an MJ Tetrad using the following conditions:

94 ºC for 30 sec,
40 cycles of;
- 94ºC for 5 sec,
  - 5 cycles of;
    - 52 ºC for 5 sec,
    - 80 ºC for 5 sec,
- then 72ºC for 3 min
- and 15ºC for 15 min.

Plates were processed by adding 6 mg ion-exchange resin per well and 16ul MilliQ water. Plates were sealed, rotated for 30min and then centrifuged to pellet the resin prior to 'spotting' samples onto SpectroCHIPS and running on the Mass-Spectrometer. Data were inspected and genotypes checked using the SEQUENOM® Typer 4.03 software. Data were downloaded and stored in a central database where any further curation was undertaken. All genotype data were maintained according to the sequence strand used for the assay design process.

Sequenom Assay details:

Supplementary Tables 22-24 contain information on the primers and assays designs.

Genetic Heterogeneity

To assess evidence for genetic heterogeneity across severe malaria subtypes CM and SMA both within and across populations, we make model comparisons in a Bayesian statistical framework. To facilitate computation, we use Approximate Bayes Factors (ABFs) in place of Bayes factors to estimate the posterior probabilities of each model of association as described in Band et al. [123]. The ABF differs from the Bayes Factor in that it depends on an approximation of the marginal likelihood function (up to a constant) by a multivariate normal density. The ABF for each model is calculated as the ratio of the approximate marginal likelihood of that model to that of the null model where the variant has no effect on any of the subtypes; note that the ABF for the null model is then, of course, equal to 1. Under the assumption that exactly one of the models is correct and all models are equally likely *a priori*, the unweighted posterior probability of a given model is calculated as the ABF for that model divided by the sum of the ABFs for all models under consideration. If any of the models are assumed *a priori* to be more likely, then we need to weigh the ABFs accordingly. For example, if, before seeing data, the null model is given 80% probability and the other nine models are assumed equally probable with each other, then the corresponding posterior probabilities are calculated by weighing the ABFs by 0.8 for the null model and 0.2 / 9=0.022 for any other model. (See Supplementary figure 5)

Calculation of the marginal likelihood requires specification of a prior distribution for the SNP effects on each phenotype at each site as well as maximum likelihood (ML) point estimates of these effects with their asymptotic standard errors. Suppose in general that we have *P* phenotypes and *S* sites. We assume a multivariate prior distribution for the SNP effects with mean zero and a covariance matrix in block form

$$\boldsymbol{\Sigma} = \sigma^2 \begin{bmatrix} A_{11} & A_{12} & \cdots & A_{1S} \\ A_{12} & A_{22} & \cdots & A_{2S} \\ \vdots & \vdots & \ddots & \vdots \\ A_{1S} & \cdots & \cdots & A_{SS} \end{bmatrix}$$

where

- σ is the standard deviation;
- for $s, t = 1, \ldots, S, t \geq s$, A_{st} are matrices of the form

$$A_{ss} = \begin{bmatrix} 1 & \rho_{12}^{ss} & \cdots & \rho_{1P}^{ss} \\ \rho_{12}^{ss} & 1 & \cdots & \rho_{2P}^{ss} \\ \vdots & \vdots & \ddots & \vdots \\ \rho_{1P}^{ss} & \rho_{2P}^{ss} & \cdots & 1 \end{bmatrix} \text{ when } s{=}t \text{ and } A_{st} = \begin{bmatrix} \rho_{11}^{st} & \rho_{12}^{st} & \cdots & \rho_{1P}^{st} \\ \rho_{12}^{st} & \rho_{22}^{st} & \cdots & \rho_{2P}^{st} \\ \vdots & \vdots & \ddots & \vdots \\ \rho_{1P}^{st} & \rho_{2P}^{st} & \cdots & \rho_{PP}^{st} \end{bmatrix} \text{ when } s{\neq}t$$

where ρ_{pq}^{st} denotes the prior correlation between phenotype p at site s and phenotype q at site t. Thus A_{ss} represents the prior correlation between effects on phenotypes within a site (phenotypic

heterogeneity) and; A_{st} is the prior correlation between phenotypes across sites (population heterogeneity).

By selecting different prior correlation values within and across sites, we can formally compare different models of effect heterogeneity. In our analyses, we use $\rho_{pq}^{st} = 1,0.1,$ or 0.96 to model fixed, independent and correlated effects respectively. For example, for 3 phenotypes and 2 sites:

- A model with effects fixed within site and correlated across sites

$$A_{11} = A_{22} = \begin{bmatrix} 1 & 1 & 1 \\ 1 & 1 & 1 \\ 1 & 1 & 1 \end{bmatrix} \text{ and } A_{12} = \begin{bmatrix} 0.96 & 0.96 & 0.96 \\ 0.96 & 0.96 & 0.96 \\ 0.96 & 0.96 & 0.96 \end{bmatrix}.$$

- A model with effects correlated within site and independent across sites

$$A_{11} = A_{22} = \begin{bmatrix} 1 & 0.96 & 0.96 \\ 0.96 & 1 & 0.96 \\ 0.96 & 0.96 & 1 \end{bmatrix} \text{ and } A_{12} = \begin{bmatrix} 0.1 & 0.1 & 0.1 \\ 0.1 & 0.1 & 0.1 \\ 0.1 & 0.1 & 0.1 \end{bmatrix}.$$

Let $\hat{\beta}_s = (\hat{\beta}_{s1}, \hat{\beta}_{s2}, \dots, \hat{\beta}_{sP})^t$ be a P x 1 vector of maximum likelihood (ML) estimates, and $\boldsymbol{V_{\beta_s}}$ the corresponding P x P variance-covariance matrix, for the estimated SNP effects on each phenotype at site s, s =1,…,S from a multinomial regression model. We approximate the multinomial likelihood function for site s by the multivariate normal density with mean $\hat{\beta}_s$ and variance-covariance $\boldsymbol{V_{\beta_s}}$. The approximate marginal likelihood is then given (up to a multiplicative constant) by the multivariate normal density evaluated at the ML estimate,

$$f(\hat{\beta}; \mathbf{O}, \boldsymbol{\Sigma} + \boldsymbol{V_{\beta}})$$

where

- $\hat{\beta} = (\hat{\beta}_1, \hat{\beta}_2, \dots, \hat{\beta}_S)^t$ is an (Sx P) x 1 vector comprising the estimated effects at each phenotype at each site:
- **O** is the null vector.
- $\boldsymbol{V_{\beta}}$ is an (Sx P) x (Sx P) matrix with diagonal blocks comprising the variance covariance matrix for the estimated effects at each site

$$V_{\beta} = \begin{bmatrix} V_{\beta_1} & 0 & \cdots & 0 \\ 0 & V_{\beta_2} & \cdots & 0 \\ \vdots & \vdots & \ddots & \vdots \\ 0 & 0 & \cdots & V_{\beta_S} \end{bmatrix}$$

The models examined here are similar to those employed by Bellenguez et al. [124] to look at heterogeneity of effects *within* a single site and by Band et al. [123] to look at heterogeneity of effects *across* a site. Here we are extending the method to allow for examination of effects both within *and* across sites.

Contributors to MalariaGEN Consortial Project 1

Listed below are all contributors to the MalariaGEN Consortial Project 1 (Genetic determinants of resistance to malaria). These are grouped by partner site and contributors are listed alphabetically within each site.

Each partner has also provided a more detailed description of their individual study sites. These can be found on the MalariaGEN website (see URLs). Individual links for each partner site are also included.

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MalariaGEN Programme Management Committee/Governance Committee :
http://www.malariagen.net/community/ethics-governance/gc

Tepnel BACC DNA extraction kit: http://www.gen-probe.com/pdfs/downloads/protocol%20BACC%20123%5B1%5D.pdf;
Qiagen: http://www.qiagen.com;
Invitrogen: http://www.probes.com;
Greiner Bio-One: http://www.greinerbioone.com;
Genetix Ltd: http://www.genetix.com;
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Sigma-Aldrich: https://www.sigmaaldrich.com;
Sequenom: http://www.sequenom.com;
Ensembl: http://www.ensembl.org;
RealSNP: http://www.realsnp.com;
Metabion: http://www.metabion.com/home/index.php.

References

1. Bedu-Addo, G., Meese, S. & Mockenhaupt, F.P. An ATP2B4 polymorphism protects against malaria in pregnancy. *The Journal of infectious diseases* **207**, 1600-3 (2013).
2. Timmann, C. *et al.* Genome-wide association study indicates two novel resistance loci for severe malaria. *Nature* **489**, 443-6 (2012).
3. Nagayasu, E. *et al.* CR1 density polymorphism on erythrocytes of falciparum malaria patients in Thailand. *Am J Trop Med Hyg* **64**, 1-5 (2001).
4. Zimmerman, P.A. *et al.* CR1 Knops blood group alleles are not associated with severe malaria in the Gambia. *Genes Immun* **4**, 368-73 (2003).
5. Cockburn, I.A. *et al.* A human complement receptor 1 polymorphism that reduces Plasmodium falciparum rosetting confers protection against severe malaria. *Proc Natl Acad Sci U S A* **101**, 272-7 (2004).
6. Thathy, V., Moulds, J.M., Guyah, B., Otieno, W. & Stoute, J.A. Complement receptor 1 polymorphisms associated with resistance to severe malaria in Kenya. *Malar J* **4**, 54 (2005).
7. Teeranaipong, P. *et al.* A functional single-nucleotide polymorphism in the CR1 promoter region contributes to protection against cerebral malaria. *J Infect Dis* **198**, 1880-91 (2008).
8. Sinha, S. *et al.* CR1 levels and gene polymorphisms exhibit differential association with falciparum malaria in regions of varying disease endemicity. *Hum Immunol* **70**, 244-50 (2009).
9. Soares, S.C., Abe-Sandes, K., Nascimento Filho, V.B., Nunes, F.M. & Silva, W.A., Jr. Genetic polymorphisms in TLR4, CR1 and Duffy genes are not associated with malaria resistance in patients from Baixo Amazonas region, Brazil. *Genet Mol Res* **7**, 1011-9 (2008).
10. Miller, L.H., Mason, S.J., Dvorak, J.A., McGinniss, M.H. & Rothman, I.K. Erythrocyte receptors for (Plasmodium knowlesi) malaria: Duffy blood group determinants. *Science* **189**, 561-3 (1975).
11. Tournamille, C., Colin, Y., Cartron, J.P. & Le Van Kim, C. Disruption of a GATA motif in the Duffy gene promoter abolishes erythroid gene expression in Duffy-negative individuals. *Nat Genet* **10**, 224-8 (1995).
12. Cavasini, C.E. *et al.* Duffy blood group gene polymorphisms among malaria vivax patients in four areas of the Brazilian Amazon region. *Malar J* **6**, 167 (2007).
13. Wilson, J. *et al.* Genetic variation at the IL10 gene locus is associated with severity of respiratory syncytial virus bronchiolitis. *J Infect Dis* **191**, 1705-9 (2005).
14. Wilson, J.N. *et al.* Analysis of IL10 haplotypic associations with severe malaria. *Genes Immun* **6**, 462-6 (2005).
15. Walley, A.J., Aucan, C., Kwiatkowski, D. & Hill, A.V. Interleukin-1 gene cluster polymorphisms and susceptibility to clinical malaria in a Gambian case-control study. *Eur J Hum Genet* **12**, 132-8 (2004).
16. Gyan, B. *et al.* Polymorphisms in interleukin-1beta and interleukin-1 receptor antagonist genes and malaria in Ghanaian children. *Scand J Immunol* **56**, 619-22 (2002).
17. Carpenter, D. *et al.* Genetics of susceptibility to malaria related phenotypes. *Infect Genet Evol* **9**, 97-103 (2009).
18. Mockenhaupt, F.P. *et al.* Common polymorphisms of toll-like receptors 4 and 9 are associated with the clinical manifestation of malaria during pregnancy. *J Infect Dis* **194**, 184-8 (2006).
19. Greene, J.A. *et al.* Toll-like receptor polymorphisms in malaria-endemic populations. *Malar J* **8**, 50 (2009).
20. Campino, S. *et al.* TLR9 polymorphisms in African populations: no association with severe malaria, but evidence of cis-variants acting on gene expression. *Malar J* **8**, 44 (2009).
21. Leoratti, F.M. *et al.* Variants in the toll-like receptor signaling pathway and clinical outcomes of malaria. *J Infect Dis* **198**, 772-80 (2008).
22. Soejima, M. *et al.* Nucleotide sequence analyses of human complement 6 (C6) gene suggest balancing selection. *Ann Hum Genet* **69**, 239-52 (2005).
23. Zhu, Z. *et al.* High prevalence of complement component C6 deficiency among African-Americans in the south-eastern USA. *Clin Exp Immunol* **119**, 305-10 (2000).
24. Zhu, Z.B., Totemchokchyakarn, K., Atkinson, T.P. & Volanakis, J.E. Molecular defects leading to human complement component C6 deficiency in an African-American family. *Clin Exp Immunol* **111**, 91-6 (1998).
25. Ohashi, J. *et al.* A single-nucleotide substitution from C to T at position -1055 in the IL-13 promoter is associated with protection from severe malaria in Thailand. *Genes Immun* **4**, 528-31 (2003).

26. Gyan, B.A. *et al.* Allelic polymorphisms in the repeat and promoter regions of the interleukin-4 gene and malaria severity in Ghanaian children. *Clin Exp Immunol* **138**, 145-50 (2004).
27. Verra, F. *et al.* IL4-589C/T polymorphism and IgE levels in severe malaria. *Acta Trop* **90**, 205-9 (2004).
28. Mangano, V.D. *et al.* Interferon regulatory factor-1 polymorphisms are associated with the control of Plasmodium falciparum infection. *Genes Immun* **9**, 122-9 (2008).
29. Barbier, M., Delahaye, N.F., Fumoux, F. & Rihet, P. Family-based association of a low producing lymphotoxin-alpha allele with reduced Plasmodium falciparum parasitemia. *Microbes Infect* **10**, 673-9 (2008).
30. Ackerman, H.C. *et al.* Complex haplotypic structure of the central MHC region flanking TNF in a West African population. *Genes Immun* **4**, 476-86 (2003).
31. McGuire, W., Hill, A.V., Allsopp, C.E., Greenwood, B.M. & Kwiatkowski, D. Variation in the TNF-alpha promoter region associated with susceptibility to cerebral malaria. *Nature* **371**, 508-10 (1994).
32. Wattavidanage, J. *et al.* TNFalpha*2 marks high risk of severe disease during Plasmodium falciparum malaria and other infections in Sri Lankans. *Clin Exp Immunol* **115**, 350-5 (1999).
33. Hananantachai, H. *et al.* Significant association between TNF-alpha (TNF) promoter allele (-1031C, -863C, and -857C) and cerebral malaria in Thailand. *Tissue Antigens* **69**, 277-80 (2007).
34. Hohjoh, H. *et al.* Significant association of a single nucleotide polymorphism in the tumor necrosis factor-alpha (TNF-alpha) gene promoter with human narcolepsy. *Tissue Antigens* **54**, 138-45 (1999).
35. Wilson, A.G., Symons, J.A., McDowell, T.L., McDevitt, H.O. & Duff, G.W. Effects of a polymorphism in the human tumor necrosis factor alpha promoter on transcriptional activation. *Proc Natl Acad Sci U S A* **94**, 3195-9 (1997).
36. Cabantous, S. *et al.* Alleles 308A and 238A in the tumor necrosis factor alpha gene promoter do not increase the risk of severe malaria in children with Plasmodium falciparum infection in Mali. *Infect Immun* **74**, 7040-2 (2006).
37. Meyer, C.G., May, J., Luty, A.J., Lell, B. & Kremsner, P.G. TNFalpha-308A associated with shorter intervals of Plasmodium falciparum reinfections. *Tissue Antigens* **59**, 287-92 (2002).
38. Mombo, L.E. *et al.* Human genetic polymorphisms and asymptomatic Plasmodium falciparum malaria in Gabonese schoolchildren. *Am J Trop Med Hyg* **68**, 186-90 (2003).
39. Atkinson, S.H. *et al.* Tumor necrosis factor SNP haplotypes are associated with iron deficiency anemia in West African children. *Blood* **112**, 4276-83 (2008).
40. Clark, T.G. *et al.* Tumor necrosis factor and lymphotoxin-alpha polymorphisms and severe malaria in African populations. *J Infect Dis* **199**, 569-75 (2009).
41. Diakite, M. *et al.* A genetic association study in the Gambia using tagging polymorphisms in the major histocompatibility complex class III region implicates a HLA-B associated transcript 2 polymorphism in severe malaria susceptibility. *Hum Genet* **125**, 105-9 (2009).
42. Stuber, F. *et al.* -308 tumor necrosis factor (TNF) polymorphism is not associated with survival in severe sepsis and is unrelated to lipopolysaccharide inducibility of the human TNF promoter. *J Inflamm* **46**, 42-50 (1995).
43. Clark, I.A. *et al.* Increased lymphotoxin in human malarial serum, and the ability of this cytokine to increase plasma interleukin-6 and cause hypoglycaemia in mice: implications for malarial pathology. *Trans R Soc Trop Med Hyg* **86**, 602-7 (1992).
44. Kwiatkowski, D. *et al.* TNF concentration in fatal cerebral, non-fatal cerebral, and uncomplicated Plasmodium falciparum malaria. *Lancet* **336**, 1201-4 (1990).
45. Grau, G.E., Piguet, P.F., Vassalli, P. & Lambert, P.H. Tumor-necrosis factor and other cytokines in cerebral malaria: experimental and clinical data. *Immunol Rev* **112**, 49-70 (1989).
46. Kern, P., Hemmer, C.J., Van Damme, J., Gruss, H.-J. & Dietrich, M. Elevated tumour necrosis factor alpha and interleukin-6 serum levels as markers for complicated *Plasmodium falciparum* malaria. *American Journal of Medicine* **87**, 139-143 (1989).
47. Butcher, G.A., Garland, T., Adjukiewicz, A.B. & Clark, I.A. Serum TNF associated with malaria in patients in the Solomon Islands. *Trans. R. Soc. Trop. Med. Hyg.* **85**, 658-661 (1990).
48. Bayley, J.P., Ottenhoff, T.H. & Verweij, C.L. Is there a future for TNF promoter polymorphisms? *Genes Immun* **5**, 315-29 (2004).
49. Randall, L.M. & Engwerda, C.R. TNF family members and malaria: old observations, new insights and future directions. *Exp Parasitol* **126**, 326-31 (2010).

50. Fry, A.E. *et al.* Positive selection of a CD36 nonsense variant in sub-Saharan Africa, but no association with severe malaria phenotypes. *Hum Mol Genet* **18**, 2683-92 (2009).
51. Omi, K. *et al.* Polymorphisms of CD36 in Thai malaria patients. *Southeast Asian J Trop Med Public Health* **33 Suppl 3**, 1-4 (2002).
52. Omi, K. *et al.* CD36 polymorphism is associated with protection from cerebral malaria. *Am J Hum Genet* **72**, 364-74 (2003).
53. Aitman, T.J. *et al.* Malaria susceptibility and CD36 mutation. *Nature* **405**, 1015-6 (2000).
54. Pain, A. *et al.* A non-sense mutation in Cd36 gene is associated with protection from severe malaria. *Lancet* **357**, 1502-3 (2001).
55. Fernandez-Reyes, D. *et al.* A high frequency African coding polymorphism in the N-terminal domain of ICAM-1 predisposing to cerebral malaria in Kenya. *Hum Mol Genet* **6**, 1357-60 (1997).
56. Amodu, O.K. *et al.* Plasmodium falciparum malaria in south-west Nigerian children: is the polymorphism of ICAM-1 and E-selectin genes contributing to the clinical severity of malaria? *Acta Trop* **95**, 248-55 (2005).
57. Athreya, B.H. & Coriell, L.L. Relation of blood groups to infection. I. A survey and review of data suggesting possible relationship between malaria and blood groups. *Am J Epidemiol* **86**, 292-304 (1967).
58. Rowe, J.A., Opi, D.H. & Williams, T.N. Blood groups and malaria: fresh insights into pathogenesis and identification of targets for intervention. *Curr Opin Hematol* **16**, 480-7 (2009).
59. Fry, A.E. *et al.* Common variation in the ABO glycosyltransferase is associated with susceptibility to severe Plasmodium falciparum malaria. *Hum Mol Genet* **17**, 567-76 (2008).
60. Mockenhaupt, F.P. *et al.* Toll-like receptor (TLR) polymorphisms in African children: common TLR-4 variants predispose to severe malaria. *J Commun Dis* **38**, 230-45 (2006).
61. Mockenhaupt, F.P. *et al.* Toll-like receptor (TLR) polymorphisms in African children: Common TLR-4 variants predispose to severe malaria. *Proc Natl Acad Sci U S A* **103**, 177-82 (2006).
62. Zakeri, S., Pirahmadi, S., Mehrizi, A.A. & Djadid, N.D. Genetic variation of TLR-4, TLR-9 and TIRAP genes in Iranian malaria patients. *Malar J* **10**, 77 (2011).
63. Basu, M. *et al.* Genetic association of Toll-like-receptor 4 and tumor necrosis factor-alpha polymorphisms with Plasmodium falciparum blood infection levels. *Infect Genet Evol* **10**, 686-96 (2010).
64. May, L. *et al.* Polymorphisms in TLR4 and TLR2 genes, cytokine production and survival in rural Ghana. *Eur J Hum Genet* **18**, 490-5 (2010).
65. Flatz, G., Pik, C. & Sundharagiati, B. Malaria And Haemoglobin E In Thailand. *Lancet* **2**, 385-7 (1964).
66. Allison, A.C. Genetic factors in resistance to malaria. *Ann N Y Acad Sci* **91**, 710-29 (1961).
67. Kruatrachue, M., Na-Nakorn, S., Charoenlarp, P. & Suwanakul, L. Haemoglobin E and malaria in south-east Thailand. *Ann Trop Med Parasitol* **55**, 468-73 (1961).
68. Chotivanich, K. *et al.* Hemoglobin E: a balanced polymorphism protective against high parasitemias and thus severe P falciparum malaria. *Blood* **100**, 1172-6 (2002).
69. Allison, A.C. Protection afforded by sickle-cell trait against subtertian malarial infection. *Br Med J* **1**, 290-4 (1954).
70. Herrick, J.B. Peculiar elongated and sickle-shaped red blood corpuscles in a case of severe anemia. 1910. *Yale J Biol Med* **74**, 179-84 (2001).
71. Savitt, T.L. & Goldberg, M.F. Herrick's 1910 case report of sickle cell anemia. The rest of the story. *Jama* **261**, 266-71 (1989).
72. Ingram, V.M. Abnormal human haemoglobins. III. The chemical difference between normal and sickle cell haemoglobins. *Biochim Biophys Acta* **36**, 402-11 (1959).
73. Williams, T.N. Human red blood cell polymorphisms and malaria. *Curr Opin Microbiol* **9**, 388-94 (2006).
74. Allison, A.C. Sickle-cell anaemia and haemoglobin C. *Trans R Soc Trop Med Hyg* **50**, 185-96; discussion, 197-203 (1956).
75. Allison, A.C. The sickle-cell and haemoglobin C genes in some African populations. *Ann Hum Genet* **21**, 67-89 (1956).
76. Modiano, D. *et al.* Haemoglobin C protects against clinical Plasmodium falciparum malaria. *Nature* **414**, 305-8 (2001).
77. Rihet, P., Flori, L., Tall, F., Traore, A.S. & Fumoux, F. Hemoglobin C is associated with reduced Plasmodium falciparum parasitemia and low risk of mild malaria attack. *Hum Mol Genet* **13**, 1-6 (2004).

78. Koch, O. *et al.* Investigation of malaria susceptibility determinants in the IFNG/IL26/IL22 genomic region. *Genes Immun* **6**, 312-8 (2005).
79. Facer, C.A. Erythrocytes carrying mutations in spectrin and protein 4.1 show differing sensitivities to invasion by Plasmodium falciparum. *Parasitol Res* **81**, 52-7 (1995).
80. Auburn, S. *et al.* Further evidence supporting a role for gs signal transduction in severe malaria pathogenesis. *PLoS One* **5**, e10017 (2010).
81. Kun, J.F. *et al.* Polymorphism in promoter region of inducible nitric oxide synthase gene and protection against malaria. *Lancet* **351**, 265-6 (1998).
82. Burgner, D. *et al.* Inducible nitric oxide synthase polymorphism and fatal cerebral malaria. *Lancet* **352**, 1193-4 (1998).
83. Burgner, D. *et al.* Nucleotide and haplotypic diversity of the NOS2A promoter region and its relationship to cerebral malaria. *Hum Genet* **112**, 379-86 (2003).
84. Ohashi, J. *et al.* Significant association of longer forms of CCTTT Microsatellite repeat in the inducible nitric oxide synthase promoter with severe malaria in Thailand. *J Infect Dis* **186**, 578-81 (2002).
85. Boutlis, C.S. *et al.* Inducible nitric oxide synthase (NOS2) promoter CCTTT repeat polymorphism: relationship to in vivo nitric oxide production/NOS activity in an asymptomatic malaria-endemic population. *Am J Trop Med Hyg* **69**, 569-73 (2003).
86. Hobbs, M.R. *et al.* A new NOS2 promoter polymorphism associated with increased nitric oxide production and protection from severe malaria in Tanzanian and Kenyan children. *Lancet* **360**, 1468-75 (2002).
87. Bellamy, R., Kwiatkowski, D. & Hill, A.V. Absence of an association between intercellular adhesion molecule 1, complement receptor 1 and interleukin 1 receptor antagonist gene polymorphisms and severe malaria in a West African population. *Trans R Soc Trop Med Hyg* **92**, 312-6 (1998).
88. Ohashi, J. *et al.* Absence of association between the allele coding methionine at position 29 in the N-terminal domain of ICAM-1 (ICAM-1(Kilifi)) and severe malaria in the northwest of Thailand. *Jpn J Infect Dis* **54**, 114-6 (2001).
89. Auburn, S. *et al.* Association of the GNAS locus with severe malaria. *Hum Genet* **124**, 499-506 (2008).
90. Griffiths, M.J. *et al.* Genomewide analysis of the host response to malaria in Kenyan children. *J Infect Dis* **191**, 1599-611 (2005).
91. Sabeti, P. *et al.* CD40L association with protection from severe malaria. *Genes Immun* **3**, 286-91 (2002).
92. Inoue, S. *et al.* Enhancement of dendritic cell activation via CD40 ligand-expressing gammadelta T cells is responsible for protective immunity to Plasmodium parasites. *Proc Natl Acad Sci U S A* **109**, 12129-34 (2012).
93. Piguet, P.F. *et al.* Role of CD40-CVD40L in mouse severe malaria. *Am J Pathol* **159**, 733-42 (2001).
94. Luzzatto, L., Usanga, F.A. & Reddy, S. Glucose-6-phosphate dehydrogenase deficient red cells: resistance to infection by malarial parasites. *Science* **164**, 839-42 (1969).
95. Gilles, H.M. *et al.* Glucose-6-phosphate-dehydrogenase deficiency, sickling, and malaria in African children in South Western Nigeria. *Lancet* **1**, 138-40 (1967).
96. Bienzle, U., Ayeni, O., Lucas, A.O. & Luzzatto, L. Glucose-6-phosphate dehydrogenase and malaria. Greater resistance of females heterozygous for enzyme deficiency and of males with non-deficient variant. *Lancet* **1**, 107-10 (1972).
97. Nkhoma, E.T., Poole, C., Vannappagari, V., Hall, S.A. & Beutler, E. The global prevalence of glucose-6-phosphate dehydrogenase deficiency: a systematic review and meta-analysis. *Blood Cells Mol Dis* **42**, 267-78 (2009).
98. Sirugo, G. *et al.* G6PD A- deficiency and severe malaria in The Gambia: heterozygote advantage and possible homozygote disadvantage. *Am J Trop Med Hyg* **90**, 856-9 (2014).
99. Armah, H.B. *et al.* Cerebrospinal fluid and serum biomarkers of cerebral malaria mortality in Ghanaian children. *Malar J* **6**, 147 (2007).
100. Sheikh, F. *et al.* Cutting edge: IL-26 signals through a novel receptor complex composed of IL-20 receptor 1 and IL-10 receptor 2. *J Immunol* **172**, 2006-10 (2004).
101. Kingo, K. *et al.* Association analysis of IL20RA and IL20RB genes in psoriasis. *Genes Immun* **9**, 445-51 (2008).
102. Verloo, P. *et al.* Plasmodium falciparum-activated chloride channels are defective in erythrocytes from cystic fibrosis patients. *J Biol Chem* **279**, 10316-22 (2004).
103. van de Vosse, E. *et al.* Susceptibility to typhoid fever is associated with a polymorphism in the cystic fibrosis transmembrane conductance regulator (CFTR). *Hum Genet* **118**, 138-40 (2005).

104. Finney, C.A., Lu, Z., LeBourhis, L., Philpott, D.J. & Kain, K.C. Disruption of Nod-like receptors alters inflammatory response to infection but does not confer protection in experimental cerebral malaria. *Am J Trop Med Hyg* **80**, 718-22 (2009).
105. Hysi, P. *et al.* NOD1 variation, immunoglobulin E and asthma. *Hum Mol Genet* **14**, 935-41 (2005).
106. Johnson, W.E. & Sawyer, S.L. Molecular evolution of the antiretroviral TRIM5 gene. *Immunogenetics* **61**, 163-76 (2009).
107. Toyota, T. *et al.* Molecular analysis, mutation screening, and association study of adenylate cyclase type 9 gene (ADCY9) in mood disorders. *Am J Med Genet* **114**, 84-92 (2002).
108. Perkmann, T., Winkler, H., Graninger, W., Kremsner, P.G. & Winkler, S. Circulating levels of the interleukin (IL)-4 receptor and of IL-18 in patients with Plasmodium falciparum malaria. *Cytokine* **29**, 153-8 (2005).
109. Saeftel, M. *et al.* Mice deficient in interleukin-4 (IL-4) or IL-4 receptor alpha have higher resistance to sporozoite infection with Plasmodium berghei (ANKA) than do naive wild-type mice. *Infect Immun* **72**, 322-31 (2004).
110. Baud, V. *et al.* EMR1, an unusual member in the family of hormone receptors with seven transmembrane segments. *Genomics* **26**, 334-44 (1995).
111. Ntoumi, F. *et al.* Influence of carriage of hemoglobin AS and the Fc gamma receptor IIa-R131 allele on levels of immunoglobulin G2 antibodies to Plasmodium falciparum merozoite antigens in Gabonese children. *J Infect Dis* **192**, 1975-80 (2005).
112. Israelsson, E. *et al.* Differences in Fcgamma receptor IIa genotypes and IgG subclass pattern of anti-malarial antibodies between sympatric ethnic groups in Mali. *Malar J* **7**, 175 (2008).
113. Harrison, T. *et al.* Erythrocyte G protein-coupled receptor signaling in malarial infection. *Science* **301**, 1734-6 (2003).
114. Simone, O. *et al.* TLRs innate immunereceptors and Plasmodium falciparum erythrocyte membrane protein 1 (PfEMP1) CIDR1alpha-driven human polyclonal B-cell activation. *Acta Trop* **119**, 144-50 (2011).
115. Wautier, J.L. & Wautier, M.P. [Erythrocyte adhesion to the vascular endothelium]. *Transfus Clin Biol* **6**, 397-402 (1999).
116. Callaghan, M.J. *et al.* Haplotypic diversity in human CEACAM genes: effects on susceptibility to meningococcal disease. *Genes Immun* **9**, 30-7 (2008).
117. Sinnis, P., Willnow, T.E., Briones, M.R., Herz, J. & Nussenzweig, V. Remnant lipoproteins inhibit malaria sporozoite invasion of hepatocytes. *J Exp Med* **184**, 945-54 (1996).
118. Aucan, C., Walley, A.J. & Hill, A.V. Common apolipoprotein E polymorphisms and risk of clinical malaria in the Gambia. *J Med Genet* **41**, 21-4 (2004).
119. Wozniak, M.A. *et al.* Does apolipoprotein E polymorphism influence susceptibility to malaria? *J Med Genet* **40**, 348-51 (2003).
120. Wozniak, M.A., Riley, E.M. & Itzhaki, R.F. Apolipoprotein E polymorphisms and risk of malaria. *J Med Genet* **41**, 145-6 (2004).
121. Zhang, L. *et al.* Whole genome amplification from a single cell: implications for genetic analysis. *Proc Natl Acad Sci U S A* **89**, 5847-51 (1992).
122. Eng, B., Ainsworth, P. & Waye, J.S. Anomalous migration of PCR products using nondenaturing polyacrylamide gel electrophoresis: the amelogenin sex-typing system. *J Forensic Sci* **39**, 1356-9 (1994).
123. Band, G. *et al.* Imputation-based meta-analysis of severe malaria in three African populations. *PLoS Genet* **9**, e1003509 (2013).
124. Bellenguez, C. *et al.* Genome-wide association study identifies a variant in HDAC9 associated with large vessel ischemic stroke. *Nature genetics* **44**, 328-33 (2012).