

Supplementary information

Population genomic evidence of adaptive response during the invasion history of *Plasmodium falciparum* in the Americas

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Supplementary Table S1: Number of *P. falciparum* isolates by country in the final dataset.

Region	Country	Number of isolates	Sources
Central Africa	Democratic Republic of Congo	138	MalariaGen Project (Pearson <i>et al.</i> , 2019)
West Africa	Cameroon	108	
	Burkina Faso	16	
	Benin	25	
	Ghana	364	
	Guinea	67	
	Ivory Coast	42	
	Mali	224	
	Senegal	55	
	Gambia	107	
	Mauritania	38	
East Africa	Malawi	96	
	Kenya	54	
	Ethiopia	13	
	Madagascar	19	
	Tanzania	161	
	Uganda	5	
South Asia	Bangladesh	36	
West South-East Asia	Thailand	405	
	Myanmar	103	
East South-East Asia	Cambodia	228	
	Laos	66	
	Vietnam	83	
Oceania	Papua New Guinea	77	
	Indonesia	35	
Central and South Americas	Colombia	12	
	Peru	5	
	Brazil	5	SRA database project number PRJNA312679 (Moser <i>et al.</i> , 2020)
	French Guiana	18	SRA database project number PRJNA242163 (Pelleau <i>et al.</i> , 2015)
	Haiti	8	SRA database project number PRJNA603776 (Tagliamonte <i>et al.</i> , 2020)

<i>P. praefalciparum</i>	3	Sample accessions SAMEA2464702, SAMEA2073285, and SAMEA2493921 on ENA (Otto <i>et al.</i> , 2018)
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Supplementary Table S2: List of genes in which evidence of positive selection was observed only in the SAM North cluster (Colombia - Haiti) with *XP-EHH*, *Rsb* and *ABS*.

Chr ^a	Test	ID ^b	Name	Functions	Biological processes
1	XP-EHH, Rsb	PF3D7_0104100	<i>Unknown</i>	<i>Unknown</i>	Modulation by symbiont of host immune response
5	XP-EHH, Rsb	PF3D7_0511300	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0520600	Ap4AH	Bis(5'-nucleosyl)-tetraphosphatase (asymmetrical) activity	AMP biosynthetic process; ATP biosynthetic process
5	ABS	PF3D7_0520700	<i>Unknown</i>	RNA polymerase II complex binding	Positive regulation of transcription elongation from RNA polymerase II promoter; recruitment of 3'-end processing factors to the RNA polymerase II holoenzyme complex
5	ABS	PF3D7_0520800	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0520900	SAHH	Adenosylhomocysteinase activity; protein binding	S-adenosylmethionine cycle
5	ABS	PF3D7_0521000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0521100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0521200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
6	XP-EHH, Rsb	PF3D7_0619500	ACS12	Medium-chain fatty acid-CoA ligase activity	Fatty acid metabolic process
6	ABS	PF3D7_0626500	CEP135	<i>Unknown</i>	<i>Unknown</i>
6	ABS	PF3D7_0626600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
6	ABS	PF3D7_0626700	<i>Unknown</i>	ATP binding; ATP hydrolysis activity	<i>Unknown</i>
6	ABS	PF3D7_0626800	PyrK	RNA binding; pyruvate kinase activity	Glycolytic process; protein homotetramerization
6	ABS	PF3D7_0626900	<i>Unknown</i>	Structural constituent of ribosome	<i>Unknown</i>
6	ABS	PF3D7_0627000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
6	ABS	PF3D7_0627100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
6	ABS	PF3D7_0627200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
6	ABS	PF3D7_0627300	RNF5	Ubiquitin protein ligase activity; ubiquitin-like protein conjugating enzyme binding; zinc ion binding	ER-associated misfolded protein catabolic process; ubiquitin-dependent protein catabolic process
6	ABS	PF3D7_0627400	TIM22	Mitochondrion targeting sequence binding; protein transmembrane transporter activity	Protein insertion into mitochondrial inner membrane; protein targeting to mitochondria

6	ABS	PF3D7_0627500	DJ1	Peptidase activity; protein deglycase activity	Guanine deglycation, glyoxal removal; protein deglycation; protein deglycation, glyoxal removal; protein folding; thiamine biosynthetic process
6	ABS	PF3D7_0627600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
6	ABS	PF3D7_0627700	<i>Unknown</i>	Nuclear import signal receptor activity; nuclear localization sequence binding; protein transmembrane transporter activity	Protein import into nucleus
6	ABS	PF3D7_0627800	ACAS	Acetate-CoA ligase activity	Acetyl-CoA biosynthetic process; chromatin organization; generation of precursor metabolites and energy; histone acetylation; response to xenobiotic stimuli
6	ABS	PF3D7_0627900	POP4	Ribonuclease P RNA binding; ribonuclease activity	rRNA processing
9	ABS	PF3D7_0931900	AKLP2	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0932000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0932100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0932200	PFN	Actin binding; actin monomer binding; phospholipid binding; proline-rich region binding; protein binding	Actin cytoskeleton organization; cell motility; cytoplasmic actin-based contraction involved in cell motility; entry into host; sequestering of actin monomers
9	ABS	PF3D7_0932300	M18AAP	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0932400	RF1	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0932500	DHHC6	Palmitoyltransferase activity; protein-cysteine S-palmitoyltransferase activity	Peptidyl-L-cysteine S-palmitoylation; protein palmitoylation; protein targeting to membrane
9	ABS	PF3D7_0932600	RPS6	Small ribosomal subunit rRNA binding; structural constituent of ribosome	<i>Unknown</i>
9	ABS	PF3D7_0932700	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0932800	CSE1	Nuclear export signal receptor activity	Protein export from nucleus; protein import into nucleus
9	ABS	PF3D7_0932900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0933000	<i>Unknown</i>	mRNA binding	Pre-mRNA cleavage required for polyadenylation
9	ABS	PF3D7_0933100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0933200	<i>Unknown</i>	<i>Unknown</i>	Protein stabilization; regulation of protein stability

9	ABS	PF3D7_0933300	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0933400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
9	ABS	PF3D7_0933500	<i>Unknown</i>	Gamma-tubulin binding	Cytoplasmic microtubule organization; meiotic cell cycle; microtubule nucleation by interphase microtubule organizing center; mitotic cell cycle; spindle assembly
12	XP-EHH	PF3D7_1208200	CRMP3	<i>Unknown</i>	Intracellular receptor signaling pathway; intracellular transport
12	Rsb	PF3D7_1239800	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1346600	C2AP4	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1346700	P48/45	Protein binding	<i>Unknown</i>
13	ABS	PF3D7_1346800	P47	Host cell surface receptor binding	Evasion of host immune response; modulation by symbiont of host cellular process; suppression by symbiont of host innate immune response
13	ABS	PF3D7_1346900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1347000	WDR92	Methylated histone binding; ubiquitin binding	Histone lysine methylation
13	ABS	PF3D7_1347100	TOP3	DNA binding; DNA topoisomerase activity; protein binding	DNA topological change; DNA unwinding involved in DNA replication
13	ABS	PF3D7_1347200	NT1	Nucleoside transmembrane transporter activity; purine nucleoside transmembrane transporter activity	Adenosine transport; purine nucleobase transport; purine nucleoside transmembrane transport; response to xenobiotic stimulus
13	ABS	PF3D7_1347300	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1347400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1347500	ALBA4	DNA binding; RNA binding; mRNA binding; protein-containing complex binding	Regulation of translation
13	ABS	PF3D7_1347600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1347700	ECT	Ethanolamine-phosphate cytidyltransferase activity	Phospholipid biosynthetic process
13	ABS	PF3D7_1347800	CEP72	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1347900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1348000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1348100	<i>Unknown</i>	GTP binding; GTPase activity	Small GTPase mediated signal transduction

13	ABS	PF3D7_1348200	<i>Unknown</i>	<i>Unknown</i>	RNA splicing
13	ABS	PF3D7_1348300	<i>Unknown</i>	GTP binding; GTPase activity; ribosome binding; translation elongation factor activity	Mature ribosome assembly; translational elongation
13	ABS	PF3D7_1348400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1348500	<i>Unknown</i>	GTPase activator activity	Activation of GTPase activity; intracellular protein transport
13	ABS	PF3D7_1348600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1348700	WDR16	<i>Unknown</i>	<i>Unknown</i>
13	ABS	PF3D7_1348800	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	XP-EHH, Rsb	PF3D7_1352900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
14	ABS	PF3D7_1407600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
14	ABS	PF3D7_1407700	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
14	ABS	PF3D7_1407800	PM4	RNA binding; aspartic-type endopeptidase activity	Hemoglobin catabolic process
14	ABS	PF3D7_1407900	PMI	Aspartic-type endopeptidase activity	Hemoglobin catabolic process
14	ABS	PF3D7_1408000	PMII	Aspartic-type endopeptidase activity	Hemoglobin catabolic process; response to xenobiotic stimuli
14	ABS	PF3D7_1408100	PMIII	Aspartic-type endopeptidase activity	Response to xenobiotic stimuli
14	ABS	PF3D7_1408200	AP2-G2	DNA-binding transcription factor activity; protein binding; sequence-specific DNA binding	Regulation of transcription, DNA-templated
14	ABS	PF3D7_1408300	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
14	ABS	PF3D7_1408400	FANCJ	ATP binding; DNA helicase activity; DNA polymerase binding	DNA duplex unwinding; negative regulation of DNA recombination; negative regulation of t-circle formation; regulation of double-strand break repair via homologous recombination; telomeric loop disassembly
14	ABS	PF3D7_1408500	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
14	ABS	PF3D7_1408600	<i>Unknown</i>	RNA binding; structural constituent of ribosome	Maturation of SSU-rRNA from tricistronic rRNA transcripts (SSU-rRNA, 5.8S rRNA, LSU-rRNA); translation
14	ABS	PF3D7_1408700	<i>Unknown</i>	K63-linked polyubiquitin modification-dependent protein binding; thiol-dependent deubiquitinase	Plastid organization; protein deubiquitination involved in ubiquitin-dependent protein catabolic processes

^aChr: chromosome.

^bGene identifier from *Plasmodb*.

Genes discussed in this article are in bold.

Supplementary Table S3: List of genes where evidence of positive selection was observed only in the SAM South cluster (Brazil – French Guiana) with *XP-EHH*, *Rsb* and *ABS*.

Chr ^a	Test	ID ^b	Name	Functions	Biological processes
4	ABS	PF3D7_0416300	MCM9	ATP-dependent activity, acting on DNA; DNA replication origin binding; single-stranded DNA binding	DNA replication initiation; double-strand break repair via homologous recombination
4	ABS	PF3D7_0416400	HAT1	H4 histone acetyltransferase activity	Histone H4 acetylation
4	ABS	PF3D7_0416500	MAF1	RNA polymerase III core binding	Negative regulation of transcription by RNA polymerase III
4	ABS	PF3D7_0416600	PHBL	<i>Unknown</i>	Regulation of the mitochondrial membrane potential
4	ABS	PF3D7_0416700	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
4	ABS	PF3D7_0416800	SAR1	GTPase activity	Endoplasmic reticulum to Golgi vesicle-mediated transport; intracellular protein transport; membrane organization; positive regulation of protein exit from endoplasmic reticulum; regulation of COPII vesicle coating; vesicle organization
4	ABS	PF3D7_0416900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
4	ABS	PF3D7_0417000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
4	ABS	PF3D7_0417100	PUF2	RNA binding; mRNA binding; protein binding	Negative regulation of translation; posttranscriptional regulation of gene expression
4	ABS	PF3D7_0417200	DHFR-TS	RNA binding; thymidylate synthase activity	dTMP biosynthetic process; response to drugs; response to xenobiotic stimuli
4	ABS	PF3D7_0417300	<i>Unknown</i>	<i>Unknown</i>	Cell metal ion homeostasis
4	ABS	PF3D7_0417400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0522400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0522500	RPL17	Structural constituent of ribosome	Translation
5	ABS	PF3D7_0522600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0522700	SufA	2 iron, 2 sulfur cluster binding	Iron-sulfur cluster assembly; protein maturation by iron-sulfur cluster transfer

5	ABS	PF3D7_0522800	BUD31	<i>Unknown</i>	RNA splicing; alternative mRNA splicing, via spliceosome; mRNA splicing, via spliceosome
5	ABS	PF3D7_0522900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0523000	MDR1	ATPase-coupled transmembrane transporter activity; protein binding	Response to drugs; response to xenobiotic stimuli; transmembrane transport
5	ABS	PF3D7_0523100	QCR2	Metalloendopeptidase activity; ubiquinol-cytochrome-c reductase activity	Protein processing involved in protein targeting to mitochondria
5	ABS	PF3D7_0523200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0523300	ApiCOX18	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0523400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0523500	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0523600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	PF3D7_0523700	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0707200	<i>Unknown</i>	Lysine-acetylated histone binding	<i>Unknown</i>
7	ABS	PF3D7_0707300	RAMA	Protein binding	Cell-cell adhesion; cellular protein localization; entry into host
7	ABS	PF3D7_0707400	<i>Unknown</i>	Zinc ion binding	Mitochondrion organization
7	ABS	PF3D7_0707500	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0707600	MED10	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0707700	<i>Unknown</i>	Chaperone binding; ubiquitin protein ligase activity	Cell response to misfolded proteins; positive regulation of proteolysis; proteasome-mediated ubiquitin-dependent protein catabolic process; protein polyubiquitination; protein quality control for misfolded or incompletely synthesized proteins
7	ABS	PF3D7_0707800	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0707900	<i>Unknown</i>	<i>Unknown</i>	Maturation of 5.8S rRNA; maturation of LSU-rRNA
7	ABS	PF3D7_0708000	<i>Unknown</i>	Alpha-tubulin binding	Microtubule cytoskeleton organization; post-chaperonin tubulin folding pathway; tubulin complex assembly

7	ABS	PF3D7_0708100	RPB10	DNA-directed 5'-3' RNA polymerase activity; zinc ion binding	tRNA transcription by RNA polymerase III; transcription by RNA polymerase I; transcription by RNA polymerase II
7	ABS	PF3D7_0708200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0708300	BUD32	Protein binding; protein serine/threonine kinase activity	Protein phosphorylation; tRNA threonylcarbamoyladenosine metabolic process
7	ABS	PF3D7_0708400	HSP90	ATP hydrolysis activity; RNA binding; protein binding; unfolded protein binding	Cell response to heat; protein folding; protein stabilization
7	ABS	PF3D7_0708500	<i>Unknown</i>	<i>Unknown</i>	Regulation of gene expression; response to heat; response to unfolded protein
7	ABS	PF3D7_0708600	IMC1d	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0708700	COX4	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0708800	HSP110c	ATP hydrolysis activity; protein binding	Protein folding; response to heat
7	ABS	PF3D7_0708900	SCO1	<i>Unknown</i>	Mitochondrial cytochrome C oxidase assembly
7	ABS	PF3D7_0709000	CRT	Ferric iron transmembrane transporter activity; xenobiotic transmembrane transporter activity	Glutathione transport; peptide transport; response to drugs; response to xenobiotic stimuli
7	ABS	PF3D7_0709100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0709200	GLP3	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0709300	MED14	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0709400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0709500	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	ABS	PF3D7_0709700	PARE	Acylglycerol lipase activity; hydrolase activity; hydrolase activity, acting on ester bonds; lipase activity	Monoacylglycerol catabolic process; phospholipid metabolic process; response to xenobiotic stimuli
7	ABS	PF3D7_0709800	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	XP-EHH, Rsb	PF3D7_0710100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	XP-EHH, Rsb	PF3D7_0809200	pfa55-14	Histone acetyltransferase activity; peptide alpha-N-acetyltransferase activity	N-terminal peptidyl-methionine acetylation; histone H3 acetylation; histone H4 acetylation
8	XP-EHH, Rsb	PF3D7_0809400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>

8	ABS	PF3D7_0815200	<i>Unknown</i>	Nuclear import signal receptor activity; nuclear localization sequence binding	NLS-bearing protein import into nucleus; protein import into nucleus
8	ABS	PF3D7_0815300	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0815400	ATPTG3	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0815500	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0815600	EIF3G	mRNA binding; translation initiation factor activity	Translation; translational initiation
8	ABS	PF3D7_0815700	Ub	ATP hydrolysis activity	Regulation of cell cycle process; ubiquitin-dependent ERAD pathway
8	ABS	PF3D7_0815800	VPS9	Guanyl-nucleotide exchange factor activity	Golgi to endosome transport
8	ABS	PF3D7_0815900	aLipDH	Dihydrolipoyl dehydrogenase activity; flavin adenine dinucleotide binding; protein homodimerization activity	Acetyl-CoA biosynthetic process from pyruvate; oxidation-reduction process
8	ABS	PF3D7_0816000	RRB1	<i>Unknown</i>	Ribosome biogenesis
8	ABS	PF3D7_0816100	PPCDC	FMN binding; phosphopantothenoylecysteine decarboxylase activity	Coenzyme A biosynthetic process
8	ABS	PF3D7_0816200	VPS2	<i>Unknown</i>	Endosome transport via multivesicular body sorting pathway; late endosome to vacuole transport; protein transport
8	ABS	PF3D7_0816300	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0816400	<i>Unknown</i>	Calcium ion binding	<i>Unknown</i>
8	ABS	PF3D7_0816500	HSP20	Protein self-association; unfolded protein binding	Protein complex oligomerization; protein folding; response to heat; response to hydrogen peroxide; response to reactive oxygen species; response to salt stress; response to unfolded proteins
8	ABS	PF3D7_0816600	ClpB1	ATP hydrolysis activity	Cellular response to heat; response to unfolded proteins
8	ABS	PF3D7_0816700	TRAPPC2L	<i>Unknown</i>	Endoplasmic reticulum to Golgi vesicle-mediated transport
8	ABS	PF3D7_0816800	DMC1	ATP-dependent activity, acting on DNA; DNA strand exchange activity; double-stranded DNA binding; single-stranded DNA binding	DNA recombinase assembly; chromosome organization involved in meiotic cell cycle; mitotic recombination; reciprocal meiotic recombination; response to ionizing radiation; strand invasion

8	ABS	PF3D7_0816900	AK2	Adenylate kinase activity; protein binding	Nucleoside diphosphate metabolic process; purine nucleotide metabolic process
8	ABS	PF3D7_0817000	UBA3	NEDD8 activating enzyme activity	Protein modification by small protein conjugation; protein neddylation
8	ABS	PF3D7_0817100	<i>Unknown</i>	GTPase activity; ferrous iron transmembrane transporter activity	tRNA wobble uridine modification
8	ABS	PF3D7_0817200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0817300	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0817400	<i>Unknown</i>	Double-stranded DNA binding; polydeoxyribonucleotide 5'-hydroxyl-kinase activity; polynucleotide 3'-phosphatase activity	DNA repair; nucleotide phosphorylation
8	ABS	PF3D7_0823400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0823500	IMC1i	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0823600	LipB	Lipoate-protein ligase activity	Lipoate biosynthetic process; protein lipoylation
8	ABS	PF3D7_0823700	TOM7	<i>Unknown</i>	Protein targeting to mitochondria
8	ABS	PF3D7_0823800	<i>Unknown</i>	RNA binding; unfolded protein binding	Chaperone cofactor-dependent protein refolding; protein refolding
8	ABS	PF3D7_0823900	DTC	Dicarboxylic acid transmembrane transporter activity; oxoglutarate:malate antiporter activity	Alpha-ketoglutarate transport; dicarboxylic acid transport; malate transport; mitochondrial transport
8	ABS	PF3D7_0824000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0824100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0824200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0824300	Obg2	GTP binding	<i>Unknown</i>
8	ABS	PF3D7_0824400	NT2	Nucleoside transmembrane transporter activity	Nucleoside transport
8	ABS	PF3D7_0824500	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0824600	DRE2	<i>Unknown</i>	Iron-sulfur cluster assembly
8	ABS	PF3D7_0824700	LMF1	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0824800	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0824900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>

8	ABS	PF3D7_0825000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0825100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	PF3D7_0825200	IF3a	Ribosome binding; translation initiation factor activity	Ribosome disassembly
8	ABS	PF3D7_0825300	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
10	ABS	PF3D7_1036500	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
10	ABS	PF3D7_1036600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
10	ABS	PF3D7_1036700	PhLP2	<i>Unknown</i>	<i>Unknown</i>
10	ABS	PF3D7_1036800	ACT	Solute:proton symporter activity	Response to xenobiotic stimuli
10	ABS	PF3D7_1037100	PyKII	Pyruvate kinase activity	Glycolytic process
10	ABS	PF3D7_1037200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
10	ABS	PF3D7_1037300	AAC1	ATP:ADP antiporter activity; RNA binding	<i>Unknown</i>
10	ABS	PF3D7_1037400	<i>Unknown</i>	Ubiquitin protein ligase activity	Protein monoubiquitination; protein polyubiquitination
10	ABS	PF3D7_1037500	DYN2	GTPase activity; microtubule binding	Mitochondrial fission; organelle fission
10	ABS	PF3D7_1037600	XPB	3'-5' DNA helicase activity; ATP hydrolysis activity; DNA binding; DNA helicase activity; damaged DNA binding; helicase activity; transcription factor binding	Nucleotide-excision repair, DNA duplex unwinding; nucleotide-excision repair, DNA incision; response to UV; transcription by RNA polymerase II; transcription initiation from RNA polymerase II promoter
10	ABS	PF3D7_1037700	ERH	mRNA binding	<i>Unknown</i>
10	ABS	PF3D7_1037800	<i>Unknown</i>	Dynein heavy chain binding; dynein light chain binding	Cilium movement; microtubule-based movement
12	ABS	PF3D7_1225100	api-IRS	Isoleucine-tRNA ligase activity	Isoleucyl-tRNA aminoacylation; response to xenobiotic stimuli
12	ABS	PF3D7_1225200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1225300	<i>Unknown</i>	Small ribosomal subunit rRNA binding	<i>Unknown</i>
12	ABS	PF3D7_1225400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1225500	<i>Unknown</i>	rRNA (pseudouridine) methyltransferase activity; rRNA binding	rRNA base methylation
12	ABS	PF3D7_1225600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1225700	<i>Unknown</i>	<i>Unknown</i>	Phosphatidylinositol biosynthetic process; positive regulation of kinase activity

12	ABS	PF3D7_1225800	UBA1	Ubiquitin activating enzyme activity	Cell response to DNA damage stimulus; protein modification by small protein conjugation; protein ubiquitination; ubiquitin-dependent protein catabolic process
12	ABS	PF3D7_1225900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1226000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1226100	HAD3	Catalytic activity; hydrolase activity; magnesium ion binding; phosphatase activity	<i>Unknown</i>
12	ABS	PF3D7_1226200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1226300	HAD2	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1226400	<i>Unknown</i>	<i>Unknown</i>	Regulation of autophagy
12	ABS	PF3D7_1243400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1243500	SNF7	<i>Unknown</i>	Late endosome to vacuole transport via multivesicular body sorting pathway; vesicle budding from membrane
12	ABS	PF3D7_1243600	<i>Unknown</i>	RNA binding; translation initiation factor activity	Translational initiation
12	ABS	PF3D7_1243700	<i>Unknown</i>	Ubiquitin conjugating enzyme activity	Cell response to DNA damage stimulus; protein polyubiquitination
12	ABS	PF3D7_1243800	WDR82	Chromatin binding	Histone H3-K4 methylation; histone H3-K4 trimethylation
12	ABS	PF3D7_1243900	DOC2	Calcium-dependent phospholipid binding	Entry into host
12	ABS	PF3D7_1244000	<i>Unknown</i>	Flavin adenine dinucleotide binding	Mitochondrial tRNA wobble uridine modification; tRNA methylation; tRNA wobble uridine modification
12	ABS	PF3D7_1244100	<i>Unknown</i>	<i>Unknown</i>	N-terminal peptidyl-methionine acetylation
12	ABS	PF3D7_1244200	TFB2	Double-stranded DNA binding	Nucleotide-excision repair; phosphorylation of RNA polymerase II C-terminal domain; transcription by RNA polymerase II
12	ABS	PF3D7_1244400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1244500	PIMMS57	<i>Unknown</i>	<i>Unknown</i>
12	ABS	PF3D7_1244600	ARFGAP1	DNA binding; GTPase activator activity	COPI coating of Golgi vesicles
14	ABS	PF3D7_1440800	MFS6	<i>Unknown</i>	<i>Unknown</i>

14	ABS	PF3D7_1440900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
14	ABS	PF3D7_1441000	NCS2	Sulfurtransferase activity	tRNA thio-modification; tRNA wobble position uridine thiolation
14	ABS	PF3D7_1441100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
14	ABS	PF3D7_1441200	<i>Unknown</i>	RNA binding; structural constituent of ribosome	Maturation of LSU-rRNA; translation
14	ABS	PF3D7_1441300	<i>Unknown</i>	Protein serine/threonine kinase activity	Protein phosphorylation
14	ABS	PF3D7_1441400	FACT-S	DNA binding; RNA binding; histone binding; nucleosome binding; single-stranded DNA binding	<i>Unknown</i>
14	ABS	PF3D7_1441500	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
14	ABS	PF3D7_1441600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
14	ABS	PF3D7_1441700	ATP23	<i>Unknown</i>	Mitochondrial protein processing; mitochondrial proton-transporting ATP synthase complex assembly
14	ABS	PF3D7_1441800	VPS60	<i>Unknown</i>	Late endosome to vacuole transport via the multivesicular body sorting pathway; vesicle budding from membrane
14	ABS	PF3D7_1441900	TFB5	<i>Unknown</i>	Nucleotide-excision repair; nucleotide-excision repair, preincision complex assembly; phosphorylation of RNA polymerase II C-terminal domain; transcription by RNA polymerase II
14	ABS	PF3D7_1442000	<i>Unknown</i>	GTP binding; GTPase activity	Positive regulation of microtubule polymerization; protein ADP-ribosylation
14	ABS	PF3D7_1442100	RPA3	Damaged DNA binding; single-stranded DNA binding	DNA replication; base-excision repair; double-strand break repair via homologous recombination; mismatch repair; nucleotide-excision repair
14	ABS	PF3D7_1442200	YihA2	GTPase activity; mitochondrial ribosome binding	<i>Unknown</i>
14	ABS	PF3D7_1442300	tRIP	RNA binding; aminoacyl-tRNA ligase activity	tRNA aminoacylation for protein translation
10	ABS	PF3D7_1036900	<i>Unknown</i>	mRNA binding	<i>Unknown</i>
10	ABS	PF3D7_1037000	REV3	DNA-directed DNA polymerase activity	Double-strand break repair via homologous recombination; error-prone translesion synthesis

^a Chr: chromosome.

^b Gene identifier In *Plasmodb*.

Genes in bold are discussed in this article.

Supplementary Table S4: List of genes where evidence of positive selection was detected in both South American clusters with *XP-EHH*, *Rsb* and *ABS*.

Chra	Northb	Southc	IDd	Name	Functions	Processes
5	ABS	ABS	PF3D7_0521300	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	ABS	PF3D7_0521400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	ABS	PF3D7_0521500	<i>Unknown</i>	Pseudouridine synthase activity; pseudouridylate synthase activity	Enzyme-directed rRNA pseudouridine synthesis; rRNA processing
5	ABS	ABS	PF3D7_0521600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	ABS	PF3D7_0521700	DDX1	<i>Unknown</i>	rRNA processing
5	ABS	ABS	PF3D7_0521800	<i>Unknown</i>	ATP hydrolysis activity	<i>Unknown</i>
5	ABS	ABS	PF3D7_0521900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	ABS	PF3D7_0522000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	ABS	PF3D7_0522100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
5	ABS	ABS	PF3D7_0522200	TAF10	Protein binding	Transcription by RNA polymerase II
5	ABS	ABS	PF3D7_0522300	<i>Unknown</i>	S-adenosylmethionine-dependent methyltransferase activity; rRNA (guanine) methyltransferase activity	rRNA (guanine-N7)-methylation
6	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0619600	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0704600	UT	Ubiquitin-protein transferase activity	Response to drugs; response to xenobiotic stimuli
7	Rsb	ABS	PF3D7_0709600	POP1	Ribonuclease MRP activity; ribonuclease P activity	RNA phosphodiester bond hydrolysis, endonucleolytic; tRNA processing
7	XP-EHH	ABS	PF3D7_0709900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0710000	<i>Unknown</i>	rRNA binding	Ribosomal large subunit assembly

7	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0710200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0710400	RAD14	Damaged DNA binding	UV-damage excision repair; base-excision repair; nucleotide-excision repair involved in interstrand cross-link repair; nucleotide-excision repair, DNA damage recognition; nucleotide-excision repair, DNA incision
7	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0711000	CDC48	ATP hydrolysis activity; polyubiquitin modification-dependent protein binding; ubiquitin binding	ER-associated misfolded protein catabolic process; autophagosome maturation; macroautophagy; mitotic spindle disassembly; regulation of cell cycle process; retrograde protein transport, ER to cytosol; ubiquitin-dependent ERAD pathway
7	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0711200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	XP-EHH, Rsb	XP-EHH	PF3D7_0711500	<i>Unknown</i>	Chromatin binding	Ran protein signal transduction; chromosome condensation; chromosome segregation; regulation of mitotic spindle assembly
7	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0713500	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
7	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0713600	<i>Unknown</i>	Structural constituent of ribosome	Translation
7	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0713900	<i>Unknown</i>	N-acetyltransferase activity	<i>Unknown</i>
8	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_0809600	<i>Unknown</i>	Cysteine-type endopeptidase activity	Meiotic chromosome separation
8	ABS	ABS	PF3D7_0817700	RON5	RNA binding; host cell surface binding	<i>Unknown</i>
8	ABS	ABS	PF3D7_0817800	C3AP3	<i>Unknown</i>	<i>Unknown</i>

8	ABS	ABS	PF3D7_0817900	HMGB2	DNA binding; DNA binding, bending	Positive regulation of cytokine production involved in immune response; regulation of transcription by RNA polymerase II; regulation of transcription by RNA polymerase III; regulation of transcription, DNA-templated
8	ABS	ABS	PF3D7_0818000	SNRNP27	<i>Unknown</i>	<i>Unknown</i>
8	ABS	ABS	PF3D7_0818100	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
8	ABS	ABS	PF3D7_0818200	14-3-3I	RNA binding; histone binding; protein binding	Entry into host
8	ABS	ABS	PF3D7_0818300	<i>Unknown</i>	Dynein complex binding	Mitotic spindle organization
8	ABS	ABS	PF3D7_0818400	FCF1	<i>Unknown</i>	<i>Unknown</i>
8	ABS	ABS	PF3D7_0818500	<i>Unknown</i>	Zinc ion binding	<i>Unknown</i>
8	ABS	ABS	PF3D7_0818600	PBLP	Lipase activity; palmitoyl-(protein) hydrolase activity	Cell maturation; entry into host; lipid metabolic process
8	ABS	ABS	PF3D7_0818700	<i>Unknown</i>	ATP-dependent activity, acting on DNA; DNA binding; chromatin binding	ATP-dependent chromatin remodeling
11	XP-EHH, Rsb	Rsb	PF3D7_1133400	AMA1	Host cell surface binding; protein binding	Entry into host
12	ABS	ABS	PF3D7_1206800	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	ABS	PF3D7_1206900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	ABS	PF3D7_1207000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	ABS	PF3D7_1207100	<i>Unknown</i>	RNA binding	rRNA processing
12	ABS	ABS	PF3D7_1207200	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	ABS	PF3D7_1207300	LIMP	<i>Unknown</i>	Cell gliding; entry into host
12	ABS	ABS	PF3D7_1207400	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	ABS	PF3D7_1207500	<i>Unknown</i>	RNA binding	<i>Unknown</i>

12	ABS	ABS	PF3D7_1207600	MiaA	ATP binding; tRNA binding; tRNA dimethylallyltransferase activity	tRNA modification; tRNA processing
12	ABS	ABS	PF3D7_1207700	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	ABS	PF3D7_1207800	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	ABS	PF3D7_1207900	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
12	ABS	ABS	PF3D7_1208000	<i>Unknown</i>	<i>Unknown</i>	<i>Unknown</i>
13	XP-EHH, Rsb	XP-EHH, Rsb	PF3D7_1335900	TRAP	Host cell surface receptor binding	Cell gliding; entry into host; movement of cell or subcellular component

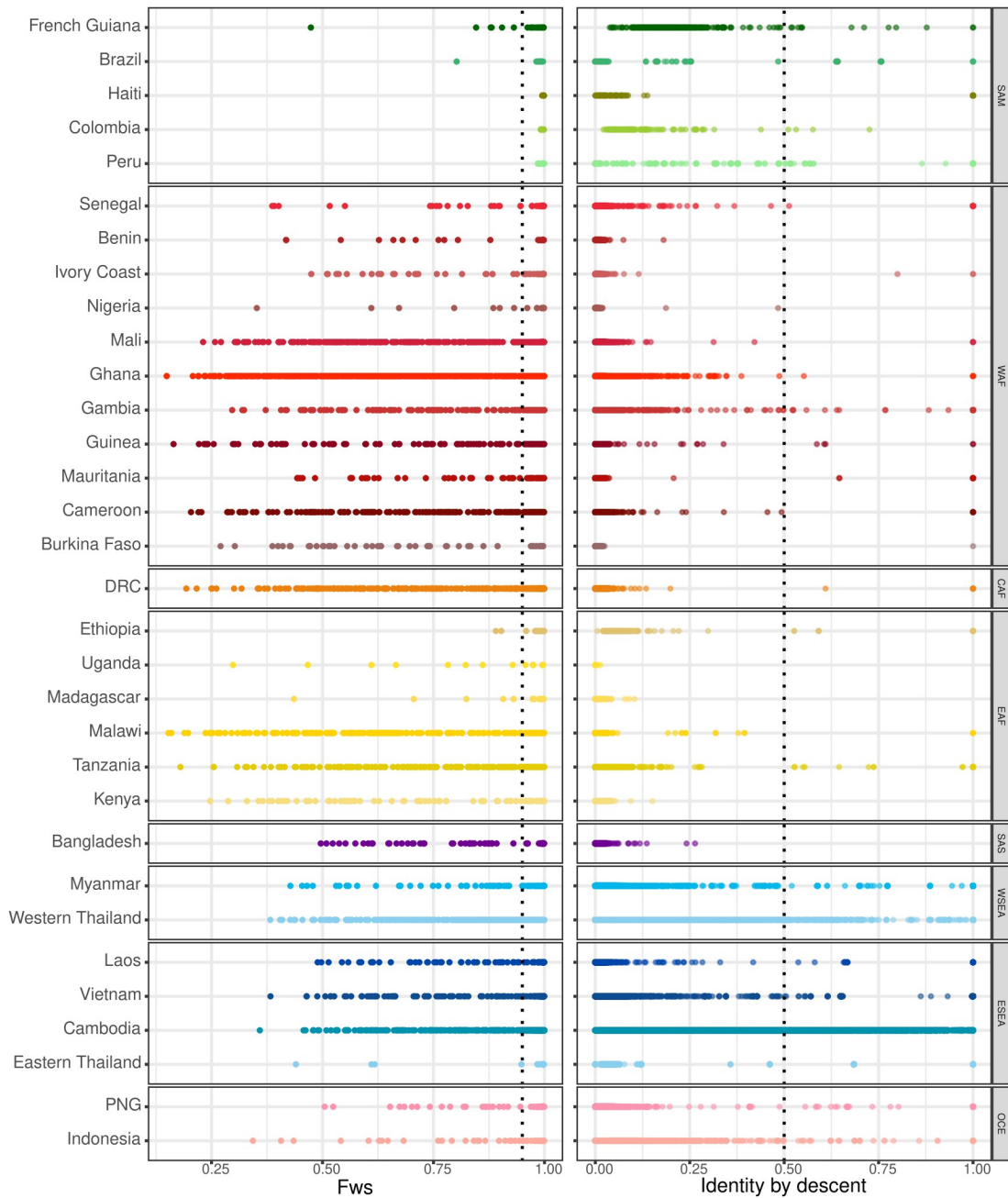
^a Chr: chromosome

^b Test in which this signal was found in the SAM North cluster (Colombia - Haiti).

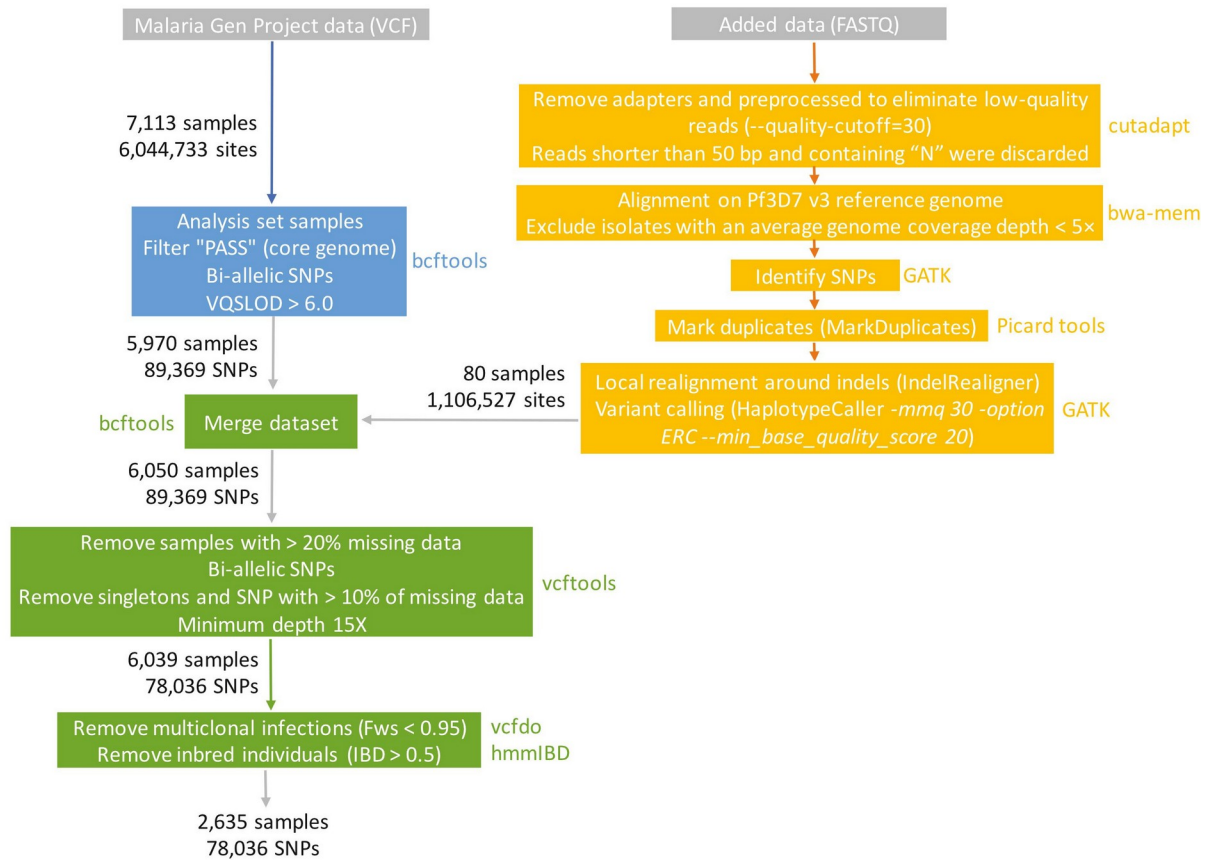
^c Test in which this signal was found in the SAM South cluster (Brazil - French Guiana).

^d Gene identifier in *Plasmodb*.

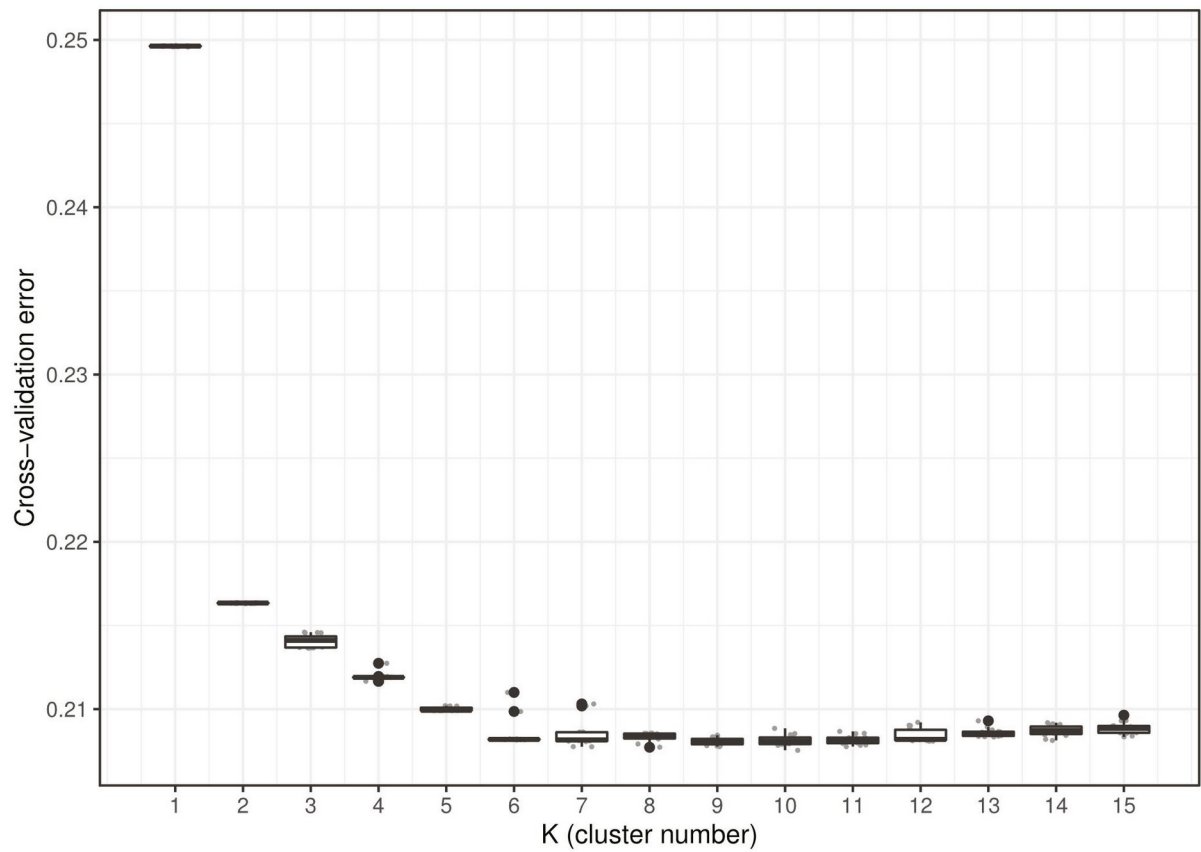
Genes in bold are discussed in this article.



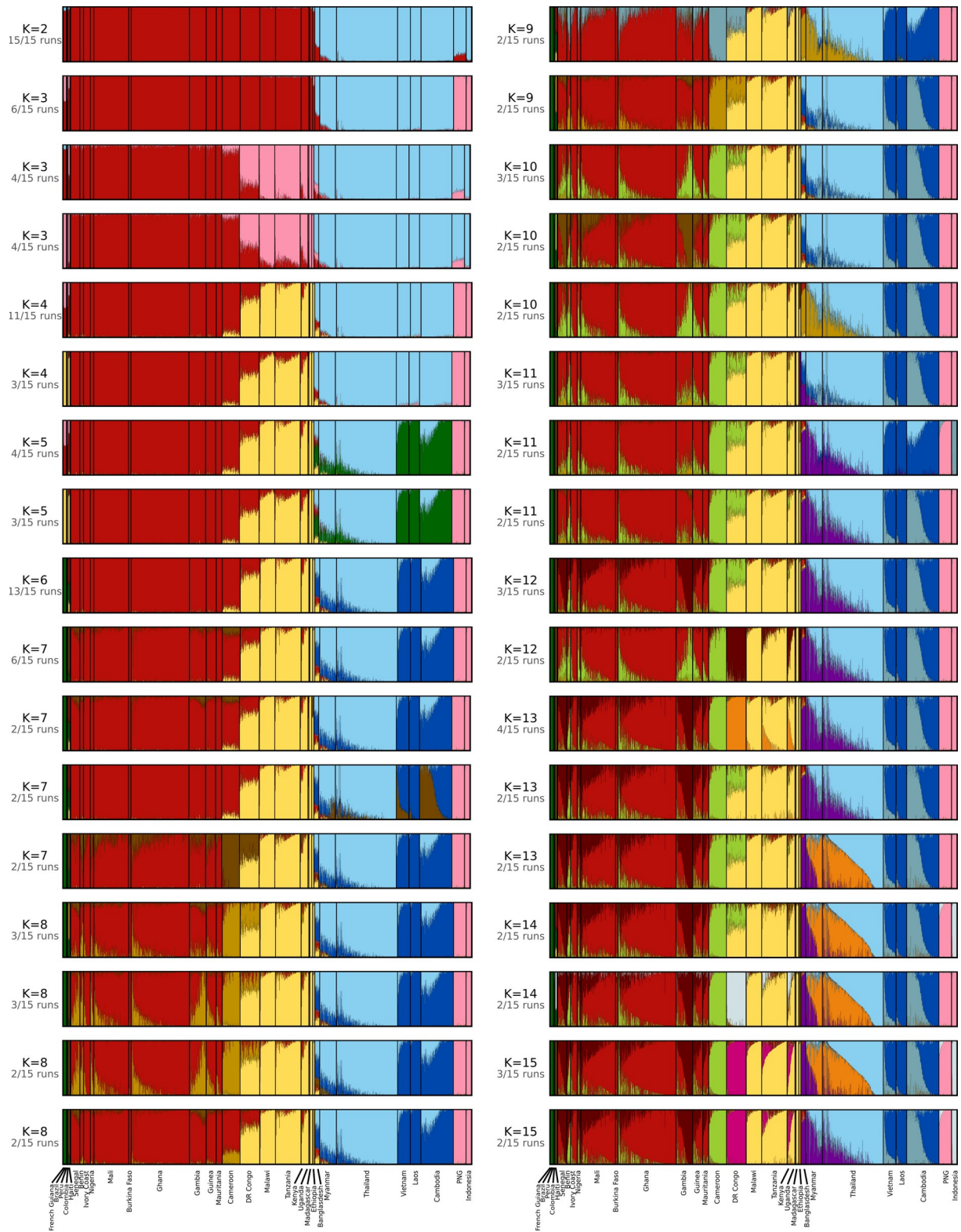
Supplementary Figure S1: Within-sample infection complexity (F_{WS} index) and consanguinity (identity by descent) in *P. falciparum* populations. The F_{WS} index provides a proxy of the diversity within individual infections, from 0 (high diversity) to 1 (no diversity). F_{WS} values >0.95 (dotted line) usually indicate monoclonal infections. Identity by descent (IBD) indicates the percentage of the genome resulting from inbreeding between pairs of individuals of the same population. One individual was excluded for all strain pairs displaying a pairwise-IBD >0.5 (dotted line).



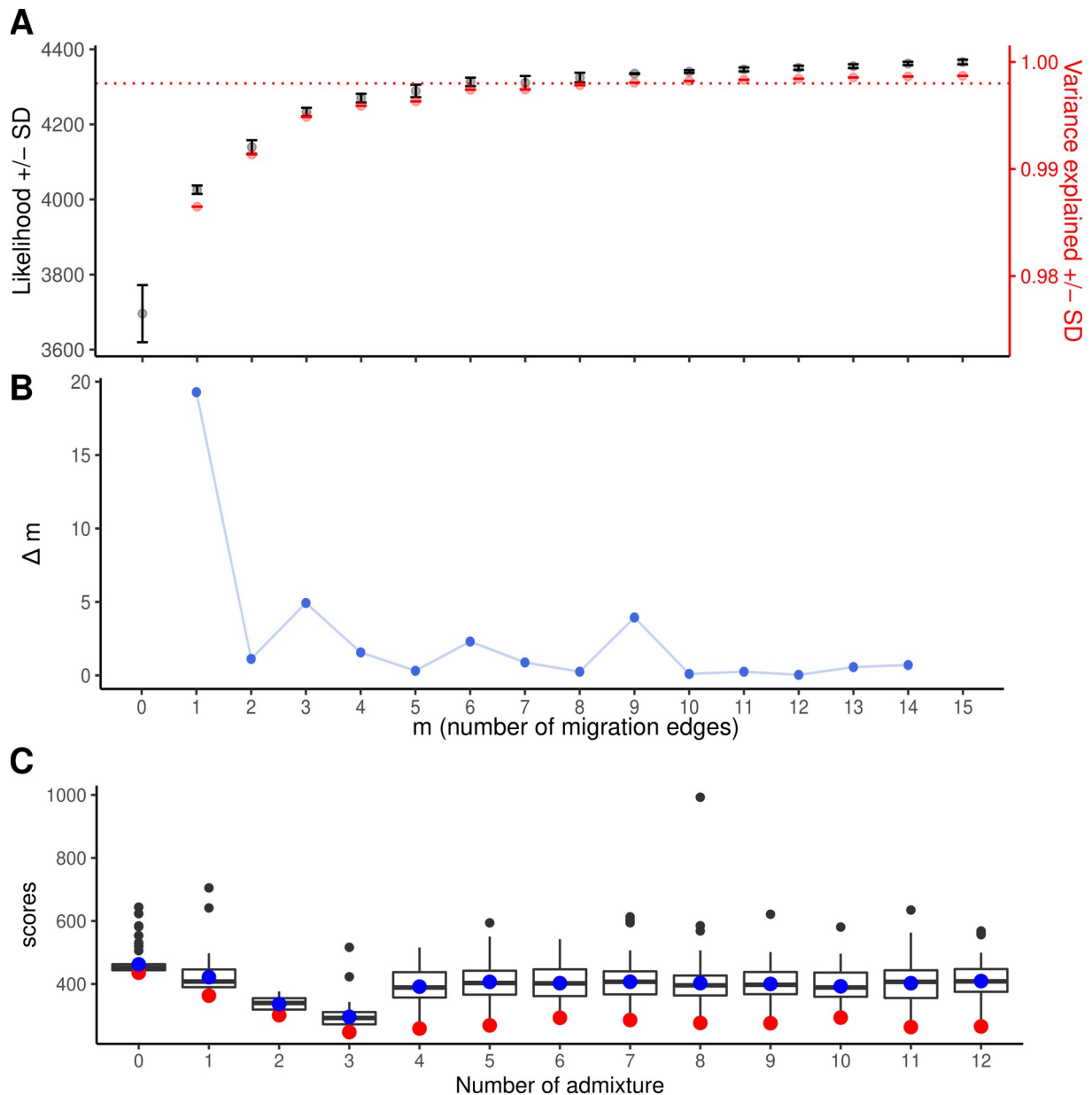
Supplementary Figure S2: Filtering and dataset creation steps. Each box represents a filtering step and the tool used. After each filtering step, the number of remaining samples and sites/SNPs is specified.



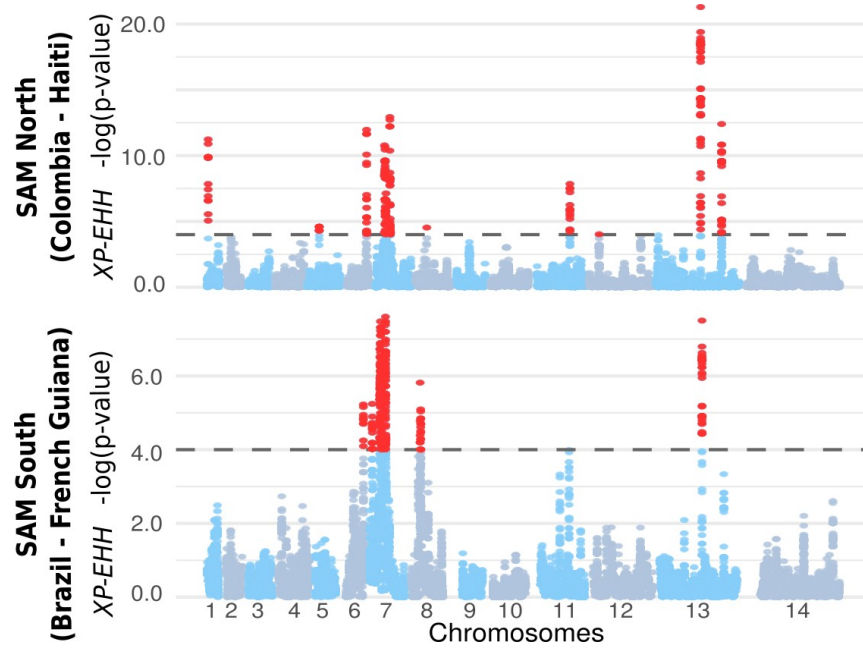
Supplementary Figure S3: Box plot displaying the cross-validation error rate in function of the increasing number of clusters (K). With K between 1 and 15 (15 replicates for each K value), K=9 was chosen to analyze the SNP data, as the value that minimizes the cross-validation error rate.



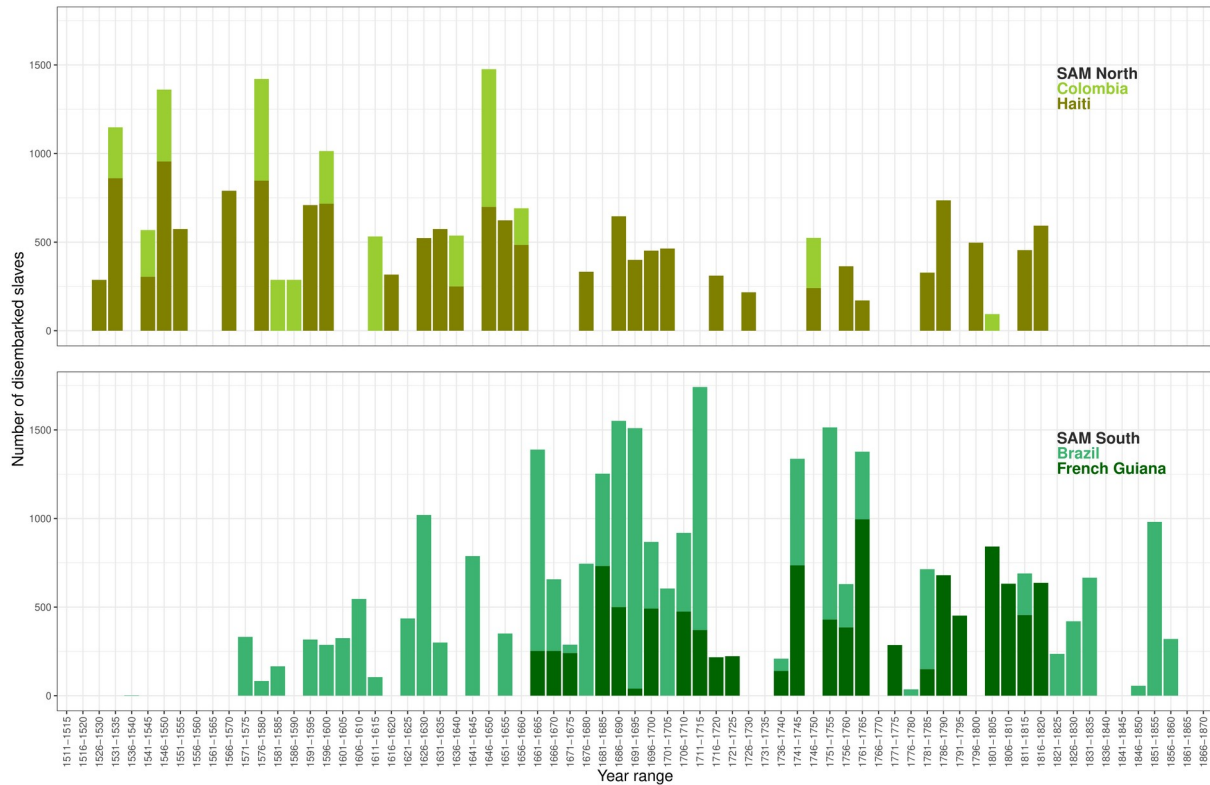
Supplementary Figure S4: Genetic ancestry of *P. falciparum* populations worldwide estimated with ADMIXTURE (K=2 to K=15). The number of clusters tested is described by the K value on the left, with the number of congruent runs. Only results with more than one congruent run are shown.



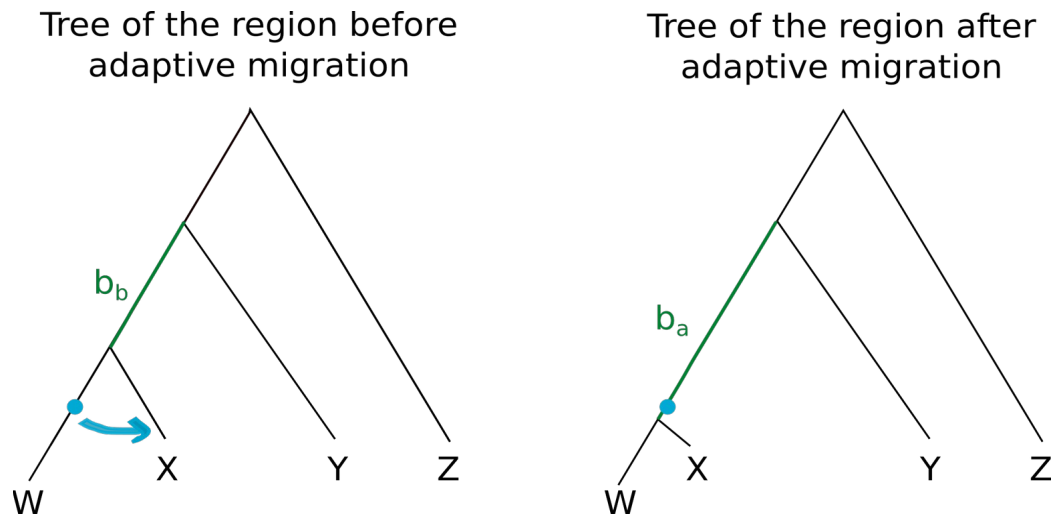
Supplementary Figure S5: Identification of the optimal number of migration edges in *P. falciparum* populations worldwide. **A.** Changes in the mean likelihood score (\pm SD) and the mean total fraction of the genetic variance explained (\pm SD) in function of the number of migration edges (TreeMix analysis). **B.** The second-order rate of change in likelihood (Δm) across values of migration edges (m). For both panels, the OptM package and the Evanno method were used, with 15 replicates for each migration edge number, from 0 to 15. The inflection point for both statistics was observed at $m=3$. **C.** Boxplots of the likelihood score for each number of admixture events, with 100 replicates in the ADMIXTOOLS2 analysis. Blue dots represent the mean, and red dots the minimum value.



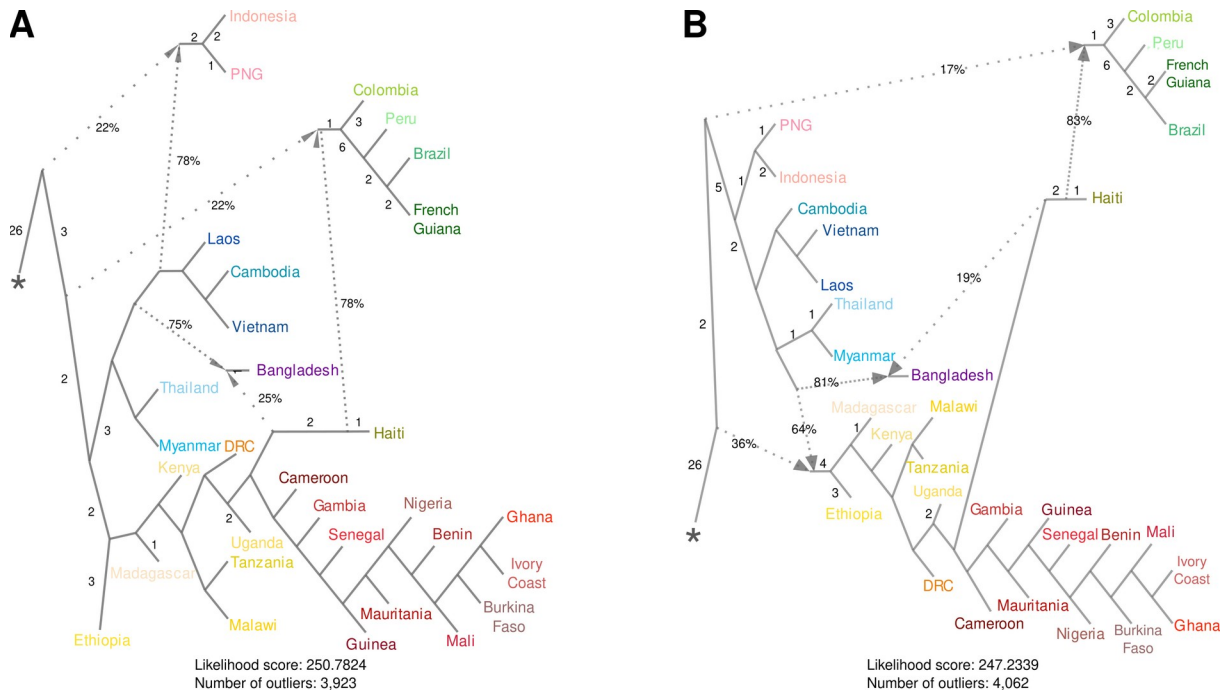
Supplementary Figure S6: Manhattan plots showing the $XP-EHH$ scores for SAM North (Colombia - Haiti) and SAM South (Brazil - French Guiana), compared with the African reference population (Senegal). The dotted lines represent the significance threshold value of $-\log(p\text{-value}) = 4$. Red, SNPs marking a selective sweep in the SAM cluster (negative $XP-EHH$ values).



Supplementary Figure S7: Number of disembarked slaves for each disembarkation region during the transatlantic slave trade. The bar plots are stacked and the colors represent the countries of arrival. The data come from www.slavevoyages.org (accessed on 02/02/2023). For Haiti, we obtained the data corresponding to Hispaniola and Santo Domingo, while for Colombia we obtained Spanish Americas.



Supplementary Figure S8: Tree topologies of genomic regions before and after an adaptive introgression. With ABS, we obtain a score based on the length of the ancestral branch (green, called b in the figure). In the case of an adaptive migration (blue arrow) of an allele (blue point) between the target populations (W and X), the ancestral branch is longer after the event (b_a) than before (b_b).



Supplementary Figure S9: Best ADMIXTOOLS2 trees. **A.** Tree with the best goodness of fit (fewest number of f_4 statistics outliers over 107,880 f_4 statistics in total) and the second best likelihood score. This tree is the one presented in Figure 2. **B.** Tree with the second best goodness of fit (second fewer number of f_4 statistics outliers over 107,880 f_4 statistics in total) and best likelihood score.