

S1 Table. Geographic origin and drug resistance genotypes of *Plasmodium falciparum* lines.

Parasite ^a	Edited ^b	Original ID	Source	Parental line (year)	K13	<i>pfcr</i> ^c	<i>pfmdr1</i>	CN ^d	<i>dhfr</i> ^e
Cam3.II K13 ^{WT}	Yes ^f		Fidock lab	W. Cambodia (2010)	WT				
Cam3.II K13 ^{R539T}	No ^g	RF 967	R. Fairhurst		R539T	Dd2	Y184F	1	Triple
Cam3.II K13 ^{C580Y}	Yes		Fidock lab		C580Y				
V1/S K13 ^{WT}	Yes ^h		Fidock lab	Vietnam (1976)	WT				
V1/S K13 ^{R539T}	Yes	V1/S	Fidock lab		R539T	Dd2	N86Y	1	Quad
V1/S K13 ^{C580Y}	Yes		Fidock lab		C580Y				

^aParasite lines were previously reported by Straimer *et al.* (2015, *Science*).

^bZinc-finger nucleases were used to generate gene-edited parasites expressing the wild-type (WT) or mutant alleles along with binding-site mutations.

^cDd2: M74I/N75E/K76T/A220S/Q271E/N326S/I356T/R371I.

^dCN, *pfmdr1* copy number.

^eTriple, N51I/C59R/S108N; Quad, quadruple N51I/C59R/S108N/I164L.

^fCam3.II K13^{R539T} parental line reverted to the WT allele. Previously denoted Cam3.II^{rev} in Straimer *et al.*

^gUnedited parental line bearing the K13 R539T allele.

^hEditing control. V1/S parasite bearing the K13 WT allele plus zinc-finger binding-site mutations.