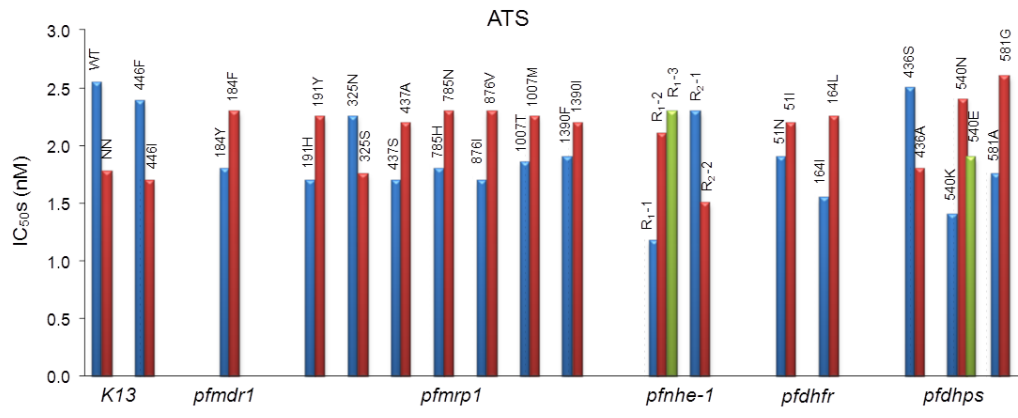
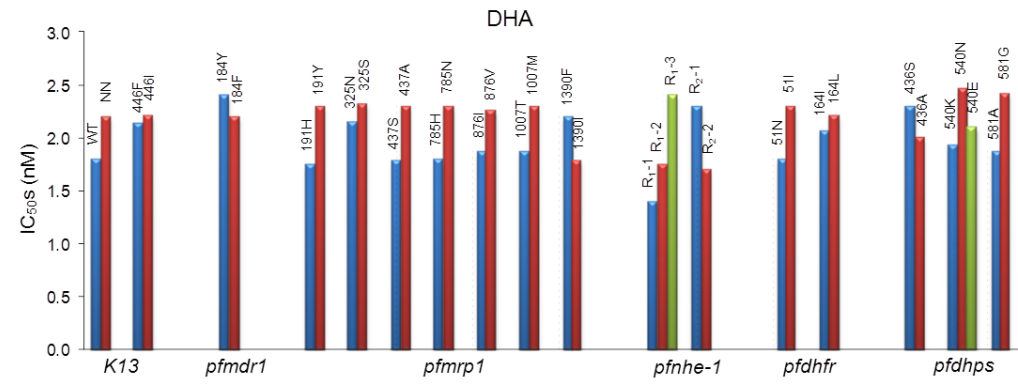
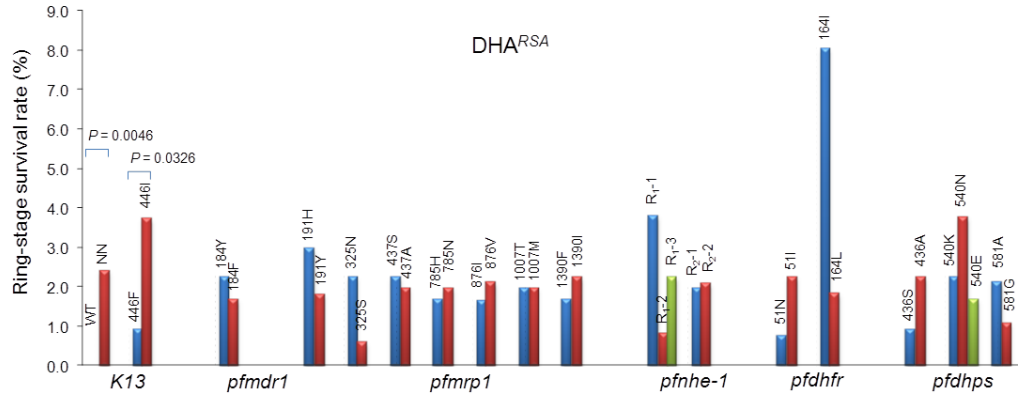
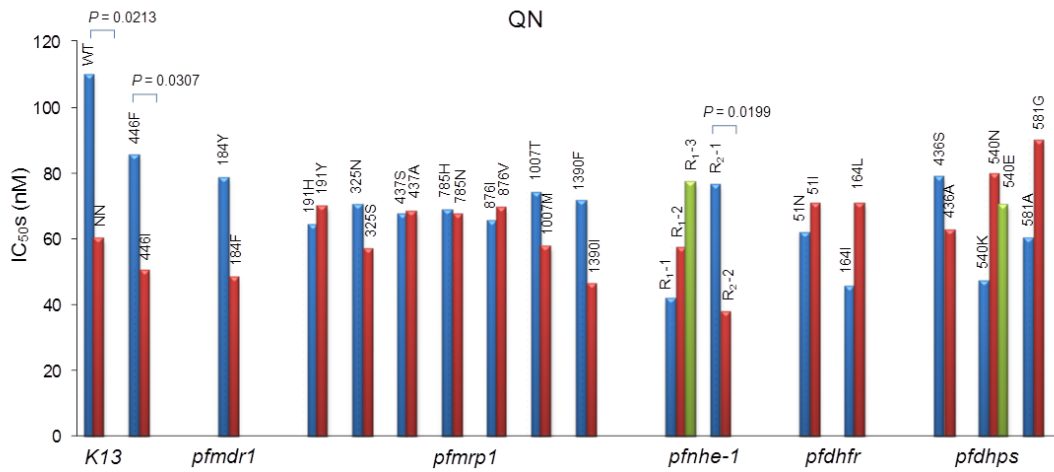
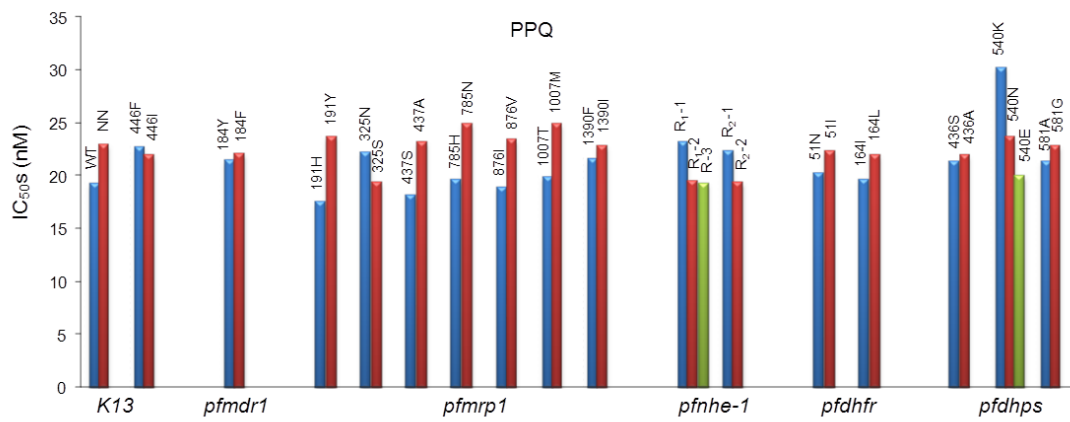
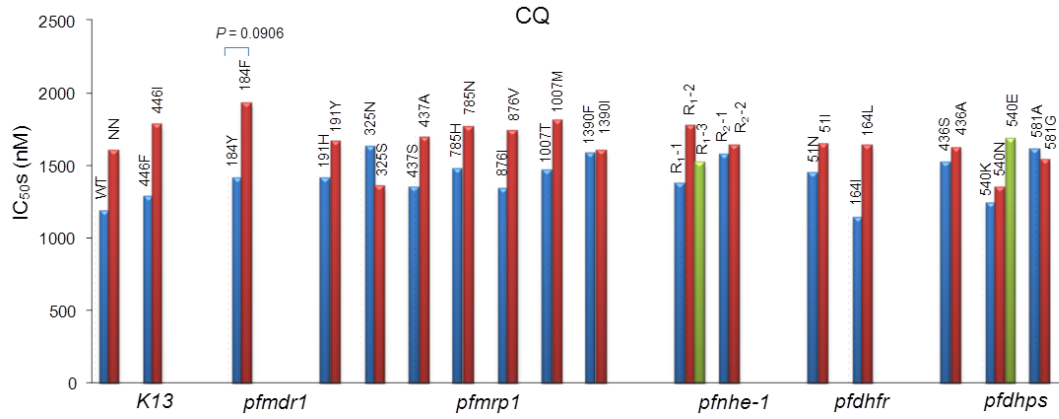
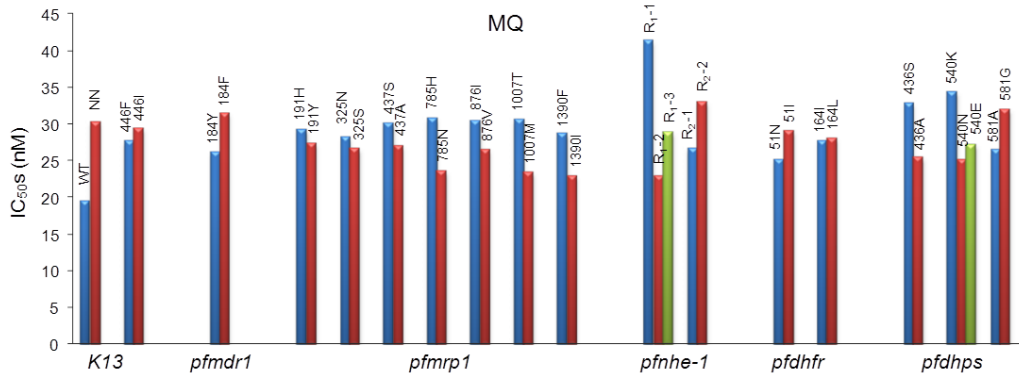
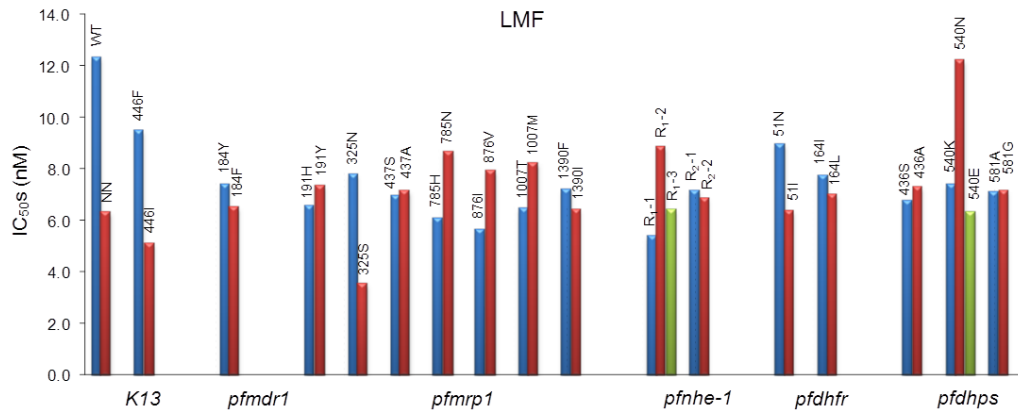
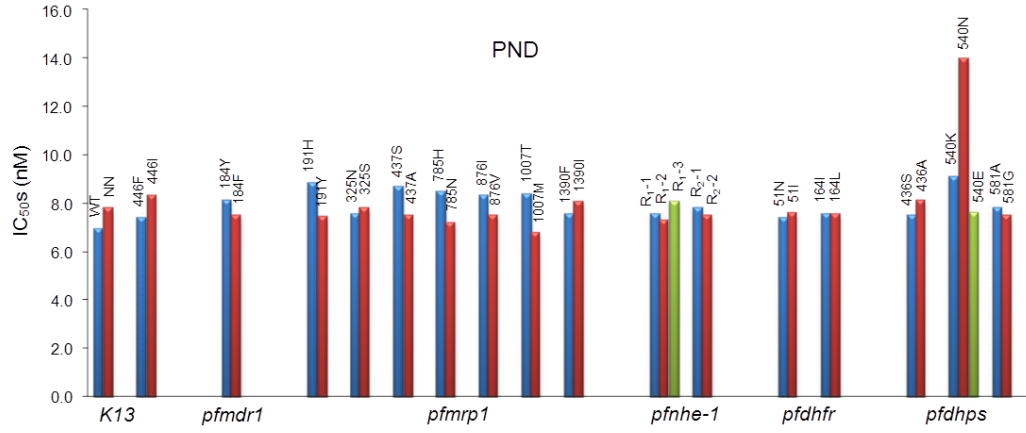


## Supplementary data

**Supplementary figure 1. Association of polymorphisms in candidate genes with drug sensitivities.** The associations between susceptibilities to eight antimalarial drugs and an insert in *K13*, the number variation of repeat R<sub>1</sub> and R<sub>2</sub> in *pfmhe-1*, and SNPs in *K13*, *pfmdr1*, *pfmrp1*, *pfdhfr* and *pfdhps* were analyzed by Mann-Whitney *U* test or Kruskal-Wallis test. Significant levels are indicated by the *P* values. DHA<sup>RSA</sup> were ring-stage survival rate (%) determined by RSA. The remaining values were IC<sub>50</sub>s determined using the SYBR Green I-based assay. The RSA result and IC<sub>50</sub> values of DHA, ATS and PND are shown as median, whereas the rest of the drugs are shown as mean. ATS, artesunate; CQ, chloroquine; PPQ, piperaquine; QN, quinine; PND, pyronaridine; LMF, lumefantrine; MQ, mefloquine.







**Supplementary figure 2. Alignment of the 6 *pfnhe-1* ms4760 alleles.** Two repeats (R1, DNNND, and R2, NHNDNHNNDDDD) are highlighted in grey. Mutation shows in red.

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1   KKKKISGSNDNDNNNDNNND-----DKNNKNDDDNHNDNHNNDDDNHNDNHNNDD-----NNNDNHDDDDNNSSHYNKEKE
3   KKKKISGSNDNDNNNDNNND-----NHNDKNNKNDDDNHNDNHNNDDDNHNDNHNNDD-----NNNDNHDDDDNNSSHYNKEKE
6   KKKKISGSNDNDNNNDNNND-----NHNDKNNKNDDDNHNDNHNNDD-----NNNDNHDDDDNNSSHYNKEKE
7   KKKKISGSNDNDNNNDNNNDNNNDNHNDKNNKNDDDNHNDNHNNDD-----NNNDNHDDDDNNSSHYNKEKE
12  KKKKISGSNDNDNNND-----DKNNKNDDDNHNDNHNNDDDNHNDNHNNDDDNHNDNHNNDDNNNDNHDDDDNNSSHYNKEKE
18  KKKKISGSNDNDNNNDNNND-----NHNDKNNKNDDDNHNDNHNNDDDNHNDNHNNDD-----NNNDNHDDDDNNSSHYNKEKE

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**Supplementary figure 3. Schematic illustration of the multilocus genotypes of the *P. falciparum* isolates.** A total of 34 haplotypes were identified and clustered based on their phylogenetic relationship. Empty and red-filled blocks indicate wild-type and mutated amino acids, respectively. Frequencies (%) of haplotypes are shown in the right column.



\*The order of haplotypes is based on the frequency.

**Supplementary table 1.** Comparison of the frequencies [N (%)] of mutations in six genes associated with drug resistance between day 3-positive and -negative isolates.

<b>Gene</b>	<b>Mutation /repeat</b>	<b>Day 3 positive</b>	<b>Day 3 negative</b>	<b>P-value*</b>	<b>Total</b>
<i>pfdhfr</i>	N51 <b>I</b>	14 (82.4)	12 (57.1)	0.1612	16 (68.4)
	C59 <b>R</b>	16 (94.1)	21 (100)	0.4474	37 (97.4)
	S108 <b>N</b>	16 (94.1)	21 (100)	0.4474	37 (97.4)
	I164 <b>L</b>	14 (82.4)	20 (95.2)	0.3068	34 (89.5)
<i>pfdhps</i>	S436 <b>A</b>	13 (76.5)	12 (57.1)	0.3068	25 (65.8)
	A437 <b>G</b>	16 (94.1)	20 (95.2)	1.000	36 (94.7)
	K540 <b>E/N</b>	13 (76.5)	20 (95.2)	0.1524	33 (86.8)
	A581 <b>G</b>	3 (17.6)	7 (33.3)	0.4604	10 (26.3)
<i>pfprt</i>	S72 <b>C</b>	17 (100)	21 (100)	1.000	38 (100)
	M74 <b>I</b>	17 (100)	21 (100)	1.000	38 (100)
	N75 <b>E</b>	17 (100)	21 (100)	1.000	38 (100)
	K76 <b>T</b>	17 (100)	21 (100)	1.000	38 (100)
	A220 <b>S</b>	17 (100)	21 (100)	1.000	38 (100)
<i>pfmndr1</i>	N86 <b>Y/T</b>	0 (0)	0 (0)	1.000	0 (0)
	Y184 <b>F</b>	7 (41.2)	6 (28.6)	0.5017	13 (34.2)
	N1042 <b>D</b>	0 (0)	0 (0)	1.000	0 (0)
<i>pfmrpl</i>	H191 <b>Y</b>	10 (58.8)	16 (76.2)	0.3073	26 (68.4)
	N325 <b>S</b>	1 (5.9)	5 (23.8)	0.1965	6 (15.8)
	S437 <b>A</b>	11 (64.7)	16 (76.2)	0.491	27 (71.1)
	H785 <b>N</b>	8 (47.1)	7 (33.3)	0.5091	15 (39.5)
	I876 <b>V</b>	10 (58.8)	14 (66.6)	0.7396	24 (63.2)
	T1007 <b>M</b>	8 (47.1)	6 (28.6)	0.3176	14 (36.8)
	F1390 <b>I</b>	3 (17.6)	2 (9.5)	0.6396	5 (13.2)
<i>pfmhe-1</i>	Rep-1	15 (88.2)	20 (95.2)	0.5768	35 (92.1)
	Rep-2	3 (17.6)	5 (23.8)	0.7087	8 (21.1)

\* Comparison between the two groups (Fisher's exact test).