Table S1. Significance tests (p-values; Student's t-test, unpaired) of compound activities (MMV007839 – 7839; BH267.meta – 267.*m*; and BH296 – 296) against 3D7 parasites and selected resistant strains with PfFNT mutations G107S, G21E, and V196L. Non-significance ($p > 0.05$) is indicated by yellow cell shading, borderline significance by a hash (#).

	3D7 7839	**G107S** 7839	**G21E** 7839	**V196L** 7839	**3D7** 267.*m*	**G107S** 267.*m*	**G21E** 267.*m*	**V196L** 267.*m*	**3D7** 296	**G107S** 296	**G21E** 296	**V196L** 296
3D7 7839	—	<0.0001	0.0044	<0.0001	0.0008	<0.0001	0.0061	<0.0001	<0.0001	<0.0001	0.0001	0.0010
G107S 7839		—	<0.0001	<0.0001	<0.0001	**#0.0401**	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	**0.0846**
G21E 7839			—	<0.0001	0.0081	<0.0001	0.0058	<0.0001	0.0011	0.0001	0.0002	0.0012
V196L 7839				—	<0.0001	0.0001	<0.0001	**0.1370**	<0.0001	0.0024	0.0092	0.0235
3D7 267.*m*					—	<0.0001	0.0041	<0.0001	0.0001	<0.0001	0.0001	0.0010
G107S 267.*m*						—	<0.0001	0.0003	<0.0001	<0.0001	<0.0001	0.0259
G21E 267.*m*							—	<0.0001	0.0001	<0.0001	0.0001	0.0010
V196L 267.*m*								—	0.0001	0.0010	0.0047	**#0.0454**
3D7 296									—	0.0006	0.0006	0.0017
G107S 296										—	**0.3687**	0.0016
G21E 296											—	0.0077
V196L 296												—

Table S2. Primers for genomic *fnt* fragment amplification, sequencing, and point mutations

Primers for fragment amplification from gDNA
Set 1 (1111 bp):
Primer 54 forward CGAT GCGGCCGC TAA GAGGGTTGTTTTATTATCAC
Primer 56 reverse CTGACCTAGGACTACCGCTGCCGGACCCAGATCCTGAACCATTTCGTAATTCTATAGATAAA
Set 2 (1889 bp):
Primer 300 forward CCATTTGATTATTGTGATTGAAAGTG
Primer B14 reverse ACACCTGGGATAATTAAATAATCATTTATTTTTTGAG
Primers for fragment sequencing
Primer 54 forward, seq. s. above
Primer B14 reverse, seq. s. above
Primer 186 forward TATAGCGGCCGCTAACCACCAAATAATTCCAAATATGTTTTAGATCC
Primer B13 forward TATCATATATTTTATCATTTATTCCATCA
Primer B12 reverse TGTACAAAGTATAAACACTTTATGCATACAC
Primers for point mutations (mutation site in lower case, codon underlined)
Primer G21E forward CAAAAGCGTGTGCGGA<u>GaG</u>GAAGAAAGCTATATC
Primer V196L forward GGTTGTAACATATTT<u>tTA</u>TGCTTGGCGGTGTAT

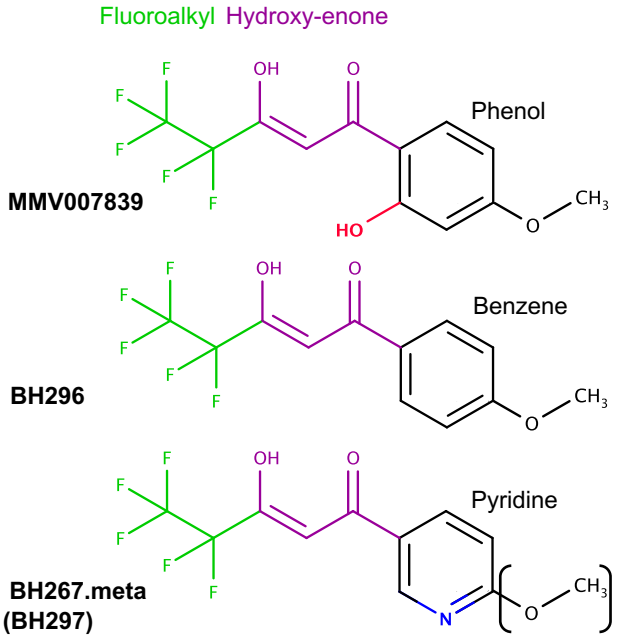

Fig. S1. Molecular structures of the PfFNT inhibitors used in this study.

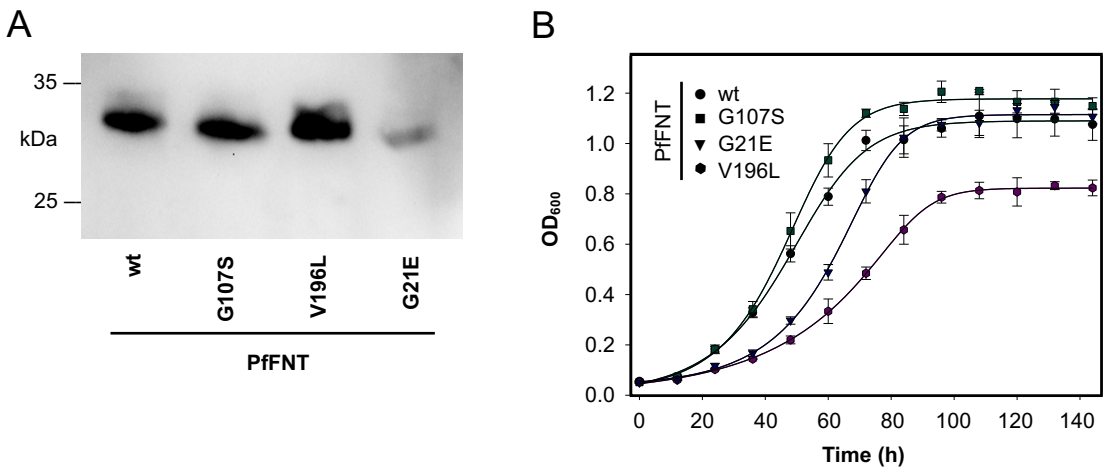

Fig. S2. Expression of wildtype and mutant PfFNT in yeast and growth on lactate media. **A.** Western blot using a primary antibody directed against an N-terminally engineered hemagglutinin epitope. **B.** Yeast lacking endogenous monocarboxylate transporters but expressing PfFNT wildtype or G107S, G21E, or V196L mutants were grown in liquid media containing lactate as the sole carbon source.

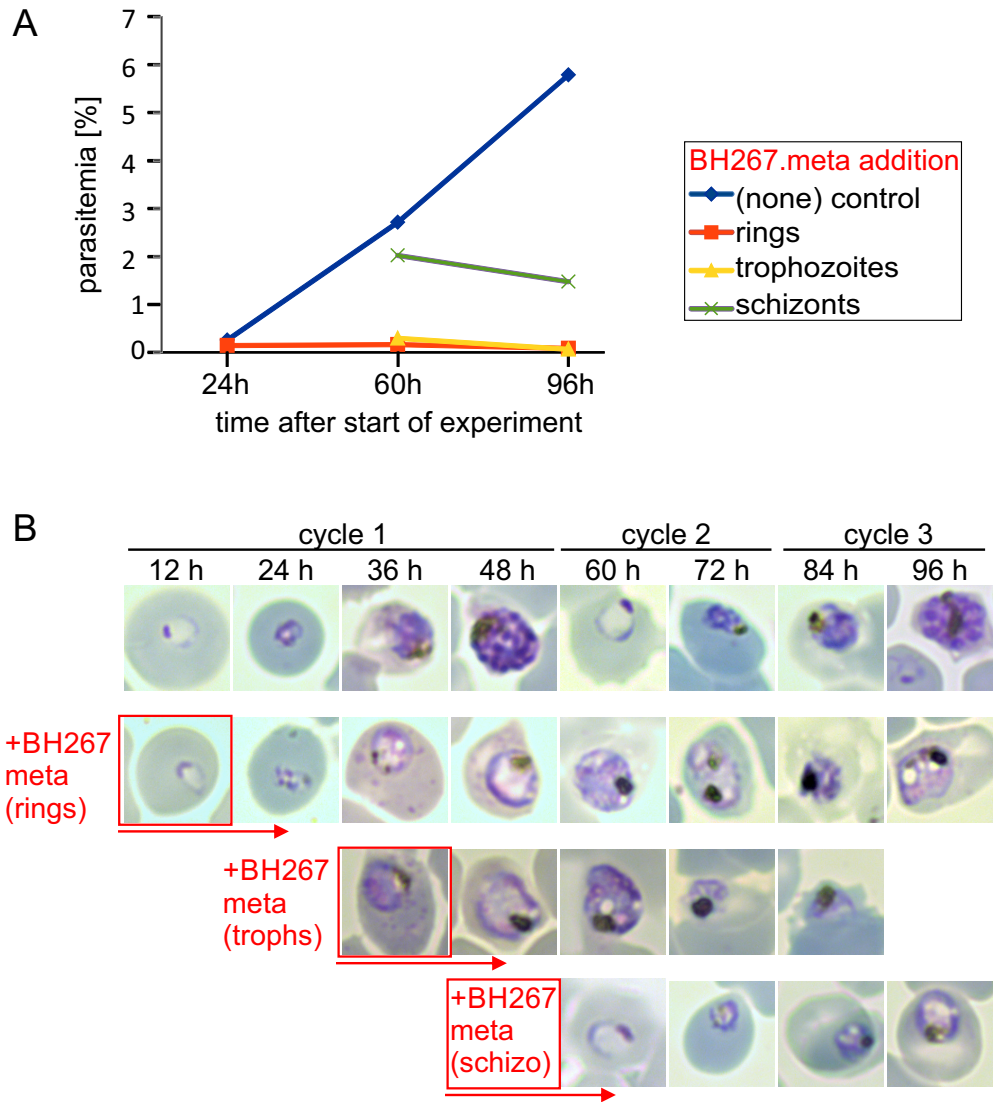

Fig. S3. Experiment similar to that shown in Fig. 3 of the main paper showing growth (A) and the parasite stage in Giemsa smears (B) in a synchronised culture split into 4 dishes consisting of a control (no drug), or cultures where BH267.meta was added at the ring stage, the trophozoite stage or the schizont stage. Parasitemia (A) and Giemsa smears (B) were taken at the indicated time points.

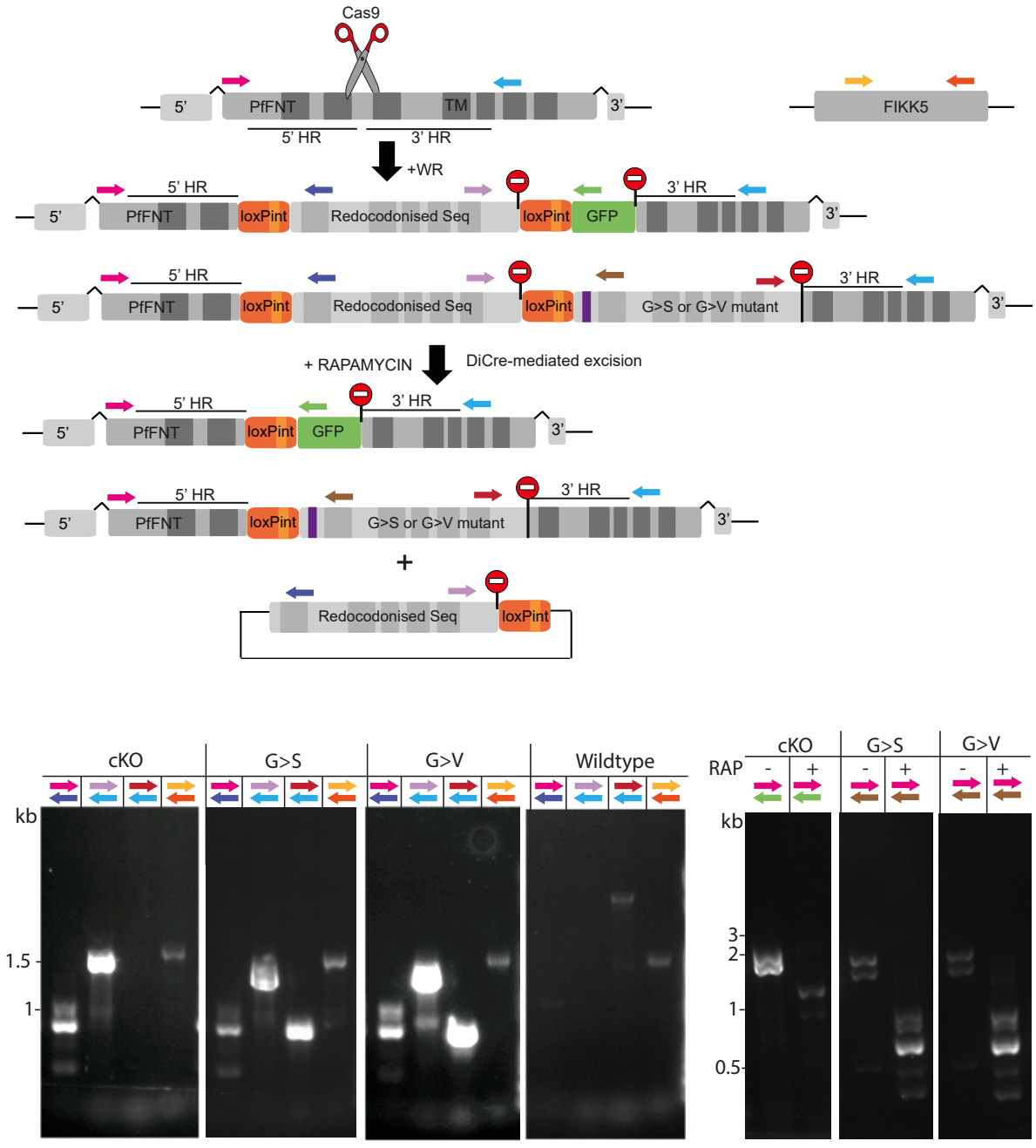

Fig. S4. Schematic of the conditional knockout and mutation construction (A) and confirmation by PCR (B). See Methods section in the main paper for details.