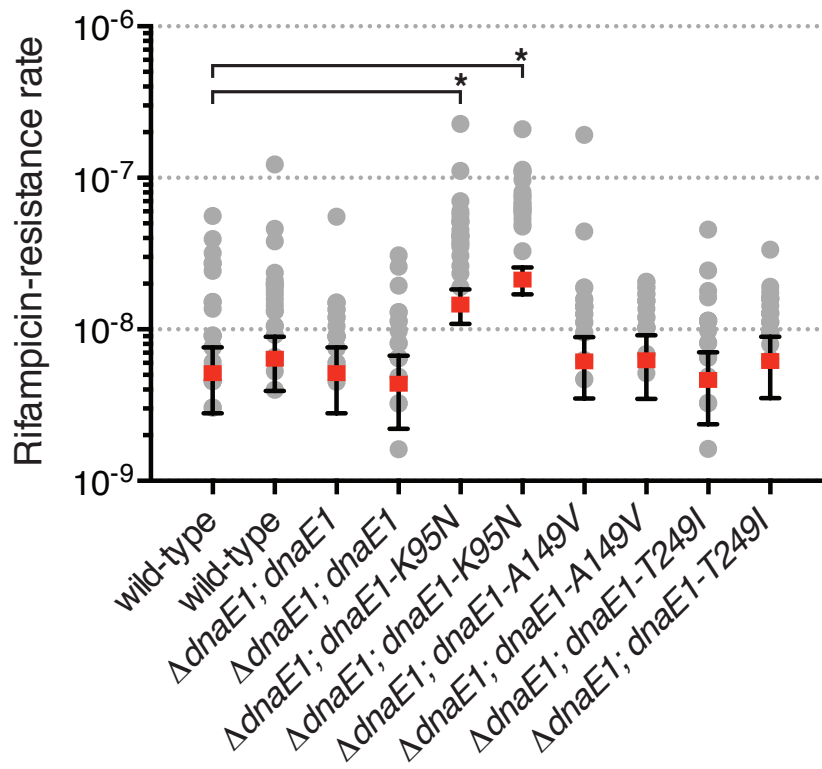


A

Genome Coordinate	Reference Base	Alternative Base	Effect	SNP Prevalence
1747837	C	G	silent_T46	1 in 1725
1747972	C	T	silent_D91	6 in 1725
1747984	G	T	K95N	1 in 1725
1747987	C	G ; T	silent_A96 ; silent_A96	22 in 1725 ; 1 in 1725
1748131	C	T	silent_L144	6 in 1725
1748145	C	T	A149V	1 in 1725
1748152	C	T	silent_G151	1 in 1725
1748445	C	T	T249I	52 in 1725

B

Supplemental Figure 7. Loss-of-function mutations in the *dnaE1* PHP domain are rarely found in clinical *M. tuberculosis* isolates.

(A) *dnaE1* (*Rv1547*) PHP domain single nucleotide polymorphisms (SNPs) observed in clinical *M. tuberculosis* isolates. SNP prevalence refers to the number of clinical strains containing the indicated SNP as compared to the total number of clinical strains analyzed. See Supplemental Table 3 for additional information. (B) Fluctuation analysis was used to determine the rates at which the indicated *M. smegmatis* strains acquired resistance to rifampicin. With the exception of wild-type *M. smegmatis*, these strains harbor a deletion of the endogenous *dnaE1* (*Ms3178*) gene and have been complemented with the indicated *M. tuberculosis dnaE1* (*Rv1547*) gene. Circles represent mutant frequency (number of rifampicin-resistant mutants per cell plated in a single culture). The red bar represents the estimated mutation rate (mutations conferring rifampicin resistance per generation), with error bars representing the 95% confidence interval (CI). * $P < 0.05$ in comparison of mutant frequencies by Wilcoxon rank-sum test.