SUPPLEMENTARY INFORMATION

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Susceptibility of *Mycobacterium tuberculosis* cytochrome *bd* oxidase mutants to compounds targeting the terminal respiratory oxidase, cytochrome *c*

Table S1. *M. tuberculosis* strains used in this study

Strain name	Genotype	Whole-genome sequence analysis	Reference
H37RvMA	Wild-type; ATCC27294	See reference (1)	(1)
cydKO	*cydC*::*aph*; constructed in H37Rv (ATCC27294)	ND	(2, 3)
Δ*cydA*	Allelic exchange mutant of H37RvMA carrying *cydA* deletion allele from base pair 121 to 1329 resulting in 1209 bp in-frame deletion in the 1458 bp *cydA* (*Rv1623c*) gene.	Rv1616:F77L, Rv1617/*pykA*:R17F, (Rv1628c:T126T)	This study
Δ*cydAB*	Allelic exchange mutant of H37RvMA carrying *cydAB* deletion allele from base pair 121 of *cydA* to 2418 of *cydB* resulting in 2298 bp deletion in the *cydA-cydB* locus (*Rv1623c-Rv1622c*)	*pepN*:V526A, *ppsE*:G146*	This study

SUPPLEMENTARY REFERENCES

1. **Ioerger TR, Feng Y, Ganesula K, Chen X, Dobos KM, Fortune S, Jacobs WR, Jr., Mizrahi V, Parish T, Rubin E, Sassetti C, Sacchettini JC.** 2010. Variation among genome sequences of H37Rv strains of *Mycobacterium tuberculosis* from multiple laboratories. J Bacteriol **192:**3645-3653.
2. **Arora K, Ochoa-Montano B, Tsang PS, Blundell TL, Dawes SS, Mizrahi V, Bayliss T, Mackenzie CJ, Cleghorn LA, Ray PC, Wyatt PG, Uh E, Lee J, Barry CE, 3rd, Boshoff HI.** 2014. Respiratory flexibility in response to inhibition of cytochrome C oxidase in *Mycobacterium tuberculosis*. Antimicrob Agents Chemother **58:**6962-6965.
3. **Shi L, Sohaskey CD, Kana BD, Dawes S, North RJ, Mizrahi V, Gennaro ML.** 2005. Changes in energy metabolism of *Mycobacterium tuberculosis* in mouse lung and under *in vitro* conditions affecting aerobic respiration. Proc Natl Acad Sci U S A **102:**15629-15634.

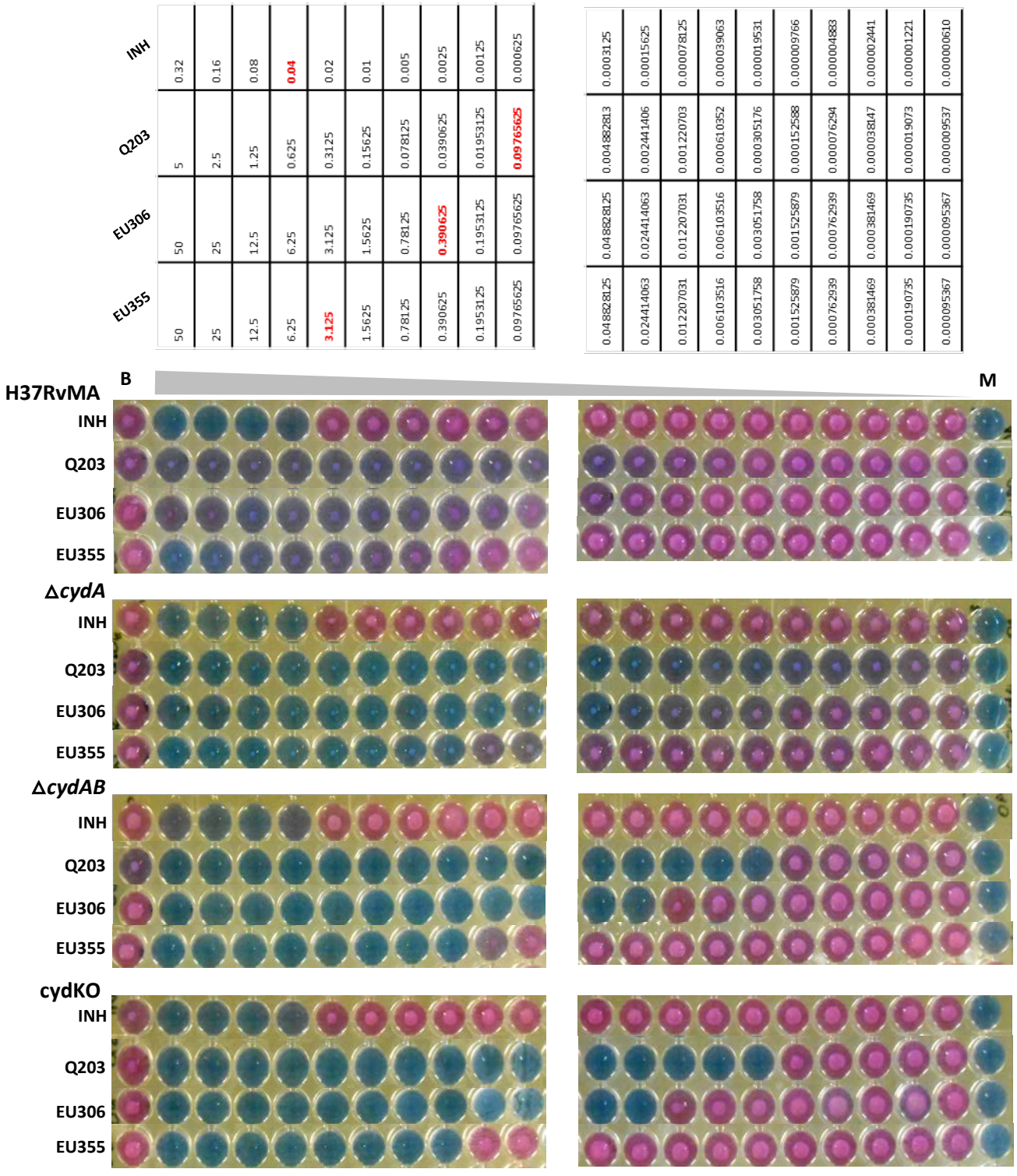

FIG S1 Treatment of *M. tuberculosis* H37Rv and *cyd* operon mutants with inhibitors of the cytochrome bc_1 complex confirms inhibition of Alamar Blue reduction in the wild-type strain. This effect is eliminated in the *cyd* operon mutants which retain full susceptibility over the 14-day assay. Isoniazid (INH) is included as a control; note also that the left-most column on each plate contains bacilli only (**B**, no drug control) and the right-most column is the media-only (**M**) control. Drug concentrations (μg/ ml) are shown in the tables above the plates; values in bold **red** typeface indicate the MICs inferred for wild-type H37RvMA.