

**Table S2** Genome editing of regions with “weak” PAM sequences in *M. tuberculosis*.

Gene name	sgRNA targeting sequence +PAM sequence <sup>a</sup>	Fold repression <sup>b</sup>	No. of mutant / No. of test
Rv1991c	actgacctcaccgaccgag <u>TTGGGGAG</u>	24.7	10/16
Rv1991c	gtacggatctgactggatta <u>CGAGCAC</u>	11.9	16/16
Rv2801c	gtgatgcgccggtgagat <u>TTGGCAG</u>	4.0	14/24
Rv2801c	accttggcgatgttgctcgtca <u>CCGGCAC</u>	2.7	19/24

<sup>a</sup> PAM sequences are shown underlined and capitalized.

<sup>b</sup> The PAM fold repression was adopted from Ref (1). A cutoff score of greater than 25-fold repression was suggested for CRISPRi; thus PAMs with less than 25-fold repression are considered “weak”.

## Reference

1. Rock JM, Hopkins FF, Chavez A, Diallo M, Chase MR, Gerrick ER, Pritchard JR, Church GM, Rubin EJ, Sasseti CM, Schnappinger D, Fortune SM. 2017. Programmable transcriptional repression in mycobacteria using an orthogonal CRISPR interference platform. *Nat Microbiol* 2:16274.