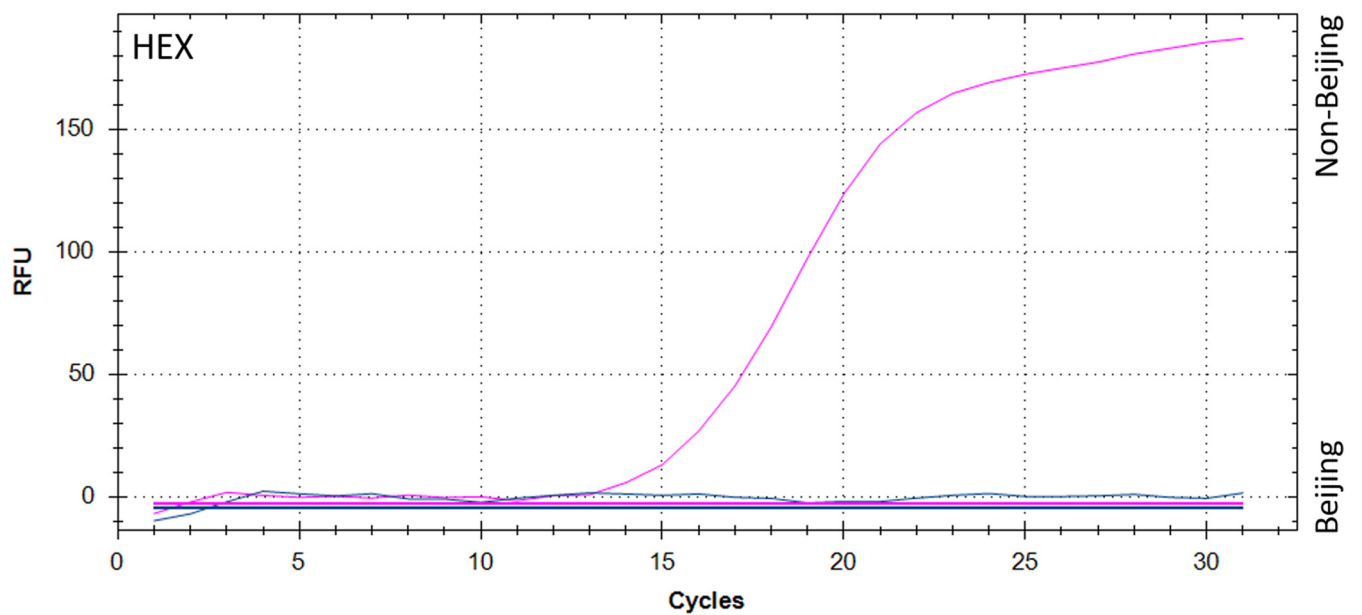


(a)



(b)

Figure S1. Fluorescence curves of a real-time PCR assay targeting the *dnaA-dnaN*::IS6110 region of *M. tuberculosis* L2/Beijing genotype: (a) L2/Beijing genotype-specific signal (FAM channel); (b) Non-Beijing genotype-specific signal (HEX channel). The design of the PCR assay was described by Mokrousov et al. [18].

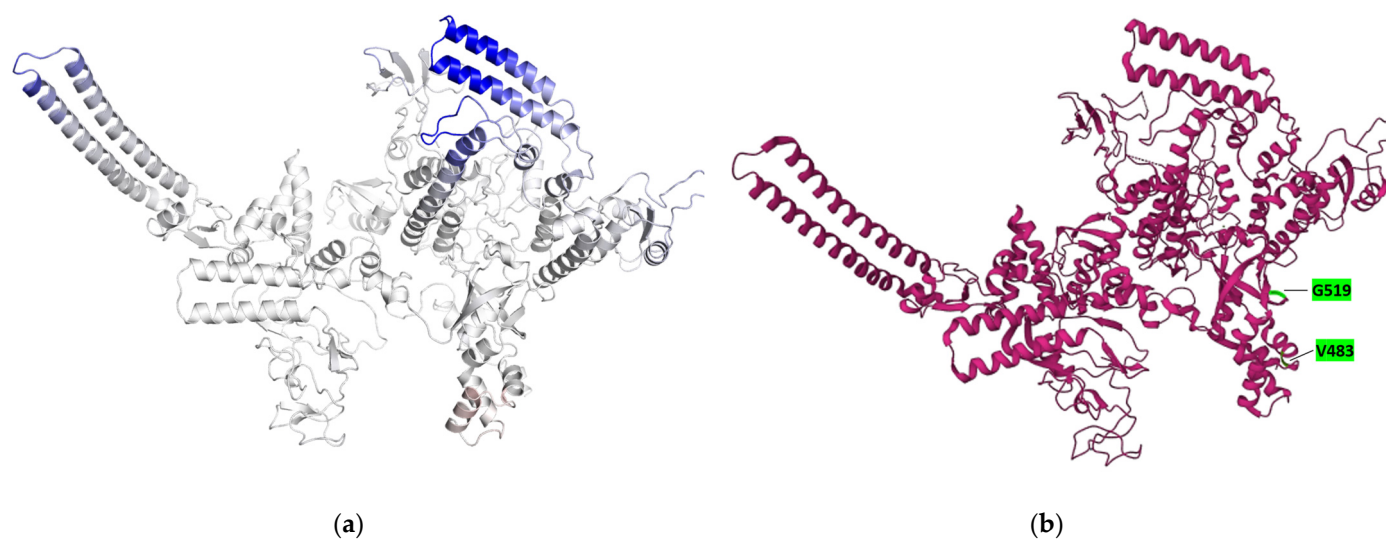


Figure S2. Three-dimensional representation of compensatory mutations on the crystal structure of Mtb DNA-directed RNA polymerase (RNAP) subunit beta (PDB: 6c04). **(a)** Decreased flexibility of RNAP subunit beta upon V483G mutation. Amino acids are colored according to vibrational entropy change (blue: rigidification of structure; red: gain in flexibility). **(b)** RNAP subunit beta structure with V483 and G519 WT alleles (green).