

Original Article**Identification of drug resistance-related virulence gene mutations in 667 clinical *Mycobacterium tuberculosis* isolates**Yu Zhang¹, Xinchang Chen¹, Shiyong Wang¹, Ning Jiang², Lingyun Shao¹, Jiazhen Chen¹¹ Department of Infectious Diseases, Shanghai Key Laboratory of Infectious Diseases and Biosafety Emergency Response, National Medical Center for Infectious Diseases, Huashan Hospital, Shanghai Medical College, Fudan University, China² State Key Laboratory of Genetic Engineering, School of Life Sciences, Fudan University, Shanghai, China**Abstract**

Introduction: Drug-resistant tuberculosis is a severe global public health threat. Virulence factors and antibiotic resistance are generally considered to play a significant role in bacterial pathogenesis. However, the interaction between resistance and virulence in *Mycobacterium tuberculosis* (MTB) remains unclear.

Methodology: Here, we used whole genome sequences from 667 MTB isolates from 14 countries to complete an *in silico* evaluation of the correlations between virulence gene mutations, drug resistance, and lineage classification. The chi-square (χ^2) test was used to determine whether specific virulence gene mutations and drug resistance were related.

Results: Our results showed that Mce1R_G171R and Pks15_V333A, were positively correlated with streptomycin and ethambutol resistance, respectively, and Pks15_T46I was correlated with isoniazid, rifampin, ethambutol, pyrazinamide and streptomycin resistance. We also identified an additional 24 and 40 single nucleotide polymorphisms as well as 6 and 2 insertions or deletions in various virulence genes that are likely to be associated with changes in drug susceptibility in L2 and L4, respectively.

Conclusions: Taken together our data suggest that there may be some degree of co-selection between virulence and resistance factors, which may help MTB more easily adapt to new environments.

Key words: *Mycobacterium tuberculosis*; virulence genes; drug resistance; correlation evaluations.

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Introduction

Tuberculosis, an infectious disease caused by *Mycobacterium tuberculosis* (MTB), is a severe and growing global public health threat. The COVID-19 pandemic has had a continuous damaging impact on access to TB diagnosis and treatment and the burden of TB disease since 2019. According to the Global Tuberculosis Report for 2022, an estimated 10.6 million people fell ill with TB in 2021, an increase of 4.5% from 10.1 million in 2020. Globally, the estimated number of people who developed MDR-TB or RR-TB each year was relatively stable between 2015 and 2020 but grew in 2021. There were an estimated 450,000 incident cases in 2021, up 3.1% from 437,000 in 2020 [1]. MTB is an ancient causative agent and has infected a quarter of the global human population by developing highly sophisticated mechanisms of pathogenesis and immune evasion in its host [2].

Virulence and resistance have evolved over very different timescales. Changes in the virulence mechanisms of this bacteria have developed in response

to the coevolution of this pathogen and its host, with its pathogenic behavior changing to adapt to the evolving immune response of its host environment. However, the evolution and spread of antibiotic resistance is relatively recent having predominantly occurred over the past 50 years following the advent and widespread adoption of various antimicrobial agents. Despite the differences in the evolution of these processes, they share some common characteristics. Genetically encoded antibiotic resistance to some degree can be considered a subtype of virulence factor as it facilitates host pathogenesis, allowing persistent or chronic diseases [3]. Some characteristics including efflux pumps [4], porins [5], and cell wall alterations [6] are also involved in both virulence and resistance [7].

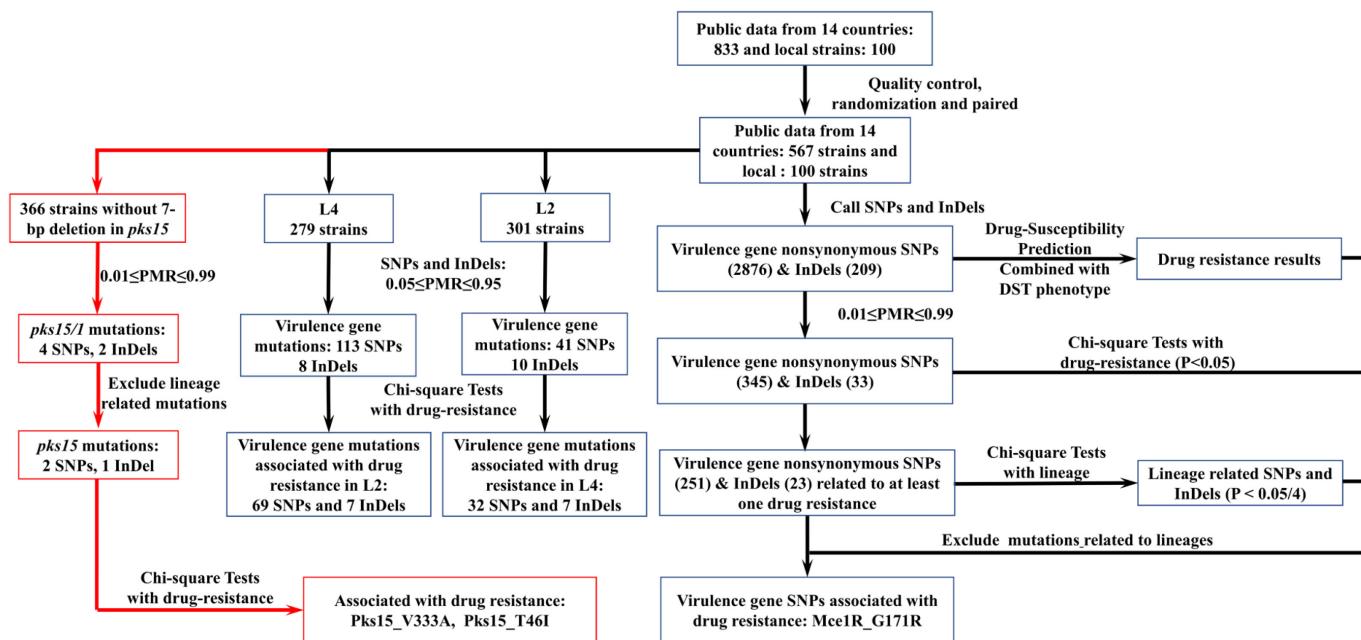
The evolution of these bacteria is the result of adaptation to the widespread, and often unnecessary and nonstandard application, of multiple antibiotics by the host and the variation in immune status caused by multiple chronic diseases, resulting in a series of new lineages of MTB. This is further complicated by the fact

that several of these endemic lineages are usually more drug-resistant and virulent than their common ancestor. As an example, B0/W-148, a rapid transmission subtype found in Russia, is characterized by increased virulence and drug resistance [8]. Many studies have shown that virulence factors are associated with antibiotic resistance in pathogenic bacteria [9,10]. The relationship between virulence genes and drug resistance in MTB remains unclear. It is reasonable to expect that enhanced virulence may be linked to drug resistance. For example, mutations in the mutator genes *mutT2* and *mutT4* in modern Beijing strains increase virulence and enhance drug resistance by improving bacterial adaptation to the host [11]. However, some resistance mutations are likely to compromise virulence, e.g., the deletion of *KatG*, which confers high-level resistance to isoniazid but results in the attenuation of bacterial virulence *in vivo* [12]. Because the targets of anti-tuberculosis drugs often have important physiological functions, mutations in these targets may produce resistance with the cost of reducing fitness [13], which is manifested as slow growth and decreased transmission. Under these conditions, MTB may likely adopt a co-selection approach to allow for improved drug resistance with reduced fitness costs. In this case, we propose that there are some drug resistance-related mutations in the virulence genes, and identifying these mutations will help us better

understand the transmission and development of MDR-TB.

Differences in lipid metabolism and associated genes often contribute to lineage-specific virulence patterns in different MTBC lineages in both *in vitro* and *in vivo* infection models [14]. In particular, the “modern” sub-lineage is globally distributed and is closely associated with MDR-TB, extensively drug-resistant-TB, and hypervirulent TB [15]. Some virulence gene mutations are specific to high-level drug-resistant lineages and may act as potential lineage markers under these conditions. For example, C1881090T, located in virulence gene *pks7*, is considered to be the definitive marker of lineage 2.1 [16]. This study was designed to identify new single nucleotide polymorphisms (SNPs) and insertions and deletions (InDels) in virulence genes that correlate with changes in the drug resistance of their lineage after excluding the specific lineage markers. We accomplished this by analyzing the whole genome sequences of 667 clinical MTB strains from 14 countries worldwide and then evaluating the relationship between specific SNPs in specific virulence genes and drug resistance in each of these isolates. Our data provide important clues for better understanding the evolution of MDR-TB.

Figure 1. Whole workflow of analyzing correlation of virulence gene mutations and drug resistance. The red arrows show the workflow of analyzing correlation of mutations in *pks15* and *pks1* with each drug resistance in the 366 strains without 7-bp deletion (GGGCCGC) in *pks15*.



Methodology

Strain selection

Our study included hundreds of global MTB strains whose genome sequences and phenotypes were available in previous studies from a public database [17-21] or formed part of our laboratory collection. We first randomly included and downloaded 833 whole MTB genome sequences from China, India, Pakistan, South Africa, Congo, Swaziland, Ivory Coast, Belgium, the Netherlands, Italy, Russia, Canada, Peru, and Australia from the Sequence Read Archive (SRA) database and then completed a quality control process on these downloads to ensure that each download included enough reads of comparable quality and depth, at a minimum coverage of 60x. Fastp (v0.20.1, parameters: -q 15 -u 10 -l 90) (Figure 1) was used to exclude low-quality reads. After trimming, samples whose total bases were no fewer than 264,691,920bp (60 times that of MTB H37Rv genome size as reference) were used for further analysis. We then balanced the geographical distribution of our samples to better evaluate the correlations between drug resistance and virulence genes, leaving 30 MDR and 15 non-MDR strains from each country. In the case of countries like Canada, Ivory Coast, and the Netherlands, which did not have enough MDR strains, all the MDR strains meeting the inclusion criteria were enrolled and 15 non-MDR strains were randomly selected, and in the case of Congo-Kinshasa, all 6 MDR and 4 non-MDR strains from this region were included in our evaluations (Table 1).

We also included an additional 100 randomly selected clinical strains from our laboratory collection consisting of 71 MDR strains and 29 non-MDR strains, archived between 2014 and 2019, in this cohort. Thus, our final dataset included 667 clinical MTB strains from

14 countries, including 567 strains from a public database and 100 strains collected by our lab (Table 1).

Virulence gene selection

We evaluated the genetic polymorphisms in 332 virulence genes (Supplementary Table 1), including those encoding toxin-antitoxin (TA) systems, cell-wall proteins, lipid synthesis proteins, and type VII secretion systems and infection survival required genes [22-25], in an effort to establish the correlation between these mutations and drug resistance in our MTB strains.

DNA extraction, sequencing, and SNP calling

MTB colonies were scraped from the Löwenstein-Jensen medium and genomic DNA was extracted using the DNeasy Blood & Tissue Kit (QIAGEN, Valencia, CA, USA), following the manufacturer's instructions. All sequencing libraries were prepared using the Nextera XT Sample Prep Kit (Illumina, San Diego, CA, USA) as described by the manufacturer and sequenced on the Illumina MiSeq, Illumina Hiseq, and BGISEQ-500 platforms., with at least a 60-fold coverage. Low-quality reads were then filtered out with fastp (v0.20.1, parameters: -q 15 -u 10 -l 90), and the remaining reads were aligned to MTB H37Rv reference genome (GenBank: NC_000962.3) using Bowtie2 (version 2.3.3.1) set to its default parameters. SNPs and InDels were then detected using SAMtools (version 1.6) with a minimum sequencing depth of 10 reads without strand bias and a frequency of $\geq 85\%$ for SNPs and $\geq 60\%$ for InDels. SNP genotyping was used to determine the lineage of each MTB strain as previously described [16].

Table 1. Country and lineage distribution for all 667 clinical isolates evaluated in this study.

Geography	MDR ^a	Non-MDR ^b	L1	L2	L3	L4	L5	L6
Australia	30	15	2	34	2	7	-	-
Belgium	30	15	1	18	-	26	-	-
Canada	25	15	8	22	2	8	-	-
China	30	15	-	37	1	7	-	-
Congo-Kinshasa	6	4	-	-	1	9	-	-
Italy	30	15	1	18	1	24	-	1
Ivory Coast	18	15	-	-	-	31	1	1
Netherland	20	15	2	10	6	17	-	-
Pakistan	30	15	2	3	34	6	-	-
Peru	29	15	1	3	-	40	-	-
Russia	30	15	-	32	-	13	-	-
South Africa	30	15	3	7	-	35	-	-
Swaziland	30	15	10	5	2	28	-	-
Thailand	30	15	5	37	-	3	-	-
Our lab (China)	71	29	-	75	-	25	-	-
Total	439	228	35	301	49	279	1	2

a. Multi-drug resistant; b. Non-multi-drug resistant.

Drug-susceptibility testing (DST) and genotypic resistance by prediction

Phenotypic DST of all 100 strains from our lab was performed as described by the Clinical and Laboratory Standards Institute [26,27] which determined that the critical concentration for isoniazid (INH) was 0.2 mg/L; rifampin (RIF), 40.0 mg/L; ethambutol (EMB), 2.0 mg/L; levofloxacin (LFX), 2.0 mg/L; streptomycin (SM), 4.0 mg/L; amikacin (AM), 30.0 mg/L; kanamycin (KM), 30.0 mg/L; and capreomycin (CM), 40.0 mg/L. These results were all determined following 3 weeks of incubation at 37 °C. Apart from pyrazinamide (PZA), the DSTs were performed using the proportion method on Löwenstein–Jensen medium (Baso, Zhuhai, Guangzhou Province, China). The susceptibility of the MTB isolates to PZA was evaluated using an automated Mycobacterial Growth Indicator Tube 960 system (Becton Dickinson Diagnostic Systems, Franklin Lakes, NJ, USA), as described by the manufacturer, at a critical concentration of 100.0 mg/L.

We then evaluated the antimicrobial resistance of the 567 strains from the public database using their phenotypic resistance where available and genetic drug resistance prediction where necessary. Genetic resistance to INH, RIF, PZA, EMB, LFX, AM, KM, CM, and SM was predicted using whole genome sequencing data as previously described [26]. Collectively, previous studies showed that the genotype DST prediction performed well in the mentioned nine drugs with sensitivity higher than 85% and specificity higher than 80% [17,26].

Correlation analysis

In this study, chi-square tests were performed with (minimal case number < 5) or without (minimal case number ≥ 5) Yates's Correction for Continuity. The population mutation rate was determined as the proportion of mutated samples in total samples. SNPs and InDels with too low (< 1%) or too high (> 99%) population mutation rates were excluded from further analysis. We determined the correlation between virulence gene mutations and drug resistance, using the proportions of each SNP or InDel in each virulence gene from each population (drug-resistant/sensitive), where the average mutation rates were between 1% and 99%. These were then compared using a chi-square test, and the *p* value less than 0.05 was considered statistically significant. We then used the chi-square test by SPSS (v26.0) to determine the correlation between specific virulence gene mutations and lineage. In this study, Bonferroni Correction was conducted in Lineage

1 to 4 due to the small population sizes of Lineage 5 and 6. Thus, the *p*-value less than 0.0125 (0.05/4) was considered significant. Since it has been known that a 7-bp deletion (GGGCCGC) in *pks15* disrupted the fused *pks15/1* gene, leading to the abolition of synthesis of phenolic glycolipid (PGL), which is associated with resistance to intracellular killing by macrophage, we excluded the strains with a 7-bp deletion in *pks15* and then reanalyzed the correlation of mutations in *pks15* and *pks1* with each drug resistance in the remaining 366 strains without 7-bp deletion (Figure 1, red arrow part).

Since lineage-specific SNPs may interfere with the analysis of the virulence genes and the sample size of L2 (301 strains) and L4 (279 strains) was relatively large, we performed separate analyses for each of these 2 lineages. We used the chi-square test to evaluate the relationship between drug resistance and virulence gene mutations whose population mutation rates were between 5% and 95%. This whole workflow is described in Figure 1.

Homology models

The homology models for protein mce1R and *pks15*, as well as models for their mutations (Mce1R_G171R, Pks15_T46I, Pks15_V333A), were searched and built using SWISS-MODEL (<https://swissmodel.expasy.org/>) [28], and assessed by MolProbity (ver. 4.4) [29]. Distances between amino acid residues in protein conformations were calculated using UCSF ChimeraX (ver. 1.3, <https://www.cgl.ucsf.edu/chimerax/>) [30].

Results

Dataset characteristics

A total of 667 clinical MTB isolates were suitable for further evaluations with these samples representing strains from 14 countries across five continents, including 567 strains from the public database and 100 strains from our laboratory collection (Figure 2). There were 45 isolates each from Australia, Belgium, China (public data), Italy, Pakistan, Russia, Swaziland, South Africa, and Thailand; 40, 10, 33, 35, and 44 isolates from Canada, Congo-Kinshasa, Ivory Coast, the Netherlands, and Peru, respectively.

Drug resistance in our 667-strain cohort

For nine common antituberculosis drugs, namely, INH, RIF, EMB, PZA, LFX, SM, AM, KM, and CM, we completed drug-resistance testing for 100 local isolates and prediction for strains from a public database for which the drug sensitivity phenotype was not available. Among the 667 strains, 460, 455, 298,

Table 2. Drug susceptibility and resistance to common antibiotics for MTB.

	INH	RIF	EMB	PZA	LFX	SM	AM	KM	CM
R strains	460	455	298	268	125	305	48	60	49
S strains	207	212	369	399	542	362	619	607	618

INH: isoniazid; RIF: rifampin; EMB: ethambutol; PZA: pyrazinamide; LFX: levofloxacin; SM: streptomycin; AM: amikacin; KM: kanamycin; CM: capreomycin; R: resistant; S: susceptible.

268, 125, 305, 48, 60, and 49 strains were resistant (R) to INH, RIF, EMB, PZA, LFX, SM, AM, KM, and CM, respectively (Table 2). Accessions, locations, and drug susceptibility results of phenotype or genotype prediction of all 667 isolates were shown in Supplementary Table 2.

Virulence gene SNPs and InDels correlating with lineage type

We detected 2876 SNPs and 209 InDels in the virulence genes evaluated, and of these, 345 SNPs and 33 InDels had a mutation rate between 1% and 99%. Of the 345 SNPs, 126, 306, 71, and 294 SNPs correlated with lineages L1, L2, L3, and L4, respectively. Among these mutations, only Rv0165c(Mce1R)G171R showed no significant differences in distributions across lineages, whereas the remaining 344 SNPs and 33 InDels were correlated with specific lineages and therefore considered as lineage markers (Supplementary Table 3). For analysis of mutations on *pks15* and *pks1*, 7-bp deletion in *pks15* was found in all L4 strains and some of other lineages. We excluded the

strains with 7-bp deletion in *pks15*, and then analyzed the correlation of mutations in *pks15* and *pks1* with each lineage in the remaining 366 strains without the deletion. Among 4 SNPs and 2 InDels in *pks15*, 2 SNPs and 1 InDel were related to specific lineages (Supplementary Table 3).

Correlation between specific virulence gene mutations and drug resistance

We evaluated the correlation between the 345 nonsynonymous SNPs and 33 InDels with their specific lineages and associated drug resistance phenotype, which revealed that 251 of these SNPs and 23 of the InDels were directly correlated with the strains' resistance of at least one drug (Supplementary Table 3). All of the InDels were excluded from these evaluations because they demonstrated significant differences in occurrence between the lineages, suggesting that they were lineage-specific mutations. After excluding the lineage-related SNPs, Mce1R_G171R was found to have a significant positive correlation with SM resistance phenotype (Table 3). For analysis of *pks15*

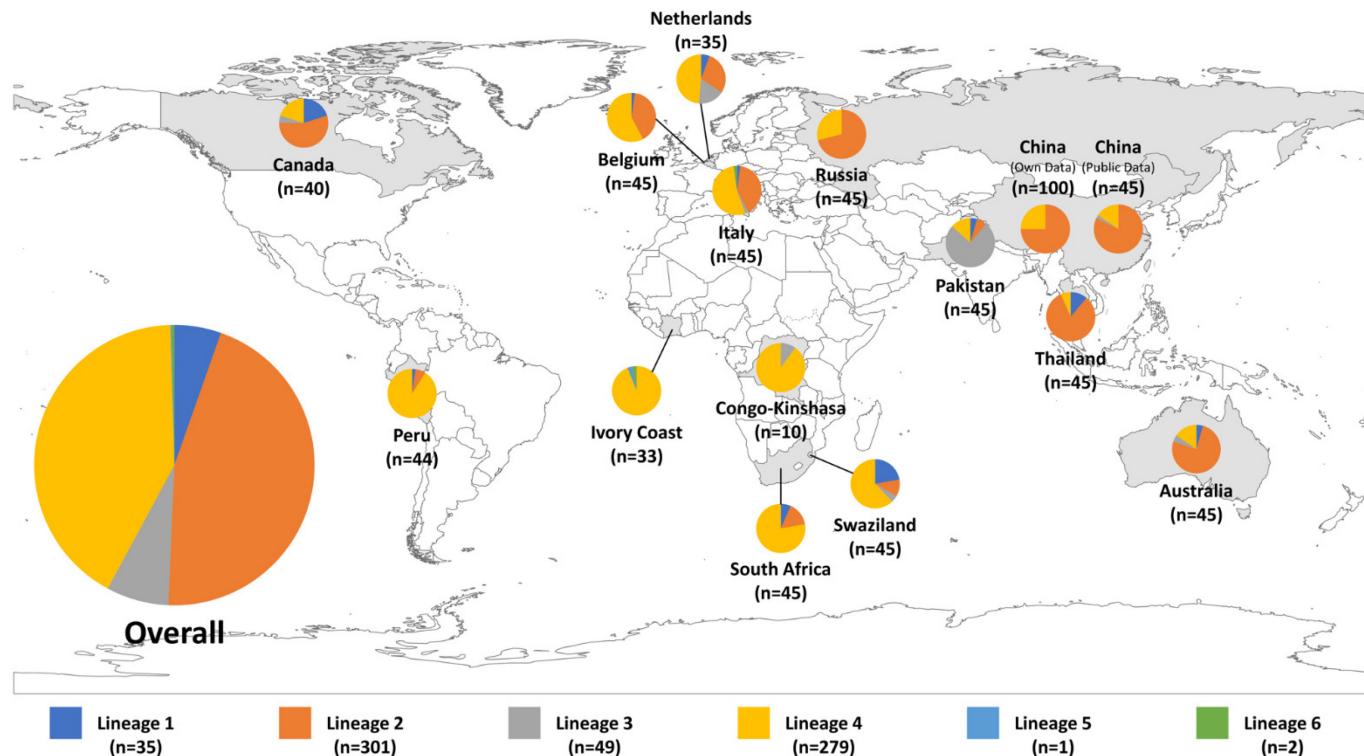
Figure 2. The global distribution of 667 clinical MTB isolates.

Table 3. Virulence gene mutation rates were significantly different in resistant strains.

Gene	Rv no.	Mutation	Gene function	Mutation rate	Drug	p value	P/N
<i>mce1R</i>	Rv0165c	G171R	Probable transcriptional regulatory protein Mce1R (GntR-family)	1.50%	SM	0.0120	P
<i>pks15^a</i>	Rv2947c	T46I	Putative inactive phenolphthiocerol synthesis polyketide synthase type I Pks15	4.37%	INH rifampin PZA SM	0.0473 0.0397 0.0242 0.0035	P P N P
<i>pks15^a</i>	Rv2947c	V333A	Putative inactive phenolphthiocerol synthesis polyketide synthase type I Pks15	91.80%	EMB	0.0331	P

INH: isoniazid; RIF: rifampin; EMB: ethambutol; PZA: pyrazinamide; SM: streptomycin. P/N, mutation is positively or negatively related to corresponding drug resistance. ^a Chi-square test was performed based on the population excluded strains with 7-bp deletion in *pks15*.

and *pks1*, after excluding the strains with 7-bp deletion in *pks15*, the correlation of mutations in *pks15* and *pks1* with each drug resistance was analyzed in the remaining 366 strains. After excluding the lineage-related mutations, the occurrence of Pks15_T46I was found to be associated with resistance of INH, RIF, PZA, and SM, and Pks15_V333A was associated with EMB resistance.

Correlation between virulence gene mutations and drug resistance in L2 and L4 strains

Strains from lineages L2 and L4 accounted for 45.1% and 41.8% of all of the samples, respectively. When we analyzed the correlation between virulence gene mutations and drug resistance in L2 and L4, 32 nonsynonymous SNPs, 7 InDels, and 69 nonsynonymous SNPs, 7 InDels were noted to show significant differences in resistance to at least one drug in L2 and L4, respectively (Supplementary Table 4,5).

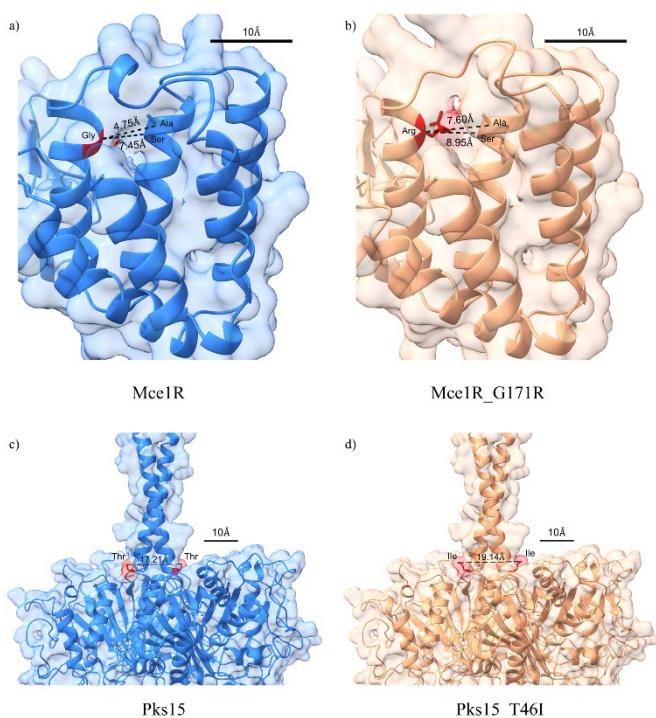
Protein homology models of *Mce1R* and *Pks15*

We identified the protein families and determined mutation-affected domains in both *Mce1R* (UniProtKB entry: Q79G00) and *Pks15* (P96284) using EMBL-EBI InterPro (<https://www.ebi.ac.uk/interpro>). The *Mce1R_G171R* mutation is located within the C-terminal of GntR (InterPro entry: IPR011711), which is known to bind to effector molecules and regulate the transcription of its target genes through the action of its N-terminal DNA-binding domain. *Pks15_T46I* and *Pks15_V333A* are located in the N-terminal and C-terminal (IPR014031) of beta-ketoacyl-ACP synthase (EC: 2.3.1.41), which catalyzes the production of long-chain fatty acids.

Homology modelling results revealed very likely conformational changes at *Mce1R_G171R* and *Pks15_T46I* (Figure 3). *Mce1R_G171R* attributes to glycine to arginine substitution that results in the nonpolar side chain of Gly (-H) replaced by a larger and charged aliphatic side chain of Arg (-CH₂)₃-

NHC(NH)NH₂). As a part of an α -helix motif, 171Arg is pushed back by 140Ala and 141Ser which are on the opposite side of another α -helix causing an enlarged interval between two motifs and a significant change in its conformation (Figure 3a, b). *Pks15_T46I* is located at the end of an α -helix motif and next to a random coil. Due to the substitution of a non-polar side chain of Ile (-CH(CH₃)CH₂CH₃) for a smaller polar side chain of Thr (-C(OH)CH₃), the distance between two isoleucine residues of the *Pks15_T46I* homo-dimers increased leading to conformational changes of the α -helix motif (Figure 3c, d). Models of *Pks_V333A* substitution

Figure 3. Protein homology models of *Mce1R* and *Pks15*. Homology modelling results of a) *Mce1R*, b) *Mce1R_G171R*, c) *Pks15*, d) *Pks15_T46I*. a) and b) The interval between two α -helices was enlarged in *Mce1R_G171R* compared to the wild type; c) and d) the distance between two isoleucine residues of *Pks15_T46I* homo-dimers increased leading to the conformational change.



versus Pks15 did not reveal significant change between their conformations.

Discussion

MTB has not been shown to participate in any form of horizontal gene transfer meaning that it usually acquires MDR via the accumulation of different genetic mutations [31]. In addition, the increasing trend of drug resistance in MTB is a concern since it drastically limits the range of therapeutic alternatives for these infections. Thus, understanding the mechanism and transmission of drug-resistance MTB may be crucial to the development of novel therapeutic strategies. Here, we focused on the first-line anti-tuberculosis drugs (INH, RIF, EMB, PZA, and SM) and important second-line anti-tuberculosis drugs (LFX, AM, KM, and CM), and explored the relationship between virulence gene mutations and drug resistance. Our correlation analysis revealed that two mutations, *Mce1R_G171R* and *Pks15_V333A*, were positively correlated with SM and EMB resistance in MTB, respectively.

The *mce1R* gene encodes transcriptional regulatory protein Mce1R, which negatively regulates the *mce1* operon in intracellular MTB [32] that is duplicated four times within the genome (*mce1-4*) [33], because it encodes the ATP-binding cassette (ABC) transporter [34], known to help regulate immunopathological responses in the infected host and is important for lipid metabolism/transport, host invasion, modulation nicely [35]. A previous study revealed that an MTB mutant in which the expression of *mce1R* gene was disrupted *in vivo* induced an accelerated immunopathological response in the infected animal [36], while another study showed that the absence of the Mce1R protein increases MTB virulence in a mouse model [37]. Our finding, that *Mce1R_G171R* occurs more frequently in SM-resistant strains might correlate with greater virulence which is consistent with the results of a previous study. Homology modeling revealed Mce1R possesses a C-terminal domain comprising a bundle of six α -helices, which was consistent with previous research [35]. Interestingly, G171R of Mce1R is not only located in the α -helix bundle but also very close to a cavity formed by the bundle, which may bind a specific ligand with high affinity [35]. While G171R as well as 140Ala and 141Ser are so close to the residues constituting the cavity. The conformational change caused by G171R will likely lead to the change of the cavity and affect the affinity to the ligand.

The *pks15* gene encodes inactive phenolphthiocerol synthesis polyketide synthase type I and is involved in the biosynthesis of PGL [38]. When *pks15* is fused to

pks1 these isolates produce PGLs, while in strains like H37Rv with split *pks15* and *pks1* loci, PGL is not produced [39]. A 7-bp or 1-bp insertion causes a frameshift in the *pks15* taking H37Rv as a reference, resulting in an intact Pks15/1 with additional codons. Similar results have been shown in other W-Beijing strains, *M. africanum*, *M. bovis*, and in the other *M. tuberculosis* lineages such as EAI, and Dehli. The disruption of the *pks15/1* gene of *M. bovis* BCG abolishes the production of the *M. bovis*-specific PGL [34]. Which, depending on the host genetic background, can be associated with changes in the pro-inflammatory cytokine response in human macrophages [40]. A polyketide synthase-derived PGL produced by a subset of MTB isolates belonging to the W-Beijing family 8 demonstrates “hyperlethality” in murine disease models, while disruption of this PGL synthesis results in the loss of this hypervirulence [41]. Thus, we can reasonably assume that mutations in *pks15* may disturb its expression disrupting PGL synthesis and decreasing virulence.

We also found that 32 nonsynonymous SNPs and 7 InDels showed significant differences in at least one kind of drug resistance in L2 strains (Supplementary Table 4) and that the ins314A and ins726G mutation of *mce2B* were negatively correlated with at least two kinds of drugs resistance, suggesting that these mutations may occur more frequently in sensitive strains. Mce2B (Rv0590) is an *mce* family protein thought to be involved in host cell invasion [42]. Thus, we can infer that the ins314A and ins726G mutation is likely to disturb *mce2B* expression, which is in agreement with the results of a previous study, in which label-free comparative proteomics showed that *mce2B* was specifically upregulated in drug-resistant strains when compared to drug-sensitive strains [43].

Despite the value of our findings, there are a few limitations to this study that are worth mentioning. First, our samples include lineages 1–6, but they are not proportionately represented with L5 and L6 being significantly underrepresented in this dataset. Thus, we failed to analyze the correlation between virulence gene mutations and L5, L6, and other lineages not included in this study. Second, because of the limited accuracy and specificity of molecular resistance predictions, some second-line drugs such as MFX were not included in this study. Third, while a series of mutations were found to be independently correlated with drug resistance in L2 and L4 strains, these mutations might be sub-lineage markers and need further verification. Despite these limitations, this study suggested that there is some relationship between specific virulence gene

mutations and drug resistance in MTB which sheds new light on the importance of identifying the novel resistance mechanisms mediated by virulence genes.

Conclusions

We found some virulence gene mutations of which the occurrence has a certain association with some antibiotic resistance. Our data suggest that there may be some degree of co-selection between virulence and resistance factors, which may help MTB more easily adapt to new environments.

Acknowledgements

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Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Corresponding author

Jiazen Chen

Department of Infectious Diseases,
Huashan Hospital, Fudan University,
Rm 524, Building No.5, No.12 Middle Wulumuqi Rd.,
Shanghai 200040, China.
Phone: 86-21-52887961
Fax: 86-21-62489015
Email: jiazen_chen@163.com

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Annex – Supplementary Items

Supplementary Table 1. 332 virulence genes included in this study.

Locus	gene name	Locus	gene name	Locus	gene name
Rv0015c	<i>pknA</i>	Rv0587	<i>yrbE2A</i>	Rv1185c	<i>fadD21</i>
Rv0098	<i>Rv0098</i>	Rv0588	<i>yrbE2B</i>	Rv1192	<i>Rv1192</i>
Rv0099	<i>fadD10</i>	Rv0589	<i>mce2A</i>	Rv1204c	<i>Rv1204c</i>
Rv0100	<i>Rv0100</i>	Rv0590	<i>mce2B</i>	Rv1211	<i>Rv1211</i>
Rv0101	<i>nrp</i>	Rv0591	<i>mce2C</i>	Rv1221	<i>sigE</i>
Rv0126	<i>treS</i>	Rv0592	<i>mce2D</i>	Rv1224	<i>Rv1224</i>
Rv0153c	<i>ptbB</i>	Rv0593	<i>lprL</i>	Rv1235	<i>lpqY</i>
Rv0165c	<i>mce1R</i>	Rv0594	<i>mce2F</i>	Rv1236	<i>sugA</i>
Rv0167	<i>yrbE1A</i>	Rv0636	<i>Rv0636</i>	Rv1237	<i>sugB</i>
Rv0168	<i>yrbE1B</i>	Rv0642c	<i>mma44</i>	Rv1238	<i>sugC</i>
Rv0169	<i>mcelA</i>	Rv0643c	<i>mma43</i>	Rv1244	<i>lpqZ</i>
Rv0170	<i>mcelB</i>	Rv0655	<i>Rv0655</i>	Rv1272c	<i>Rv1272c</i>
Rv0171	<i>mcelC</i>	Rv0670	<i>end</i>	Rv1284	<i>Rv1284</i>
Rv0172	<i>mcelD</i>	Rv0687	<i>Rv0687</i>	Rv1304	<i>atpB</i>
Rv0173	<i>lprK</i>	Rv0735	<i>sigL</i>	Rv1323	<i>fad44</i>
Rv0174	<i>mcelF</i>	Rv0757	<i>phoP</i>	Rv1332	<i>Rv1332</i>
Rv0175	<i>Rv0175</i>	Rv0758	<i>phoR</i>	Rv1333	<i>Rv1333</i>
Rv0176	<i>Rv0176</i>	Rv0820	<i>phoT</i>	Rv1338	<i>murI</i>
Rv0182c	<i>sigG</i>	Rv0821c	<i>phoY2</i>	Rv1345	<i>mbtM</i>
Rv0198c	<i>zmp1</i>	Rv0899	<i>ompA</i>	Rv1348	<i>irtA</i>
Rv0199	<i>Rv0199</i>	Rv0930	<i>pstA1</i>	Rv1349	<i>irtB</i>
Rv0204c	<i>Rv0204c</i>	Rv0931c	<i>pknD</i>	Rv1371	<i>Rv1371</i>
Rv0211	<i>pckA</i>	Rv0934	<i>pstS1</i>	Rv1405c	<i>Rv1405c</i>
Rv0216	<i>Rv0216</i>	Rv0950c	<i>Rv0950c</i>	Rv1410c	<i>P55</i>
Rv0218	<i>Rv0218</i>	Rv0969	<i>ctpV</i>	Rv1411c	<i>lprG</i>
Rv0249c	<i>Rv0249c</i>	Rv0981	<i>mpmA</i>	Rv1422	<i>Rv1422</i>
Rv0326	<i>Rv0326</i>	Rv0982	<i>mpmB</i>	Rv1460	<i>Rv1460</i>
Rv0348	<i>Rv0348</i>	Rv0983	<i>pepD</i>	Rv1465	<i>Rv1465</i>
Rv0353	<i>hspR</i>	Rv0990c	<i>Rv0990c</i>	Rv1469	<i>ctpD</i>
Rv0410c	<i>pknG</i>	Rv1013	<i>pks16</i>	Rv1514c	<i>Rv1514c</i>
Rv0414c	<i>thiE</i>	Rv1016c	<i>lpqT</i>	Rv1524	<i>Rv1524</i>
Rv0427c	<i>xthA</i>	Rv1021	<i>Rv1021</i>	Rv1527c	<i>pks5</i>
Rv0432	<i>sodC</i>	Rv1028c	<i>kdpD</i>	Rv1539	<i>lspA</i>
Rv0450c	<i>mmpL4</i>	Rv1092c	<i>coaA</i>	Rv1560	<i>Rv1560</i>
Rv0467	<i>icll</i>	Rv1099c	<i>Rv1099c</i>	Rv1568	<i>bioA</i>
Rv0470c	<i>pcaA</i>	Rv1109c	<i>Rv1109c</i>	Rv1569	<i>bioF</i>
Rv0475	<i>hhbA</i>	Rv1111c	<i>Rv1111c</i>	Rv1589	<i>bioB</i>
Rv0490	<i>senX3</i>	Rv1128c	<i>Rv1128c</i>	Rv1590	<i>Rv1590</i>
Rv0491	<i>regX3</i>	Rv1144	<i>Rv1144</i>	Rv1640c	<i>lysX</i>
Rv0566c	<i>Rv0566c</i>	Rv1183	<i>mmpL10</i>	Rv1653	<i>argJ</i>
Rv0586	<i>mce2R</i>	Rv1184c	<i>Rv1184c</i>	Rv1660	<i>pks10</i>
Rv1661	<i>pks7</i>	Rv2115c	<i>mpa</i>	Rv2869c	<i>rip</i>
Rv1696	<i>recN</i>	Rv2136c	<i>Rv2136c</i>	Rv2869c	<i>rip</i>
Rv1710	<i>Rv1710</i>	Rv2200c	<i>ctaC</i>	Rv2885c	<i>Rv2885c</i>
Rv1743	<i>pknE</i>	Rv2211c	<i>gcvT</i>	Rv2912c	<i>Rv2912c</i>
Rv1795	<i>eccD5</i>	Rv2224c	<i>caeA</i>	Rv2921c	<i>fisY</i>
Rv1807	<i>Rv1807</i>	Rv2231c	<i>cobC</i>	Rv2930	<i>fadD26</i>
Rv1811	<i>mgtC</i>	Rv2234	<i>ptpA</i>	Rv2936	<i>drrA</i>
Rv1821	<i>secA2</i>	Rv2234	<i>ptpA</i>	Rv2937	<i>drrB</i>
Rv1857	<i>modA</i>	Rv2241	<i>aceE</i>	Rv2938	<i>drrC</i>
Rv1915	<i>aceAa</i>	Rv2246	<i>kasB</i>	Rv2941	<i>fadD28</i>
Rv1916	<i>aceAb</i>	Rv2275	<i>Rv2275</i>	Rv2942	<i>mmpL7</i>
Rv1930c	<i>Rv1930c</i>	Rv2277c	<i>Rv2277c</i>	Rv2945c	<i>lppX</i>
Rv1931c	<i>Rv1931c</i>	Rv2335	<i>cysE</i>	Rv2946c	<i>pks1</i>
Rv1932	<i>tpx</i>	Rv2349c	<i>plcC</i>	Rv2947c	<i>pks15</i>
Rv1936	<i>Rv1936</i>	Rv2350c	<i>plcB</i>	Rv2976c	<i>ung</i>
Rv1937	<i>Rv1937</i>	Rv2351c	<i>plcA</i>	Rv2981c	<i>ddlA</i>
Rv1938	<i>ephB</i>	Rv2359	<i>furB</i>	Rv2998	<i>Rv2998</i>
Rv1939	<i>Rv1939</i>	Rv2374c	<i>hrcA</i>	Rv3042c	<i>serB2</i>
Rv1963c	<i>mce3R</i>	Rv2383c	<i>mbtB</i>	Rv3050c	<i>Rv3050c</i>
Rv1964	<i>yrbE3A</i>	Rv2387	<i>Rv2387</i>	Rv3061c	<i>fadE22</i>
Rv1965	<i>yrbE3B</i>	Rv2388c	<i>hemN</i>	Rv3082c	<i>virS</i>
Rv1966	<i>mce3A</i>	Rv2391	<i>nirA</i>	Rv3083	<i>Rv3083</i>
Rv1967	<i>mce3B</i>	Rv2395	<i>Rv2395</i>	Rv3084	<i>lipR</i>
Rv1968	<i>mce3C</i>	Rv2396	<i>PE_PGRS41</i>	Rv3085	<i>Rv3085</i>
Rv1969	<i>mce3D</i>	Rv2428		Rv3086	<i>adhD</i>
Rv1970	<i>lprM</i>	Rv2437	<i>Rv2437</i>	Rv3087	<i>Rv3087</i>
Rv1971	<i>mce3F</i>	Rv2445c	<i>ndkA</i>	Rv3088	<i>tgs4</i>
Rv1974	<i>Rv1974</i>	Rv2472	<i>Rv2472</i>	Rv3089	<i>fadD13</i>
Rv1979c	<i>Rv1979c</i>	Rv2483c	<i>Rv2483c</i>	Rv3103c	<i>Rv3103c</i>
Rv1980c	<i>mpf64</i>	Rv2502c	<i>accD1</i>	Rv3114	<i>Rv3114</i>
Rv1981c	<i>nrdF1</i>	Rv2553c	<i>Rv2553c</i>	Rv3132c	<i>devS</i>
Rv2004c	<i>Rv2004c</i>	Rv2692	<i>trkB</i>	Rv3133c	<i>devR</i>
Rv2027c	<i>dosT</i>	Rv2696c	<i>Rv2696c</i>	Rv3151	<i>nuoG</i>
Rv2031c	<i>hspX</i>	Rv2702	<i>ppgK</i>	Rv3168	<i>Rv3168</i>
Rv2032	<i>acg</i>	Rv2703	<i>sigA</i>	Rv3178	<i>Rv3178</i>

Rv2038c	<i>Rv2038c</i>	Rv2707	<i>Rv2707</i>	Rv3210c	<i>Rv3210c</i>
Rv2040c	<i>Rv2040c</i>	Rv2711	<i>ideR</i>	Rv3223c	<i>sigH</i>
Rv2048c	<i>pks12</i>	Rv2734	<i>Rv2734</i>	Rv3229c	<i>desA3</i>
Rv2051c	<i>ppm1</i>	Rv2745c	<i>clgR</i>	Rv3236c	<i>kefB</i>
Rv2063A	<i>mazF7</i>	Rv2808	<i>Rv2808</i>	Rv3246c	<i>mtrA</i>
Rv2069	<i>sigC</i>	Rv2813	<i>Rv2813</i>	Rv3258c	<i>Rv3258c</i>
Rv2072c	<i>cobL</i>	Rv2845c	<i>proS</i>	Rv3270	<i>ctpC</i>
Rv2097c	<i>pafA</i>	Rv2857c	<i>Rv2857c</i>	Rv3277	<i>Rv3277</i>
Rv3286c	<i>sigF</i>	Rv3542c	<i>Rv3542c</i>	Rv3758c	<i>proV</i>
Rv3310	<i>sapM</i>	Rv3543c	<i>fadE29</i>	Rv3763	<i>lpqH</i>
Rv3335c	<i>Rv3335c</i>	Rv3544c	<i>fadE28</i>	Rv3781	<i>Rv3781</i>
Rv3371	<i>Rv3371</i>	Rv3545c	<i>cyp125</i>	Rv3794	<i>embA</i>
Rv3375	<i>amiD</i>	Rv3551	<i>Rv3551</i>	Rv3804c	<i>fbpA</i>
Rv3400	<i>Rv3400</i>	Rv3556c	<i>fadA6</i>	Rv3805c	<i>Rv3805c</i>
Rv3409c	<i>choD</i>	Rv3560c	<i>fadE30</i>	Rv3810	<i>pirG</i>
Rv3414c	<i>sigD</i>	Rv3563	<i>fadE32</i>	Rv3823c	<i>mmpL8</i>
Rv3416	<i>whiB3</i>	Rv3568c	<i>hsaC</i>	Rv3849	<i>espR</i>
Rv3419c	<i>gcp</i>	Rv3574	<i>Rv3574</i>	Rv3855	<i>Rv3855</i>
Rv3472	<i>Rv3472</i>	Rv3588c	<i>Rv3588c</i>	Rv3864	<i>Rv3864</i>
Rv3484	<i>cpsA</i>	Rv3614c	<i>espD</i>	Rv3866	<i>espG1</i>
Rv3489	<i>Rv3489</i>	Rv3615c	<i>espC</i>	Rv3867	<i>espH</i>
Rv3494c	<i>mce4F</i>	Rv3616c	<i>espA</i>	Rv3868	<i>eccA1</i>
Rv3495c	<i>lprN</i>	Rv3631	<i>Rv3631</i>	Rv3869	<i>eccB1</i>
Rv3496c	<i>mce4D</i>	Rv3649	<i>Rv3649</i>	Rv3870	<i>eccCa1</i>
Rv3497c	<i>mce4C</i>	Rv3651	<i>Rv3651</i>	Rv3871	<i>eccCb1</i>
Rv3498c	<i>mce4B</i>	Rv3663c	<i>dppD</i>	Rv3872	<i>Rv3872</i>
Rv3499c	<i>mce4A</i>	Rv3664c	<i>dppC</i>	Rv3873	<i>Rv3873</i>
Rv3500c	<i>yrbE4B</i>	Rv3665c	<i>dppB</i>	Rv3874	<i>esxB</i>
Rv3501c	<i>yrbE4A</i>	Rv3666c	<i>dppA</i>	Rv3875	<i>esxA</i>
Rv3502c	<i>Rv3502c</i>	Rv3671c	<i>Rv3671c</i>	Rv3876	<i>Rv3876</i>
Rv3519	<i>Rv3519</i>	Rv3682	<i>ponA2</i>	Rv3877	<i>eccD1</i>
Rv3523	<i>Rv3523</i>	Rv3683	<i>Rv3683</i>	Rv3882c	<i>Rv3882c</i>
Rv3534c	<i>Rv3534c</i>	Rv3701c	<i>Rv3701c</i>	Rv3883c	<i>mycP1</i>
Rv3540c	<i>ltp2</i>	Rv3717	<i>Rv3717</i>	Rv3910	<i>Rv3910</i>
Rv3541c	<i>Rv3541c</i>	Rv3723	<i>Rv3723</i>		

Supplementary Table 2. Accessions, locations and drug susceptibility results of phenotype or genotype prediction of all 667 isolates.

Strain ID	Accessions	Source	Country	MDR/non-MDR	Lineage	Drug susceptibility result								
						INH	RIF	EMB	PZA	LFX	SM	AM	KM	CM
SRR5817466	SRR5817466	Public database	Australia	MDR	Lineage 4	R	R	R	R	S	R	S	S	S
SRR5817467	SRR5817467	Public database	Australia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR5817470	SRR5817470	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	S	S	S	S
SRR5817473	SRR5817473	Public database	Australia	MDR	Lineage 1	R	R	S	R	S	S	S	S	S
SRR5817481	SRR5817481	Public database	Australia	MDR	Lineage 2	R	R	R	S	S	R	S	S	S
SRR6079919	SRR6079919	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6079920	SRR6079920	Public database	Australia	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR6079921	SRR6079921	Public database	Australia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR6079924	SRR6079924	Public database	Australia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR6079925	SRR6079925	Public database	Australia	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR6079930	SRR6079930	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6079931	SRR6079931	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6079933	SRR6079933	Public database	Australia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR6079934	SRR6079934	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6079935	SRR6079935	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6079937	SRR6079937	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6079942	SRR6079942	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6079944	SRR6079944	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6079945	SRR6079945	Public database	Australia	non-MDR	Lineage 2	R	R	S	S	S	S	R	S	S
SRR6079953	SRR6079953	Public database	Australia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR6079956	SRR6079956	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6079960	SRR6079960	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6079964	SRR6079964	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6079965	SRR6079965	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6079966	SRR6079966	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6079967	SRR6079967	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6117321	SRR6117321	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6117322	SRR6117322	Public database	Australia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR6117325	SRR6117325	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6117326	SRR6117326	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6117328	SRR6117328	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6117329	SRR6117329	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6117337	SRR6117337	Public database	Australia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR6117339	SRR6117339	Public database	Australia	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR6117344	SRR6117344	Public database	Australia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR6117345	SRR6117345	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6117346	SRR6117346	Public database	Australia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR6117348	SRR6117348	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6339640	SRR6339640	Public database	Australia	MDR	Lineage 1	R	R	S	R	S	R	S	S	S
SRR6339642	SRR6339642	Public database	Australia	MDR	Lineage 4	R	R	R	R	S	R	S	S	S
SRR6339649	SRR6339649	Public database	Australia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR6339653	SRR6339653	Public database	Australia	MDR	Lineage 4	R	R	R	R	S	R	S	S	S
SRR6367398	SRR6367398	Public database	Australia	MDR	Lineage 3	R	R	S	R	S	S	S	S	S
SRR6369876	SRR6369876	Public database	Australia	MDR	Lineage 2	R	R	S	R	S	S	S	S	S
SRR6369878	SRR6369878	Public database	Australia	MDR	Lineage 1	R	R	S	R	S	R	S	S	S
ERR2516166	ERR2516166	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2516169	ERR2516169	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516176	ERR2516176	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2516181	ERR2516181	Public database	Belgium	MDR	Lineage 4	R	R	R	R	R	R	R	R	R
ERR2516193	ERR2516193	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516195	ERR2516195	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516199	ERR2516199	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2516209	ERR2516209	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	S	R	R	R
ERR2516216	ERR2516216	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516222	ERR2516222	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516224	ERR2516224	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516226	ERR2516226	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2516230	ERR2516230	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2516231	ERR2516231	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516232	ERR2516232	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2516234	ERR2516234	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516237	ERR2516237	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	R	S	S	S
ERR2516239	ERR2516239	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2516241	ERR2516241	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516242	ERR2516242	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516246	ERR2516246	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516250	ERR2516250	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516261	ERR2516261	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2516263	ERR2516263	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2516264	ERR2516264	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	R	S
ERR2516266	ERR2516266	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	R	S	R	R
ERR2516280	ERR2516280	Public database	Belgium	MDR	Lineage 1	R	R	R	R	S	S	R	S	S
ERR2516285	ERR2516285	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	R	R	R
ERR2516301	ERR2516301	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	R	S	S	S
ERR2516302	ERR2516302	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	R	S	S	S
ERR2516308	ERR2516308	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	R	S	R
ERR2516326	ERR2516326	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516347	ERR2516347	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	R	S	S	S
ERR2516349	ERR2516349	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2516350	ERR2516350	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516351	ERR2516351	Public database	Belgium	MDR	Lineage 4	R	R	R	R	S	R	S	S	S
ERR2516352	ERR2516352	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	R	R	R
ERR2516356	ERR2516356	Public database	Belgium	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
ERR2516359	ERR2516359	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	R	R
ERR2516365	ERR2516365	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2516367	ERR2516367	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2516371	ERR2516371	Public database	Belgium	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR2516377	ERR2516377	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2516396	ERR2516396	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	R	S
ERR2516399	ERR2516399	Public database	Belgium	MDR	Lineage 2	R	R	R	R	S	R	S	R	R
SRR6152683	SRR6152683	Public database	Canada	non-MDR	Lineage 1	S	S	R	R	S	S	S	S	S
SRR6152771	SRR6152771	Public database	Canada	non-MDR	Lineage 1	S	S	R	R	S	S	S	S	S

SRR6152779	SRR6152779	Public database	Canada	non-MDR	Lineage 1	S	S	R	S	S	S	S	S	S	S	S
SRR6152800	SRR6152800	Public database	Canada	MDR	Lineage 3	R	R	S	S	S	R	S	S	S	S	S
SRR6152846	SRR6152846	Public database	Canada	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S	S	S
SRR6152999	SRR6152999	Public database	Canada	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
SRR6153110	SRR6153110	Public database	Canada	non-MDR	Lineage 1	S	S	R	S	S	S	S	S	S	S	S
SRR6153117	SRR6153117	Public database	Canada	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S	S	S
SRR6397333	SRR6397333	Public database	Canada	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S	S	S
SRR6397399	SRR6397399	Public database	Canada	MDR	Lineage 2	R	R	R	R	S	S	R	R	R	R	R
SRR6397408	SRR6397408	Public database	Canada	MDR	Lineage 2	R	R	R	R	R	S	R	S	S	S	S
SRR6397420	SRR6397420	Public database	Canada	MDR	Lineage 1	R	R	S	S	S	S	S	S	S	S	S
SRR6397425	SRR6397425	Public database	Canada	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
SRR6397467	SRR6397467	Public database	Canada	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
SRR6397471	SRR6397471	Public database	Canada	MDR	Lineage 2	R	R	R	R	S	R	S	S	S	S	S
SRR6397477	SRR6397477	Public database	Canada	MDR	Lineage 2	R	R	R	R	S	R	S	S	S	S	S
SRR6397521	SRR6397521	Public database	Canada	MDR	Lineage 1	R	R	S	R	S	R	S	S	S	S	S
SRR6397630	SRR6397630	Public database	Canada	MDR	Lineage 2	R	R	S	R	S	R	S	S	S	S	S
SRR6397665	SRR6397665	Public database	Canada	MDR	Lineage 2	R	R	S	S	R	S	S	S	S	S	S
SRR6397671	SRR6397671	Public database	Canada	MDR	Lineage 2	R	R	R	R	R	S	R	S	S	S	S
SRR6397697	SRR6397697	Public database	Canada	MDR	Lineage 2	R	R	S	S	S	S	S	S	S	S	S
SRR6397708	SRR6397708	Public database	Canada	MDR	Lineage 2	R	R	R	R	S	R	S	S	S	S	S
SRR6397716	SRR6397716	Public database	Canada	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
SRR6397730	SRR6397730	Public database	Canada	MDR	Lineage 2	R	R	R	R	S	R	S	S	S	S	S
SRR6397748	SRR6397748	Public database	Canada	MDR	Lineage 2	R	R	R	R	S	R	S	S	S	S	S
SRR6397753	SRR6397753	Public database	Canada	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
SRR6397784	SRR6397784	Public database	Canada	MDR	Lineage 2	R	R	R	R	S	R	S	S	S	S	S
SRR6397810	SRR6397810	Public database	Canada	MDR	Lineage 3	R	R	R	R	S	R	S	S	S	S	S
SRR6397917	SRR6397917	Public database	Canada	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
SRR6397947	SRR6397947	Public database	Canada	MDR	Lineage 2	R	R	R	R	S	R	S	S	S	S	S
SRR6397949	SRR6397949	Public database	Canada	MDR	Lineage 1	R	R	S	R	S	S	S	S	S	S	S
SRR6397957	SRR6397957	Public database	Canada	MDR	Lineage 1	R	R	S	R	S	S	S	S	S	S	S
SRR6397962	SRR6397962	Public database	Canada	MDR	Lineage 2	R	R	S	R	S	R	S	S	S	S	S
SRR6398008	SRR6398008	Public database	Canada	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
SRR6398011	SRR6398011	Public database	Canada	MDR	Lineage 2	R	R	R	R	S	R	S	S	R	S	S
SRR6398041	SRR6398041	Public database	Canada	MDR	Lineage 2	R	R	S	S	S	S	S	S	S	S	S
SRR6398050	SRR6398050	Public database	Canada	MDR	Lineage 2	R	R	S	S	S	R	S	S	S	S	S
SRR6398076	SRR6398076	Public database	Canada	MDR	Lineage 2	R	R	S	S	S	S	S	S	S	S	S
SRR6398091	SRR6398091	Public database	Canada	MDR	Lineage 2	R	R	S	R	S	R	S	S	S	S	S
SRR6398095	SRR6398095	Public database	China	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
276	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	R	S	S	S	S	S	S	S	S	S	S
646	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S	S	S
654	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
703	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	R	R	R
905	UPLOADING	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	R	R	R	R	S	S	S
911	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
1267	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
1370	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
1400	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	R	S	S	S	S
1474	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	R	S	S	S	S
1647	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	R	R	R	R	R
1711	UPLOADING	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	R	R	R	R	S	S	S
1788	SAMN10961303	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	R	S	S	S	S
2036	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
2174	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
2185	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S	S	S
2213	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	R	R	R
2291	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	R	S	S	S	S	S	S	S	S	S	S
2502	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
2521	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
14-1096	SAMN10961304	Own laboratory collection	China	MDR	Lineage 4	R	R	S	S	S	S	S	S	S	S	S
14-1521	SAMN10961309	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
14-1566	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	S	S	S	S	S
14-157	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
14-1886	SAMN10961310	Own laboratory collection	China	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S	S	S
14-1910	SAMN10961311	Own laboratory collection	China	MDR	Lineage 2	R	R	S	S	S	S	S	S	S	S	S
14-259	SAMN10961313	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
14-304	SAMN10961315	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	R	R	R	R	S	S	S
14-311	SAMN10961316	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S	S	S
14-32	SAMN10961317	Own laboratory collection	China	MDR	Lineage 2	R	R	S	S	S	R	R	S	S	S	S
14-325	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
14-38	SAMN10961320	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
14-453	SAMN10961323	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
14-456	SAMN10961324	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	R	R	R
14-50	SAMN10961325	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	S	S	S	R	S	S	S
14-547	SAMN10961327	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
14-66	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
14-80	SAMN10961330	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	R	R	R	R	S	S	S
14-84	SAMN10961331	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	R	S	S	S	S
14-87	SAMN10961332	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	S	S	S	S	S
15-1002	SAMN10961334	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	S	R	S	S	S
15-129	SAMN10961336	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	R	R	S	S	S
15-1455	SAMN10961337	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	R	R	R	R	R
15-1543	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S	S	S
15-1948	SAMN10961339	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	R	S	S	S	S
15-2011	SAMN10961340	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S	S	S
15-2170	SAMN10961342	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	S	S	S	S	S	S
15-2190	UPLOADING	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	R	R	R	R	S	S	S
15-2203	UPLOADING	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	S	R	R	S	S	S	S
15-2325	SAMN10961344	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	R	R
15-310	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	S	S	S
15-333	SAMN10961346	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	S	R	R	R	S	S	S
15-408	SAMN10961347	Own laboratory collection	China	non-MDR	Lineage 2	S	R	S	S	R	R	S	S	S	S	S
16-008	SAMN10961349	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	S	R	R	S	S	S	S
16-1136	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	R	R	S	S	S
16-122	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	R	R	R	R	R	R	R	S	S	S
16-1299	SAMN10961354	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	S	R	S	R	S	S	S

16-1785	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	R	S	S	R	S	S	S	S
16-1989	SAMN10961361	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
16-2222	SAMN10961367	Own laboratory collection	China	MDR	Lineage 2	R	R	R	S	R	R	S	S	S
16-2284	SAMN10961368	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
16-2352	SAMN10961371	Own laboratory collection	China	MDR	Lineage 2	R	R	S	R	R	R	S	S	S
16-308	SAMN10961375	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	R
16-349	SAMN10961376	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
16-3957	SAMN10961377	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
16-4165	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	R
16-4234	SAMN10961379	Own laboratory collection	China	MDR	Lineage 2	R	R	S	R	R	R	R	S	S
16-442	SAMN10961381	Own laboratory collection	China	MDR	Lineage 2	R	R	S	S	S	S	S	S	S
16-5553	SAMN10961383	Own laboratory collection	China	MDR	Lineage 2	R	R	S	S	S	S	S	S	S
16-5679	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
16-5703	SAMN10961385	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
16-705	UPLOADING	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	R	S	S	S	S
16-763	SAMN10961387	Own laboratory collection	China	MDR	Lineage 2	R	R	S	S	S	S	S	S	S
16-765	SAMN10961388	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
16-815	SAMN10961389	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
16-917	SAMN10961392	Own laboratory collection	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	R
16-994	SAMN10961393	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
17-5169	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
17-6233	UPLOADING	Own laboratory collection	China	MDR	Lineage 2	R	R	S	S	R	S	S	S	S
17-6382	SAMN10961396	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	R	S	S	S
17-6470	SAMN10961397	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
61-3	SAMN10961398	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	R	S	S	S	S
B273	SAMN10961401	Own laboratory collection	China	MDR	Lineage 4	R	R	S	S	S	S	S	S	S
C234	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
C245	SAMN10961403	Own laboratory collection	China	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
C252	SAMN10961404	Own laboratory collection	China	MDR	Lineage 4	R	R	S	S	R	S	S	S	S
C306	SAMN10961405	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	S	R	S	S	S
C526	SAMN10961406	Own laboratory collection	China	MDR	Lineage 2	R	R	S	R	S	R	S	S	S
C780	UPLOADING	Own laboratory collection	China	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
C794	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	R	S	S	S	S	S
D156	SAMN10961409	Own laboratory collection	China	MDR	Lineage 4	R	R	S	S	S	R	S	S	S
D371	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
D855	SAMN10961412	Own laboratory collection	China	MDR	Lineage 2	R	R	S	R	S	R	S	S	S
H20	SRR10333502	Own laboratory collection	China	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
H3	SRR10333503	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
L03-33	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
L03-34	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
L03-35	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
L03-36	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 4	R	S	S	S	S	S	S	S	S
L03-37	UPLOADING	Own laboratory collection	China	non-MDR	Lineage 2	S	S	S	S	R	S	S	S	S
SRR2024881	SRR2024881	Public database	China	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
SRR2024891	SRR2024891	Public database	China	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR2024892	SRR2024892	Public database	China	MDR	Lineage 2	R	R	S	R	S	R	S	S	S
SRR2024896	SRR2024896	Public database	China	MDR	Lineage 4	R	R	R	R	R	S	R	S	S
SRR2024901	SRR2024901	Public database	China	MDR	Lineage 4	R	R	R	R	R	S	R	S	S
SRR2024912	SRR2024912	Public database	China	MDR	Lineage 2	R	R	R	R	R	S	R	S	S
SRR2024913	SRR2024913	Public database	China	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR2024918	SRR2024918	Public database	China	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR2024920	SRR2024920	Public database	China	MDR	Lineage 2	R	R	R	R	R	S	R	S	S
SRR2024923	SRR2024923	Public database	China	MDR	Lineage 2	R	R	R	R	R	S	R	S	S
SRR2024928	SRR2024928	Public database	China	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR2024935	SRR2024935	Public database	China	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR2024945	SRR2024945	Public database	China	MDR	Lineage 2	R	R	S	S	S	S	S	S	S
SRR2024949	SRR2024949	Public database	China	MDR	Lineage 4	R	R	R	R	R	S	R	S	R
SRR2024961	SRR2024961	Public database	China	MDR	Lineage 2	R	R	R	R	R	R	S	R	S
SRR2024967	SRR2024967	Public database	China	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
SRR2024971	SRR2024971	Public database	China	MDR	Lineage 2	R	R	S	R	R	S	S	S	S
SRR2024978	SRR2024978	Public database	China	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR2024980	SRR2024980	Public database	China	MDR	Lineage 2	R	R	S	R	R	S	S	S	S
SRR2024993	SRR2024993	Public database	China	MDR	Lineage 2	R	R	R	R	R	S	R	S	S
SRR671769	SRR671769	Public database	China	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
SRR671784	SRR671784	Public database	China	MDR	Lineage 2	R	R	S	S	R	R	S	S	S
SRR671785	SRR671785	Public database	China	MDR	Lineage 2	R	R	S	R	R	R	R	S	S
SRR671786	SRR671786	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	R	S	S	S
SRR671787	SRR671787	Public database	China	MDR	Lineage 2	R	R	R	R	R	R	R	S	S
SRR671788	SRR671788	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671790	SRR671790	Public database	China	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
SRR671792	SRR671792	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671798	SRR671798	Public database	China	MDR	Lineage 2	R	R	S	R	R	R	S	S	S
SRR671799	SRR671799	Public database	China	MDR	Lineage 2	R	R	R	R	R	R	R	R	R
SRR671802	SRR671802	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671803	SRR671803	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671808	SRR671808	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671811	SRR671811	Public database	China	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
SRR671814	SRR671814	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671816	SRR671816	Public database	China	MDR	Lineage 2	R	R	S	R	R	S	S	S	S
SRR671823	SRR671823	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671828	SRR671828	Public database	China	MDR	Lineage 2	R	R	S	R	R	R	S	S	S
SRR671830	SRR671830	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671870	SRR671870	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671872	SRR671872	Public database	China	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR671873	SRR671873	Public database	China	non-MDR	Lineage 3	S	S	S	S	S	S	S	S	S
SRR671876	SRR671876	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671877	SRR671877	Public database	China	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
SRR671878	SRR671878	Public database	China	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR3724660	SRR3724660	Public database	Congo-Kinshasa	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
SRR3724755	SRR3724755	Public database	Congo-Kinshasa	non-MDR	Lineage 4	S	S	S	S	S	R	S	S	S
SRR3724799	SRR3724799	Public database	Congo-Kinshasa	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
SRR3724809	SRR3724809	Public database	Congo-Kinshasa	non-MDR	Lineage 4	S	S	S	S	S	S	R	S	S
SRR3724817	SRR3724817	Public database	Congo-Kinshasa	non-MDR	Lineage 4	S	S	S	S	S	S	R	S	S
SRR3724946	SRR3724946	Public database	Congo-Kinshasa	non-MDR	Lineage 3	S	S	S	S	S	S	S	S	S
SRR3724950	SRR3724950	Public database	Congo-Kinshasa	MDR	Lineage 4	R	R	S	S	S	S	S	S	S

SRR7517770	SRR7517770	Public database	Peru	MDR	Lineage 4	R	R	S	R	S	S	S	S	S
SRR7517772	SRR7517772	Public database	Peru	MDR	Lineage 4	R	R	S	R	S	S	S	S	S
SRR7517786	SRR7517786	Public database	Peru	MDR	Lineage 4	R	R	S	S	S	R	S	S	S
SRR7517787	SRR7517787	Public database	Peru	MDR	Lineage 4	R	R	S	S	S	R	S	S	S
SRR7517809	SRR7517809	Public database	Peru	MDR	Lineage 4	R	R	S	S	S	S	S	S	S
SRR7517810	SRR7517810	Public database	Peru	MDR	Lineage 4	R	R	S	R	S	S	S	S	S
SRR7517811	SRR7517811	Public database	Peru	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR7517813	SRR7517813	Public database	Peru	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
SRR7517814	SRR7517814	Public database	Peru	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
SRR7517815	SRR7517815	Public database	Peru	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
SRR7517816	SRR7517816	Public database	Peru	MDR	Lineage 4	S	R	S	R	S	S	S	S	S
SRR7517831	SRR7517831	Public database	Peru	MDR	Lineage 4	R	R	S	R	S	S	S	S	S
SRR7517834	SRR7517834	Public database	Peru	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
SRR7517835	SRR7517835	Public database	Peru	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR7517836	SRR7517836	Public database	Peru	MDR	Lineage 4	S	R	S	R	S	S	S	S	S
ERR067585	ERR067585	Public database	Russia	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR067590	ERR067590	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR108425	ERR108425	Public database	Russia	MDR	Lineage 4	R	R	S	S	S	R	S	S	S
ERR108441	ERR108441	Public database	Russia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
ERR108447	ERR108447	Public database	Russia	non-MDR	Lineage 2	R	S	S	S	S	R	S	S	S
ERR108458	ERR108458	Public database	Russia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
ERR108482	ERR108482	Public database	Russia	MDR	Lineage 4	R	R	S	S	S	R	S	S	S
ERR108489	ERR108489	Public database	Russia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
ERR117454	ERR117454	Public database	Russia	MDR	Lineage 2	R	R	S	R	S	R	R	S	R
ERR117457	ERR117457	Public database	Russia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
ERR133819	ERR133819	Public database	Russia	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR133846	ERR133846	Public database	Russia	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR133888	ERR133888	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	S	R	S	S
ERR133913	ERR133913	Public database	Russia	non-MDR	Lineage 2	R	S	S	S	S	S	S	S	S
ERR133967	ERR133967	Public database	Russia	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR133981	ERR133981	Public database	Russia	MDR	Lineage 4	R	R	S	S	S	S	S	S	S
ERR137192	ERR137192	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR137204	ERR137204	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR137216	ERR137216	Public database	Russia	non-MDR	Lineage 2	R	S	S	R	S	R	S	S	S
ERR137223	ERR137223	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR137274	ERR137274	Public database	Russia	MDR	Lineage 4	R	R	S	S	S	R	S	S	S
ERR144549	ERR144549	Public database	Russia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
ERR144559	ERR144559	Public database	Russia	non-MDR	Lineage 4	R	S	S	S	S	S	S	S	S
ERR144564	ERR144564	Public database	Russia	non-MDR	Lineage 2	R	S	S	S	S	R	S	S	S
ERR144579	ERR144579	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	S	R	S	S
ERR144620	ERR144620	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR144628	ERR144628	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	S	R	S	S
ERR144633	ERR144633	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR158572	ERR158572	Public database	Russia	non-MDR	Lineage 2	S	S	R	S	S	S	S	S	S
ERR158579	ERR158579	Public database	Russia	MDR	Lineage 4	R	R	S	R	S	R	R	R	R
ERR229984	ERR229984	Public database	Russia	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
ERR229991	ERR229991	Public database	Russia	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
ERR229997	ERR229997	Public database	Russia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
ERR230003	ERR230003	Public database	Russia	MDR	Lineage 4	R	R	S	S	S	S	S	S	S
ERR234561	ERR234561	Public database	Russia	non-MDR	Lineage 4	S	S	S	R	S	S	S	S	S
ERR234565	ERR234565	Public database	Russia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
ERR234570	ERR234570	Public database	Russia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
ERR234574	ERR234574	Public database	Russia	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
ERR234590	ERR234590	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	R	R	S	S
ERR234596	ERR234596	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	S	R	S	S
ERR234598	ERR234598	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	R	R	S	S
ERR234617	ERR234617	Public database	Russia	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
ERR234633	ERR234633	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR234645	ERR234645	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	S	R	S	S
ERR234646	ERR234646	Public database	Russia	MDR	Lineage 2	R	R	R	R	S	S	R	S	S
ERR2515112	ERR2515112	Public database	South Africa	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
ERR2515182	ERR2515182	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2515293	ERR2515293	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2515348	ERR2515348	Public database	South Africa	MDR	Lineage 1	R	R	R	R	S	S	R	S	S
ERR2515498	ERR2515498	Public database	South Africa	non-MDR	Lineage 4	S	R	S	S	S	S	S	S	S
ERR2515517	ERR2515517	Public database	South Africa	non-MDR	Lineage 2	S	S	S	S	S	S	S	S	S
ERR2515542	ERR2515542	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2515663	ERR2515663	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2515684	ERR2515684	Public database	South Africa	MDR	Lineage 2	R	R	R	R	R	R	R	R	R
ERR2515735	ERR2515735	Public database	South Africa	MDR	Lineage 2	R	R	R	R	R	R	R	R	R
ERR2515934	ERR2515934	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2515938	ERR2515938	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2515950	ERR2515950	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2515956	ERR2515956	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
ERR2516018	ERR2516018	Public database	South Africa	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
ERR2516031	ERR2516031	Public database	South Africa	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
ERR2516069	ERR2516069	Public database	South Africa	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
SRR1011449	SRR1011449	Public database	South Africa	MDR	Lineage 2	R	R	R	R	R	R	R	R	R
SRR1062863	SRR1062863	Public database	South Africa	non-MDR	Lineage 1	S	S	S	S	S	S	S	S	S
SRR1140949	SRR1140949	Public database	South Africa	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
SRR1140950	SRR1140950	Public database	South Africa	non-MDR	Lineage 4	R	S	R	S	S	S	S	S	S
SRR1140959	SRR1140959	Public database	South Africa	non-MDR	Lineage 1	R	S	R	S	S	S	S	S	S
SRR1140965	SRR1140965	Public database	South Africa	MDR	Lineage 4	R	R	R	R	R	R	S	S	S
SRR1180396	SRR1180396	Public database	South Africa	MDR	Lineage 2	R	R	R	R	R	R	S	S	S
SRR1181168	SRR1181168	Public database	South Africa	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR1181211	SRR1181211	Public database	South Africa	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR1181301	SRR1181301	Public database	South Africa	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR1181313	SRR1181313	Public database	South Africa	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR1184002	SRR1184002	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	R	R	S	S
SRR1184027	SRR1184027	Public database	South Africa	non-MDR	Lineage 4	R	S	R	S	S	S	S	S	S
SRR1184340	SRR1184340	Public database	South Africa	MDR	Lineage 4	R	R	S	R	S	R	R	R	R
SRR1184356	SRR1184356	Public database	South Africa	non-MDR	Lineage 4	S	S	S	S	S	S	S	S	S
SRR833055	SRR833055	Public database	South Africa	MDR	Lineage 4	R	R	S	R	S	S	S	S	S
SRR833080	SRR833080	Public database	South Africa	MDR	Lineage 4	R	R	R	R	S	S	S	S	S
SRR833095	SRR833095	Public database	South Africa	non-MDR	Lineage 4	S	S	S	R	S	S	S	S	S

SRR5710017	SRR5710017	Public database	Thailand	MDR	Lineage 4	R	R	R	R	R	S	S	S	S
SRR5710025	SRR5710025	Public database	Thailand	MDR	Lineage 2	R	R	S	S	S	R	S	S	S
SRR5837707	SRR5837707	Public database	Thailand	MDR	Lineage 2	R	R	R	R	S	R	S	S	S
SRR5837710	SRR5837710	Public database	Thailand	MDR	Lineage 2	R	R	R	R	R	R	R	R	R
SRR5837712	SRR5837712	Public database	Thailand	MDR	Lineage 2	R	R	S	S	S	R	S	S	S

P value of SNPs.

Virulence gene SNPs	Population mutation rate	Lineage					Drug resistance								
		L1	L2	L3	L4	INH	RIF	EMB	PZA	LFX	SM	AM	KM	CM	
Rv0015c(Q369R)	29.69%	0.000162	2.72409E-75	4.67396E-06	7.639E-46	0.013755	0.002141	0.5464	0.031465	1.87126E-08	1.04316E-14	0.011023	0.002544	0.076428	
Rv01015c(T370P)	29.39%	0.000182	1.21081E-74	5.51074E-06	3.31233E-45	0.011067	0.001683	0.353049	0.013504	1.05434E-08	9.77589E-15	0.00941	0.002067	0.680816	
Rv0015c(S385R)	6.00%	0.240389	7.60111E-09	0.126113434	6.44631E-14	0.618227	0.276534	0.966265	0.00836	0.531786287	0.002354649	0.009301	0.01211	0.000151	
Rv0101(A1048T)	2.85%	0.601384	0.000148551	0.421864589	7.06787E-07	0.118437	0.047707	0.485809	0.763352	0.390643819	0.209131637	0.434713	0.325296	0.424186	
Rv0101(L1280F)	1.35%	0.696326	0.015803151	0.833095439	0.00133539	0.215635	0.644895	0.304544	0.444819	0.30747805	0.408275927	0.847916	0.716497	0.835759	
Rv0101(S2432N)	1.35%	1.85E-33	0.015803151	0.833095439	0.02565826	0.831621	0.644895	0.725069	0.936604	0.30747805	0.276470255	0.847916	0.716497	0.835759	
Rv0101(S454P)	1.20%	0.900792	0.025484851	0.902152465	0.020859628	0.449898	0.425728	0.036326	0.017137	0.06820493	0.024137915	0.008084	0.026877	0.00913	
Rv0165c(G171A)	1.35%	0.969326	0.000282651	0.833095439	0.025658226	0.092619	0.079348	0.318086	0.444819	0.48425361	0.108182405	0.847916	0.716497	0.835759	
Rv0165c(G171R)	1.50%	0.969165	0.057564553	0.771806707	0.016861839	0.072966	0.058961	0.192765	0.754082	0.760047009	0.012009899	0.786543	0.074702	0.774456	
Rv0167(T51)	4.80%	4.1E-129	3.43323E-07	0.197005618	2.01E-06	0.229417	0.177752	0.177173	0.49242	0.010707503	0.818017073	0.206258	0.132026	0.198692	
Rv0168(A167)	3.15%	0.546973	1.002E-06	0.373272123	0.000184309	0.333622	0.370897	0.106633	0.24652	0.240775997	0.130497623	0.992302	0.763024	0.971031	
Rv0168(G248C)	6.60%	0.204016	1.09966E-09	1.6744E-127	1.30325E-08	0.825165	0.139655	0.602877	0.136545	0.133452534	0.328607167	0.314485	0.426672	0.300302	
Rv0169(G398E)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.08272	0.155111	0.909823	0.078513785	0.0012445	0.462096	0.920709	0.451352	
Rv0169(K63E)	3.75%	0.4556	0.94967E-08	0.294284865	3.59098E-05	0.060582	0.163691	0.631575	0.219171	0.922944968	0.000206596	0.30547	0.212741	0.296314	
Rv0169(S313A)	56.22%	0.000138	2.64623E-86	1.22298E-08	1.7558E-134	3.91E-05	1.41E-05	0.009772	0.185050	2.94812E-08	2.49471E-21	0.225474	0.087363	0.66418	
Rv0170(A162V)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.191488	0.244129	0.508259	0.736383	0.261900673	0.184943224	0.786543	0.656359	0.774456	
Rv0170(V87A)	2.25%	0.734072	0.00094987	0.544317466	1.44228E-05	0.9302	0.177472	0.247476	0.003553	0.121955981	0.00085714	0.670857	0.890614	0.690304	
Rv0171(G340R)	5.25%	0.295911	8.29312E-08	9.1078E-100	5.77698E-07	0.282703	0.042285	0.356989	0.464967	0.015476006	0.294969281	0.989953	0.831035	0.962195	
Rv0172(A265V)	8.25%	0.130624	4.84077E-12	0.055293993	4.52527E-19	0.776953	0.359247	0.466336	0.047536	0.036183533	0.000202572	0.570322	0.604589	0.110302	
Rv0172(I188T)	41.98%	5.31E-07	0.359048E-12	1.35556E-09	1.22214E-77	2.42E-05	6.37E-05	0.060335	0.02035	2.86684E-07	9.79195E-27	0.017162	0.003028	0.10247	
Rv0172(I67T)	2.55%	0.663188	0.000375477	0.478260314	3.19682E-06	0.034815	0.08272	0.155111	0.909823	0.078513785	0.0012445	0.462096	0.920709	0.451352	
Rv0172(V212M)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.08272	0.155111	0.909823	0.078513785	0.0012445	0.462096	0.920709	0.451352	
Rv0173(V121A)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.037472	0.08272	0.155111	0.909823	0.078513785	0.0012445	0.462096	0.920709	0.451352	
Rv0174(G408A)	2.10%	0.773616	0.00151206	0.581738545	3.06225E-05	0.000326	0.004798	0.001768	0.004747	0.141573761	0.007865663	0.595808	0.473443	0.625453	
Rv0174(L370P)	92.50%	0.026807	5.40998E-05	0.053033185	0.00035321	0.081405	0.002694	0.484464	0.566737	0.204112475	0.000146572	0.955442	0.79632	0.922254	
Rv0175(M138T)	8.10%	0.136004	7.98295E-12	0.058416209	7.82871E-19	0.702833	0.509561	0.747846	0.016217	0.26547397	0.00142588	0.24558	0.287821	0.028214	
Rv0175(N164S)	3.00%	0.573341	9.34292E-05	0.396688426	3.31875E-07	0.184046	0.163639	0.063438	0.363075	0.466412212	0.947157238	0.957458	0.812394	0.978662	
Rv0175(R89P)	6.90%	0.188045	4.15083E-10	8.95565E-134	5.94748E-09	0.673457	0.065109	0.633481	0.087475	0.086380719	0.21589886	0.631835	0.733320	0.606547	
Rv0182c(D324Y)	43.33%	4.26E-07	2.22211E-135	4.50198E-10	5.6809E-82	2.91E-06	7.67E-06	0.029126	0.017171	6.60993E-10	5.2388E-25	0.005395	0.001045	0.042624	
Rv0182c(G287D)	43.33%	4.26E-07	2.22211E-135	4.50198E-10	5.6809E-82	2.91E-06	7.67E-06	0.029126	0.017171	6.60993E-10	5.2388E-25	0.005395	0.001045	0.042624	
Rv0182c(Q204H)	2.55%	0.663188	0.000375477	0.478260314	3.19682E-06	0.044941	0.106903	0.234674	0.677239	0.090836555	0.000334269	0.491628	0.979972	0.480673	
Rv0182c(R269P)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.077866	0.037427	0.32638	0.548072	0.93186319	0.284597945	0.462096	0.920709	0.451352
Rv0182c(V39M)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.08272	0.155111	0.909823	0.078513785	0.0012445	0.462096	0.920709	0.451352	
Rv0198c(A276V)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.191488	0.244129	0.508259	0.736383	0.261900673	0.184943224	0.786543	0.656359	0.774456	
Rv0199v(V143L)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.098336	0.155111	0.909823	0.078513785	0.0012445	0.462096	0.920709	0.451352	
Rv0204c(R33C)	1.20%	0.900792	0.025484851	0.902152465	0.020859628	0.120916	0.464663	0.957656	0.835844	0.362403306	0.194526129	0.917004	0.784814	0.90482	
Rv0211(M108I)	1.80%	0.862825	0.003843533	0.667479646	3.0478E-05	0.0013146	0.000276	0.004675	0.004393	0.010234	0.191717675	0.003541886	0.681935	0.55521	0.670081
Rv0211(N101T)	2.70%	0.631269	0.006592381	0.448984342	0.000121806	0.830764	0.963492	0.346664	0.708309	0.592872168	0.712196678	0.849919	0.920709	0.870742	
Rv0218(C316R)	87.86%	0.35848	0.002449624	0.261153493	0.00793549	0.633276	0.407317	0.363503	0.552896	0.115604552	0.006505995	0.319345	0.260888	0.351745	
Rv0326(T44A)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.098336	0.155111	0.909823	0.078513785	0.0012445	0.462096	0.920709	0.451352	
Rv0410c(F706S)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.191488	0.244129	0.229417	0.177752	0.751308	0.010705703	0.818017073	0.206258	0.132026	0.198692
Rv0414c(L102P)	2.10%	0.773616	0.00151206	0.581738545	3.59087E-05	0.000276	0.004675	0.001768	0.004747	0.141573761	0.007865663	0.595808	0.473443	0.625453	
Rv0450c(A190T)	1.35%	0.969326	0.015803151	0.833095439	0.00133539	0.215635	0.269452	0.746427	0.936604	0.87246319	0.351970192	0.631835	0.733320	0.606547	
Rv0450c(D456N)	1.65%	1.61E-41	0.00614221	0.716942349	0.011114988	0.954822	0.942354	0.113858	0.71899	0.223786869	0.034199161	0.731554	0.60296	0.719571	
Rv0470c(H231Y)	1.95%	0.816388	0.002409209	0.622622622	4.50256E-05	9.06E-06	0.001806	0.002785	0.006965	0.164599513	0.002209407	0.636895	0.512261	0.625192	
Rv0588(A107T)	4.80%	4.1E-129	3.43323E-07	0.197005618	2.01E-06	0.229417	0.177752	0.177173	0.751308	0.1608973	0.206258	0.132026	0.206258	0.198692	
Rv0588(V113T)	37.93%	4.43E-06	1.9496E-108	2.79436E-08 </											

Rv1144(T11S)	6.90%	0.188045	4.15083E-10	8.9556E-134	5.54748E-09	0.673457	0.065109	0.63341	0.162356	0.086380719	0.351970192	0.631835	0.733332	0.606547	
Rv1183(K384T)	1.20%	0.900792	0.025484851	0.902152465	0.002859628	0.434157	0.425728	0.442163	0.017137	0.362403306	0.024137915	0.917004	0.784814	0.90482	
Rv1183(T408A)	43.33%	2.46E-07	2.2221E-135	4.50198E-10	5.6809E-82	6.55E-06	0.000125	0.042908	0.02695	2.30205E-09	2.65454E-24	0.005395	0.001045	0.042624	
Rv1184c(D232H)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.784767	0.825827	0.051976	0.523333	0.261900673	0.012009869	0.786543	0.656359	0.774456	
Rv1184c(M296I)	4.50%	0.365912	8.80768E-07	0.220629041	1.6022E-10	0.350832	0.068815	0.548497	0.000652	0.765802776	0.003798165	0.039987	0.03111	0.006561	
Rv1224(W8G)	55.77%	0.000844	1.31048E-86	8.58351E-09	4.5298E-132	3.79E-05	0.000197	0.020303	0.174921	1.59755E-08	7.02923E-21	0.114662	0.040013	0.424665	
Rv1244(A119T)	4.50%	1.6E-120	8.80768E-07	0.220629041	4.59639E-06	0.277411	0.073235	0.17651	0.687951	0.014197801	0.787685697	0.230422	0.151106	0.222412	
Rv1244(D208H)	3.15%	0.546973	5.84787E-05	3.89708E-58	0.000184309	0.333622	0.046815	0.050637	0.843045	0.004006154	0.246674752	0.992302	0.763024	0.971031	
Rv1272c(F301L)	1.05%	1.9E-25	0.041311055	0.980790878	0.060199544	0.169579	0.554176	0.00995	0.03727	0.429252966	0.079505325	0.995603	0.863263	0.983451	
Rv1304(F222L)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.191488	0.212591	0.508259	0.736383	0.261900673	0.184943224	0.786543	0.656359	0.774456	
Rv1348(A48V)	7.05%	0.180553	2.54518E-10	6.326E-137	3.61326E-09	0.847974	0.153355	0.543073	0.69378	0.104124855	0.172526667	0.605482	0.700318	0.580598	
Rv1348(V322F)	4.20%	5.4E-112	2.25132E-06	0.247363745	1.048E-05	0.584471	0.457616	0.175263	0.921452	0.018830662	0.93932338	0.257681	0.173106	0.249217	
Rv1371(R442S)	1.20%	0.900792	0.005645062	0.902152465	0.039198877	0.127402	0.425728	0.957656	0.835844	0.994548382	0.006087006	0.917004	0.784814	0.90482	
Rv1405c(G198D)	4.35%	3E-116	1.40876E-06	0.233568863	6.94287E-06	0.411752	0.122976	0.800597	0.016350181	0.920800285	0.243636	0.161711	0.2354		
Rv1405c(R184L)	1.80%	0.862825	0.003843533	0.667479646	0.000138146	0.000276	0.003373	0.004393	0.010234	0.191717675	0.035341886	0.681935	0.55521	0.670081	
Rv1460(P252L)	1.05%	0.823692	0.041311055	0.980790878	0.006151821	0.05592	0.063381	0.213573	0.309016	0.429252966	0.194526129	0.995603	0.863263	0.983451	
Rv1469(L96P)	1.50%	0.969165	0.001477142	0.771806707	0.016861839	0.784767	0.825827	0.7303025	0.754082	0.760047009	0.553125373	0.786543	0.656359	0.774456	
Rv1469(R294H)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.191488	0.212591	0.508259	0.736383	0.261900673	0.184943224	0.786543	0.656359	0.774456	
Rv1469(V525F)	4.35%	3E-116	1.40876E-06	0.233568863	6.94287E-06	0.411752	0.122976	0.800597	0.016350181	0.920800285	0.243636	0.161711	0.2354		
Rv1527c(A191SS)	1.05%	1.9E-25	0.041311055	0.980790878	0.060199544	0.169579	0.145652	0.00995	0.03727	0.429252966	0.079505325	0.995603	0.863263	0.983451	
Rv1527c(G130R)	2.55%	0.663188	0.00375477	0.478260314	3.19682E-06	0.883527	0.760872	0.43051	0.35895	0.288499825	0.702810939	0.491628	0.376806	0.480673	
Rv1527c(L1903R)	5.40%	0.283773	5.15388E-08	0.157447101	1.50724E-12	0.001077	0.000809	0.00051	0.000496	0.0206221489	0.03607567	0.469551	0.297823	0.452159	
Rv1527c(L2061Q)	4.65%	0.350537	1.22047E-09	0.208458995	3.04071E-06	0.004641	0.026145	0.008164	2.52E-06	0.00113211	1.53136E-08	1.45E-06	5.22E-11	2.14E-06	
Rv1527c(L2061R)	36.58%	8.47E-06	2.0216E-102	7.04785E-08	3.69354E-62	0.00366	0.003394	0.62916	0.627304	4.47023E-06	2.42501E-12	0.447701	0.564444	0.981572	
Rv1527c(P532T)	4.35%	1E-103	5.73564E-06	0.227662046	3.92382E-06	0.21824	0.070199	0.122532	0.800597	0.016350181	0.63083102	0.243636	0.161711	0.2354	
Rv1527c(P878Q)	1.35%	0.969326	0.002882651	0.833095439	0.025658262	0.096219	0.079348	0.318086	0.545176	0.118882705	0.795583645	0.847916	0.418044	0.835759	
Rv1527c(T1230A)	3.00%	0.573341	9.34292E-05	0.396688426	3.31875E-07	0.378881	0.096944	0.626891	0.363075	0.885218234	0.601658255	0.957458	0.812394	0.978662	
Rv1569(A161T)	1.80%	0.862825	0.003843533	0.667479646	0.000138146	0.000276	0.003373	0.004393	0.010234	0.191717675	0.035341886	0.681935	0.55521	0.670081	
Rv1569(A171G)	5.25%	0.295911	8.29312E-08	0.166480262	3.29693E-12	0.004347	0.024395	0.008164	2.52E-06	0.00113211	1.53136E-08	1.45E-06	5.22E-11	2.14E-06	
Rv1640c(D1001G)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.784767	0.825827	0.051976	0.523333	0.261900673	0.012009869	0.786543	0.656359	0.774456	
Rv1640c(I701T)	37.03%	6.84E-06	2.1341E-104	5.19976E-08	3.92378E-63	0.000658	0.004476	0.119759	0.015807	2.08546E-05	1.71918E-23	0.010711	0.000961	0.071961	
Rv1640c(I494V)	4.35%	3E-116	1.40876E-06	0.233568863	6.94287E-06	0.411752	0.122976	0.122532	0.800597	0.016350181	0.920800285	0.243636	0.161711	0.2354	
Rv1640c(S330A)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.191488	0.212591	0.508259	0.736383	0.261900673	0.184943224	0.786543	0.656359	0.774456	
Rv1640c(T652A)	1.80%	0.862825	0.003843533	0.667479646	0.000138146	0.000276	0.003373	0.004393	0.010234	0.191717675	0.035341886	0.681935	0.55521	0.670081	
Rv1653(S403N)	2.55%	0.663188	0.000375477	0.478260314	3.19682E-06	0.0083527	0.000125405	0.0053895	0.288499825	0.702810939	0.491628	0.376806	0.480673		
Rv1661(A2014S)	2.85%	0.601384	0.000148551	0.421864589	7.06787E-07	0.118437	0.062266	0.485809	0.763352	0.390643819	0.209131637	0.434713	0.325296	0.424186	
Rv1661(E814A)	41.98%	5.31E-07	3.59048E-128	1.35569E-08	1.22214E-77	5.70E-05	6.37E-05	0.011812	0.003077	2.32337E-10	1.59924E-20	0.002786	0.000442	0.025455	
Rv1661(O655P)	1.50%	0.969165	0.001477142	0.771806707	0.016861839	0.191488	0.212591	0.508259	0.736383	0.261900673	0.184943224	0.786543	0.656359	0.774456	
Rv1661(T558K)	5.25%	0.295911	7.99231E-11	0.166480262	5.77698E-07	0.0238872	0.194544	0.464967	0.024369244	0.036630222	0.493639	0.317093	0.475855		
Rv1661(V479G)	4.80%	4.1E-129	3.43323E-07	0.197005616	2.91E-06	0.0229417	0.177752	0.32458	0.49242	0.010707503	0.552660022	0.206258	0.132026	0.198692	
Rv1710(V561)	1.95%	0.81638	0.002409209	0.622622423	6.50256E-05	0.234053	0.261144	0.913903	0.657268	0.164595513	0.975118902	0.636895	0.512261	0.625192	
Rv1743(V91A)	1.20%	0.900792	0.005645062	0.902152465	0.039198877	0.127402	0.107222	0.168263	0.090823	0.099454832	0.006087006	0.917004	0.784814	0.90482	
Rv1795(T213A)	1.35%	0.969326	0.015803151	0.833095439	0.00135359	0.348221	0.298418	0.01885	0.000828	0.872467315	0.795583645	0.847916	0.716497	0.835759	
Rv1795(T415A)	1.35%	0.969326	0.015803151	0.833095439	0.00135359	0.348221	0.298418	0.01416112	0.0092631	0.872467315	0.795583645	0.847916	0.716497	0.835759	
Rv1811(R182H)	6.00%	0.240389	7.6011E-09	0.166482349	4.46431E-14	0.002473	0.0001204	0.008087	0.036804703	0.00755026	0.384338	0.947152738	0.957458	0.812394	0.978662
Rv1811(V871Y)	1.80%	0.573341	9.34292E-05	0.396688426	3.31875E-07	0.184044	0.138171	0.063438	0.363075	0.466412212	0.94757238	0.957458	0.812394	0.978662	
Rv1915(G179D)	69.12%	0.027848	8.36734E-40	0.131982E-11	1.9129E-135	1.18368E-09	2.1243E-110	1.01E-06	9.92E-08	0.072145	0.043325	5.58758E-22	<b		

Rv2051c(T240A)	3.00%	0.573341	9.34292E-05	0.396688426	3.31875E-07	0.184046	0.138171	0.063438	0.363075	0.466412212	0.947157238	0.957458	0.812394	0.978662	
Rv2051c(T467I)	4.35%	3E-116	1.40876E-06	0.233568863	6.94287E-06	0.411752	0.316346	0.122532	0.800597	0.016350181	0.920800285	0.243636	0.161711	0.2354	
Rv2063A(N105D)	1.05%	0.823692	0.011107921	0.980790878	0.060199544	0.169579	0.159273	0.775844	0.594203	0.854639262	0.011860066	0.995603	0.863263	0.983451	
Rv2063A(R101P)	3.90%	1.6E-103	5.73564E-06	0.277620046	2.38328E-05	0.403704	0.108456	0.03028	0.85534	0.024988424	0.65550349	0.288524	0.198542	0.2796	
Rv2072c(A284T)	2.55%	0.663188	0.000375477	0.478260314	3.19682E-06	0.044941	0.125551	0.234674	0.677239	0.090836555	0.000334269	0.491628	0.979972	0.480673	
Rv2072c(E17G)	1.05%	0.823692	0.011107921	0.980790878	0.060199544	0.05592	0.298107	0.631561	0.808573	0.429252966	0.59293467	0.995603	0.863263	0.983451	
Rv2072c(L205P)	86.36%	0.523958	2.43978E-10	0.173090573	4.12277E-12	0.058516	0.027887	0.760517	0.30737	0.041441251	2.50431E-05	0.131938	0.267217	0.151781	
Rv2211c(Q3R)	2.85%	0.601384	0.000148551	0.48260314	2.48563E-52	0.000146976	0.482296	0.076893	0.061844	0.862122	0.001177698	0.430265117	0.904877	0.864901	0.925936
Rv2224c(P65L)	2.25%	0.734072	0.00094987	0.544317466	1.44228E-05	0.185626	0.549977	0.712449	0.988531	0.121955981	0.652462772	0.558166	0.438211	0.546814	
Rv2234(A37T)	3.60%	0.476553	1.45707E-05	0.312078685	1.59386E-08	0.04081	0.068163	0.254897	0.78505	0.031188159	0.012655901	0.534107	0.804262	0.557072	
Rv2275(D131G)	4.50%	1.6E-120	8.80768E-07	0.220629041	4.95639E-06	0.495032	0.164486	0.084103	0.983591	0.014197801	0.915818212	0.230422	0.151106	0.222412	
Rv2349c(D267V)	1.20%	0.900792	0.005645062	0.902152465	0.039198877	0.449895	0.393448	0.507744	0.835854	0.999454832	0.54779371	0.917004	0.784814	0.90482	
Rv2349c(G361C)	41.23%	8.04E-07	2.6058E-124	2.44812E-09	2.55761E-75	7.21E-05	0.000188	0.148302	0.044813	2.85741E-07	1.73631E-23	0.028197	0.004782	0.148044	
Rv2350c(L469S)	2.55%	0.663188	0.000375477	0.478260314	3.19682E-06	0.359866	0.826775	0.841447	0.276963	0.090836555	0.545294223	0.491628	0.376806	0.480673	
Rv2351c(D284Y)	2.55%	0.663188	0.000375477	0.478260314	3.19682E-06	0.88352	0.760872	0.43051	0.35895	0.288499825	0.702810939	0.491628	0.376806	0.480673	
Rv2351c(P96R)	1.20%	0.900792	0.005645062	0.902152465	0.039198877	0.127402	0.393448	0.957656	0.835844	0.999454832	0.006080706	0.917004	0.784814	0.90482	
Rv2351c(T446A)	41.83%	5.78E-07	1.643E-127	5.57216E-09	3.59807E-77	0.000127	0.00305	0.102251	0.081006	7.72652E-08	7.91222E-23	0.016117	0.006593	0.09774	
Rv2359(H64R)	4.80%	8.1E-125	5.50161E-07	0.208458995	3.04071E-06	0.4178	0.06025	0.086541	0.751308	0.01070503	0.818017073	0.206258	0.132026	0.198692	
Rv2374c(S133L)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.191488	0.212591	0.508259	0.736383	0.261900673	0.184943224	0.786543	0.656359	0.774456	
Rv2383c(D713N)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.191488	0.241419	0.508259	0.736383	0.261900673	0.184943224	0.786543	0.656359	0.774456	
Rv2383c(V674L)	43.78%	1.88E-07	7.3557E-138	3.08185E-10	1.83545E-83	3.17E-06	7.96E-06	0.033522	0.007942	4.7577E-09	1.08887E-24	0.006648	0.001372	0.050107	
Rv2391(I71C)	1.20%	0.900792	0.025484851	0.902152465	4.02859626	0.449898	0.425728	0.036326	0.999454832	0.910083136	0.917004	0.784814	0.90482		
Rv2391(L372R)	1.20%	0.900792	0.025484851	0.902152465	4.02859626	0.434157	0.425728	0.036326	0.999454832	0.910083136	0.917004	0.784814	0.90482		
Rv2395(N30S)	6.90%	0.188045	4.15083E-10	8.95556E-134	5.54748E-09	0.673457	0.096793	0.63341	0.162356	0.086380719	0.351970192	0.631835	0.733332	0.606547	
Rv2395(S548P)	5.25%	4.1E-129	3.43323E-07	0.197005618	2.01E-06	0.053793	0.016103	0.240167	0.277901	0.24969821	0.174949	0.107795	0.168027		
Rv2437(Y36F)	6.00%	0.240389	2.54543E-12	0.126113434	7.10009E-08	0.361957	0.802635	0.204157	0.72141	1.13614E-05	0.22466651	0.694944	0.953564	0.783996	
Rv2483c(C189G)	4.80%	3E-116	1.40876E-06	0.233568863	6.94287E-06	0.229417	0.023326	0.086541	0.49242	0.01070503	0.552660022	0.206258	0.132026	0.198692	
Rv2483c(M161S)	2.85%	0.601384	0.000148551	0.421864589	7.06782E-07	0.118437	0.0477007	0.485809	0.763352	0.390643819	0.209131637	0.434713	0.325296	0.424186	
Rv2502c(A243V)	6.90%	0.188045	4.15083E-10	8.95556E-134	5.54748E-09	0.673457	0.096793	0.63341	0.162356	0.086380719	0.215898868	0.631835	0.733332	0.606547	
Rv2502c(F325V)	41.68%	6.28E-07	1.2925E-126	1.7203E-09	1.05341E-76	1.78E-05	0.000315	0.062404	0.02198	1.86214E-07	1.00803E-26	0.015126	0.00255	0.093178	
Rv2502c(M439I)	4.65%	8.1E-125	5.50161E-07	0.208458995	3.04071E-06	0.197104	0.042045	0.243875	0.584957	0.012329549	0.664306118	0.21798	0.141229	0.210193	
Rv2502c(V137A)	1.65%	0.913516	0.00614221	0.716942349	0.00293763	0.297224	0.326177	0.71899	0.223786869	0.3504040805	0.044447	0.108482	0.048653		
Rv2692(I133V)	55.02%	0.000616	1.632E-86	3.18994E-07	3.7018E-128	5.81E-05	0.000296	0.01207	0.175173	5.65167E-08	1.18953E-21	0.092304	0.02981	0.364602	
Rv2702(A244S)	1.35%	0.969326	0.002882651	0.833095439	0.025658262	0.831621	0.794958	0.746427	0.936604	0.35095333	0.847916	0.716497	0.835759		
Rv2702(A93S)	3.60%	0.476553	1.45707E-05	0.312078685	1.59386E-08	0.110472	0.132207	0.254897	0.78505	0.031188159	0.012655901	0.534107	0.804262	0.557072	
Rv2702(G29A)	2.25%	8.84E-58	0.00094987	0.544317466	0.002138348	0.447769	0.210559	0.083169	0.988531	0.121955981	0.0536306636	0.558166	0.438211	0.546814	
Rv2702(I203T)	94.75%	0.788668	0.001981334	0.956119381	0.01075474	0.053793	0.06903	0.567433	0.739971	0.230849234	0.01135721	0.989953	0.810335	0.962195	
Rv2702(N140S)	2.85%	0.601384	0.000148551	0.421864589	7.06782E-07	0.57879	0.326967	0.479244	0.261358	0.526955667	0.727816863	0.904877	0.925936		
Rv2813(T16V)	4.65%	5.4E-112	2.25132E-06	4.23736745	5.4E-08	0.197104	0.015719	0.423875	0.356888	0.012329549	0.421866606	0.21798	0.141229	0.210193	
Rv2869c(K95F)	1.05%	0.823692	0.000745203	0.980790878	0.060199544	0.275558	0.330919	0.631561	0.073083	0.854639262	0.819545904	0.995603	0.863263	0.983451	
Rv2869c(V259F)	55.47%	0.000745	2.64313E-86	3.83478E-08	1.725E-130	1.37E-05	0.00089	0.1379786	1.05454E-08	1.90781E-21	0.105256	0.035623	0.399964		
Rv2912c(D121M)	6.75%	0.195861	6.76058E-10	1.2388E-130	8.50753E-09	0.511925	0.036659	0.731531	0.1988	0.070841085	0.424518299	0.659167	0.767497	0.633496	
Rv2921c(a67G)	2.55%	0.663188	0.000375477	0.478260314	3.19682E-06	0.88352	0.831487	0.43051	0.35895	0.288499825	0.702810939	0.491628	0.376806	0.480673	
Rv2930(M240V)	4.80%	0.913516	0.000375477	0.478260314	6.94287E-06	0.229417	0.033236	0.086541	0.49242	0.26190673	0.350522477	0.102261	0.625192		
Rv2930(T164V)	37.93%	4.43E-06	1.9496E-108	8.9241E-66	0.00020260	0.000343	0.109691	0.010961	0.02460173	3.61799E-24	0.006623	0.0006624	0.049788		
Rv2981c(T365A)	82.91%	0.629573	5.71166E-14	0.187215497	7.68627E-16	0.718595	0.541172	0.294436	0.93692	0.15164059	0.26722	0.09405	0.029405		
Rv2998(A116P)	1.50%	0.969165	0.009837697	0.771806707	0.000625624	0.019322	0.112148	0.535104	0.736383	0.21690673	0.0780644	0.786543	0.656359	0.774456	
Rv3042c(G116E)	87.56%	0.742756	3.47551E-10	0.465780624	2.28903E-11	0.00191	0.003421	0.335417	0.746806	0.023150137	0.357528	0.52947	0.392311		
Rv3082c(D209E)	2.55%	0.663188</													

Rv3551(A7S)	5.10%	8.1E-125	5.5016E-07	0.208458995	3.04071E-06	0.189468	0.019204	0.088553	0.339286	0.008075492	0.584543315	0.184785	0.115443	0.177652		
Rv3556c(P208R)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.098336	0.155111	0.0909823	0.078513785	0.0012445	0.462096	0.920709	0.451352		
Rv3560c(G251D)	2.85%	0.601384	3.78198E-06	0.421864589	0.000416976	0.006627	0.005628	0.100206	0.01479	0.145698457	4.55559E-06	0.434713	0.864901	0.424186		
Rv3563(W275S)	56.22%	6.4E-06	1.24205E-83	1.22298E-08	1.7558E-134	3.91E-05	0.0002	0.015232	0.243553	9.06713E-08	1.10643E-20	0.225474	0.087363	0.66418		
Rv3616c(T128V)	4.95%	0.321932	2.14037E-07	0.186220391	1.56787E-11	0.631866	0.485532	0.242203	0.526128	0.587874839	0.696053505	0.545567	0.359445	0.527021		
Rv3616c(T192I)	92.95%	0.48864	0.001732758	0.254584151	0.000561912	0.264254	5.14E-05	0.761236	0.971581	0.483310285	0.001441007	0.605482	0.700318	0.580598		
Rv3649(A558G)	6.45%	0.212528	1.7864E-09	2.2119E-124	1.99425E-08	0.646726	0.054996	0.70085	0.089665	0.111278257	0.399393906	0.71685	0.839273	0.690482		
Rv3649(L93P)	55.47%	0.000745	2.26431E-86	3.83478E-07	7.235E-130	1.37E-05	7.85E-05	0.013927	0.185363	1.05454E-08	8.47562E-21	0.105256	0.035623	0.39964		
Rv3651(I179T)	7.05%	0.180553	2.54518E-10	6.326E-137	3.61326E-09	0.60395	0.053666	0.761236	0.13172	0.104124855	0.28894742	0.605482	0.700318	0.580598		
Rv3664c(A189S)	1.80%	0.862825	0.003843553	0.667479646	0.000138146	0.000276	0.004675	0.004393	0.010234	0.191717675	0.003541886	0.681935	0.55521	0.670081		
Rv3665c(T194I)	5.25%	0.295911	7.99231E-11	0.166480262	5.77698E-07	0.238872	0.194544	0.356989	0.464967	0.024369244	0.36630222	0.493639	0.317093	0.475855		
Rv3666c(E311K)	4.35%	3E-116	1.40876E-06	0.233568863	6.94287E-06	0.21824	0.159633	0.122532	0.800597	0.016350181	0.92080285	0.243636	0.161711	0.2354		
Rv3666c(P272L)	1.20%	0.090792	0.025484851	0.902152465	0.002859628	0.989424	0.393448	0.507744	0.35096	0.362403306	0.54779731	0.917004	0.784814	0.90482		
Rv3666c(Q4R)	55.62%	0.000212	3.65343E-87	2.22588E-07	2.812E-131	2.29E-05	1.84E-05	0.006862	0.114353	1.16029E-09	1.1642E-20	0.057393	0.018784	0.26325		
Rv3666c(R443Q)	4.80%	3E-116	1.40876E-06	0.233568863	6.94287E-06	0.229417	0.083005	0.086541	0.49242	0.010705703	0.552660022	0.206258	0.132026	0.198692		
Rv3671c(I363V)	55.62%	0.000105	3.65343E-87	4.90247E-07	2.812E-131	4.78E-05	1.84E-05	0.010875	0.155619	1.29886E-08	8.14756E-22	0.10988	0.037764	0.412203		
Rv3671c(V172A)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.08272	0.155111	0.0909823	0.078513785	0.0012445	0.462096	0.920709	0.451352		
Rv3682(A1619T)	41.38%	7.41E-10	4.4847E-125	2.17777E-09	8.80905E-76	5.82E-05	0.000153	0.064526	0.035619	6.5025E-26	0.013298	0.002141	0.084546			
Rv3682(P780R)	5.55%	0.272189	3.19941E-08	7.3075E-106	2.0481E-07	0.849996	0.256754	0.229624	0.18217	0.00852601	0.094860537	0.915204	0.919161	0.887525		
Rv3701(cP58Q)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.089336	0.155111	0.0909823	0.078513785	0.0012445	0.462096	0.920709	0.451352		
Rv3723(G37T)	2.85%	0.601384	0.000148551	0.421864589	7.06787E-07	0.118437	0.047707	0.485809	0.763352	0.390643819	0.209131637	0.434713	0.325296	0.424186		
Rv3723(G37V)	2.55%	0.663188	0.000375477	0.478260314	3.98162E-06	0.088305	0.155619	0.43051	0.35895	0.288499825	0.702810939	0.491628	0.376806	0.480673		
Rv3758c(N84D)	36.88%	7.35E-06	7.97992E-104	5.75718E-08	5.98535E-63	0.000417	0.003052	0.103269	0.013096	6.69061E-06	7.48965E-24	0.009981	0.00087	0.068232		
Rv3763(cC158S)	1.95%	0.81638	0.002409209	0.62262423	6.50256E-05	0.778068	0.662564	0.216871	0.06121	0.501572972	0.41669094	0.636895	0.746223	0.625192		
Rv3794(A813G)	1.20%	1.9E-29	0.025484851	0.902152465	0.039198877	0.127402	0.425728	0.004974	0.097268	0.362403306	0.042452222	0.917004	0.784814	0.90482		
Rv3794(P913S)	5.10%	9.3E-138	1.33E-07	0.176058873	7.8614E-07	0.090516	0.019204	0.319796	0.5508844	0.008075492	0.584543315	0.184785	0.115443	0.177652		
Rv3794(V206M)	1.20%	1.9E-29	0.025484851	0.902152465	0.039198877	0.989424	0.973962	0.957656	0.835844	0.362403306	0.408275927	0.917004	0.784814	0.90482		
Rv3805c(D397G)	43.63%	2.06E-07	4.9861E-137	3.49914E-10	5.79816E-83	4.05E-06	0.041739	0.01635	1.09266E-09	2.51384E-24	0.006205	0.001254	0.047503			
Rv3805c(K522R)	1.80%	0.862825	0.003843553	0.667479646	0.000138146	0.000276	0.003373	0.004393	0.010234	0.191717675	0.003541886	0.681935	0.55521	0.670081		
Rv3805c(V293M)	1.20%	1.9E-29	0.025484851	0.902152465	0.039198877	0.127402	0.425728	0.004974	0.097268	0.362403306	0.042452222	0.917004	0.784814	0.90482		
Rv3810(P268H)	2.85%	0.601384	3.78198E-06	0.421864589	0.000416976	0.026971	0.018848	0.034684	0.261358	0.145698457	3.83739E-05	0.054755	0.007426	0.060486		
Rv3823c(G235R)	5.70%	4.2E-142	2.89312E-08	0.166480262	5.77698E-07	0.060091	0.020316	0.176506	0.265452	0.00459041	0.425544248	0.148604	0.08841	0.142294		
Rv3823c(L38V)	2.25%	0.734072	0.00094987	0.544317466	1.44228E-05	0.9302	0.177472	0.247476	0.003553	0.121955981	0.00085741	0.670857	0.890614	0.690304		
Rv3823c(P696S)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.784767	0.88314	0.051976	0.523333	0.26190673	0.012009869	0.786559	0.656359	0.774456		
Rv3823c(V526A)	4.80%	3E-116	1.40876E-06	0.233568863	6.94287E-06	0.229417	0.083005	0.086541	0.49242	0.010705703	0.552660022	0.206258	0.132026	0.198692		
Rv3864(G6D)	1.50%	1.75E-37	0.009837699	0.771806707	0.016861839	0.677698	0.825827	0.051976	0.335462	0.26190673	0.012009869	0.786543	0.656359	0.774456		
Rv3864(L21V)	7.20%	0.17337	1.55855E-10	0.081199459	1.05948E-16	0.720819	0.467815	0.663153	0.040193	0.084343419	0.001441007	0.370163	0.373797	0.046049		
Rv3866(D103G)	2.55%	0.663188	0.000375477	1.46585E-46	0.000943577	0.683018	0.106903	0.1261118	0.932341	0.02438495	0.702810939	0.792571	0.979972	0.813056		
Rv3866(V21A)	2.40%	0.697367	0.000597085	0.509940621	5.91716E-06	0.014583	0.04312	0.146655	0.284842	0.10519372	0.005352521	0.523354	0.957172	0.512396		
Rv3867(K93N)	2.25%	0.734072	0.000994987	0.544317466	1.44228E-05	0.447697	0.549977	0.875465	0.604246	0.121955981	0.941079	0.558166	0.438211	0.546814		
Rv3868(E132A)	2.70%	0.631269	0.000236168	0.448984342	1.50377E-06	0.034815	0.08272	0.155111	0.0909823	0.078513785	0.0012445	0.462096	0.920709	0.451352		
Rv3868(E68K)	5.70%	0.261112	1.98386E-08	0.140880732	3.13045E-13	0.000886	0.000182	0.495032	0.392383	0.084103	0.687951	0.01417801	0.915818212	0.230422	0.151106	0.222412
Rv3869(M170I)	6.60%	0.204016	1.09966E-09	1.6744E-127	1.30325E-08	0.821565	0.139655	0.602877	0.241754	0.057386887	0.506817825	0.687498	0.802813	0.616466		
Rv3869(S215L)	1.35%	0.015803151	0.833095439	0.025658226	0.215635	0.269542	0.318086	0.444819	0.30747805	0.276470255	0.847916	0.716497	0.835759			
Rv3871(A386S)	3.75%	0.4556	6.64967E-08	0.294284865	3.59098E-05	0.001382	0.013211	0.00509738	0.005495919	8.91014E-08	1.34E-08	1.86E-14	2.18E-08			
Rv3871(P288S)	1.20%	0.900792	0.025484851	0.902152465	0.039198877	0.127402	0.425728	0.036326	0.35096	0.362403306	0.123340222	0.917004	0.784814	0.90482		
Rv3872(E99*)	93.55%	0.008423	7.58455E-05	0.684708321	0.001058108	0.365529	0.429586	0.570561	0.579585	0.40593892	0.004249777	0.804582	0.839273	0.836695		
Rv3874(E68K)	5.70%	0.261112	1.98386E-08	0.1408807												

P value of InDels

Virulence gene InDels	Population mutation rate	Lineage						Drug resistance						
		L1	L2	L3	L4	INH	RIF	EMB	PZA	LFX	SM	AM	KM	CM
Rv0165c(510InCC)	49.93%	2.82E-09	4.59E-51	7.55E-13	1.2E-104	0.162462	0.420749	0.260523	0.448419	0.906213	8.77E-11	0.756225	0.172105	0.87342
Rv0427c(567InGTA)	1.80%	1.45E-45	0.003844	0.66748	0.007344	0.887765	0.844219	0.015307	0.483804	0.191718	0.003376	0.681935	0.55521	0.670081
Rv0590(314InA)	4.50%	0.365912	2.4E-09	0.220629	4.6E-06	0.495032	0.829965	0.597961	0.983591	0.856466	0.915818	0.230422	0.896795	0.222412
Rv0590(762InG)	49.48%	2.01E-09	2.07E-49	4.64E-13	8.3E-103	0.081289	0.251988	0.182202	0.570251	0.975315	2.08E-11	0.707545	0.150267	0.822178
Rv0592(1388InC)	11.39%	0.055806	7.11E-16	5.32E-40	0.025156	0.153862	0.314406	0.001496	0.008818	0.8131	0.001812	0.824875	0.721609	0.845646
Rv0670(171DelC)	7.05%	0.180553	2.55E-10	0.085782	2.38E-16	0.397691	0.200654	0.361032	0.001799	0.276294	0.000148	0.034182	0.046085	0.001296
Rv0934(64InA)	2.70%	0.631269	0.000236	0.448984	1.5E-06	0.830764	0.88621	0.645192	0.388953	0.078514	0.712197	0.462096	0.349952	0.451352
Rv1028c(200DelCA)	5.25%	4.2E-142	8.29E-08	0.16648	5.78E-07	0.120386	0.028441	0.240167	0.464967	0.007013	0.726234	0.174949	0.107975	0.168027
Rv1192(470DelCG)	2.70%	0.631269	0.000236	0.448984	1.5E-06	0.077866	0.092454	0.616509	0.909823	0.319228	0.284598	0.462096	0.349952	0.451352
Rv1204c(105DelGGT)	5.25%	4.2E-142	8.29E-08	0.16648	5.78E-07	0.120386	0.028441	0.240167	0.464967	0.007013	0.726234	0.174949	0.107975	0.168027
Rv1660(835DelG)	4.95%	2E-133	2.14E-07	0.18622	1.33E-06	0.287025	0.083656	0.126354	0.646481	0.009299	0.97428	0.195208	0.123446	0.18786
Rv1661(170DelG)	1.80%	0.862825	0.003844	0.66748	0.000138	0.151845	0.171461	0.61378	0.915575	0.191718	0.245213	0.065091	0.148091	0.070747
Rv1661(579DelGGGC)	1.50%	1.75E-37	0.009838	0.771807	0.016862	0.191488	0.212591	0.508259	0.736383	0.261901	0.184943	0.786543	0.656359	0.774456
Rv1915(882InT)	64.92%	8.19E-05	1.16E-15	1.89E-07	2.01E-37	0.553413	0.5565	0.929033	0.013177	0.020471	0.001917	0.191486	0.988806	0.134724
Rv2275(647InG)	5.25%	4.2E-142	8.29E-08	0.16648	5.78E-07	0.120386	0.028441	0.240167	0.464967	0.007013	0.726234	0.174949	0.107975	0.168027
Rv2275(791DelCGC)	2.55%	0.663188	0.000375	0.47826	3.2E-06	0.883527	0.831487	0.43051	0.35895	0.2885	0.702811	0.491628	0.376806	0.480673
Rv2351c(1066InCACG)	6.75%	0.195861	6.76E-10	1.2E-130	8.51E-09	0.747325	0.153726	0.513374	0.109632	0.070841	0.156088	0.659167	0.767497	0.633496
Rv2388c(225InG)	1.20%	3.83E-22	0.12865	0.902152	0.039199	0.449898	0.973962	0.036326	0.35096	0.362403	0.188489	0.917004	0.784814	0.904482
Rv2553c(171DelGGT)	4.05%	0.416923	1.82E-08	0.261997	1.58E-05	0.099469	0.276018	0.414932	0.388598	0.778004	0.000643	0.27262	0.185358	0.263927
Rv2553c(171InGGT)	7.65%	0.004922	1.58E-09	0.068874	1.25E-09	0.066442	0.315159	0.034479	0.180283	0.184044	0.006406	0.5094	0.833694	0.890446
Rv2703(248DelCCG)	1.20%	0.900792	0.005645	0.902152	0.039199	0.127402	0.425728	0.957656	0.835844	0.999455	0.006087	0.917004	0.784814	0.904482
Rv3872(4DelA)	4.80%	0.91214	0.000416	0.208459	8.1E-06	0.449512	0.648682	0.913853	0.428516	0.246339	0.389264	0.206258	0.132026	0.198692
Rv3876(1395DelG)	1.35%	1.85E-33	0.015803	0.833095	0.025658	0.608093	0.644895	0.746427	0.936604	0.307478	0.27647	0.847916	0.716497	0.835759
Rv3876(1453InA)	1.50%	1.75E-37	0.009838	0.771807	0.016862	0.191488	0.212591	0.508259	0.736383	0.261901	0.184943	0.786543	0.656359	0.774456
Rv1028c(2543DelAC)	3.75%	0.4556	6.95E-08	0.294285	3.59E-05	0.001382	0.017113	0.005097	1.38E-05	0.005496	8.91E-08	1.34E-08	1.86E-14	2.18E-08
Rv1128c(918DelC)	44.53%	1.2E-07	4.4E-142	1.62E-10	5.31E-86	4.74E-06	9.04E-05	0.01645	0.008088	3.93E-10	2.09E-24	0.000456	0.000101	0.006111
Rv1371(614DelICC)	28.49%	0.000256	4.15E-71	8.96E-06	2.51E-43	0.0265	0.083638	0.847774	0.32213	2.01E-05	1.64E-10	0.150906	0.241229	0.501936
Rv1971(64DelGTGCT)	6.75%	0.195861	7.73E-14	0.095744	8.51E-09	0.001586	0.005913	0.002123	0.331993	0.158269	6.68E-10	0.09902	0.032987	0.110912
Rv1979e(14181InGCC)	1.80%	0.862825	0.003844	0.66748	0.000138	0.000276	0.003373	0.004393	0.010234	0.191718	0.003542	0.681935	0.55521	0.670081
Rv2027c(775DelG)	36.13%	1.05E-05	1.8E-100	9.51E-08	5.48E-61	0.016256	0.136586	0.30501	0.602658	0.704664	7.81E-16	0.146391	0.008645	0.184498
Rv2383c(2576DelC))	1.80%	0.862825	0.003844	0.66748	0.000138	0.000276	0.003373	0.004393	0.010234	0.191718	0.003542	0.681935	0.55521	0.670081
Rv2437(106DelA)	44.53%	1.2E-07	4.4E-142	1.62E-10	5.31E-86	3.75E-07	1E-05	0.010604	0.001777	3.93E-10	7.95E-26	0.000456	0.000101	0.006111
Rv2885c(1306InC)	54.27%	2.23E-06	6.59E-74	2.53E-09	2.3E-124	4.31E-05	0.000119	0.025718	0.13007	5.42E-07	1.72E-20	0.073579	0.021921	0.310208

Those in Lineage column with p values less than 0.05/4 are highlighted in bold and in Drug resistance column less than 0.05 are highlighted in bold and italic.

P values of mutations on pks15_1

pks15_1 SNPs & InDels	Population mutation rate	Lineage						Drug resistance					
		L1	L2	L3	INH	RIF	EMB	PZA	LFX	SM	AM	KM	CM
Rv2947c(V333A)	91.80%	0.469612	0.747531	0.840894	0.697325	0.496907	0.033072	0.95973	0.136255	0.606108	0.89156	0.972636	0.977624
Rv2946c(Q918R)	7.38%	3.88E-70	1.71E-24	0.076137	0.092438	0.014446	0.454643	0.522714	0.002565	0.046744	0.176837	0.103058	0.199382
Rv2947c(G374R)	7.65%	5.57E-73	1.88E-25	0.068812	0.122351	0.021887	0.348546	0.687918	0.002044	0.07144	0.164502	0.094131	0.18621
Rv2947c(T46I)	4.37%	0.449492	0.072218	0.234835	0.047271	0.039662	0.256465	0.024204	0.659954	0.003517	0.400141	0.283871	0.432329
Rv2946c(4126InACGG G)	1.91%	0.918256	0.362426	0.649078	0.453522	0.502437	0.48986	0.701397	0.758743	0.497952	0.861279	0.716503	0.898682
Rv2946c(714InC)	2.46%	1.29E-21	4.48E-08	0.50827	0.280664	0.324286	0.933832	0.805726	0.149389	0.03051	0.713591	0.572627	0.750526

Those in Lineage column with p values less than 0.05/3 are highlighted in bold and in Drug resistance column less than 0.05 are highlighted in bold and italic.