Table S1: Mutations in *pncA* and its UFR in PZA^{R} *M. tuberculosis* clinical isolates

Locus	Nucleotide change	Codon change	Amino acid change	PZase activity[a]	No. of isolates
UFR	A -11G	-	-	N	5
	A -11 C	-	-	N	1
	T-12 C	-	-	N	1
	C -70[#]	insertion	Frameshift	WP	1
	T -122	deletion	Frameshift	P	1
	C -131[#]	insertion	Frameshift	P	1
	C -114, A -11G	deletion + substitution	Frameshift + substitution	P[##]	1
pncA+UFR	A -17[#], G255[#]	insertion	Frameshift	N	1
	C -110G, C169T	CAC → TAC	His57Tyr	N	1
	C-112ins, T476G	CTG → CGG	Leu159Arg	N	2
	G -115C, C512T	GCG → GTG	Ala171Val	N	2
	G -119C, T355G	TGG → GGG	Trp119 Gly[#]	N	1
	A-144ins, A403C	ACC → CCC	Thr135 Pro	N	1
	A-144ins, A422C	CAG → CCG	Gln141 Pro	N	2
	T-155A, T416C	GTG → GCG	Val139Ala	N	2
pncA^{C}	T2C	ATG → ACG	Met1Thr	N	1
	C8A	GCG → GAG	Ala3Glu	N	2
	T11G	TTG → TCG	Leu4Ser	N	2
	T20G	GTC → GGC	Val7Gly	N	3
	T20C	GTC → GCC	Val7Ala[#]	N	2
	CGACGTG 21-27[#]	deletion	Frameshift	N	2
	A23G	GAC → GGC	Asp8Gly	N	3
	C24G, G25C, A478C	GAC → GAG, GTG → CTG, ACA → CCA	Asp8Glu, Val9Leu, Thr160Pro	N	1
	C28T	CAG → TAG	Gln10Stop	N	1
	A29G	CAG → CGG	Gln10Arg	N	3
	A29C	CAG → CCG	Gln10Pro	N	1
	A35G	GAC → GGC	Asp12Gly[#]	N	1
	C51[#]	deletion	Frameshift	N	2
	T52[#]	deletion	Frameshift	N	2
	C52[#]	insertion	Frameshift	N	1
	GCTGGCG 54-60[#]	insertion	Frameshift	N	1
	G71A[#]	GGC → GAC	Gly24Asp	N	1
	T80G[#]	CTG → CGG	Leu27Arg	N	3
	C83A	GCC → GAC	Ala28Asp	N	2
	T104C	CTG → CCG	Leu35Pro	N	1
	A128[#]	deletion	Frameshift	N	2
	G133T[#]	GTG → TTG	Val45Leu	N	3
	C137A	GCA → GAA	Ala46Glu	N	3
	A142T[#]	AAG → TAG	Lys48Stop	N	1
	A143G	AAG→ AGG	Lys48Arg	N	2
	A146G	GAC → GGC	Asp49Gly	N	2
	A152G	CAC → CGC	His51Arg	N	1
	A152C	CAC → CCC	His51Pro	N	1
	C161T	CCG → CTG	Pro54Leu	N	3
	C161A	CCG → CAG	Pro54 Gln[#]	N	1
	G162A	CCG → CCA	Pro54Pro	P	2
	G162	deletion	Frameshift	N	2
	T165[#]	deletion	Frameshift	N	3
	A170C	CAC → CCC	His57Pro	N	2
	T173C	TTC → TCC	Phe58Ser	N	2
	ACACCGGACT 181-190[#]	deletion	Frameshift	N	2
	C185T	CCG → CTG	Pro62Leu	N	2
	C189A	GAC → GAA	Asp63Glu	N	3
	T196C	TCG → CCG	Ser66Pro	N	2
	T199C	TCG → CCG	Ser67Pro	N	2
	A212G	CAT → CGT	His71Arg	N	3
	A226C	ACT → CCT	Thr76 Pro	N	3
	G233A	GGC → GAC	Gly78Asp	N	2
	T246[#]	deletion	Frameshift	N	1

	T254G	CTG → CGG	Leu85Arg	N	2
	T254C	CTG → CCG	Leu85Pro	N	3
	C263A	TCG → TAG	Ser88Stop	N	2
	T269G	ATC → AGC	ile90Ser	N	3
	G279[#]	insertion	Frameshift	N	2
	T281G[#]	TTC → TGC	Phe94Cys	N	2
	C282G[#]	TTC → TTG	Phe94Leu	N	2
	A286G	AAG → GAG	Lys96Glu	N	2
	A287G	AAG → AGG	Lys96Arg	N	1
	G290A	GGT → GAT	Gly97Asp	N	4
	A296[#]	deletion	Frameshift	N	1
	A298C[#]	ACC → CCC	Thr100Pro	N	3
	C299T[#]	ACC → ATC	Thr100Ile	N	2
	G304C	GCG → CCG	Ala102Pro[#]	N	2
	T307C	TAC → CAC	Tyr103His	N	1
	C309A	TAC → TAA	Tyr103Stop	N	3
	C309G	TAC → TAG	Tyr103Stop	N	3
	G311T[#]	AGC → ATC	Ser104Ile	N	3
	C312A	AGC → AGA	Ser104Arg	N	2
	G313T[#]	GGC → TGC	Gly105Cys	N	2
	G313[#]	insertion	Frameshift	N	2
	G314A	GGC → GAC	Gly105Asp	N	1
	CTTCGAAGGAGTCGA 314-329[#]	insertion	Frameshift	N	2
	A320[#]	deletion	Frameshift	N	2
	A340C	ACG → CCG	Thr114Pro	N	2
	G356A[#]	TGG → TAG	Trp119Stop	N	2
	T359C	CTG → CGG	Leu120Pro	N	2
	A365, A366[#]	deletion	Frameshift	N	3
	T383, G546[#]	insertion	Frameshift	N	1
	TGTGGTCGG 387-395[#]	deletion	Frameshift	N	2
	GGTCG 389-394[#]	deletion	Frameshift	N	2
	G390	insertion	Frameshift	N	3
	G391	insertion	Frameshift	N	2
	G395A	GGT → GAT	Gly132Asp	N	2
	T396, T397[#]	deletion	Frameshift	N	1
	A407G	GAT → GGT	Asp136Gly	N	4
	T408[#]	insertion	Frameshift	N	2
	G415C	GTG → CTG	Val139Leu	N	2
	T416G	GTG → GGG	Val139Gly	N	3
	T416C	GTG → GCG	Val139Ala	N	3
	C421T	CAG → TAG	Gln141Stop	N	1
	A424C	ACG → CCG	Thr142Pro	N	3
	A424G	ACG → GCG	Thr142Ala	N	2
	C425T	ACG → ATG	Thr142Met	N	4
	C437T	GCG → GTG	Ala146Val	N	2
	TTGGCCACCAGGGTG 451-465[#]	deletion	Frameshift	N	3
	T452C[#]	TTG → TCG	Leu151Ser	N	2
	C455[#]	deletion	Frameshift	P	1
	G461[#]	insertion	Frameshift	WP	2
	GTGGACCTGACA 469-480[#]	deletion	Frameshift	N	1
	G483	insertion	Frameshift	N	2
	G485A	GGT → GAT	Gly162Asp	N	1
	T490C	TCG → CCG	Ser164Pro	N	1
	C494[#]	deletion	Frameshift	N	2
	CGCCAGCGTCGA 531-542[#]	deletion	Frameshift	N	1
	T545G	TTG → TGG	Leu182Trp[#]	N	2
	T545C	TTG → TCG	Leu182Ser	N	1

UFR: mutations only in upstream flaking region (UFR) of *pncA*. *pncA*+UFR: mutations both in UFR and *pncA*.. *pncA*^{C}: mutations only in the coding region of *pncA*. [a] P: positive, N: negative, WP: Weakly positive, ins: insertion; del, deletion. P[##]: novel phenomena first-time in this study. [#] indicates the novel mutations in PZA^{R} strains in this study.

Table S2: Results of sequencing analysis of *rpsA, panD, Rv2783c* and *Rv2044c-pncA-Rv2042c* in PZA^R isolates

Genes	Nucleotide position	Codon change	Amino acid change	PZase activity[a]	No. of isolates
Rv2044c	T208C, T212A, T238G	TAC→ CAC, ATC→ AAC, TGG→ GGG	Tyr70His[#], Ile71Asn[#], Trp80Gly[#]	N	1
	G239T, C245A	TGG→ TTG, GCC→ GAC	Trp80Leu[#], Ala82Asp[#]	N	1
rpsA	A485G	CAG → CGG	Gln162Arg[#]	P	3
	C1235T	GCC→ GTC	Ala412Val[#]	P	2
	C86T	ACG→ ATG	Thr29Met	P	2
panD	T395C	Leu→ Pro	Leu132 Pro[#]	P	2
	C400T	Pro→ Ser	Pro134Ser	P	2
Rv2783c	T445C, C1893T	TCC→ CCC, ATC→ ATT	Ser149Pro[#], Ile631Ile	P	1
	G444T, T445C	GCG→ GCT, TCC→ CCC	Ala148Ala, Ser149Pro[#]	P	2

[a] Negative (N), Positive (P). [#] indicates the novel mutations in *Rv2044c, rpsA, panD* and *Rv2783c* genes.
rpsA gene frequently showed A636C, Arg→Arg synonymous mutation in both PZA^S and PZA^R strains.
*Note: All 448 tested *M. tuberculosis* strains had WT *clpC1* without any mutation in coding or its upstream region.

Table S3: Mutations distribution in PZA^{S} *M. tuberculosis* clinical isolates

pncA			***rpsA***	***panD***	***Rv2783c***	***clpC1***	**PZase activity**	**No. of isolates**
Nucleotide change	**Codon change**	**Amino acid change**						**n = 179**
T92G	ATC → AGC	Ile 31 Ser	WT	WT	WT	WT	P	2
A139G	ACC → GCC	Thr 47Ala	WT	WT	WT	WT	P	1
A159	insertion	Frameshift	WT	WT	WT	WT	P	1
T213C	CAT → CAC	His 71 His	WT	WT	WT	WT	P	1
C428T	GCC → GTC	Ala 143 Val	WT	WT	WT	WT	P	1
A446G	AAT → AGT	Asn 149 Ser	WT	WT	WT	WT	P	1
G477A	CTG → CTA	Leu 159 Leu	WT	WT	WT	WT	P	1
T488C	GTG → GCG	Val 163 Ala	WT	WT	WT	WT	P	1
G513T	GCG → GCT	Ala 171 Ala	WT	WT	WT	WT	P	1
WT	WT	WT	WT	WT	WT	WT	P	169

* PZase = Pyrazinamidase ; P = Positive ; WT = Wild-type