

Genome-wide analysis to detect multi-drug resistance genes in *Mycobacterium tuberculosis* strains SWLPK and MNPK resourced from Pakistan

Supplementary Material

Table S1. 24 multi-drug resistance proteins in *M. tuberculosis* strains SWLPK, MNPK, and H37Rv (NuoG)

MDR Proteins Name	SWLPK	H37RV (NuoG)	MNPK
RpoB	+	+	+
RpoA	+	+	+
RpoC	+	+	+
KatG	+	+	+
InhA	+	+	+
OxyR	+	+	+
AhpC	+	+	+
kasA	+	+	+
RpsA	+	+	+
FurA	+	+	+
EmbA	+	+	+
EmbB	+	+	+
EmbC	+	+	+
PncA	+	+	+
RpsL	+	+	+
GidB	+	+	+
PrcA	+	+	+
EthR	+	+	+
Pare1	+	+	+
ThyA	+	+	+
Ddl	+	+	+
CycA	+	+	+
RibD	+	+	+
FolC	+	+	+

Table S2. *M. tuberculosis* H37Rv genes with high probabilities of being essential

Rv no.	Gene description	Probability (%)
0404	Acyl-CoA synthase (fadD30)	83
2006	Trehalose-6-phosphatase	83
3193c	Probable integral membrane protein	83
2024c	Conserved hypothetical protein	82
3859c	Glutamate synthase (gltB)	82
1536	Isoleucyl-tRNA synthase	81
1161	Nitrate reductase [a] subunit (narG)	79
0041	Leucyl-tRNA synthase (leuS)	79
2524c	Fatty acid synthase (FasI)	78
0064	Probable membrane protein	77
1640c	C-term Lysyl-tRNA synthase (lysX)	76
2476c	Conserved hypothetical protein	75
1753c	PPE-family protein	75
0107c	Probable Mg transport ATPase	75
2967c	Pyruvate carboxylase	75

(Rv numbers refer to the annotated gene numbers in *M. tuberculosis* H37Rv)

Table S3. Families of 24 drug resistance proteins from *M. tuberculosis* strains SWLPK, MNPK and H37Rv (NuoG)

Proteins Name	Drugs name	Strains containing genes	Domains	E value	Identities (%)
RpoC	Rifampin	SWLPK & MNPK	DNA-directed RNA polymerase, subunit beta prime	0.0	95
		H37Rv (NuoG)	DNA-directed RNA polymerase, subunit beta prime		
RpoB	Rifampin	SWLPK & MNPK	DNA-directed RNA polymerase, subunit beta prime	0.0	90
		H37Rv (NuoG)	DNA-directed RNA polymerase, subunit beta prime		
RpoA	Rifampin	SWLPK & MNPK	DNA-directed RNA polymerase, subunit beta prime	0.0	99
		H37Rv (NuoG)	DNA-directed RNA polymerase, subunit beta prime		
PrcA	Fluoro-quinolones	SWLPK & MNPK	Proteasome, subunit alpha/beta	0.0	98
		H37Rv (NuoG)	Proteasome, subunit alpha/beta		
KatG	Isoniazid	SWLPK & MNPK	Catalase-peroxidase haem	0.0	99
		H37Rv (NuoG)	Catalase-peroxidase haem		
InhA	Isoniazid	SWLPK & MNPK	Enoyl-[acyl-carrier-protein] reductase (NADH)	0.0	100
		H37Rv (NuoG)	Enoyl-[acyl-carrier-protein] reductase (NADH)		
OxyR	Isoniazid	SWLPK & MNPK	Winged helix-turn-helix DNA-binding domain	1 ⁻¹⁴	34
		H37Rv (NuoG)	Winged helix-turn-helix DNA-binding domain		
AhpC	Isoniazid	SWLPK & MNPK	Peroxiredoxin, AhpC-type	1 ^{-14b}	100
		H37Rv (NuoG)	Peroxiredoxin, AhpC-type		
KasA	Isoniazid	SWLPK & MNPK	Thiolase-like	0.0	99
		H37Rv (NuoG)	Thiolase-like		
RpsA	Pyrazinamide	SWLPK & MNPK	Isochorismatase-like	0.0	100
		H37Rv (NuoG)	Isochorismatase-like		
FurA	Isoniazid	SWLPK & MNPK	Ferric-uptake regulator	3 ⁻⁸⁶	99
		H37Rv (NuoG)	Ferric-uptake regulator		
EmbA	Ethambutol	SWLPK & MNPK	Arabinofuranosyltransferase, N-terminal	0.0	99
		H37Rv (NuoG)	Arabinofuranosyltransferase, N-terminal		
EmbB	Ethambutol	SWLPK & MNPK	Arabinofuranosyltransferase, N-terminal	0.0	98
		H37Rv (NuoG)	Arabinofuranosyltransferase, N-terminal		
EmbC	Ethambutol	SWLPK & MNPK	Arabinofuranosyltransferase, N-terminal	0.0	97
		H37Rv (NuoG)	Arabinofuranosyltransferase, N-terminal		
PncA	Pyrazinamide	SWLPK & MNPK	Isochorismatase-like	1 ⁻¹¹⁰	95
		H37Rv (NuoG)	Isochorismatase-like		
RpsL	Streptomycin	SWLPK & MNPK	Ribosomal protein S12/S23	1 ⁻⁸⁷	100
		H37Rv (NuoG)	Ribosomal protein S12/S23		
GidB	Streptomycin	SWLPK & MNPK	rRNA small subunit methyltransferase G	1 ⁻⁸⁹	100
		H37Rv (NuoG)	rRNA small subunit methyltransferase G		
ParE1	Fluoro-quinolones	SWLPK & MNPK	Toxin-antitoxin system, RelE/ParE toxin family	1 ⁻⁷¹	100
		H37Rv (NuoG)	Toxin-antitoxin system, RelE/ParE toxin family		
EthR	Ethionamide	SWLPK & MNPK	DNA-binding HTH domain, TetR-type	e ⁻¹⁶⁰	100
		H37Rv (NuoG)	DNA-binding HTH domain, TetR-type		
ThyA	Para-Amino Salicylic Acid	SWLPK & MNPK	Thymidylate synthase	0.0	99
		H37Rv (NuoG)	Thymidylate synthase		
RibD	Para-Amino Salicylic Acid	SWLPK & MNPK	Riboflavin biosynthesis protein rib	0.0	90
		H37Rv (NuoG)	Riboflavin biosynthesis protein rib		
FolC	Para-Amino Salicylic Acid	SWLPK & MNPK	Folypolyglutamate synthetase	0.0	90
		H37Rv (NuoG)	Folypolyglutamate synthetase		
Ddl	Cycloserine	SWLPK & MNPK	D-alanine--D-alanine ligase	0.0	80
		H37Rv (NuoG)	D-alanine--D-alanine ligase		
CycA	Cycloserine	SWLPK & MNPK	Amino acid/polyamine transporter I	0.0	100
		H37Rv (NuoG)	Amino acid/polyamine transporter I		

Table S4. Multi-drug resistance proteins docked with the proteins of *M. tuberculosis* strains SWLPK, MNPK, H37Rv (NuoG) and their binding energy values using PatchDock.

MDR Proteins	PDB ID	<i>M. tuberculosis</i> SWLPK (PatchDock)	<i>M. tuberculosis</i> MNPK (PatchDock)	<i>M. tuberculosis</i> H37Rv (NuoG) (PatchDock)
RpoB	5UH5	-17.40	-589.61	- 2.87
RpoA	5ZX2	-21.93	4.39	-13.64
RpoC	5UH5	-1.0	-8.93	- 3.46
KatG	2CCA	-12.67	-7.71	-15.80
InhA	6SQ5	-20.38	-14.38	-54.72
AhpC	2BMX	-16.91	-13.17	-4.63
KasA	4C6U	-16.67	-4.44	-17.35
RpsA	4NNI_	-1.16	-10.08	-12.72
EmbA	7BVF	-6.42	-34.57	-38.46
EmbB	7BVF	-42.91	-54.32	-28.06
PncA	3PL1	-16.12	-24.84	-16.72
RpsL	5V93	- 3.36	-16.29	-3.87
PrcA	3H6F	-15.62	- 10.55	-3.00
EthR	3G1L	-34.65	-5.83	-9.17
ThyA	4FOG	-42.94	-52.40	-29.07
Ddl	3LWB	-33.63	-14.87	-32.92
FolC	2VOR	-5.42	-15.28	-29.28

Table S5. Molecular docking analysis and interacting residues with *M. tuberculosis* strains SWLPK, MNPK and H37Rv (NuoG)

MDR Proteins	<i>M. tuberculosis</i> SWLPK	<i>M. tuberculosis</i> MNPK	<i>M. tuberculosis</i> H37Rv (NuoG)
RpoB	Leu64, Ala65, Asn81, Pro82, Val83, Glu88, Tyr91, Gly92, Ile328, Thr329, Ser330, Ser331, Thr332	Asn5, Phe6, Phe7, Asp8, Gly9, Leu10, Arg11, Ile12, Arg13, Lys14, Ala15, Glu598, His599, Asp600, Asp601, Ala602, Asn603	Glu13, Gly23, Val24, Gly25, Ile26, Val399, Glu402, Arg403, Asn419, Arg421, Pro422, Asp761, Gly765, Ala766, Glu768
RpoA	Gln5, Arg6, Pro7, Thr8, Leu9, Tyr146, Val147, Pro148, Ile151, Asp152, Gln155, Gln156	Gln5, Arg6, Pro7, Thr8, Leu9, Lys407, Gly408, Lys409, Gln410	Gln5, Arg6, Pro7, Thr8, Leu9, Pro422, Asp761, Gly765, Ala766, Glu768
RpoC	Asp3, Val4, Phe6, Arg54, Gln55, Ser56, Lys260, Gly261, Gly262, Lys458, Leu459, Asp462, Leu463	Gly287, Gln288, Leu290, Arg291, Gln435, Lys437, Gly604, Asp605, Pro606, His607, Gly608	Asp3, Val4, Arg21, Tyr25, Ile73, Ile74, Cys75, Arg75, Cys76, Gly77, Arg419, His420, Arg421, Val422, Pro423
KatG	Meth26, Lys27, Tyr28, Asp42, Pro43, Gly44, Ala45, Gly46, Asn47, Gly289, Ala290, Ala291, Gly294, Gln255, Meth256	Tyr28, Pro29, Val30, Gly31, Gln32, Leu42, Lys43, Leu48, His49, Lys152, Lys153, Lys154, Ser138, Val139, Asp140, Gly141, Gly142	Pro43, Gly44, Ala45, Gly46, Asn47, Gly289, Ala290, Ala291, Gly294, Gln255, Meth256, Cys76, Gly77, Arg419, His420, Arg421, Val422, Pro423
InhA	Pro43, Gly44, Tyr72, Asn73, Arg153, Ala154, Glu209, Glu210, Ala211, Thr253, Thr254, Gly255, Asp256	Leu42, Arg43, Leu44, Arg45, Glu98, Glu100, Leu101, Asp150, Pro151, Ser152, Val432, Gly433, Pro434, Gln435	Glu98, Glu100, Leu101, Asp150, Pro151, Ser152, Val432, Gly433, Pro434, Gln435
AhpC	Asp22, Leu23, Ser24, Asp40, Pro43, Gly44, Ala45, Gly46, Asn47, Ala49, Asp50, Gln55, Ser56, Gly57	Pro2, Leu4, Asp8, Gln9, Pro12, Tyr13, Lys14, Val26, Asp27, Ala28, Lys29, Gln30, Pro31, Gly32, Asp33	Gln120, Ala121, Ala122, Gly123, Asn126, Ala127, Asp128, Pro140, Asn141, Asn142
kasA	Gln3, Pro4, Phe11, Arg107, Gly111, Leu112, Ala119, Leu120, Ser70, Asn73, Asp74, Arg76, Ala77, His78	Phe7, Asp8, Gly9, Asp69, Met77, Gly115, Leu116, Ala119, Glu120, Val123, Tyr126	Met129, Asn130, Pro134, Arg135, Val142, Pro143, Asn144, Ser272, Ala273, Phe274, His275, Met276
RpsA	Leu37, Ala38, Leu39, Asp40, Asp42, Pro43, Gly44, Ala45, Gly46, Ala327, Glu328, Arg329, His330, Met432, Glu433, Lys434, Phe435, Ala436, Ala437, Ala438	Asp42, Pro43, Gly44, Ala45, Gly46, Ala327, Glu328, Arg329, His330, Met432, Glu433, Lys434, Phe435, Ala436, Ala437, Ala438	Arg54, Ser55, Gln56, Arg329, His330, Met432, Glu433, Lys434, Phe435, Ala436, Ala437, Ala438
EmbA	Asn73, Arg76, Ser80, Val81, Asn82, Ala83, Val84, Asn85, Leu86, Glu87, Phe248, Ala249, Leu252, Ala255, Ala256, Ala259, Arg353, Val354, Phe362	Leu86, Glu87, Phe248, Ala249, Leu252, Ala255, Ala256, Ala259, Arg353, Val354, Phe362	Leu252, Ala255, Ala256, Ala259, Arg353, Val354, Phe362, Arg413, Asn414, Asn415
EmbB	Val29, Ile36, Leu40, Arg213, Thr216, Val227, Ala228, Val230, Val231, Ile234, Trp237, Arg238, Gln241, Arg413, Asn414, Asn415, Gly416, Tyr417, Gln418	Val230, Val231, Ile234, Trp237, Arg238, Gln241, Arg413, Asn414, Asn415, Gly416, Tyr417, Gln418	Trp237, Arg238, Gln241, Arg413, Asn414, Asn415, Gly416, Tyr417, Gln418, Gln452, Pro453, Gly454, Arg455
PncA	Met1, Tyr34, Ala38, Ala39, Asp40, Tyr41, Leu117, Arg121, Arg148, Asn149, Gly150, Leu151, Ala152, Thr153, Arg154, Ser406, Val407, Leu409, Asp410	Arg148, Asn149, Gly150, Leu151, Ala152, Thr153, Arg154, Ser406, Val407, Leu409, Asp410, Arg413, Asn414	Arg148, Asn149, Gly150, Leu151, Ala152, Thr153, Arg154, Ser406, Val407, Leu409, Asp410, Arg413
RpsL	Pro2, Thr3, Gln5, Gln6, Leu7, Val8, Lys9, Gly10, Arg11, Arg12, Asp42, Pro43, Gly44	Phe6, Phe7, Asp8, Glu9, Lys71, Leu7, Val8, Arg9, Lys10, Gly11, Arg12, Arg13, Asp14, Lys15, Ile16, Ser17, Lys18, Val19, Lys20, Val21, Lys22, Thr23, Ala24	Met1, Thr2, Gln3, Ala4, Ala5, Val11, Gln14, Gly11, Arg12, Arg13, Asp14, Lys15, Ile16, Ser17, Lys18, Val19, Lys20, Val21, Lys22, Thr23, Ala24
PrcA	Lys28, Pro43, Gly44, Ala45, Ala49, Asp50, Glu43, Pro46, Arg48, Ser49, Leu50, Gln51, Arg413, Asn414, Asn414, Gly415	Glu43, Pro46, Arg48, Ser49, Leu50, Gln51, Arg456, Ile457, Leu478, Trp656, Gln657, Pro658, Gly659	Pro1, Glu2, Met13, Glu43, Pro46, Arg48, Ser49, Leu50, Gln51, Met1, Thr2, Gln3, Ala4, Ala5, Val11, Gln14
EthR	Gly22, Asp23, Asp24, Leu27, Ala28, Asp77, Arg78, Asn81, Gln82, Ala83, Asp84, Arg413, Asn414, Asn414, Gly415	Ala28, Asp77, Arg78, Asn81, Gln82, Ala83, Asp84, Arg456, Ile457, Leu478, Trp656, Gln657, Pro658, Gly659	Met1, Thr2, Gln3, Ala4, Ala5, Val11, Gln14, Gly22, Asp23, Asp24, Leu27, Ala28, Asp77, Arg78, Asn81
ThyA	Met1, Thr2, Pro3, Asp6, Gln33, Met34, Arg35, Asp37, Ser39, Ala40, Gly41, Arg413, Asn414, Asn414, Gly415	Pro3, Asp6, Gln33, Met34, Arg35, Asp37, Ser39, Ala40, Gly41, Arg456, Ile457, Leu478, Trp656, Gln657, Pro658	Met1, Thr2, Gln3, Ala4, Ala5, Val11, Gln14, Pro3, Asp6, Gln33, Met34, Arg35, Asp37, Ser39, Ala40, Gly41
Ddl	Pro43, Gly44, Ala45, Ala49, Asp50, Gly19, Ala20, Val29, Ile50, Thr51, Pro52, Ala53, Gly119, Pro120, Tyr121, Gly122, Ser200, Ser201, Ile202	Thr51, Pro52, Ala53, Gly119, Pro120, Tyr121, Gly122, Ser200, Ser201, Ile202, Arg456, Ile457, Leu478, Trp656, Gln657, Pro658, Gly659	Thr2, Gln3, Ala4, Ala5, Val11, Gln14, Ala53, Gly119, Pro120, Tyr121, Gly122, Ser200, Ser201, Ile202
FoIC	Pro47, Ser48, Leu49, Thr50, Ser53, Ala54, Arg413, Asn414, Asn414, Gly415	Ser48, Leu49, Thr50, Ser53, Ala54, Trp656, Gln657, Pro658, Gly659	Gln3, Ala4, Ala5, Val11, Gln14, Pro47, Ser48, Leu49, Thr50, Ser53, Ala54