

Whole genome sequencing of multidrug-resistant *Mycobacterium tuberculosis* isolates collected in the Czech Republic, 2005-2020

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Supplementary table 1. Transmission clusters of MDR, pre-XDR and XDR *M. tuberculosis* isolates from Czech Republic

Cluster (sublineage)	Isolates (year of the first diagnosis of TB)	Resistance profile (determined by WGS)	Location
1 (Haarlem 4.1.2.1)	CZ286 (2008)	MDR	Prague
	CZ188 (2004)	XDR	Prague
	CZ8842 (2014)	MDR	Nový Jičín
	CZ218 (2004)	Pre-XDR	Prague
	CZ188-16 (2016)	MDR	Prague
2 (Beijing 2.2.1)	CZ800-17 (2017)	MDR	Roudnice nad Labem
	CZ388-19 (2014)	MDR	Prague
3 (Beijing 2.2.1)	CZ553-17 (2017)	XDR	Pilsen
	CZ628-17 (2014)	MDR	Prague
	CZ29-19 (2019)	MDR	Pilsen
	CZ149-18 (2014)	MDR	Prague
	CZ139-19 (2019)	Pre-XDR	Prague
4 (Beijing 2.2.1)	CZ291 (2009)	XDR	Kladno
	CZ372-15 (2015)	MDR	Prague
5 (Beijing 2.2.1)	CZ279 (2008)	XDR	Šenov
	CZ276 (2007)	MDR	Liberec
	CZ178-18 (2017)	MDR	Šenov
6 (Beijing 2.2.1)	779-16 (2016)	MDR	Prague
	1019-16 (2016)	MDR	Mělník

Supplementary table 2. Study data and drug resistance related mutations in candidate genes

Cluster	Sample	Year	Sex	Age	Rifampicin	Isoniazid	Ethambutol	Pyrazinamide	Streptomycin	Aminoglycosides	Ethionamide	Fluoroquinolones	PAS	Linezolid	Delamanid
1	188/16	2016	M	53	Euro-American (Haarlem) 4.1.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Leu		rrs r.513a>c	efmA c.1054_1054del				
1	8842	2014	M	49	Euro-American (Haarlem) 4.1.2.1	rpoB p.Ser450Leu, rpoC p.Leu527Val	katG p.Ser315Thr	embB p.Met306Leu		rrs r.514a>c	efmA c.1054_1054del				
1	188	2005	F	56	Euro-American (Haarlem) 4.1.2.1	rpoB p.Ser450Leu, rpoC p.Leu527Val	katG p.Ser315Thr	embB p.Met306Leu		rrs r.906a>g	efmA c.1054_1054del	gyrA p.Ala90Val			
1	286	2008	M	70	Euro-American (Haarlem) 4.1.2.1	rpoB p.Ser450Leu, rpoC p.Leu527Val	katG p.Ser315Thr	embB p.Met306Leu		rrs r.906a>g	efmA c.1054_1054del				
1	218	2005	M	54	Euro-American (Haarlem) 4.1.2.1	rpoB p.Ser450Leu, rpoC p.Leu527Val	katG p.Ser315Thr	embB p.Met306Leu		rrs r.514a>c	efmA c.1054_1054del	gyrA p.Asp94Gly			
2	800/17	2017	M	32	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Val	pncA p.Thr160Ala	rpsL p.Lys43Arg					
2	388/19	2019	M	38	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Val	pncA p.Thr160Ala	rpsL p.Lys43Arg					
2	149/18	2018	M	37	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	pncA c.405_406insCACC		rpsL p.Lys43Arg				gpcC p.Cys154Arg	
3	29/19	2019	M	53	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embA c.-8C>A (only PhyResSe)		rpsL p.Lys43Arg					
3	139/19	2019	F	26	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Gln497Arg	pncA c.405_406insCACC	rpsL p.Lys43Arg		gyrA p.Asp94Gly, gyrA p.Ala90Val		rplC p.Cys154Arg	
3	628/17	2017	M	36	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr		pncA c.405_406insCACC	rpsL p.Lys43Arg					
3	553/17	2017	F	29	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	pncA p.Thr160Pro		rpsL p.Lys43Arg	rrs r.1401a>g	gyrA p.Asp94Gly			
4	372/15	2015	M	43	East-Asian (Beijing) 2.2.1	rpoB p.Ser451Leu	katG p.Ser315Thr	embB p.Ile131Ser	pncA p.Ile131Ser	rpsL p.Lys43Arg					
4	291	2009	F	49	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Gly406Ala	pncA p.Ile131Ser	rpsL p.Lys43Arg	rrs r.1401a>g	efmA c.341_341del	gyrA p.Asp94Gly		
4	178/18	2018	M	51	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Gln497Arg		rpsL p.Lys43Arg			folC p.Glu40Gly		
5	279	2009	M	41	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Gln497Arg		rpsL p.Lys43Arg		gyrA p.Ala90Val			ddn p.Trp88STOP
5	276	2010	M	54	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Gln497Arg		rpsL p.Lys43Arg			folC p.Glu40Gly		
6	1019/16	2016	M	81	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Ile		rpsL p.Lys43Arg					
6	779/16	2016	M	49	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Ile		rpsL p.Lys43Arg					
-	772/17	2017	M	49	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Ile	pncA p.Thr142Ala	rpsL p.Lys43Arg	rrs r.1401a>g				
-	851/17	2017	M	48	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embA c.-16C>T, embB p.Pro404Ser	pncA p.Gln10Lys	rpsL p.Lys88Arg	rrs r.1401a>g	gyrA p.Asp94Gly	folC p.Asp49Phe		
-	868/17	2017	F	50	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embA c.-12C>T, embB p.Tyr334His	pncA p.His71Arg	rpsL p.Lys88Arg		gyrA p.Ala90Val			
-	395/18	2018	M	27	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Val	pncA p.His51Arg	rpsL p.Lys43Arg					
-	412/18	2018	M	29	Euro-American (Haarlem) 4.1.2.1	rpoB c.1302_1307del	katG p.Ser315Thr								
-	424/18	2018	M	28	Euro-American (LAM, T) 4.3.3	rpoB p.His445Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embB p.Met306Ile	pncA p.Cys138Tyr	rrs r.514a>c	fabG1 c.-15C>T				
-	505/18	2018	M	38	Euro-American (LAM, T) 4.3.4.2	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Ile				gyrA p.Asp94Asn			
-	279/19	2019	F	31	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Asp354Ala	pncA p.Asp63Ala	rpsL p.Lys43Arg	rrs r.1401a>g	gyrA p.Asp94Gly		ddn p.Trp88STOP	
-	318/19	2019	M	39	Euro-American (LAM, T) 4.3.3	rpoB p.Ser450Tyr	katG p.Ser315Thr, fabG1 c.-15C>T		rrs r.514a>c		fabG1 c.-15C>T				
-	354/19	2019	M	40	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embA c.-12C>T, embB p.Tyr334His	pncA p.His57Arg	rpsL p.Lys88Arg	fabG1 c.-15C>T				
-	389/19	2019	M	26	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Phe	katG p.Ser315Thr	embB p.Met306Val	pncA p.Leu27Pro	rpsL p.Lys43Arg	rrs r.1401a>g	gyrA p.Asp94Gly			
-	402/19	2019	M	46	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Tyr319Cys	pncA p.Asp63Ala	rpsL p.Lys43Arg	Kan. eis c.-14C>T				
-	533/18	2018	M	45	Euro-American (LAM, T) 4.3.3	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Gly406Asp		rpsL p.Lys43Arg					
-	541/18	2018	M	33	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embA c.-12C>T, embB p.Tyr334His		rpsL p.Lys88Arg	fabG1 c.-15C>T				
-	614/18	2018	M	38	East-Asian (Beijing) 2.2.1	rpoB p.Leu452Pro	katG p.Ser315Thr	embB p.Met306Val	pncA p.His51Arg	rpsL p.Lys43Arg	Kan. eis c.-12C>T				
-	757/18	2018	M	28	Euro-American (Haarlem) 4.1.2.1	rpoB p.Ser450Leu, rpoC p.Leu527Val	katG p.Ser315Thr	embB p.Met306Val	pncA p.Phe94Leu		efmA c.1054_1054del				
-	35/19	2019	M	53	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Tyr	katG p.Ser315Thr	embB p.Tyr319Ser		rpsL p.Lys43Arg	rrs r.1401a>g				
-	36/19	2019	M	41	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Val	pncA p.Pro69Leu	rpsL p.Lys43Arg	efmA p.Thr314Ile	gyrB p.Thr500Pro			
-	105/19	2019	M	55	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu, rpoC p.Phe452Ser	katG p.Ser315Thr	embB p.Met306Val	pncA p.His57Arg	rpsL p.Lys43Arg	Kan. eis c.-10G>A	gyrA p.Asp94Gly			
-	732/19	2019	M	30	Euro-American (Ural) 4.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embB p.Ser297Ala		rpsL p.Lys88Arg	Kan. eis c.-12C>T				
-	19/15	2015	M	38	Euro-American (LAM, T) 4.3.3	rpoB p.Ser450Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embB p.Gln497Arg	pncA p.Asp63Gly	rrs r.514a>c	fabG1 c.-15C>T	gyrA p.Asp94Asn			
-	416/15	2015	F	38	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Gln497Arg	pncA p.Val139Ala						
-	367/17	2017	M	52	Euro-American (Haarlem) 4.1.2.1	rpoB p.Ser450Leu, rpoC p.Leu527Val	katG p.Ser315Thr	embB p.Met306Leu	pncA p.Phe94Leu		efmA c.1054_1054del				
-	398/15	2015	M	30	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Gly406Ser	pncA p.Gln10Pro, pncA c.287_287del	rpsL p.Lys43Arg	efmA p.Arg67Pro	gyrA p.Asp94Asn, gyrA p.Ser91Pro			
-	270/20	2020	M	32	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu, rpoC p.Phe452Ser	katG p.Ser315Thr	embB p.Met306Leu	pncA p.His57Arg	rpsL p.Lys43Arg	Kan. eis c.-10G>A	gyrA p.Ser91Pro			
-	421/17	2017	M	50	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Gln497Arg	pncA p.Val139Ala						
-	318/15	2015	F	28	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu, rpoC o.Ile491Thr	katG p.Ser315Thr	embB p.Met306Val	pncA c.524_524del	rpsL p.Lys43Arg	Kan. eis c.-10G>A (low-level R)	efmA c.1010_1010del			
-	505/15	2015	M	23	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr			rpsL p.Lys43Arg					
-	9320	2014	F	29	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Ile		rpsL p.Lys43Arg					
-	8946	2014	F	30	Euro-American (LAM, T) 4.3.3	rpoB p.Ser450Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embB p.Met306Val	pncA p.Asp12Ala	rrs r.514a>c	Kan. eis c.-10G>C, Capreo. flyA c.733_742del	fabG1 c.-15C>T			
-	445/15	2015	M	43	Euro-American (Haarlem) 4.1.2.1	rpoB p.Asp435Tyr	katG p.Ser315Thr, fabG1 c.-15C>T	embB p.Met306Ile		rpsL p.Lys43Arg					
-	95/17	2017	M	32	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Val		rpsL p.Lys43Arg					
-	248/20	2009	M	34	East-Asian (Beijing) 2.2.1	rpoB p.Asp435Tyr	katG p.Ser315Thr	embB p.Met306Ile	pncA Ile133Thr	rpsL p.Lys43Arg					
-	9206	2014	F	27	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Val	pncA p.Val128Gly	rpsL p.Lys43Arg					
-	317/15	2015	M	39	East-Asian (Beijing) 2.2.1	rpoB p.Asp435Tyr, rpoB p.Ser450Leu	inhA p.Ser94Ala, fabG1 c.-15C>T	embB p.Met306Val	pncA p.Asp12Glu	rpsL p.Lys43Arg	inhA p.Ser94Ala, fabG1 c.-15C>T	gyrA p.Asp94Gly			
-	895/16	2016	M	29	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Tyr	katG p.Ser315Thr	embB p.Met306Val		rpsL p.Lys43Arg					
-	417/15	2015	M	47	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Ile		rpsL p.Lys43Arg	rrs r.1401a>g	gyrA p.Asp94Gly			
-	292	2009	M	28	East-Asian (Beijing) 2.2.1	rpoB p.His445Asp	katG p.Ser315Thr, fabG c.-8T>C	embB p.Met306Ile			fabG c.-8T>C				
-	217	2005	M	37	Euro-American (Ural) 4.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embB p.Gln497Arg		rpsL p.Lys88Arg	Kan. eis c.-12C>T				
-	223	2006	F	51	Euro-American (Ural) 4.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr, fabG1 c.-15C>T	embB p.Gly406Ala	pncA p.Tyr345TOP	rpsL p.Lys88Arg	Kan. eis c.-12C>T	fabG1 c.-15C>T			
-	280	2008	M	53	Euro-American (LAM) 4.3.1	rpoB p.Asp435Val	katG p.Ser315Thr								
-	221	2009	M	28	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu, rpoC p.Ile491Thr	katG p.Ser315Thr, fabG c.-8T>C	embB p.Met306Ile	pncA p.Tyr68Gly	rpsL p.Lys43Arg	efmA c.1386_1386del, fabG c.-8T>C				
-	297	2010	F	23	East-Asian (Beijing) 2.2.1	rpoB p.Ser450Leu	katG p.Ser315Thr	embB p.Met306Ile	pncA p.Leu19Pro	rpsL p.Lys43Arg	Kan. eis c.-12C>T				

-	222	2008	M	33	Euro-American (LAM, T) 4.3.3	<i>rpoB</i> p.His445Asp	<i>katG</i> p.Ser315Thr, <i>fabG1</i> c.-15C>T	<i>embA</i> c.-12C>T, <i>embB</i> p.Gln497Arg	<i>pncA</i> p.Asp49Gly	<i>rms</i>	Kan. eis c.-12C>T	<i>fabG1</i> c.-15C>T					
-	288	2009	M	49	East-Asian (Beijing) 2.2.1	<i>rpoB</i> p. Ser450Leu, <i>rpoC</i> p.Ile491Thr	<i>katG</i> p. Ser315Thr	<i>embB</i> p. Met306Val	<i>pncA</i> p. Gly97Arg	<i>rpsL</i> p. Lys43Arg							
-	282	2009	M	25	East-Asian (Beijing) 2.2.1	<i>rpoB</i> p. Ser450Leu	<i>katG</i> p. Ser315Thr	<i>embB</i> p. Met306Val		<i>rpsL</i> p. Lys43Arg							