Supplementary material

TABLE S1. Primers used to perform genetic sequencing of regions targeted by the GenoType MTBDR*sl*.

Drug resistance	Target gene	Gene ID	Primer sequence (5' - 3')	$T_{annealing}$ (°C)
Fluoroquinolones	*gyrA* (Rv0006)	887105	CAATGTTCGATTCCGGCTTC	58
			CTCCATCGCCAACGGG	58
Second-line injeactable drugs	*rrs* (rvnr01)	2700429	GCCGCAAGGCTAAAACTCAAAG	58
			GTACGGCTACCTTGTTACGACTTC	58
Ethambutol	*embB* (Rv3795)	886126	TTCTCCACCCGGCCGACC	65
			CAGCGCGGCCACCGC	65

T: temperature.

TABLE S2. Comparison between the GenoType MTBDR*sl* and sequencing in 175 clinical isolates tested.

	Sequence % (95% CI)
Fluoroquinolones	
Sensitivity	100 (90,8-100)
Specificity	96,3 (91,7-98,4)
PPV	88,4 (75,5-94,9)
NPV	100 (97,2-100)
Second-line injectables	
Sensitivity	100 (95,6-100)
Specificity	96,7 (90,7-98,9)
PPV	96,6 (90,4-98,8)
NPV	100 (95,8-100)
Ethambutol	
Sensitivity	100 (95,6-100)
Specificity	96,7 (90,7-98,9)
PPV	96,6 (90,4-98,8)
NPV	100 (95,8-100)

TABLE S3. Spoligotyping profiles of the 175 clinical isolates included in the evaluation of the performance of the MTBDR*sl*.

Lineage	Fluoroquinolones DST						Second-line injectable drugs DST						Ethambutol* DST					
	R		S		Tot	%	R		S		Tot	%	R		S		Tot	%
	n	%	n	%			n	%	n	%			n	%	n	%		
Beijing	26	45,6	38	32,2	64	36,6	46	54,8	18	19,8	64	36,6	44	35,5	20	39,2	64	36,6
Cameroon	2	3,5	1	0,8	3	1,7	0	0,0	3	3,3	3	1,7	1	0,8	2	3,9	3	1,7
Dehli/CAS	1	1,8	2	1,7	3	1,7	0	0,0	3	3,3	3	1,7	2	1,6	1	2,0	3	1,7
Ghana	7	12,3	27	22,9	34	19,4	8	9,5	26	28,6	34	19,4	26	21,0	8	15,7	34	19,4
Haarlem	1	1,8	7	5,9	8	4,6	2	2,4	6	6,6	8	4,6	4	3,2	4	7,8	8	4,6
LAM	3	5,3	12	10,2	15	8,6	7	8,3	8	8,8	15	8,6	9	7,3	6	11,8	15	8,6
S	4	7,0	3	2,5	7	4,0	6	7,1	1	1,1	7	4,0	7	5,6	0	0,0	7	4,0
TUR	3	5,3	13	11,0	16	9,1	1	1,2	15	16,5	16	9,1	9	7,3	7	13,7	16	9,1
Uganda I	1	1,8	2	1,7	3	1,7	2	2,4	1	1,1	3	1,7	3	2,4	0	0,0	3	1,7
Ural	5	8,8	3	2,5	8	4,6	7	8,3	1	1,1	8	4,6	6	4,8	2	3,9	8	4,6
W african	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0
X	0	0,0	1	0,8	1	0,6	1	1,2	0	0,0	1	0,6	1	0,8	0	0,0	1	0,6
Unknown	4	7,0	9	7,6	13	7,4	5	4,8	8	9,9	13	7,4	12	9,7	1	2,0	13	7,4
Total	57		118		175		85		90		175		124		51		175	

* the phenotypic DST result is adjusted according to the minimum inhibitory concentration results; DST: drug-susceptibility testing; R: resistant; S: susceptibility.

TABLE S4. Frequency of mutations affecting *gyrA* gene among Beijing and non-Beijing lineages in 54 fluoroquinolone resistant clinical isolates.

Sequence	Beijing		total w/o Beijing	
	n	**%**	**n**	**%**
WT	6	**23,1**	9	**29,0**
A90V	5	**19,2**	10	**32,3**
S91P	1	**3,8**	3	**9,7**
D94A	3	**11,5**	3	**9,7**
D94N	1	**3,8**	1	**3,2**
D94Y	2	**7,7**	0	**0,0**
D94G	8	**30,8**	5	**16,1**
D94H	0	**0,0**	0	**0,0**
Other QRDR	0	**0,0**	0	**0,0**

QRDR: quinolone-resistance determining region; w/o: without.

TABLE S5. Distribution of mutations affecting the *rrs* gene among the 84 clinical isolates phenotypically resistant to at least one second-line injectable drug.

CAP	AMK	KAN	GT-MTBDR*s*/	Sequence	n	%
na	R	na	a1484t	WT	1	1,2
na	R	na	a1401g	a1401g	1	1,2
na	R	S	WT	WT	1	1,2
na	S	R	WT	WT	3	3,6
R	S	S	WT	WT	3	3,6
R	S	R	WT	WT	2	2,4
R	S	R	a1401g	a1401g	1	1,2
R	R	R	a1401g	a1401g	44	52,4
R	R	R	a1401g-1484t	a1401g	3	3,6
R	R	R	no WT	a1402t	1	1,2
R	R	R	WT	WT	4	4,8
R	R	S	a1401g	a1401g	1	1,2
S	R	S	WT	WT	1	1,2
S	R	R	a1401g	a1401g	6	7,1
S	R	R	WT	WT	1	1,2
S	R	R	WT+a1401g	WT+a1401g	1	1,2
S	R	R	WT+a1401g	WT	1	1,2
S	S	R	WT	WT	9	10,7

CAP: capreomycin; AMK: amikacin; KAN: kanamycin; R: resistant; S: susceptible; na: not available.

TABLE S6. Frequency of mutations affecting the *rrs* gene among Beijing and non-Beijing lineages in 85 second-line injectable drug-resistant clinical isolates.

Sequence	**Beijing**		**total w/o beijing**	
	n	**%**	**n**	**%**
WT	10	**21,7**	16	**41,0**
a1401g	35	**76,1**	23	**59,0**
g1484t	0	**0,0**	0	**0,0**
Other *rrs*	1	**2,2**	0	**0,0**

w/o: without.

TABLE S7. Other mutations identified in the *embB* gene of 37 ethambutol-resistant strains showing a wild-type sequence at codon 306.

cod. 306	**Whole ERDR**	**n**
WT	WT	21
	G406A	4
	Y319C	3
	D354A+S426N	1
	D328Y	1
	G406S	1
	Y319D	1
	Y319S	2
	C361S+E405D	1
	N296H	1
	ins. ctg at cod. 332	1

Cod: codon; ERDR: ethambutol-resistance determining region; ins: insertion.

TABLE S8. Frequency of mutations affecting the *embB* gene in 125 ethambutol-resistant clinical isolates belonging or not-belonging to the Beijing lineage.

Sequence	**Beijing**		**total w/o beijing**	
	n	**%**	**n**	**%**
WT	13	**29,5**	24	**30,0**
M306V	24	**54,5**	30	**37,5**
M306I	7	**15,9**	25	**31,3**
Other *embB*	0	**0,0**	1	**1,3**

w/o: without.

TABLE S9. Comparison of the performances of the GenoType MTBDR*s/* among lineages.

	Beijing % (95% CI)	Non-Beijing % (95% CI)	Mid-p exact test
Fluoroquinolones			
Sensitivity	76,9 (58,0-89,0)	71,0 (53,4-83,9)	
Specificity	100 (90,8-100)	98,8 (93,3-99,8)	
PPV	100 (83,9-100)	95,7 (79,0-99,2)	
NPV	86,4 (73,3-93,6)	89,8 (81,7-94,5)	
Diagnostic accuracy	90,6 (81,0-95,6)	91,0 (84,2-95,0)	
Second-line injectables			
Sensitivity	78,3 (64,4-87,7)	59,0 (43,4-72,9)	***
Specificity	100 (82,4-100)	98,6 (92,6-99,8)	
PPV	100 (90,4-100)	95,8 (79,8-99,3)	
NPV	64,3 (45,8-79,3)	81,8 (72,5-88,5)	***
Diagnostic accuracy	84,4 (73,6-91,3)	84,8 (77,0-90,3)	
Ethambutol*			
Sensitivity	70,5 (55,8-81,8)	70,0 (59,2-78,9)	
Specificity	100 (83,9-100)	96,8 (83,8-99,4)	
PPV	100 (89,0-100)	98,3 90,7-99,7)	
NPV	60,6 (43,7-75,3)	55,6 (42,4-68,0)	
Diagnostic accuracy	79,7 (68,3-87,7)	77,5 (68,9-84,3)	

CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; *: the phenotypic DST result is adjusted according to the minimum inhibitory concentration results.