

1 **Suppl. Table 1. Resistance profile of MDR-TB cases in Shenzhen, stratified by**  
 2 **lineages**

	Total	Modern Beijing	Ancient Beijing	Non-Beijing	Chi square statics	
	N=417	N=216	N=135	N=66	$\chi^2$	p value
Genetic resistance						
Non-MDR	10 (2.40)	5 (2.31)	3 (2.22)	2 (3.03)	0.137	0.934
MDR/RR	274 (65.71)	135 (62.50)	86 (63.70)	53 (80.30)	7.47	0.024
Pre-XDR	114 (27.34)	64 (29.63)	41 (30.37)	9 (13.64)	7.43	0.024
XDR	19 (4.56)	12 (5.56)	5 (3.70)	2 (3.03)	1.08	0.584
First-line drug resistance						
INH	408 (97.84)	213 (98.61)	132 (97.78)	63 (95.45)	2.39	0.303
RIF	407 (97.60)	211 (97.69)	132 (97.78)	64 (96.97)	0.137	0.934
SM	277 (66.43)	180 (83.33)	82 (60.74)	15 (22.73)	86.2	<0.001
EMB	245 (58.75)	134 (62.04)	80 (59.26)	31 (46.97)	4.76	0.093
PZA	112 (26.86)	62 (28.70)	36 (26.67)	14 (21.21)	1.45	0.485
Second-line drug resistance						
FQ	107 (25.66)	58 (26.85)	39 (28.89)	10 (15.15)	4.72	0.094
AMK	45 (10.79)	31 (14.35)	12 (8.89)	2 (3.03)	7.48	0.024
KAN	28 (6.71)	14 (6.48)	10 (7.41)	4 (6.06)	0.167	0.920
CPM	23 (5.52)	12 (5.56)	10 (7.41)	1 (1.52)	2.95	0.228
PAS	31 (7.43)	11 (5.09)	18 (13.33)	2 (3.03)	10.4	0.005
ETO	54 (12.95)	40 (18.52)	5 (3.70)	9 (13.64)	16.2	<0.001

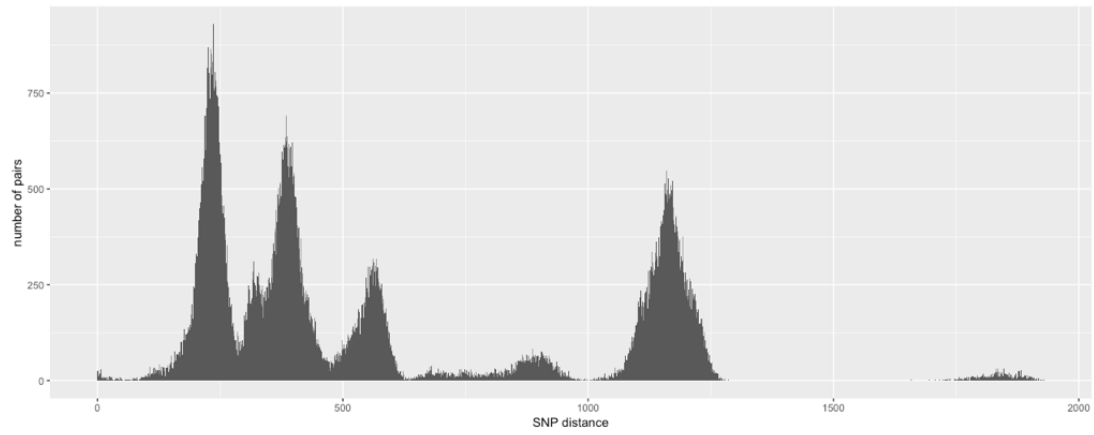
3  
 4 \* Abbreviations of anti-TB drugs: isoniazid (INH), rifampin (RIF), streptomycin  
 5 (SM), ethambutol (EMB), pyrazinamide (PZA), fluoroquinolones (FQ), amikacin  
 6 (AMK), kanamycin (KAN), capreomycin (CPM), para-aminosalicylic acid (PAS),  
 7 ethionamide (ETO), linezolid (LZD), clofazimine (CFZ), and bedaquiline (BDQ)  
 8 \*\* No mutation was detected on the resistance genes for linezolid, clofazimine,  
 9 bedaquiline

10

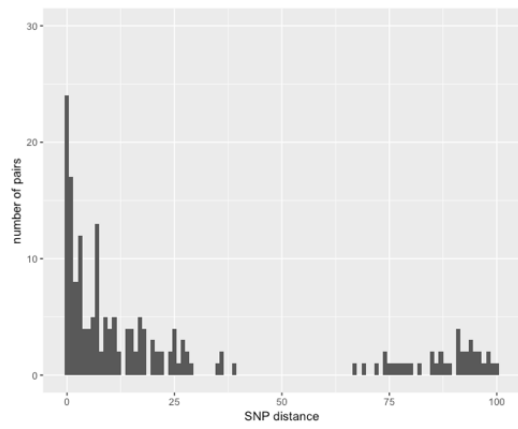
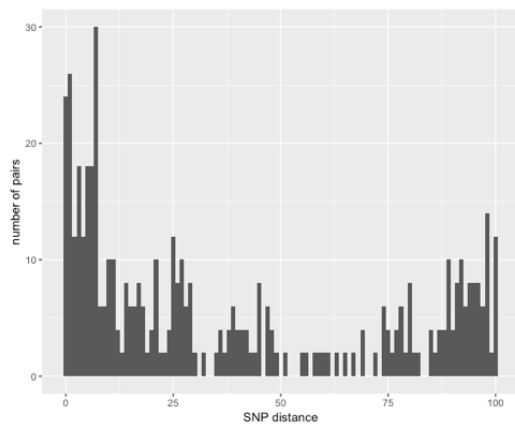
11 **Suppl. Table 2. Epidemiological links of MDR-TB cases from large genomic-clusters ( $\geq 3$  cases)**

	Cluster size	Median age (years, [IQR])	No. males	Risk factors	No. patients living in the same district	Median Pairwise geographic distance (kilometers, [IQR])	No. patients coming from the same county	No. patients receiving investigation	Known social links (n.)	Epidemiological links
Cluster 02	6	28 (23-33)	5	SZ(2) FQ(2)	6	0.6 (0.6-1.0)	2,2	3	Household (2) Community (6)	Yes
Cluster 03	3	36 (30-45)	2	FQ(1)	2	16 (1.3-16)	0	2	Community (2) Past community (2)	Probable
Cluster 08	4	37 (21-52)	2	SZ(1) Stu.(1) FQ(3)	3	4.2 (4.0-4.8)	0	2	Community (2)	Probable
Cluster 10	4	40 (31-49)	3	FQ(3)	3	16 (7.0-24)	2	3	Household (2)	Yes
Cluster 11	4	24 (23-39)	4		2	18 (13-28)	0	0	Unknown	ND
Cluster 12	3	41 (27-50)	2		2	37 (1.7-38)	0	1	Workplace (2) Community (2)	Yes
Cluster 14	5	33 (23-39)	3	Stu.(1) FQ(2)	3,2	21 (15-36)	2	1	Community (2,2) Source county(2)	Probable
Cluster 17	4	36 (30-44)	2	FQ(1)	2	9.1 (6.6-15)	0	1	Unknown	ND
Cluster 30	3	33 (30-49)	3		3	5.8 (4.0-6.3)	0	0	Community (2)	Probable
Cluster 32	3	26 (25-28)	1	FQ(1)	0	45 (24-57)	0	1	Unknown	ND
Cluster 44	4	26 (23-29)	1	FQ(1)	2	11 (1.8-13)	3	1	Source county (3)	Probable
Cluster 46	4*	17 (16-18)	2	Stu.(3) FQ(4)	0	38 (5.8-40)	2	2	School (3)	Yes
Cluster 47	4	33 (19-51)	3	Stu.(2) FQ(4)	2,2	9.4 (8.2-17)	0	3	School (3)	Yes

12 \* Baseline data was missing for one case



C.



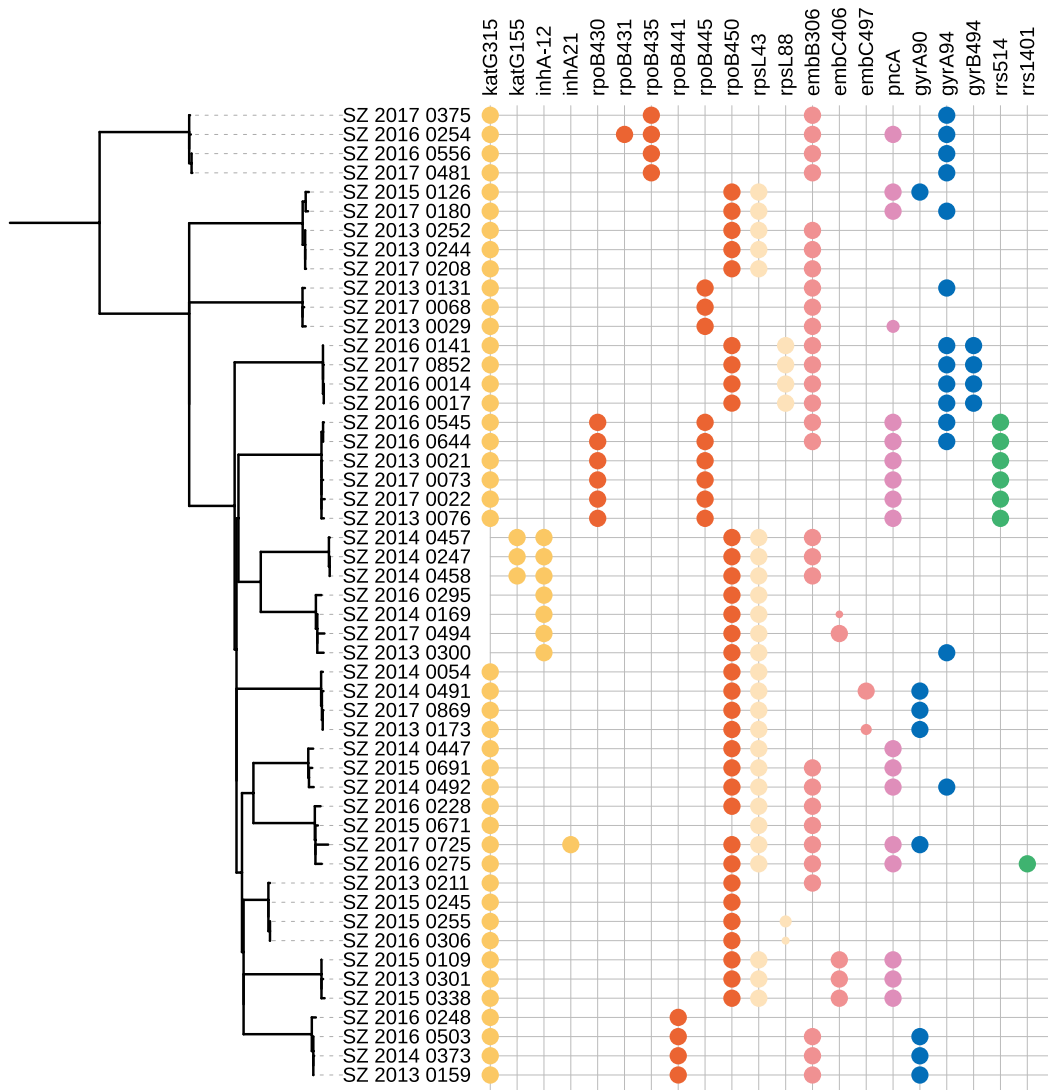
13

14 **Suppl. Figure 1.** SNP distribution of enrolled MDR strains. (A) Total distribution of

15 pairwise SNP distance. (B) Distribution of pairwise SNP distances  $\leq 100$ . (C)

16 Distribution of minimum SNP distance  $\leq 100$ .

17



18

19 **Suppl. Figure 2.** Mutations associated with drug resistance found in strains belonging  
 20 to the 13 large clusters containing three or more cases