GENETIC DIVERSITY AND POPULATION STRUCTURE OF *M.TUBERCULOSIS* STRAINS CIRCULATING IN CENTRAL RUSSIA

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Research on Tuberculosis

Study settings

- **Study population**

Epidemiologically unlinked *M. tuberculosis* strains from the Tula, Kaluga, and Moscow regions

- **Study methods**

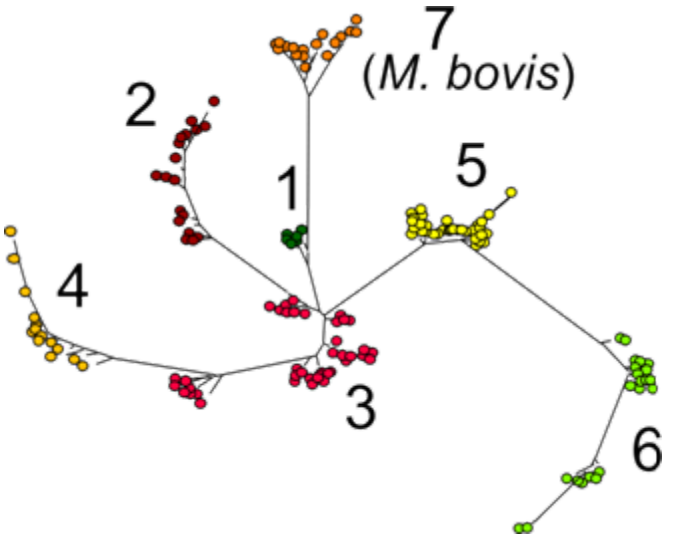
Epidemiological markers (IS*6110*-RFLP, spoligotyping,

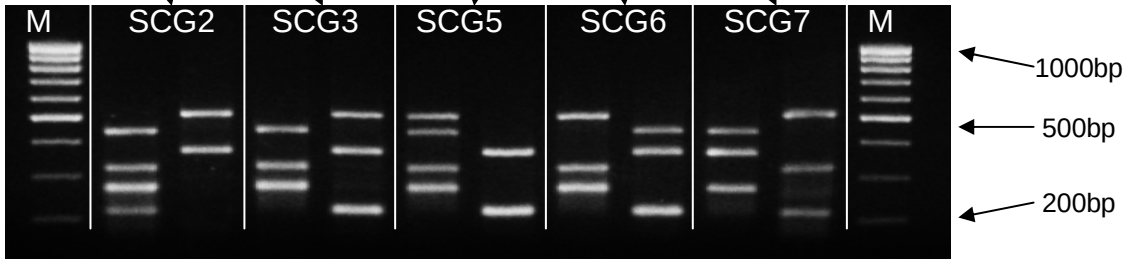
MIRU-VNTR typing)

Phylogenetic markers (SCG, PGG)

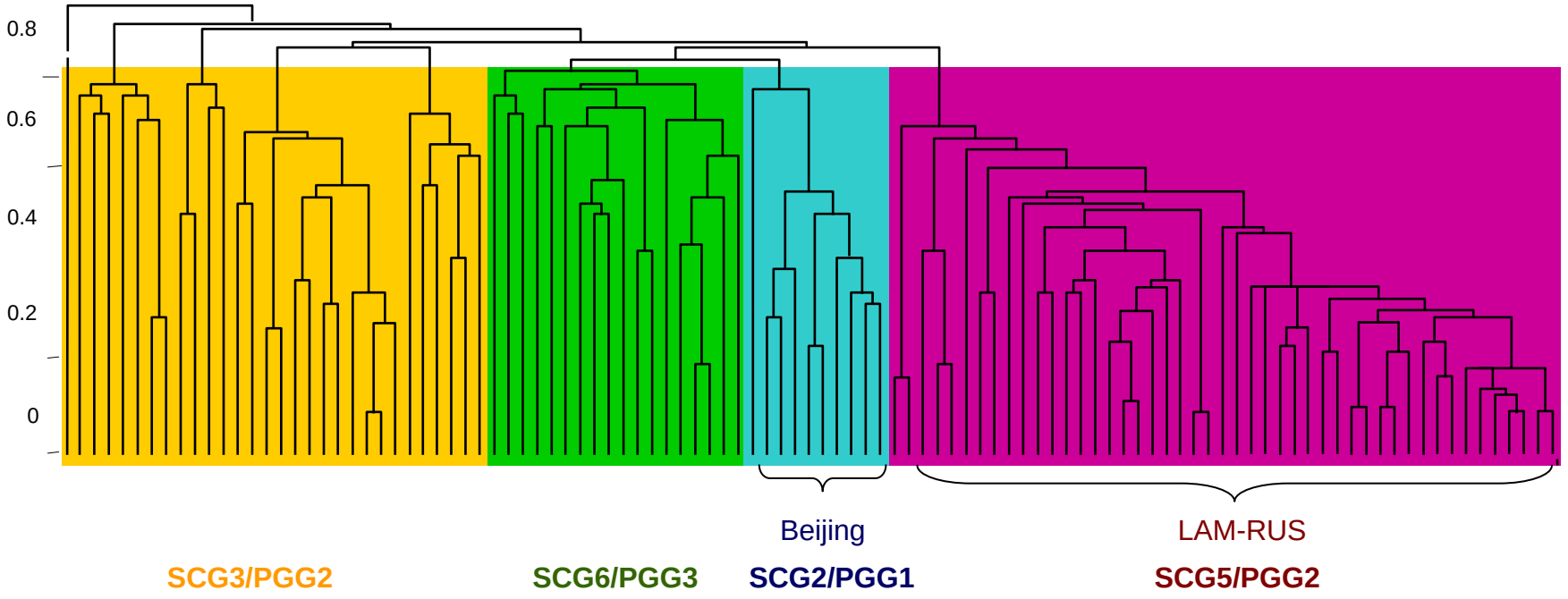
Identification of SNP Clustered Group (SCG)

Position in H37*Rv* Genome	SCG1	SCG2	SCG3	SCG4	SCG5	SCG6	SCG7
3352929	C	G	C	G	C	G	C	G	C	G	C	G	C	G
92197	G	T	G	T	G	T	G	T	G	T	G	T	G	T
473678	A	G	A	G	A	G	A		A	G	A	G	A	G
1920118	G	T	G	T	G	T	G	T	G	T	G	T	G	T
2460626	C	A	C	A	C	A	C	A	C	A	C	A	C	A
3111473	T	C	T	C	T	C	T	C	T	C	T	C	T	C



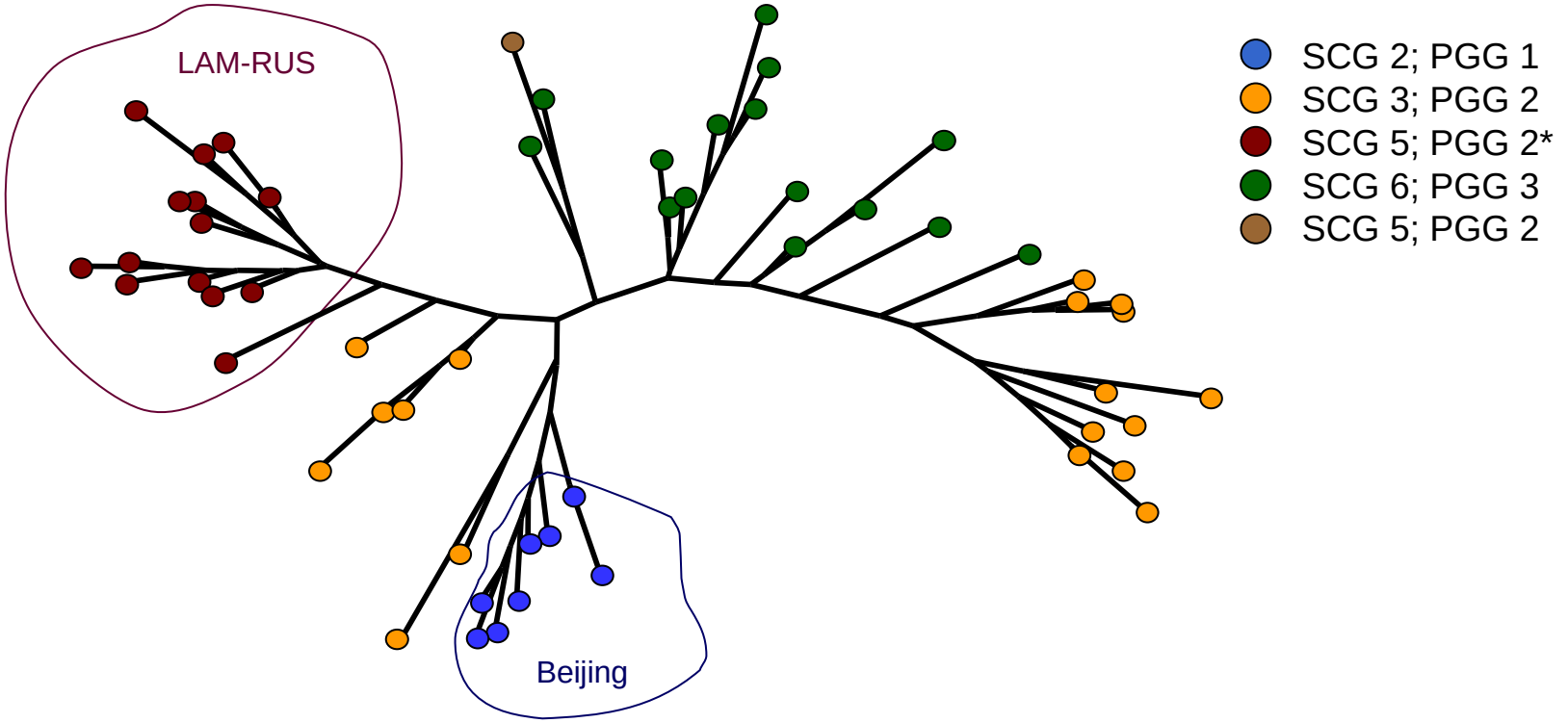


Genetic diversity of *M. tuberculosis* strains based on their IS*6110*-RFLP patterns

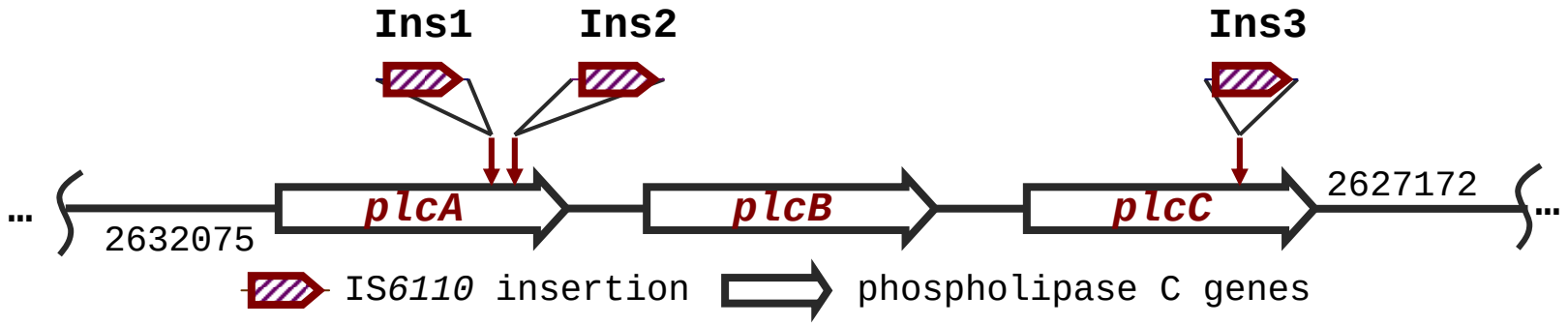


Phylogenetic tree

MIRU-VNTR typing

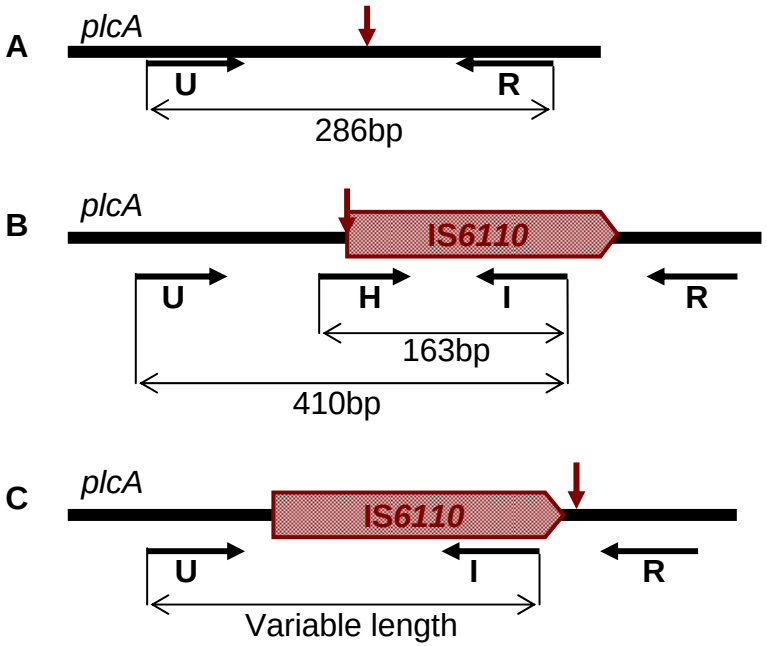


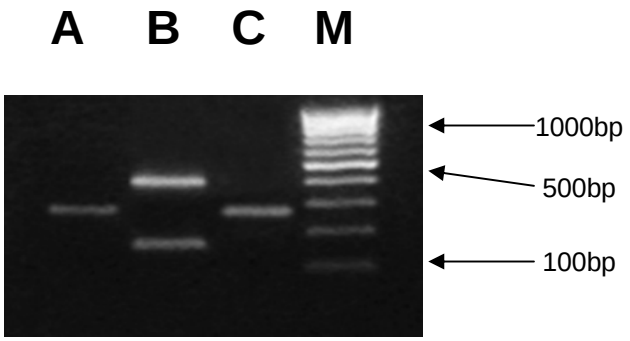
Prevalence of *plcABC*::IS*6110* genotype in different phylogenetic groups



Phylogenetic groups	Total isolate no.	Isolates with *plcABC*::IS*6110* genotype
PGG1/SCG2	10	-
PGG2/SCG3	30	-
PGG2/SCG5	47	45 (**Ins2**, *plcA*)
PGG3/SCG6	20	1 (Ins1, *plcA*) 1 (Ins3, *plcC*)

Identification of LAM-RUS strains





Study settings

Population:	1 041 641
TB incidence rate:	106.8/100 000
Incarceration rate:	10.44/1 000

Study population

sets of *M. tuberculosis* strains recovered in Tula dispensary and Ozerki prison hospital (Tula region) during one-year study

Study methods

Epidemiological markers

- IS*6110*-RFLP, spoligotyping,
- MIRU-VNTR typing

Phylogenetic markers

- SCG, PGG

Profiling of drug resistance

Patients' characteristics

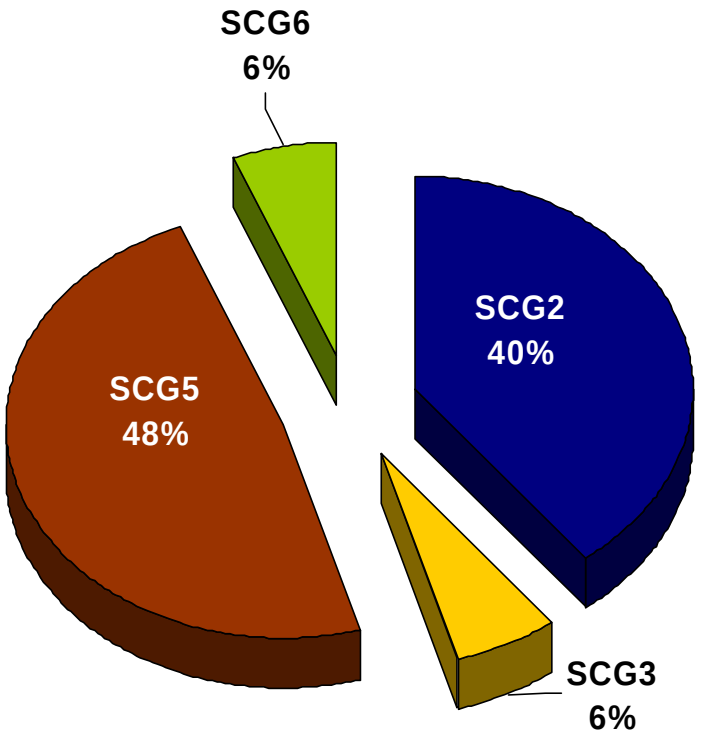
	Prison hospital	City dispensary
Patient no.	81	167
Clusters no.	11	20
Average cluster size	4.5	3.2
% Clustered cases	**72%**	36%
No. of shared clusters	7	

Prevalence of drug resistant TB among new and previously treated patients

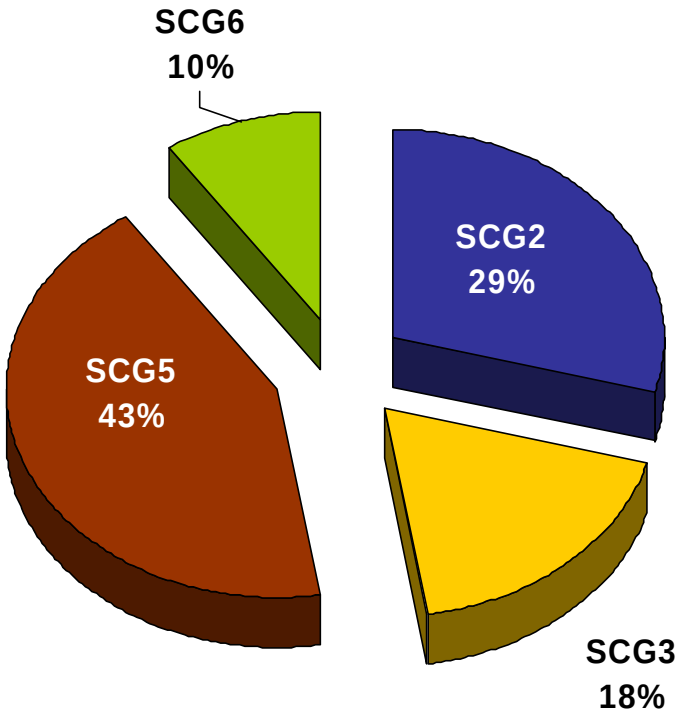
	Prison hospital		City dispensary	
	n.c.	p.t.	n.c.	p.t.
Patient no.	24	57	58	109
Susceptible	25%	5%	31%	19%
MDR	50%	**86%**	20%	**59%**
MDR+KAN	29%	**82%**	12%	**46%**

Prevalence of strains of different phylogenetic groups in prison and civilian population

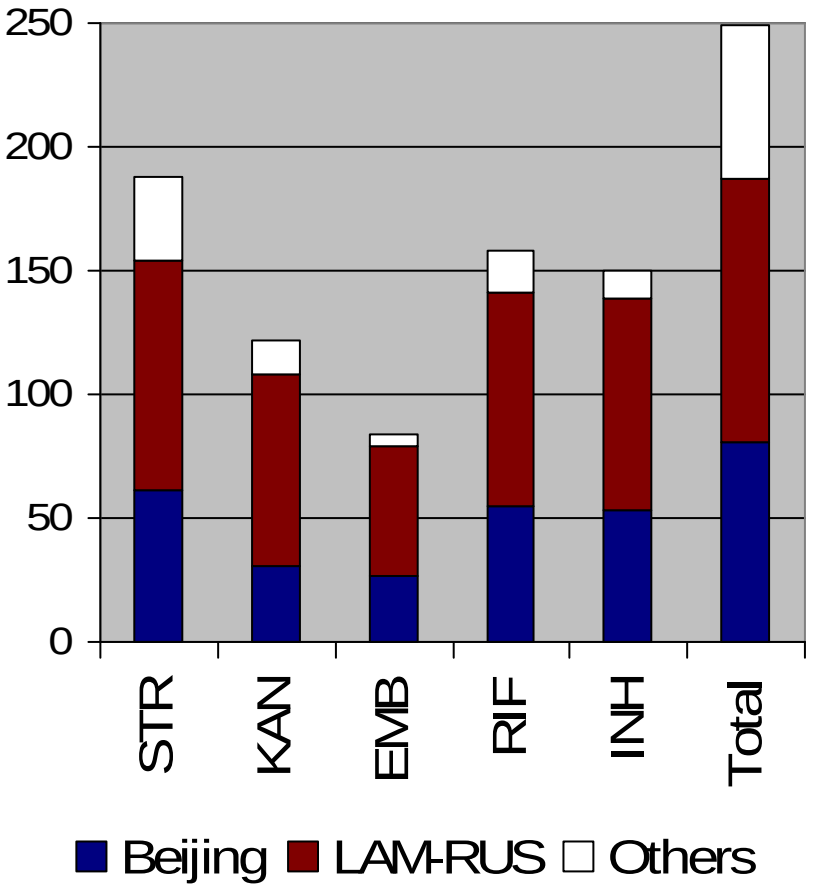
Prison hospital



City dispensary

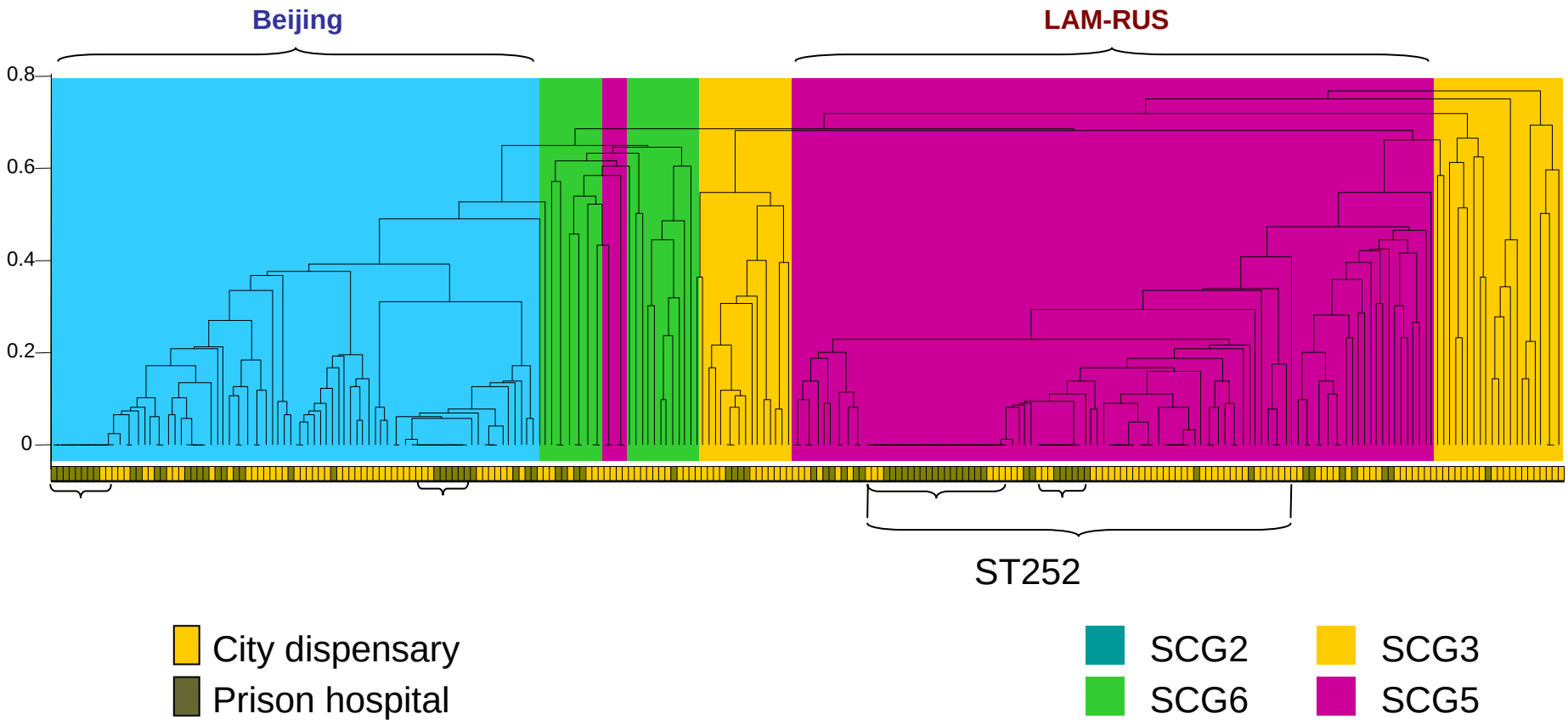


Drug resistance profiles of major *M.tuberculosis* strains



	Susc.	MDR	MDR+K
Beijing	14(17%)	44(54%)	25(31%)
LAM-RUS	10(9%)	81(74%)	73(67%)
Others	24(39%)	8(13%)	4(6%)

Major clusters identified by IS*6110*-RFLP



Neglected epidemics

- Spoligotype **ST252**: 777477607760771.
- Belongs to SCG5/PGG2, LAM-RUS strains.
- Comprises **29%** of the study sample (71 of 248 isolates).
- Prevalent in both prison and civilian population (27 and 44 cases, respectively).
- Includes 11 newly diagnosed cases.
- Drug resistance profile STR, KAN, RIF, INH, (EMB)
- Comprises **53%** of all MDR TB in the study population.
- Genetic markers for drug resistance: S315T *katG*, D516V *rpoB*, M306I *embB*.

Conclusions

- Members of tree modern SCG 3, 5 and 6, together with ancestral SCG2 are major contributors to the genetic diversity of the *M. tuberculosis* strains circulating in central Russia;
- LAM-RUS family of strains contained an insertion in a unique position in the *plcA* gene, which can serve as specific genetic marker for this group;
- Prisons have a significant impact on the TB incidence in the civilian population. Major clusters comprised from isolates recovered in both prison and civilian hospitals, emphasizing the interdependence of two populations;
- Majority of MDR TB cases in the region are due to Beijing or LAM-RUS;
- Abundance of MDR strains resistant to KAN implies that we may face the XDR epidemics in the region before long.