Transborder molecular analysis of MDR tuberculosis dynamics in Mongolia and Eastern Siberia, Russia

Svetlana Zhdanova[1], Igor Mokrousov[2], Elizaveta Orlova[1], Viacheslav Sinkov[1], and Oleg Ogarkov[1]

[1]Scientific Centre of the Family Health and Human Reproduction Problems Irkutsk Russia
[2]St Petersburg Pasteur Institute St Petersburg Russia
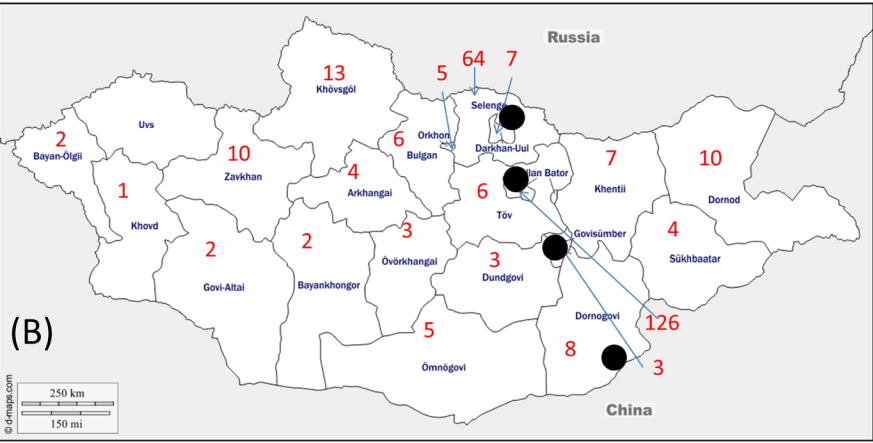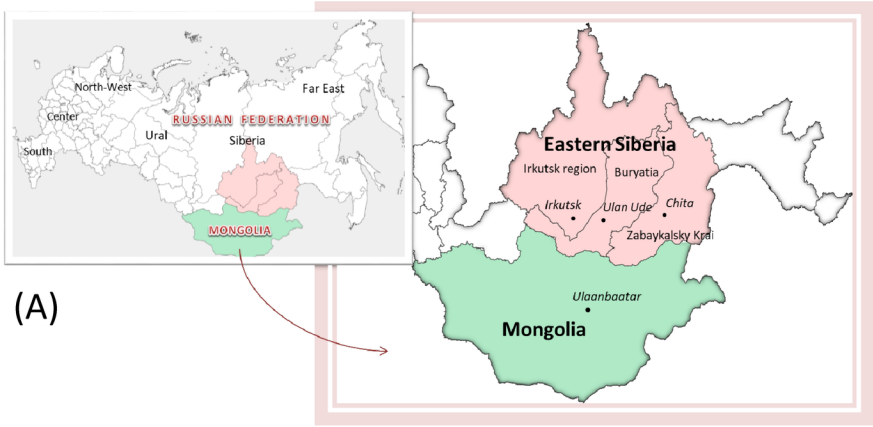
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Abstract

Mongolia and Eastern Siberia, Russia are border regions in Asia with high incidence of tuberculosis (TB). In this study, we aimed to investigate MDR -TB transborder transmission with a focus on endemic and epidemic *Mycobacterium tuberculosis* clones and drug resistance patterns. *M. tuberculosis* strains (291 from Mongolia and 754 from Russia) were collected within cross-sectional population-based surveys in 2010-2016. DNA was genotyped in 24 MIRU-VNTR loci and by PCR testing of the key SNP markers to discriminate within Beijing genotype. In total, 1045 isolates were divided into 435 MIRU-types that were assigned to Lineage 2 (Beijing isolates) and Lineage 4 (Ural, Haarlem, Latin-American-Mediterranean [LAM], S, and unclassified isolates). Beijing genotype was dominant in both countries, but most of Russian and all Mongolian Beijing strains belonged to different subtypes of the modern Beijing sublineage with only negligible overlap between the two countries. In particular, the Beijing types #342-32, #3819-32, #1773-32 (Asian African 2 group) were found only in Mongolia. LAM was the most common non-Beijing genotype (11.0% in Mongolia and 14.7% in Russia) and its isolates mostly belonged to LAM-RUS branch. MDR rate was higher in Russia compared to Mongolia among newly diagnosed patients: 29.4% versus 4.2% (p < 0.001) but similar and high in the retreatment subgroups (65.8% and 67.4%, respectively). In Russian collection, a higher MDR rate was observed in (i) Beijing compared to non-Beijing (47.5% versus 38.8%, p = 0.03), (ii) Beijing B0/W148 subtype compared to Beijing Central Asian/Russian subtype (64.5% versus 39.3%, p <0.001). In Mongolia, MDR rate was similar in Beijing (29.7%) and non-Beijing (27.5%) genotypes. In conclusion, population structures of the Beijing genotype in Mongolia and Russian borderline regions differ significantly including specific patterns of drug resistance. In contrast, largely overlapping LAM subtypes may correlate with historical endemic circulation of the LAM-RUS branch in Northern Eurasia.
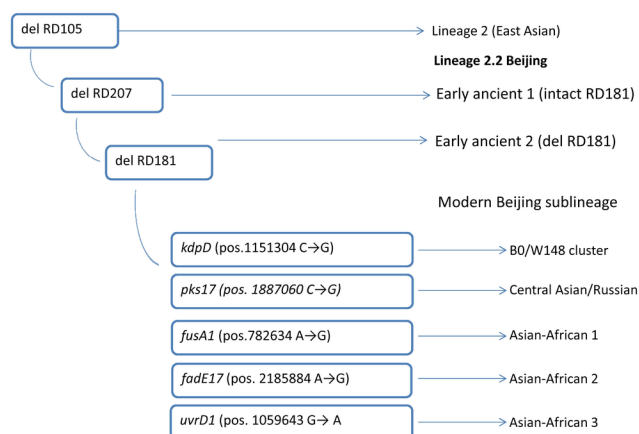
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Fig S1 UPGMA tree of all Mongolian and Russian profiles with reference (red).pdf available at https://authorea.com/users/423622/articles/528933-transborder-molecular-analysis-of-mdr-tuberculosis-dynamics-in-mongolia-and-eastern-siberia-russia

(A)

(B)

del RD105 → Lineage 2 (East Asian)

Lineage 2.2 Beijing

del RD207 → Early ancient 1 (intact RD181)

→ Early ancient 2 (del RD181)

del RD181

Modern Beijing sublineage

kdpD (pos.1151304 C→G) → B0/W148 cluster

pks17 (pos. 1887060 C→G) → Central Asian/Russian

fusA1 (pos.782634 A→G) → Asian-African 1

fadE17 (pos. 2185884 A→G) → Asian-African 2
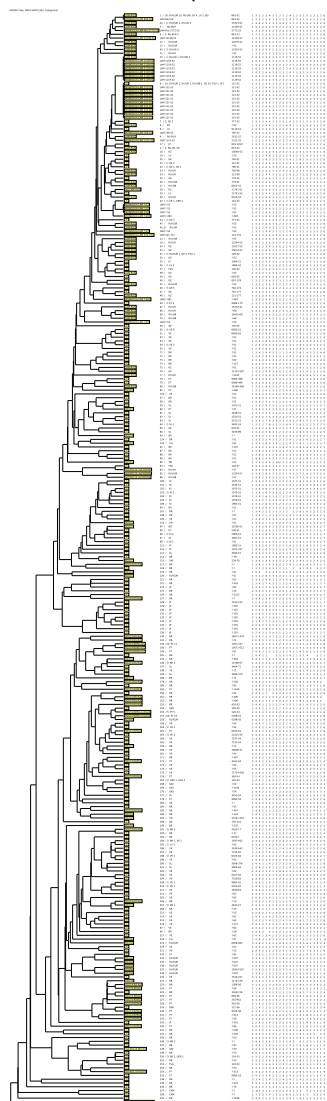
uvrD1 (pos. 1059643 G→ A) → Asian-African 3

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Fig S2 UPGMA tree of all Mongolian and Russian profiles.pdf available at https://authorea.com/users/423622/articles/528933-transborder-molecular-analysis-of-mdr-tuberculosis-dynamics-in-mongolia-and-eastern-siberia-russia

Fugure S3. UPGMA tree of 24-MIRU-VNTR of the Mongolian LAM
isolates and global LAM dataset (Mokrousov et al., 2016)

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`Table S3 Genotypic and phenotypic information.xlsx` available at https://authorea.com/users/423622/articles/528933-transborder-molecular-analysis-of-mdr-tuberculosis-dynamics-in-mongolia-and-eastern-siberia-russia

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`Supplementary Tables S1 S2 S4 S5 S6.docx` available at https://authorea.com/users/423622/articles/528933-transborder-molecular-analysis-of-mdr-tuberculosis-dynamics-in-mongolia-and-eastern-siberia-russia