



## WHOLE GENOME SEQUENCING OF KAZAKHSTANI *M.TUBERCULOSIS* STRAINS WITH DIFFERENT DRUG SUSCEPTIBILITY

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Despite the effective anti-tuberculosis chemotherapy, TB remains one of the leading infectious diseases in many countries, including Kazakhstan.

The whole genome sequencing of 20 *M.tuberculosis* clinical isolates from TB patients with different drug resistance (8 MDR, 4 XDR, 2 mono-resistant, 1 poly-resistant, 5 susceptible) were performed by NGS platform Roche 454 GS FLX+.

Bioinformatics analysis was performed and showed that relative indicators of coverage of the 20 *M.tuberculosis* strains were high enough and sufficient for further analysis. Alignment of received sequences was performed separately for each of the twenty clinical isolates. On average, among all isolates 97.8% sequences was mapped to the reference strain *M.tuberculosis* H37Rv that composed 4334396 nucleotide bases. Most of the studied isolates of *M. tuberculosis* (18) are Beijing family strains (East Asian), only two isolates belongs to families T (Euro-American) and MANU-1 (Indo-Oceanic). International «Tuberculosis Drug Resistance Mutation Database» was analyzed to study the genetic loci involved in the resistance to basic anti-TB drugs. As a result of the analysis the most common mutations in genetic loci associated with drug resistance to basic anti-TB drugs were selected. Genetic mutations in genes associated with drug resistance of *M.tuberculosis* were analyzed and found 18-27 genetic variants. All detected genomic variants with single nucleotide polymorphisms, insertions, deletions for each clinical isolates of *M.tuberculosis* indicating the description of the gene and protein, the positions on reference genome H37Rv, deep coverage of gene were prepared. Three main groups for comparative bioinformatic analysis were chosen - susceptible, MDR and XDR. 1018 genomic loci were identified as a common for all three study groups. The major parts of these genomic variants are found in "core" genes that necessary for mycobacteria life-sustaining activity. Several genomic variants have been detected in four genes PEPGRS24, PPE24, PPE5, PEPGRS56 which are typical for MDR and XDR isolates and belong to genes of protein family PE/PPE specific for species of Mycobacteria only.

The mutations specific to MDR and XDR groups of *M.tuberculosis* isolates can be one of the additional virulence factors that may provide an advantage in host-pathogen interaction and require further investigation.