MULTIDRUG-RESISTANT TUBERCULOSIS: WHOLE-GENOME SEQUENCING AND BIOINFORMATICS ANALYSIS

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Introduction: Tuberculosis (TB) remains a serious public health threat worldwide. It is estimated that approximately one-third of the world's population has been infected with multidrug-resistant tuberculosis (MDR-TB), and 1.8 million people die of this disease annually. It is extremely important to determinate susceptible and resistant strains with different mutations in genes encoding drug metabolism of Mycobacterium tuberculosis (MTB) strains in Kazakhstan.

Materials and Methods: The whole genome sequencing of 8 MDR-TB clinical isolates using next-generation sequencing platform were examined.

Results: Both missense and splice mutations, known pathogenic and novel variants were found. Genomic variants (SNPs and indels) in de novo assembled and annotated whole-genomes and specific/novel variants in drug-resistant genes of MDR strains from Kazakhstan were observed. We identified 1933 non repetitive single nucleotide variations (SNVs), among which a common pool of 1037 SNPs were shared by the 8 isolates. We found several mutations that are known to confer resistance to drugs. The majority of MTB isolates were the Beijing-type strain (lineage 2- East-Asian lineage) and their complete genomes were studied for the first time in Kazakhstan. The most frequent resistance mutations were observed in the katG and rpoB genes, conferring resistance to isoniazid and rifampicin respectively. In addition, WGS analysis allowed the detection of heteroresistance to multiple drugs.

Conclusion: These findings may provide a basis for expansion of the reference MTB database, and further investigation of virulence and transmissibility patterns in MDR strains. This study may provide a basis for creation of the reference database, the subsequent study, and comparison with the different drug-resistant MTB isolates circulating in Kazakhstan.

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