CREATING PREREQUISITES OF PERSONALIZED APPROACH IN THE DIAGNOSIS AND TREATMENT OF TUBERCULOSIS, BASED ON WHOLE GENOME-SEQUENCING OF M.TUBERCULOSIS

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INTRODUCTION.

The next generation sequencing technology provides a tool to obtain genetic data from clinically isolates *M.tuberculosis*. Using it we can clarify the factors cause of the formation of highly virulent strains of *M.tuberculosis*, the evolution of local strains, and genetic markers of drug resistance, which will pave the personalized approach in the diagnosis and treatment of TB.

OBJECTIVES.

Collect samples of *M.tuberculosis*, isolated from patients with disease, identify their microbial strains, test drug susceptibility and extract DNA. Build collections of genomic DNA samples from clinically isolated *M.tuberculosis*, and sequence the complete genome of isolates. Conduct a comparative analysis with publicly available WGS databases to identify differences in mutation type and frequency between genes drug metabolism which stipulates susceptibility to antituberculosis drugs. Identify factors that affect on the formation of highly virulent strains of *M.tuberculosis*, multidrug and extensively drug-resistant tuberculosis. Determine the genetic markers for quick and effective implementation into preventive diagnosis from drug-resistant TB. Create a database of the characteristic local *M.tuberculosis* strains, with descriptions of the study, the sample origin, microbiological tests and sequencing data.

MATERIALS AND METHODS.

Over the 2013 year disease cultures was selected from 50 patients with different types of drug resistance. Material collection and determination of drug sensitivity was performed in the reference-laboratory "National Center of the Tuberculosis".

Drug sensitivity of *M.tuberculosis* to antituberculosis drugs was determined with method of proportions to 4 antituberculosis drugs from the first lane and to 6 drugs from the second lane.

The whole genome sequencing of 3 samples were performed on Roche 454 GS FLX+ next-generation sequencing platform. The reads from three isolates were assembled into contigs using GS De Novo Assembler (Roche). All alignments were done to the reference strain Mycobacterium tuberculosis H37Rv using GS Reference Mapper.

RESULTS.

The protocols were elaborated and tested for the new generation sequencing on platforms Roche 454 GS FLX+. The whole genome sequencing was performed for 3 mycobacterium isolates. Bioinformatics analysis is ongoing for sequencing data. The numbers of SNPs and CNVs in sequenced whole genomes will be evaluated. The results of genome assembling are submitted into NCBI GenBank and available for public access.

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