Antibiotics are chemicals used to treat bacterial infections. The discovery of antibiotics by Alexander Fleming revolutionized medicine and saved millions of lives. In today's world, we can no longer imagine a world without antibiotics. Over the years, they have been widely administered to both humans and animals. In the course of time, it has become apparent that this widespread use of antibiotics also has its dark side. It has been found that bacteria are able to produce forms resistant to the effects of antibiotics. Factors leading to the appearance of drug-resistant forms are poorly selected doses of antibiotics or premature termination of therapy. Therefore, the effectiveness of currently used antibiotics is decreasing and it is necessary to search for new antibacterial compounds.

Mycobacterium tuberculosis is one of the most dangerous bacterial pathogens in the modern world. The World Health Organization estimates that 1.5 million people die from tuberculosis every year. The number of people infected with drug-resistant mycobacteria is estimated at 600,000. Unfortunately, in 2015 only 52% of people infected with drug-resistant mycobacteria were cured.

The aim of this project is to evaluate the effectiveness of an innovative method of optimizing antibacterial therapy based on the characteristic evolutionary patterns present in bacterial DNA. The research will be carried out on a model of tubercle bacilli, and it will be focused on three proteins constituting the molecular targets for currently used anti-mycobacterial drugs. We hypothesize that the identification of characteristic evolutionary patterns may 1) facilitate the identification of mutations in DNA leading to drug resistance and, that it may 2) facilitate the identification of effective antibacterial compounds.

The project is to be divided into four stages. In the first stage, we will compare thousands of bacteria with each other and identify evolutionary patterns that suggest which protein fragments are responsible for drug resistance and which protein fragments are key to its functioning. In the second stage of the project, as a result of genetic modifications, we will obtain mutants of *M. tuberculosis* in which protein regions identified in the first stage of the project will be modified. This stage is intended to confirm experimentally that the regions of proteins identified by us actually affect the functioning of bacteria. In the third stage of the project, we will use computer computational methods to identify chemical compounds that bind to the proteins. The newly identified compounds would be active against protein variants conditioning drug resistance or they will bind to particularly evolutionarily preserved protein fragments. In the last stage of the project, we will test the effectiveness of compounds identified by computer methods against *M. tuberculosis* in laboratory conditions.

Data obtained in this project may allow optimization of anti-tuberculosis therapy. If the evaluation method of optimizing antibacterial therapy proves effective here, it can be applied to other bacterial pathogens. Moreover, the data obtained in the course of this project can be used in clinical settings to identify drug-resistant infections, and to improve computational methods for molecular interactions. We may be able to identify new, effective anti-tuberculosis compounds.