

According to information provided by the World Health Organization, the problem of antibiotic resistance, including the overuse of antibiotics, is one of the primary concerns of modern healthcare systems. The antibiotic resistance poses a considerable challenge for scientists, promoting an ongoing search for novel antimicrobials. One promising area of research is phage therapy, which has shown positive results worldwide. It is a therapy that uses viruses to attack bacteria and thus eliminate them. This approach remains an experimental therapy and has yet to be introduced to clinics. In addition to the use of whole phage particles, their components with specific properties can also be utilized. An interesting group of molecules, which holds promise from a clinical perspective but remains underexplored are **Receptor Binding Proteins (RBPs)**. These groups of proteins exhibit unique properties because they allow the virus to infect the bacteria with high specificity towards particular bacteria strains. Another promising approach is therapeutic monoclonal antibodies (mAbs) which represent a strategy for the treatment of various diseases. Today, mAbs are widely used to treat oncological and immunological conditions. However, the development of mAbs for infectious diseases remains a challenge. Few antibacterial mAbs have completed clinical trials, and to date, only three mAbs have been approved by the FDA for treating infections, all of which neutralize toxins produced by bacteria. **Our research aims to integrate the mechanism of action of mAb with the properties of bacteriophage RBPs**, which are highly specific proteins that recognize bacteria. In this project, we propose to develop a molecule composed of a bacteriophage protein and the fragment of the antibody. This design combines their biological functions: (1) the bacteriophage component will enable recognition and binding of bacterial cells and (2) the antibody fragment will facilitate interaction with receptors on immunological cells such as macrophages. Macrophages are cells of the immune system that engulf bacteria and digest them thus annihilating pathogens. This process is called phagocytosis. **In this project, we propose a modular platform** for the assembly of molecules consisting of phage protein and antibody parts with the use of the SpyCatcher system, which allows the irreversible joining of two proteins. The platform will consist of molecules “blocks”. The proteins of interest will be produced using genetic engineering. Produced RBP and Fc “blocks”, when mixed, will irreversibly react. The described modular character of the platform will enable the joining of molecules in different combinations to pick the most effective combo in the functional assays. **In summary, the primary objective** of this project is to create a platform for the assembly of proteins that mimic antibodies, effectively combining different biological mechanisms to augment the natural immune response against life-threatening infections. This platform is particularly targeted at combating multidrug-resistant bacteria, such as *Pseudomonas aeruginosa* and *Escherichia coli*, which are classified as high-priority pathogens by WHO. If a functional molecule can be obtained that is effective in *in vitro* cell line studies, this will certainly contribute to the development of further bacteriophage-based solutions, which in turn will provide a remedy for difficult cases of infection with multidrug-resistant strains in the future. To achieve the project's goals, various advanced methods will be used such as flow cytometry and holotomographic microscopy to study phagocytosis, Gentamycin Protection Assay to test the killing efficiency of phagocytosed pathogens, and a panel of cytokines will be examined. All selected methods will allow us to evaluate the potential of our presented solution.