A new class of antimicrobial compounds. Design, synthesis and study of the mechanism of action.

Bacteria, though small and inconspicuous, can kill even the largest animal. In addition, they are intelligent enough that, even though the discovery of antibiotics, they can cope with them. Such capable bacteria, which can defend themselves against drugs are called antibiotic-resistant. This feature is a global problem, which is talked about not only by scientists and doctors, but even by politicians. According to statistics, nearly one million deaths per year can be related to antimicrobial-resistance and the prediction is that by 2050, 10 million people will die each year due to drug-resistant infections. It is estimated that antibiotic resistance will become the most common cause of death in the world, surpassing cancer (8.5 million) or diabetes (1.5 million). The first antibiotic was discovered by Alexander Fleming. He already warned about bacterial intelligence and said that they would certainly find their way to continue to be menacing. Antibiotics are the first defense treatment in many diseases, which were once fatal, then completely harmless, and are now again raising statistics of mortality. Unfortunately, as Fleming predicted, an uncontrolled application of antibiotics led to the appearance of resistant bacteria. This was due to the patient's passion for using antibiotics, often hasty and inaccurate diagnosis and lack of handheld diagnostic tests in in doctors' practices. Therefore, it is important to look for new antimicrobial compounds that are effective, safe and that their mechanism of action is different from those for which bacteria already have their "smart ways". The main task of this project is to develop a new class of antimicrobial compounds whose mechanism of action would be different from those currently known. The leading structure, which based upon the new structures will be designed and synthesized, is the compound called A-20, derived from human Cystatin C, the protein belonging to the first non-immune line of defense against microbes. This compound is active against resistant bacteria that cause post-operative infections, which affect the wound healing process. In the first task of the project the design of various molecules will take place by using theoretical methods, and then these molecules will be synthesized and tested against bacteria pathogenic strains. In the next three tasks, scientists will try to answer the question how these molecules act on different strains of bacteria, and what element of the bacterial cell machinery stopped, destroyed or removed as a result of activity of new compounds.