Microorganisms for centuries constituted a serious problem to life and health of both humans and animals. Since the discovery and isolation of penicillin, antibiotics have become an effective tool for fight with pathogens. However, too common and often irresponsible use of them has caused microorganisms to develop a number of defense mechanisms against them such as converting the antibiotic into harmless form by enzymatic modification, active removal of antibiotics from the cell, or modification of its components. Currently, antibiotic resistance of microorganisms is a global problem, which forces on the modern science to develop new effective biologically active substances.

In recent years many new antibacterial agents have been proposed. Particular attention should be paid to nanoparticles of metals such as silver or zinc/zinc oxide. Such materials can be obtained by physicochemical, chemical and biological methods. The most widespread are chemical methods, but recently there has been a noticeable increase of interest in biological methods which are simple, relatively inexpensive and environmentally friendly. What's more, research has shown that biologically synthesized nanoparticles have better antimicrobial properties while being less toxic to the human body. Another interesting approach in the fight against drug resistance may be the use of metal nanoparticles in combination with antibiotics. The synergistic effects of antibiotics and nanoparticles of metals such as silver, zinc, and gold have been proven in several experiments. However, the mechanism of action of the nanoparticles as well as the complexes of antibiotic and nanoparticles has not been explained so far. It is believed that nanoparticles can damage the bacterial cell wall so that they can act as a drug carrier to inside of cell.

A key role in explaining how certain stressors work and to understanding drug resistance mechanisms may be an analysis of molecular profiles, protein expression, or lipid profile of the bacteria they are exposed to stressors. Against this challenge is the use of innovative technology such as matrix-assisted laser desorption/ionization-time-of-flight mass spectrometry (MALDI-TOF MS). This technique, thanks to the use of soft ionization enables for both identification of native bacterial cells as well as the selected expression proteins, and tracing the lipid profiles. For this reason, in the proposed project will be investigate the metabolism of selected, clinically relevant bacteria treated with a specific stressor such as metal ions (eg Ag<sup>+</sup>aq, Zn<sup>2+</sup>aq, Cd<sup>2+</sup>aq), metal nanoparticles (eg AgNPs, ZnNPs/ZnONPs) and their combinations with commercially available antibiotics (eg methicillin, kanamycin, streptomycin) by electrophoretic techniques and mass spectrometry MALDI-TOF MS. Synthesized metallo-antibiotics based on protein-antibiotic and metal-antibiotic interactions may be a desirable pharmaceutical product. The results obtained during the project will help to deepen the current state of knowledge about the effects of metal ions, nanoparticles, antibiotics and their connections on bacterial cells.