Bacterial resistance to antibiotics is one of the greatest challenges facing researchers today. Years of uncontrolled use of antibiotics in medicine and animal production contributed to the drug resistance of bacteria. This problem often occurs in gram-negative bacteria, which have an additional outer lipid membrane, impermeable to many potentially bactericidal components. The negative charge of the bacterial outer membrane is often an big barrier for new antibacterial agents. Nowadays, new alternatives to antibiotics are searching. One of them can be nanomaterials. Among them, we can distinguish dendritic nanoparticles, dendrimers or metallodendrimers, often combined with metal ions such as silver to increase their bactericidal activity. Due to their positive charge, they have the ability to cross and permeabilize the bacterial membrane. In this way, they not only cause damage to the outer membrane of bacteria, but can also open the way for e.g. proteins (lysozyme or phage endolysins) that break down peptidoglycan localized in the bacterial wall.

Bacteriophage-encoded endolysins have emerged as a novel class of antibacterial agents to combat the surging antibiotic resistance. Lysins act as efficient antimicrobials with economical potential. The PG degrading effect of lysins can be seen as osmotic lysis of targeted cell, making these enzymes a desirable and efficient antibacterial agent. Lysins have specific structures and mechanisms to exert antibacterial effect against Gram-positive (G+ve). However, its use against G-ve bacteria is limited because the outer membrane (OM) of G-ve bacteria hinders the permeation of exogenously applied lysins.

Therefore, it seems promising to increase the antibacterial activity of endolysins against gram-negative bacteria by supporting them with cationic dendritic nanoparticles.

In this project, I am going to check whether the complexation of dendritic nanoparticles with phage-derived endolysin can improve their antibacterial properties against gram-negative bacteria. The project will focus on the antimicrobial properties of the dendritic nanoparticles (including metalodendrimers and dendronized metal nanoparticles) complex with endolysin, where dendritic nanoparticles act as permeabilizers of the bacterial outer membrane (OM) and thus can lead to strengthening bactericidal activity of endolysin responsible for the degradation of peptidoglycan PG. In order to answer the question whether the complexation of dendritic nanoparticles with endolysin can increase its effect on multi drug resistant bacteria (mainly gram-negative), we will focus on achieving a few specific goals. (1) Investigating whether complexation of endolysin with selected dendritic nanoparticles will preserve its antibacterial properties (2) Investigating whether dendritic nanoparticles are able to pass through the outer membrane of antibiotic-resistant bacteria strains and help endolysin reach the peptidoglycan. (3) Investigation of the inhibitory properties of bacterial biofilm by complexes of dendritic nanoparticles with endolysin.

A number of biophysical and biochemical methods will answer the final question whether the use of the above mentioned method can lead to develop of a new effective alternative to kill drug-resistant bacteria.