In recent years, the number of infections caused by antibiotic-resistant pathogens is rapidly growing. According to World Health Organization (WHO) the world stands on the edge of a post-antibiotic era, in which common infections can cause death. The awareness of consumers who expect natural and safe preservatives in food and cosmetics is also increasing. These result in a need for new substances with antimicrobial activity. One of the promising group of compounds, that act by killing microorganisms or inhibiting their growth, are bacteriocins - peptides or proteins produced by bacteria. Interestingly, some of them have also been shown to kill tumor cells. Although the first bacteriocin was identified in 1925, their antimicrobial potential has not been fully exploited yet. Only nisin, assigned as E234, is widely used as a natural preservative in the cheese production. This circumstance may result from insufficient knowledge about the molecular mechanisms of bacteriocins action. The biggest challenge is a detailed understanding of how specific bacteriocins differentiate sensitive and resistant bacteria and how they interact with sensitive cells. Previous studies showed that bacteriocins mostly use transport proteins that naturally occur in the cell membranes. During normal growth, transporters facilitate the transfer of nutrients, such as sugars, across a biological membrane. In the presence of bacteriocin, transporters serve as its receptor in the bacterial cells. In the result of bacteriocin-receptor interaction, a pore is formed, which results in the leakage of cytoplasmic metabolites and consequent cell death. Up to date high number and diversity of these compounds have been found and, it is currently believed, that bacteriocins with different structures, physicochemical properties and spectra of activity, interact with distinct receptors on target cells. Importantly, only six receptors have been identified so far. This illustrates how little is known yet and how many studies are needed for detailed understanding of the mechanisms of bacteriocins antimicrobial action.

Our research group is experienced in working on bacteriocins, also in the cooperation with leading European centers. The results of our studies question the currently accepted hypothesis about the diversity of distinct receptors specific for different bacteriocins, suggesting that membrane transporter of sugar, which is mannose, is an important receptor for many bacteriocins with different structure, physicochemical properties and spectra of activity. In this research project we would like to show the superior role of mannose transporter in the binding of various bacteriocins and fill the gap in the knowledge about bacteriocins receptors. Therefore, the primary aim of this project is the identification of at least a dozen of bacteriocins that use the mannose transporter as a receptor. In addition, we will determine their antimicrobial activity against several dozen of indicator bacteria, including pathogenic strains from the genera *Enterococcus*, *Listeria*, *Pseudomonas*, *Staphylococcus*, *Streptococcus* and *Salmonella*.

Beyond receptors identification, published research does not generally provide knowledge about the mechanisms of bacteriocin-receptor interactions. Therefore, we want to investigate how identified bacteriocins recognize and interact with their receptor. The results of our studies suggest that sensitivity to bacteriocins depends on the presence of specific regions and amino acids in mannose transporter structure. Therefore, the secondary aim of this project is the identification of mannose transporter and bacteriocins amino acids, which are responsible for their interaction one with another. To identify specific amino acids that are involved in the bacteriocin-receptor interaction we will use mutagenesis, a process by which the genetic information is changed. We will obtain mutants with changes in these regions of mannose transporter and bacteriocins, which are responsible for their mutual interactions. Thus, we will try to understated how a single transporter can serve as a receptor for so many, different bacteriocins. We hope that our research will expand knowledge about the molecular mechanisms of bacteriocins action and will widely open new possibilities for their further studies.