

Bacteria of genus *Enterococcus* are part of the natural human intestinal microflora. However, in the hospital environment, they are one of the most dangerous microorganisms, causing infections mainly in immunocompromised patients and those undergoing invasive medical procedures. Enterococci survive in extreme environmental conditions, exhibit natural resistance to many antibiotics and easily acquire new resistance mechanisms through efficient exchange of genetic material.

One of the most dangerous drug resistance types found in enterococci is resistance to glycopeptides (vancomycin and/or teicoplanin), which has become particularly prevalent in *Enterococcus faecium*, making this species a hospital alert pathogen. In recent years, an increase in the frequency of nosocomial invasive infections caused by *E. faecium* has been observed in Europe. Due to common resistance to most of the available antibiotics, new treatment options for vancomycin-resistant *E. faecium* (VRE*fm*) infections are urgently needed.

The most common and most dangerous variant of resistance to glycopeptides is the VanA phenotype, conferring a high level resistance to both vancomycin and teicoplanin, and capable of spreading rapidly by horizontal gene transfer. Detailed characterization of national and global VRE*fm* VanA populations and genetic elements encoding the VanA phenotype, especially based on genomic sequencing techniques, is crucial for a better understanding of the epidemiology of these microorganisms and for a more effective search for new treatment options and infection control strategies.

In Poland *E. faecium* VanA constitutes the main cause of vancomycin-resistant enterococcal infections and its role is still growing. However, its current epidemiology in our country has not been studied in detail. Therefore, the proposed project responds to the need for an in-depth analysis of this group of pathogens. It aims at defining the factors that shape current Polish invasive VRE*fm* VanA population from intensive care units (ICUs), with particular emphasis on the role of mobile genetic elements in spreading VanA resistance. To this end, we plan to study the clonal relationship of isolates, susceptibility to clinically important antimicrobial agents, the presence of virulence determinants and the structure of genomes, including plasmids and transposons encoding the VanA phenotype. The use of the genomic approach will allow defining a pool of genes common to the entire studied population and relationship between strains from different regions of the country. The role of particular enterococcal epidemic clones and mobile genetic elements in spreading glycopeptide resistance will be indicated. Complete genome sequences obtained in the proposed study will allow to determine the structure of chromosomes and plasmids present in these microorganisms and will enrich the global pool of *E. faecium* genomes.

The big relevance of the proposed project is based on studying the unexplored epidemiology of invasive VRE*fm* in Poland collected over the last decade, the spread of which has serious clinical consequences, especially in intensive care units. The results of the planned research will significantly enrich information on local and global epidemiology and the evolution of VRE*fm*. The acquired knowledge can potentially be used to search for new therapeutic options and create new infection control and prevention procedures.