

Antimicrobial resistance (AMR) to anti-infective agents has increased dramatically last decades and constitutes a serious threat to health and life worldwide. It is estimated that by 2050 ~10,000,000 people will die of resistant infections and the global production loss will affect notably low and middle-income countries. Particularly relevant in clinical practice is resistance to carbapenems, one of the β -lactams, considered to be the last resort agents reserved for the treatment of serious, life-threatening infections. Carbapenemase-producing *Enterobacterales* (CPE), one of the major carbapenems reservoir in nosocomial, consists resistance to almost all β -lactams, which, with co-presence of resistance determinants to other antibiotics classes significantly reduces any accessible therapeutic options, and in extreme cases even completely eliminates them. OXA-48 type enzymes belonging to the most diverse class D of β -lactamases, have spread rapidly around the world directly from Mediterranean countries. Together with the infection control measures, the epidemiological research are one of the most effective weapon against AMR. Introduction of basic molecular biology techniques has opened new frontiers into infection epidemiology investigations allowing the precise identification and epidemiological tracking of individual epidemic clones, as well as the genetic characterization of AMR determinants. However, the whole-genome sequencing (WGS) application is notably a technological revolution. In comparison to classical molecular biology procedures, the WGS generates incomparably greater amount of data obtained in a relatively short time, and has the highest discriminatory power with almost full reproducibility and comparability. These advantages allowing conducting of comparative relatedness comparisons, crucial in epidemiology, with unprecedented precision.

OXA-48-type CPE producers have been reported in Poland by the National Reference Centre for Susceptibility Testing (NRCST) in Warsaw since 2012. In the following years, the NRCST observed systematic increase in numbers of such cases. The aim of the proposed project is **genomic analysis of OXA-48-type strains from 2013 to 2023**, and refers to the first Polish epidemiological study comprising 54 isolates from 2013-Jan.2017. **Since the beginning of 2017 to the end of 2021, the total number of OXA-48-positive CPE increased 15-times overall**, making the situation alarming. **A significant OXA-48 increase in 2022**, can be associated with **COVID-19 pandemic consequences**, but also with a massive **migration crisis caused by the Russian military aggression in Ukraine**. This phenomenon severely affects the OXA-48 epidemiology in Poland.

The pilot study performed on a pool of isolates from a later period of occurrence (Feb.2017-2021), creates a basis of the project. This analysis revealed several epidemic clones domination, especially in southern Poland. Three of them were previously recorded in our country, as well as in Europe, and the fourth, observed for the first time in 2018, may be a representative of a high-risk epidemic clone appearing increasingly in Europe and worldwide.

During this project the exhaustive genomic analysis of ~2000 OXA-48-type producers will be performed, together with the comprehensive relatedness comparison against international resources deposited in GenBank. Moreover, antimicrobials susceptibility testing, including newly introduced agents will be performed, to provide potential therapeutic options against those microorganisms. The study will represent the current state-of-the-art in CPE population epidemiology studies, providing high-quality data with impact on the European and global knowledge on these infection agents of highest clinical and epidemiological relevance. The precise definition and characterization of the CPE epidemic clones circulating in individual regions/countries is crucial for infection medicine and public health, especially in the era of massive travelling and migrations. Such wide epidemiology investigation would provide a significant impact of this project among research tasks in the field conducted in other countries, and a pioneering nature in Poland.