NIVB Meeting 2022

30th November – 2nd December, 2022
Kutná Hora, Czech Republic

The first annual meeting of the National Institute of Virology and Bacteriology (NIVB)

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Book of abstracts
edited by
Šárka Šímová

National Institute of Virology and Bacteriology

The project National Institute of Virology and Bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) – Funded by the European Union – Next Generation EU.

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MINISTRY OF EDUCATION, YOUTH AND SPORTS

CZECH RECOVERY PLAN

P-56

EPIDEMIC SPREAD OF KPC-PRODUCING BACTERIA IN THE CZECH REPUBLIC

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Carbapenems are currently last-resort antibiotics for the therapy of infections caused by multidrug-resistant Gram-negative bacteria. Therefore, the resistence to those drugs represents a significant threat of current medicine. Genes encoding for carbapenemases are mainly spread on mobile-genetic elements, especially plasmids. As demonstrated by several studies, they can be efficiently spread in bacterial populations. For surveillance purpose, it is crucial to understand evolution and spread of those resistence determinants on molecular-genetic level. In the Czech Republic, carbapenemase-producing bacteria are monitored in a routine level by diagnostic clinical laboratories and confirmed at National Reference Laboratory for Antibiotics of National Institute of Public Health and at Biomedical Center of Faculty of Medicine in Pilsen, Charles University. Whole-genome-sequencing-based molecular surveillance of those bacteria has been established since 2014. Among three main molecular groups of carbapenemases, KPC-type enzymes are spread globally, causing high-level of resistence to carbapenems. In this study we present the ongoing spread of the KPC-producing strains, which is evolving to an epidemic in Czech hospitals. During the period of 2018–2019, a total of 108 KPC-producing Enterobacterales were recovered from 20 hospitals. Analysis of long-read sequencing data revealed the presence of several types of bla_{KPC}-carrying plasmids; 19 out of 25 bla_{KPC}-carrying plasmids could be assigned to R (n = 12), N (n = 5), C (n = 1) and P6 (n = 1) incompatibility (Inc) groups. Five of the remaining bla_{KPC}-carrying plasmids were multireplicon, while one plasmid couldn't be typed. Additionally, phylogenetic analysis confirmed the spread of bla_{KPC}-carrying plasmids among different clones of diverse Enterobacterales species. Our findings demonstrated that the increased prevalence of KPC-producing isolates was due to plasmids spreading among different species. In some districts, the local dissemination of IncR and IncN plasmids was observed. Additionally, the ongoing evolution of bla_{KPC}-carrying plasmids, through genetic rearrangements, favours the preservation and further dissemination of these mobile genetic elements. Therefore, the situation should be monitored, and immediate infection control should be implemented in hospitals reporting KPC-producing strains.

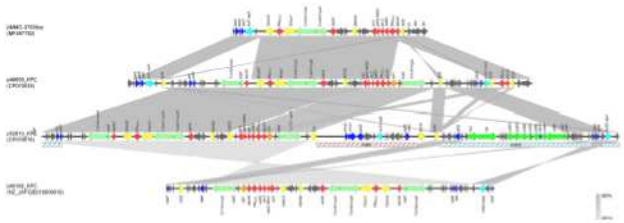

Fig. 1. **Linear comparisons of the KPC-encoding plasmids p48659_KPC and p45182_KPC.** Arrows show the direction of transcription of open reading frames (ORFs). Resistance genes are shown in red. IS elements and transposases are shown in yellow and light green, respectively. intI1 genes are shaded purple. Genes encoding replication, stability and transfer systems are shown in aqua, blue and green colors, respectively. The remaining genes are shown in gray. Homologous segments (representing ≥ 85% sequence identity) are indicated by gray shading.

Acknowledgement

This work was supported by research project grant NU20J-05-00033, provided by the Czech Health Research Council, by the Charles University Research Fund PROGRES (project number Q39), and by project CZ.02.1.01/0.0/0.0/16_019/0000787 "Fighting Infectious Diseases," provided by the Ministry of Education Youth and Sports of the Czech Republic and by the project National Institute of Virology and Bacteriology (Programme EXCELES, ID Project No. LX22NPO5103) – Funded by the European Union – Next Generation EU.