

**L-22
EMERGING PATTERNS OF MICROBIOME AND
RESISTOME IN THE HEALTHCARE ENVIRONMENT**

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The project led by Prof. Dřevínek at the 2nd Faculty of Medicine has two main research objectives (see below). Active collaboration with the groups in the consortium is planned.

**Research objective 1: Molecular epidemiology and
antimicrobial resistance in healthcare-associated pathogens**

Antimicrobial resistance (AMR) is one of the biggest public health challenges. A rapid spread of multi- and pan-resistant bacteria leads to difficult-to-treat infections and higher mortality in healthcare settings. To address this issue, Pavel Dřevínek's research team initiated several national surveillance studies in the Czech Republic and Slovakia with the goal to map the epidemiology of healthcare-associated pathogens (1-3). In addition, large sets of colistin-resistant Enterobacterales and *Burkholderia cepacia* complex isolates were collected over the years during the grant projects (4).

The aim of the project is (i) to perform the prospective surveillance of the currently important nosocomial pathogens in the Czech Republic and Slovakia, i.e. *C. difficile*, *S. aureus* (including methicillin-resistant) and coagulase-negative Staphylococci, vancomycin-resistant Enterococci, and multidrug-resistant Gram-negative bacteria with plasmid-mediated resistance to the last resort antibiotics. The second aim is (ii) to gather deeper knowledge about major clones of antibiotic-resistant nosocomial pathogens and get insight into the forces driving their spread by studying isolates acquired during the prospective surveillance and from retrospective collections of the team. Comparative analysis of genomes and antimicrobial resistance of acquired isolates will allow to elucidate of the specific resistance determinants and their genetic context (plasmid or chromosome-associated genes, mutation) and also perform a phylogenetic analysis of isolates putting them in the local and global context of respective pathogen epidemiology. In addition, the biofilm formation and growth rates of resistant isolates in different conditions will be analysed as important factors influencing the clinical success of the pathogenic bacteria.

**Research objective 2: The human virome in human disease
and its interaction with other exposome components**

The modern concept of the exposome encompasses all the multifaceted exposures acting upon the organism (the microbiota, diet, toxicants, climate), and the response of the organism induced by these exposures (e.g. changes in its transcriptome, proteome, metabolome). Microbes are very important exposome components, including bacteria, archaea,

parasites, fungi or viruses. The technical advances in metagenomics over the last decade enabled researchers to define the microbial component of the exposome with reassuring accuracy, yet the knowledge is incomplete of the association of microbes with a great range of primarily non-infectious diseases, and gaps remain also in the definition of what can be regarded as a healthy microbiome.

The proposed project is a logical extension of the works on virome exploration that the laboratory under the leadership of prof. Cinek has been conducting for over 10 years (5–8). The main objective of this part of the project is to explore the virome in longitudinal sample collections from several diagnoses of medical and societal importance. The project will study the virome during the natural disease course, in reaction to standard treatment modalities, or to targeted interventions in ongoing clinical trials. This will be done in the context of other components of the microbial exposome (bacteriome, mycobiome, parasitome), with background metadata characterizing the available non-microbial exposome (diet, physical activity etc).

Acknowledgement

This work was supported by 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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