

Migliavacca research activity

Study of pathogenicity, mechanisms of resistance, persistence and clinical impact of Multi Drug Resistant Gram-negative pathogens, i.e: *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*.

Treatment of serious infections caused by Gram-negative microorganisms is complicated due to the occurrence of multi-drug resistance.

The nowadays increasing rate of plasmid-mediated carbapenems and colistin resistance is a cause of concern worldwide.

Several distinct mechanisms of acquired antibiotic-resistance could be present in the same strain, and to exactly know the epidemiology of the circulating genes/clones is extremely important in order to set a proper antibiotic therapy.

In multi-drug resistant (MDR) isolates, the relative contributions of different molecular mechanisms toward phenotypic resistance and overall strain virulence is not fully elucidated. Molecular virulence factors characterization and clonality studies could be therefore essential in demonstrating the whole pathogen potential, the bacterial environmental persistence and ability to cause outbreaks. This analysis could be also important for documenting the start of chronic colonisation in patients for whom eradication treatment following the first isolation of a particular pathogen has failed, for demonstrating cross-colonisations between patients, or for identifying new hyper-transmissible clones.

The research plan will lead to completely characterize antibiotic-resistance, survival and persistence mechanisms of the highly successful Gram-negative strains spread in different Italian settings (both environment and health care associated). This will be instrumental for the development of novel strategies to counteract the persistence of invasive clones, for the design of novel specific inhibitors/or antimicrobials and to circumvent multidrug-resistance of these bacteria.

Recently *Klebsiella pneumoniae* producing class A carbapenemase of KPC type, and *Escherichia coli* NDM or OXA-48 producers, characterized by multidrug- or pandrug- resistance has emerged as a new important nosocomial pathogens. The dissemination of such microorganisms is of great concern to public health services worldwide. Improved detection of new resistant strains especially by using practical and affordable screening methods and by evaluating mechanisms of resistance is a priority to implement infection control measures and limit the spread of these worrisome strains.

- 1) Evaluation of the *in vitro* activity of antibiotic molecules, also carried by nanoparticles, against planktonic bacteria or organized in biofilm.
- 2) Study of colistin, tigecycline and phosphomycin resistance determinants in opportunistic pathogens with high clinical impact.
- 3) Phenotypic and molecular characterization of antimicrobial resistance and virulence in Gram-negative pathogens of medical interest (bacterial identification, antibiogram, MIC, MBC, screening tests and identification of ES β L and carbapenemases, biofilm production).
- 4) Identification and study by molecular techniques (PFGE, MLST, rep-PCR, NGS) of epidemic clones (and/or plasmids).
- 5) Epidemiology of MDR microorganisms in community, environment and hospitals (acute care and Long Term and Rehabilitation Facilities).
- 6) Maintaining a high technological standards research biobank.
- 7) Quali- and quantitative evaluation of the bacterial flora on the surface of night-time apnea devices before/after the use of recommended oral hygiene procedures.