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Emerging Carbapenemases in Gram-negative bacteria : Characterization and Epidemiology

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Antibiotic resistance is currently one of the biggest challenges for public health. This work contributes to the analysis of the emerging resistance to carbapenems, which affects the entire world.

New variants of carbapenemases have been discovered (variants of KPC-3: KPC-41 and KPC-50). These variants provide resistance to a new ceftazidim/avibactam combination, which is usually effective against producers of carbapenemases of class A, C and D. The detailed analysis of those enzymes allowed to understand their biochemical properties and the genetic context.

Currently in Europe, we are witnessing a spread of *Escherichia coli* strains producing OXA-244, a variant of OXA-48, which is difficult to detect due to its weak carbapenemase activity. Our work allowed to optimise the detection of OXA-244-producing *E. coli*. The immunochromatographic test NG-Carba 5, NG Biotech and the medium SuperCarba, ChromAgar, allow to isolate and detect all strains producing OXA-244.

As a part of a 2018 Swiss study concerning a potential presence of resistant Gram-negative organisms in animal source foods, a new metallo-β-lactamase of type B2 (PFM-1) has been discovered in a strain of *Pseudomonas synxantha*. That novel enzyme was fully characterized.

An epidemiological study was carried out on 65 clinical strains obtained from Pakistan, in order to evaluate the evolution of the resistance in this region of the world where the resistance is very high and limits the therapeutic possibilities. Very frequently, a multidrug-resistance phenomen (carbapenemases, extended-spectrum ß-lactamases, 16S rRNA methylases) was observed in many clinical strains. Another epidemiological study on 122 environmental samples (water and soil) from Nigeria revealed the presence of multidrug-resistant clinical bacteria in the environment, especially close to hospitals.

Jury: **Prof. Patrice Nordmann (thesis supervisor), Dr Jean-Winoc Decousser, Prof. Michael Walch, Dr Dominique Blanc (external co-examiners), Dr Laurent Poirel (internal examiner), Prof. Curzio Rüegg (president).**