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O0955 Rapid detection and discrimination of chromosome- and MCR-plasmid-mediated resistance to polymyxins by MALDI-TOF MS: The MALDIxin test

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Background: Polymyxins are now considered a last-resort treatment for infections caused by multidrug-resistant Gram-negative bacteria. Recently, the emergence of carbapenemase-producing *Enterobacteriaceae* has accelerated the use of polymyxins in the clinic, resulting in the rise of polymyxin-resistant bacteria. Polymyxin resistance arises through modifications of lipid A, such as the addition of phosphoethanolamine (pETN). The underlying mechanisms involve numerous chromosome-encoded genes or, more worryingly, a plasmid-encoded phosphoethanolamine transferase, named MCR. Currently, detection of polymyxin resistance is difficult and time consuming. There is no available rapid diagnostic test which can identify polymyxin resistance and at the same time differentiate between chromosome- and plasmid-encoded resistances allowing for effective patient management.

Materials/methods: Here, we develop a cost-effective tool based on MALDI-TOF mass-spectrometry that aims to detect polymyxin resistance directly on intact Enterobacteriaceae in less than 15 min. From the obtained spectra, peaks corresponding to intact lipid A and modified lipid A were analysed manually.
This patented technique as been developped using a collection of 79 *E. coli* including 33 polymyxin-resistant strains of which 29 were MCR producers (18 MCR-1, two MCR-1.5, three MCR-2, two MCR-3 and four MCR-5). The 46 polymyxin-susceptible *E. coli* strains were of various phenotypes, from wild-type to carbapenemase producers.
Then, the developed test was prospectively validated on 78 consecutive carbapenemase-producing *E. coli* received from October to November 2016

Results: Only the peak(s) corresponding to the intact lipid A (1796 m/z) has(ve) been detected for polymyxin-susceptible isolates. Independently of the resistance mechanism involved (chromosome- or plasmid-encoded), a peak at 1919 m/z corresponding to the addition of pETN to the 1796 m/z non-modified lipid A has been detected for all polymyxin-resistant isolates. In case of plasmid-mediated resistance (*mcr-like* gene), an additional specific peak, corresponding to the dephosphorylated form of the pETN modified lipid A, was observed at 1821 m/z.
During the prospective study, this technique perfectly and rapidly identified all MCR-1-producing *E. coli* (n=3) where conventional methods would have needed 24 to 48 hours delay.

Conclusions: This rapid and cost-effective technique offers a reliable tool for identification of plasmid-mediated polymyxin resistance in Enterobacteriaceae and therefore a very useful tool for preventing their spread.