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Improvement of the Xpert® Carba-R kit for the accurate detection of carbapenemase-producing Enterobacteriaceae.

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Background

Among the techniques dedicated to the rapid screening of carbapenemase producers, molecular diagnostic assays have been increasingly used. Most of them are able to detect the 'big four' carbapenemase families (KPC, NDM, VIM, and OXA-48-like) that represent more than 95% of the carbapenemase produced by Enterobacteriaceae. Among the commercial kits, only the Xpert® Carba-R kit performed on the GeneXpert (Cepheid, Sunnyvale, CA, USA) can additively detect IMP-1 group producers.(1) However, the first version of the Xpert® Carba-R kit was unable to detect some OXA-48 variants named OXA-181 and OXA-232. Although still rare in France in 2012 when the Xpert Carba-R kit started to be globally distributed, the identification of these two variants rose from 0.8% in 2012,(2) to 3.4% in 2014 and 6.7% at the mid of 2015 of the total EPC received by the Associated French National Reference Centre for Antibiotic Resistance (unpublished data).

Objectives

The aim of the present study was to determine the biological performances of the Xpert Carba-R v2 on a panel of well-characterized enterobacterial isolates with a reduced susceptibility to at least one carbapenem, reflecting the French epidemiology of carbapenemase-producing Enterobacteriaceae (CPE). This novel kit is an improvement of the commercialized Xpert Carba-R assay. Two additional targets are now detected: OXA-232 and OXA-181, OXA-48 variants that are emerging worldwide and especially in France.

Methods

The Xpert Carba-R v2 has been tested on a collection of 150 enterobacterial isolates, that were representative for the French epidemiology. This collection comprised 61 non-carbapenemase producers including 43 strains with decreased susceptibility to almost one carbapenem (imipenem, meropenem or ertapenem) according to EUCAST guidelines, 9 KPC producers, 11 NDM producers, 9 VIM producers, 5 IMP producers, 41 OXA-48 like producers (20 OXA-48, 2 OXA-162, 9 OXA-181, 5 OXA-204, 3 OXA-232 and 2 OXA-244), and 14 strains producing multiple carbapenemases (three NDM-1 + OXA-48, six NDM-1 + OXA-181, two NDM-1 + OXA-232, one NDM-5 + OXA-232, one NDM-1 + VIM-2 and one VIM-4 + OXA-48). The bacteria were isolated on ChromID® CARBA SMART (bioMérieux), a medium commonly used by clinical bacteriology laboratories in France to detect carbapenemase carriers.

Results

- The performances of the Xpert Carba-R v2 are detailed in table 1
- Globally, **the Xpert Carba-R v2** was able to detect **all KPC, all NDM, all VIM, all OXA-48 variants including OXA-181 and OXA-232** and **all multiple carbapenemase producers**. Concerning IMP-type carbapenemases, **all IMP-1 group** (IMP-1 and IMP-11 in our study) were perfectly detected. As claimed by the manufacturer, the two IMP-8 producers, that are not of the IMP-1 group, were not detected.
- In addition, **all non-carbapenemase producers were perfectly identified except two OXA-163 and one OXA-405** producers. These two β -lactamase are OXA-48 variants that possess an extended-spectrum activity towards 3rd generation cephalosporins but that were devoid of any carbapenemase activity due to deletion of four amino-acids in their active site.(3) Although OXA-405 was reported from an unique *S. marcescens* isolate recovered in France,(3) OXA-163 producers that were firstly described in Argentina have already spread in Egypt,(4) paving the way of their possible dissemination in North African countries and Europe.
- Extrapolating these results to the global French CPE epidemiology, the Xpert Carba-R v2 may be able to detect 99.6% (2018/2026) of the CPEs identified by the Associate French NRC between 2012 and 2014, missing only seven IMI-1/2 and one FRI-1 producers (3,5).

Globally, this study demonstrated that the Xpert Carba-R v2 kit is now well adapted to the French epidemiology of CPE.

Table 1: Performances of the Xpert Carba-R v2

Performances	Xpert Carba-R v2	
	This study	Global French CPE epidemiology (2012-2014)
Sensitivity	97.8 %	99.61 %
Specificity	95.3 %	99.98 %
False positive	1 OXA-405 2 OXA-163	1 OXA-405
False negative	2 IMP-8	7 IMI 1 FRI-1 ⁽⁵⁾

Conclusions

The overall performances of the Xpert Carba-R v2 is high, detecting the five major carbapenemases families (NDM, VIM, IMP, KPC, and OXA-48). On top with the inclusion of OXA-181 and OXA-232, the Xpert Carba-R v2 is perfectly in line with the current French epidemiology of CPE, which reflects that of many countries especially in northern Europe.

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