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Noncarbapenemase OXA-48 Variants (OXA-163 and OXA-405) Falsely Detected as Carbapenemases by the β Carba Test

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In *Enterobacteriaceae*, carbapenem resistance may be mediated by (i) plasmid-encoded or chromosome-encoded cephalosporinase and/or extended-spectrum β-lactamase production associated with decrease permeability of the outer membrane and (ii) carbapenemase production (1). During the last decade, the rapid dissemination of carbapenemase-producing *Enterobacteriaceae* (CPE) led to fear of a return to a preantibiotic era in which no antimicrobial molecule might be useful for the treatment of infected patients (1). To limit the spread of CPE, a lot of countries have implemented strict infection control measures for infected and colonized patients. However, implementation of these infection control measure is costly. Accordingly, there is an urgent need for accurate and fast diagnostic tests able to identify CPE among carbapenem-resistant isolates (2). For that purpose, several diagnostic tests have been developed during the last 5 years. They include (i) tests for carbapenemase inhibition activity (2); (ii) the carbapenem inactivation method (3); (iii) detection of carbapenem hydrolysis by matrix-assisted laser desorption ionization–time of flight mass spectrometry (4), biochemical tests (e.g., Carba NP test and derivatives) (5, 6), or an electrochemical method (BYG test) (7); (iv) immunochromatographic assays aiming to detect OXA-48-like CPE, IMP-like CPE, and OXA-48/KPC CPE (8–10); and (v) diverse molecular tools able to detect the most prevalent carbapenemase-encoding genes (11, 12).

Among the biochemical tests able to detect carbapenem hydrolysis activity, a new colorimetric assay, named the β Carba test (Bio-Rad, Marnes La Coquettes, France), based on the color change (yellow to red) of a chromogenic substrate in the presence of a carbapenemase has been recently commercialized. Recently, this test has been evaluated by Compain et al. on a collection of 79 enterobacterial isolates including 30 carbapenemase producers, 12 noncarbapenemase producers with decreased susceptibility to carbapenems, and 37 isolates susceptible to carbapenems (13). In that paper, it was claimed that the β Carba test was 100% specific and 100% sensitive. However, OXA-163-producing *Klebsiella pneumoniae* and OXA-405-producing *Serratia marcescens* gave positive results at 30 min, 1 h, and 3 h with the β Carba test, whereas they were not CPE. Indeed, the OXA-48 group is composed of enzymes with true carbapenemase activity (OXA-48, OXA-181, OXA-204, OXA-232, OXA-244, OXA-245, OXA-370, and OXA-484) and of enzymes devoid of any carbapenemase activity because of an amino acid deletion in their active site (OXA-163, OXA-247, and OXA-405) (14, 15). Because of their close relationship with OXA-48, these three noncarbapenemase variants usually gave false-positive results with molecular methods (11). Since Compain et al. used a molec-

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ular method as a reference, OXA-163 and OXA-405 were falsely considered true carbapenemases. Actually, they are false positive by the β Carba test. Consequently, the performance of the β Carba test on the collection tested is 100% sensitivity and 96.1% specificity at 1 h and 85.7% sensitivity and 96.1% specificity at 30 min, which is the time recommended by the manufacturer. Of note, the other colorimetric tests able to detect carbapenemase activity, named the Carba NP test, the Rapidec Carba NP (bioMérieux, La Balmes les Grottes, France), and the Rapid Carba Screen (ROSCO Diagnostica, Taastrup, Denmark), were previously shown to perfectly detect OXA-163 and OXA-405 as noncarbapenemases (5).

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