

Plasmid-Mediated Carbapenem-Hydrolyzing β -Lactamase KPC in a *Klebsiella pneumoniae* Isolate from France

Carbapenem-hydrolyzing β -lactamases can be metallo- β -lactamases (7), expanded-spectrum oxacillinases (8), or Ambler class A enzymes (1, 2, 4, 6, 9–12). The class A KPC β -lactamases hydrolyze all β -lactams except for cephamycins and have been rarely reported in studies of enterobacterial species (*Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Salmonella enterica*, *Enterobacter* sp.) found in New England and the mid-Atlantic region of the United States; when they are reported, they are found to come from New York City hospitals in particular (2, 4, 6, 9–12). We report here a *K. pneumoniae* isolate from Paris that produced β -lactamase KPC-2.

An 80-year-old man with a 5-year history of prostatic carcinoma and metastasis was admitted in February 2005 at the Cochin hospital in Paris for acute urine retention in the right nephrostomy. The bilateral nephrostomy was performed in December 2004 at a New York City hospital. No hospitalization or antibiotic treatment is known to have taken place during the period between the patient's stay in New York and his emergency hospitalization in Paris. *K. pneumoniae* YC was isolated from urine and blood cultures and, according to disk diffusion susceptibility testing, was resistant or of intermediate susceptibility to all antibiotics except colistin and fosfomycin (3). No other *K. pneumoniae* isolates with similar antibiotic resistance patterns were recovered from the Cochin hospital during this same period of time.

The MICs of β -lactams (3) for *K. pneumoniae* YC confirmed the disk diffusion results, with the MICs of expanded-spectrum cephalosporins and carbapenems being only slightly modified after the addition of clavulanic acid (Table 1). A crude β -lactamase extract of that isolate had significant imipenem hydrolysis activity (0.37 μ mol of imipenem/min/mg of total protein) (5, 8).

Plasmid analysis detected two plasmids of >100 kb and ca. 75 kb in isolate YC. Using ampicillin (100 μ g/ml) and sodium azide (100 μ g/ml; Sigma-Aldrich, Saint-Quentin-Fallavier, France) as selective agents and sodium azide-resistant *Escherichia coli* J53 as the recipient strain, the ca.-75-kb plasmid was self-conjugative and conferred β -lactam resistance patterns for *E. coli* transconjugants similar with respect to the MICs obtained, except for those for cefoxitin, cefotaxime, ceftazidime, and aztreonam, which were lower than those for the parental strain (Table 1). A β -lactamase extract from a transconjugant culture subjected to analytical isoelectric focusing (8) identified two β -lactamases with pI values of 5.4 and 6.8. Using primers for the detection of Ambler class A and class B β -lactamase genes (7, 8), PCR experiments followed by sequencing identified a β -lactamase gene coding for the carbapenemase KPC-2 (pI 6.8) and the narrow-spectrum TEM-1 (pI 5.4), which were also identified from *K. pneumoniae* YC.

Then, by the use of a series of successive PCR primers, the 2.8-kb surrounding sequences of the *bla*_{KPC-2} gene were found to be identical to those surrounding the same *bla*_{KPC-2} gene from a *Salmonella* isolate from Maryland (6).

This report identified a carbapenem-hydrolyzing β -lactamase KPC in France that likely resulted from an intercontinental transfer of the KPC producer from the United States. Up to the time of this discovery, plasmid-mediated KPC enzymes had been a unique feature of the United States, whereas most other broad-spectrum antibiotic resistance genes have been reported in the United States after their initial discoveries elsewhere. The identification of KPC enzymes is worrisome, since they hydrolyze expanded-spectrum cephalosporins and carbapenems and thus could jeopardize therapy for serious infections caused by major nosocomial pathogens. In addition, their detection, based on careful interpretation of reduced carbapenem susceptibility in *Enterobacteriaceae*, remains difficult.

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TABLE 1. MICs of β -lactams for *K. pneumoniae* YC, the transconjugant strain, and the reference strain

β -Lactam(s) ^a	MIC (μ g/ml) for:		
	<i>K. pneumoniae</i> YC	Tc <i>E. coli</i> J53	<i>E. coli</i> J53
Amoxicillin	>256	>256	4
Amoxicillin + CLA	32	32	4
Ticarcillin	>256	>256	2
Ticarcillin + CLA	>256	256	2
Piperacillin	>256	>256	1
Piperacillin + TZB	256	64	1
Cephalothin	>256	>256	4
Cefoxitin	64	2	1
Cefotaxime	64	4	0.06
Cefotaxime + CLA	16	2	0.06
Ceftazidime	64	4	0.06
Aztreonam	>256	16	0.03
Aztreonam + CLA	>256	8	0.03
Imipenem	4	8	0.12
Imipenem + CLA	2	2	0.12
Meropenem	2	2	0.03
Meropenem + CLA	1	0.25	0.03

^a CLA, clavulanic acid at a fixed concentration of 2 μ g/ml; TZB, tazobactam at a fixed concentration of 4 μ g/ml.

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