ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, July 2011, p. 3579–3583 Vol. 55, No. 7
0066-4804/11/$12.00 doi:10.1128/AAC.01783-10
Copyright © 2011, American Society for Microbiology. All Rights Reserved.

Dissemination of bla_{KPC-2} by the Spread of *Klebsiella pneumoniae* Clonal Complex 258 Clones (ST258, ST11, ST437) and Plasmids (IncFII, IncN, IncL/M) among *Enterobacteriaceae* Species in Brazil▽

Leonardo Neves Andrade,[1] Tânia Curiao,[2] Joseane Cristina Ferreira,[1] Juliana Mucedola Longo,[1] Eduardo Carneiro Clímaco,[1] Roberto Martinez,[3] Fernando Bellissimo-Rodrigues,[3] Aníbal Basile-Filho,[3] Marco Antônio Evaristo,[3] Pedro F. Del Peloso,[4] Vanessa Bley Ribeiro,[5] Afonso Luis Barth,[5] Milena Cristina Paula,[6] Fernando Baquero,[2] Rafael Cantón,[2] Ana Lúcia da Costa Darini,[1] and Teresa M. Coque[2]*

Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirao Preto, Brazil[1]; Servicio de Microbiología, Hospital Universitario Ramón y Cajal, Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS), and CIBER en Epidemiología y Salud Pública (CIBERESP), Madrid, Spain[2]; Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirao Preto, Brazil[3]; Laboratório Richet, Rio de Janeiro, Brazil[4]; Unidade de Microbiologia e Biologia Molecular, Serviço de Patologia Clínica, Hospital das Clínicas de Porto Alegre, Porto Alegre, Brazil[5]; and Laboratório Santa Casa de Franca, Franca, Brazil[6]

Received 20 December 2010/Returned for modification 6 February 2011/Accepted 1 May 2011

This article reports the spread of bla_{KPC-2} in the Sao Paulo and Rio de Janeiro states, facilitated by globally spread *K. pneumoniae* clonal complex 258 (CC258) clones (ST258, ST11, and ST437) and a diversity of plasmids (IncFII, IncN, and IncL/M, two untypeable plasmids carrying Tn*4401*a or Tn*4401*b) successfully disseminated among species of the *Enterobacteriaceae* (*Enterobacter cloacae*, *Serratia marcescens*, and *Citrobacter freundii*). It also constitutes the first description of sequence type 258 (ST258) in Brazil, which was associated with a nosocomial hospital outbreak in Ribeirao Preto city.

KPC (*Klebsiella pneumoniae* carbapenemase) enzymes are globally spread β-lactamases of Ambler class A, comprising 10 variants, KPC-2 and KPC-3 being predominant (26; http://www.lahey.org/studies/). They are mainly associated with *K. pneumoniae*, although KPC producers of other *Enterobacteriaceae* species, *Pseudomonas* and *Acinetobacter*, are increasingly reported (26, 39). The bla_{KPC} genes are part of Tn*4401*, which is often linked to mosaic platforms derived from Tn*1331*, a transposon containing bla_{OXA-9} and bla_{TEM-1} (24, 33). Expansion of clones and plasmids that have acquired Tn*4401* seems to have fuelled the recent pandemic dissemination of bla_{KPC} genes (8, 15, 20, 21, 34). To date, only sporadic cases of *K. pneumoniae*, *Enterobacter cloacae*, *Serratia marcescens*, and *Escherichia coli* KPC-2 producers have been documented in Brazil (6, 9, 11, 19, 23, 28, 35, 40).

We analyzed 64 carbapenem-resistant isolates: 57 *K. pneumoniae* isolates, 5 *E. cloacae* isolates, 1 *S. marcescens* isolate, and 1 *Citrobacter freundii* isolate from different patients at 6 hospitals in two distant Brazilian regions (Table 1 and Fig. 1). Identification and antimicrobial susceptibility testing were accomplished by using semiautomatic systems and standard methods (7, 13). Clonal relatedness was established by pulsed-field gel electrophoresis (PFGE) and also by multilocus sequence typing in the case *K. pneumoniae* isolates (http://www.pasteur.fr/recherche/genopole/PF8/mlst/Kpneumoniae.html). Characterization of KPC-2 producers included phenotypic assays, PCR, and further sequencing as reported previously (8).

The *K. pneumoniae* isolates corresponded to 5 PFGE types linked to 6 sequence types (STs): KpA-ST258 (n = 51, comprising 6 subtypes: 42 KpA, 1 KpA1, 3 KpA1′, 2 KpA2, 2 KpA4, and 1 KpA4′), KpA6-ST11 (n = 1), KpB-ST327 (n = 1), KpC-ST44 (n = 2), KpD-ST437 (n = 1), and KpE-ST48 (n = 1). All isolates were resistant to β-lactams, susceptible to colistin and tigecycline, and showed a variable phenotype against aminoglycosides, quinolones, nitrofurantoin, and trimethoprim-sulfamethoxazole (Table 1). Heteroresistance to carbapenems was observed for *K. pneumoniae* and *C. freundii* isolates, as previously reported for KPC and VIM producers (29, 36).

The detection of isolates belonging to the multidrug-resistant *K. pneumoniae* clonal complex 258 (CC258) (ST258 and its single-locus variants ST11 and ST437) is of special concern (37). The ST258 clone is now globally spread and is mostly associated with the emergence and dissemination of KPC producers in different countries of North America, Europe, and Asia (2, 3, 14, 16, 20, 25, 26, 34). The ST11-*K. pneumoniae* lineage, first reported in France in 1997, is currently predominant in China, South Korea, and Hungary and has also been detected in the Netherlands, Norway, Poland, Portugal, Spain, and Brazil (2, 9, 17, 27, 30, 32, 35, 37; Luísa Peixe, personal communication). This clone has been extensively associated with different extended-spectrum beta-lactamases (ESBLs), mainly CTX-M-15 and CTX-M-14 (17, 27, 37) and more recently the KPC-2 (2, 30, 34) and VIM enzymes (18). Only sporadic cases of ST11 have been identified in Brazil; however, its recovery in different Brazilian cities might mirror a wider

* Corresponding author. Mailing address: Servicio de Microbiología, Hospital Universitario Ramón y Cajal, Carretera de Colmenar km 9.1, Madrid 28034, Spain. Phone: 34-913368330. Fax: 34-913368809. E-mail: mcoque.hrc@salud.madrid.org.

▽ Published ahead of print on 16 May 2011.

TABLE 1. Plasmids carrying bla_{KPC-2} genes in *Enterobacteriaceae* from Brazil[a]

Inc group	Size (kb)[b]	Tn*4401* variant	Other beta-lactamases	Species	ST	PFGE pattern[c]	Susceptibility phenotype[d]	No. of isolates	Date[e]	City/state	Sample
FIIs	50, 130, 240	a	OXA-9, TEM-1, SHV-1	*K. pneumoniae*	ST258	KpA	GEN	34	03/2007–06/2008	Ribeirao Preto/SP	Several samples[f]
FIIs	50, 130, 240	a	OXA-9, TEM-1, SHV-1	*K. pneumoniae*	ST258	KpA1	GEN	1	06/2007	Ribeirao Preto/SP	Surgical wound
FIIs	50, 130, 240	a	OXA-9, TEM-1, SHV-1	*K. pneumoniae*	ST258	KpA2	GEN	2	02–06/2008	Ribeirao Preto/SP	Bronco-alveolar lavage; urine
FIIs	130, 150, 270	a	OXA-9, TEM-1, SHV-1	*K. pneumoniae*	ST258	KpA	GEN	1	04/2007	Franca/SP	Urine
FIIs	130	a	OXA-9, TEM-1, SHV-1	*K. pneumoniae*	ST258	KpA	GEN	7	07–08/2009	Ribeirao Preto/SP	Rectal swab
FIIs	130	a	OXA-9, TEM-1, SHV-1	*K. pneumoniae*	ST258	KpA1′	GEN	3	07–08/2009	Ribeirao Preto/SP	Rectal swab
FIIs	130	a	OXA-9, TEM-1, SHV-1	*K. pneumoniae*	ST258	KpA4	GEN	2	08/2009	Ribeirao Preto/SP	Rectal swab
FIIs	130	a	OXA-9, TEM-1, SHV-1	*K. pneumoniae*	ST258	KpA4′	GEN	1	08/2009	Ribeirao Preto/SP	Rectal swab
FIIs	130, 240	a	OXA-9, TEM-1, SHV-1	*K. pneumoniae*	ST11[g]	KpA6	GEN, AMI, TOB	1	07/2009	Ribeirao Preto/SP	Rectal swab
FIIs	130, 140, 160	a	OXA-9, TEM-1, SHV-1, CTX-M-2	*K. pneumoniae*	ST48	KpE	AMI, CIP, LEV, NIT, STX	1	08/2009	Ribeirao Preto/SP	Rectal swab
ut	50, 110	b	OXA-9, TEM-1, SHV-1, CTX-M-2	*K. pneumoniae*	ST44	KpC	GEN, AMI, TOB	2	2008–2009	Rio de Janeiro/RJ	Urine
N	40, 100, 150	b	OXA-9, TEM-1, SHV-1, CTX-M-2	*K. pneumoniae*	ST327	KpB	GEN, AMI, TOB	1	01/2008	Rio de Janeiro/RJ	Urine
N	40, 140	b	OXA-9, TEM-1, SHV-1, CTX-M-2	*K. pneumoniae*	ST437	KpD	GEN, AMI, TOB	1	2009	Rio de Janeiro/RJ	Urine
N	40	b	OXA-9, TEM-1	*E. cloacae*	NA	Eclα	—[j]	2	11/2007–10/2008	Porto Alegre; Lageado/RS	Fragment of foot amputated; urine
ut	20, 100, 250, 300	ut	OXA-9, TEM-1	*E. cloacae*[h]	NA	Eclβ	—	3	01–04/2009	Porto Alegre/RS	Venous catheter; urine; blood
L/M	60	b	OXA-9, TEM-1	*S. marcescens*[i]	NA	Sm	GEN	1	04/2010	Duque de Caxias/RJ	Blood
L/M	50	b	OXA-9, TEM-1	*C. freundii*	NA	Cf	AMI	1	06/2010	Duque de Caxias/RJ	Bile secretion

[a] Abbreviations: GEN, gentamicin; AMI, amikacin; TOB, tobramycin; CIP, ciprofloxacin; LEV, levofloxacin; NIT, nitrofurantoin; STX, trimethoprim-sulfamethoxazole; NA, not applicable; ut = untypeable.

[b] Underlining indicates size of the plasmid carrying bla_{KPC-2}.

[c] PFGE types are defined by capital letters. Subtypes are designated by a number (indicating the number of bands that differed from those of the index strain) and primes when necessary (to distinguish among subtypes differing in the same number of bands, with such bands being different).

[d] The following antibiotics were tested in this study: ampicillin, ampicillin-sulbactam, piperacillin, piperacillin-tazobactam, cefazolin, cefuroxime, cefuroxime-axetil, cefotetan, ceftazidime, ceftriaxone, cefepime, aztreonan, imipenen, meropenen, AMI, GEN, TOB, CIP, LEV, NIT, STX, colistin, and tigecycline.

[e] Dates are given as month/year.

[f] This clone was recovered from samples of blood ($n = 10$), peritoneal cavity ($n = 1$), oropharynx ($n = 2$), urine ($n = 7$), venous catheter ($n = 7$), rectal swab ($n = 3$), broncoalveolar lavage ($n = 1$), sputum ($n = 1$), and wound/abscess ($n = 2$).

[g] ST11 and ST258 show highly related PFGE profiles, as has also been noted in other studies (37).

[h] Strains initially described in reference 40.

[i] Strain initially described in reference 11.

[j] —, susceptible only to colistin and tigecycline according to EUCAST breakpoints (13).

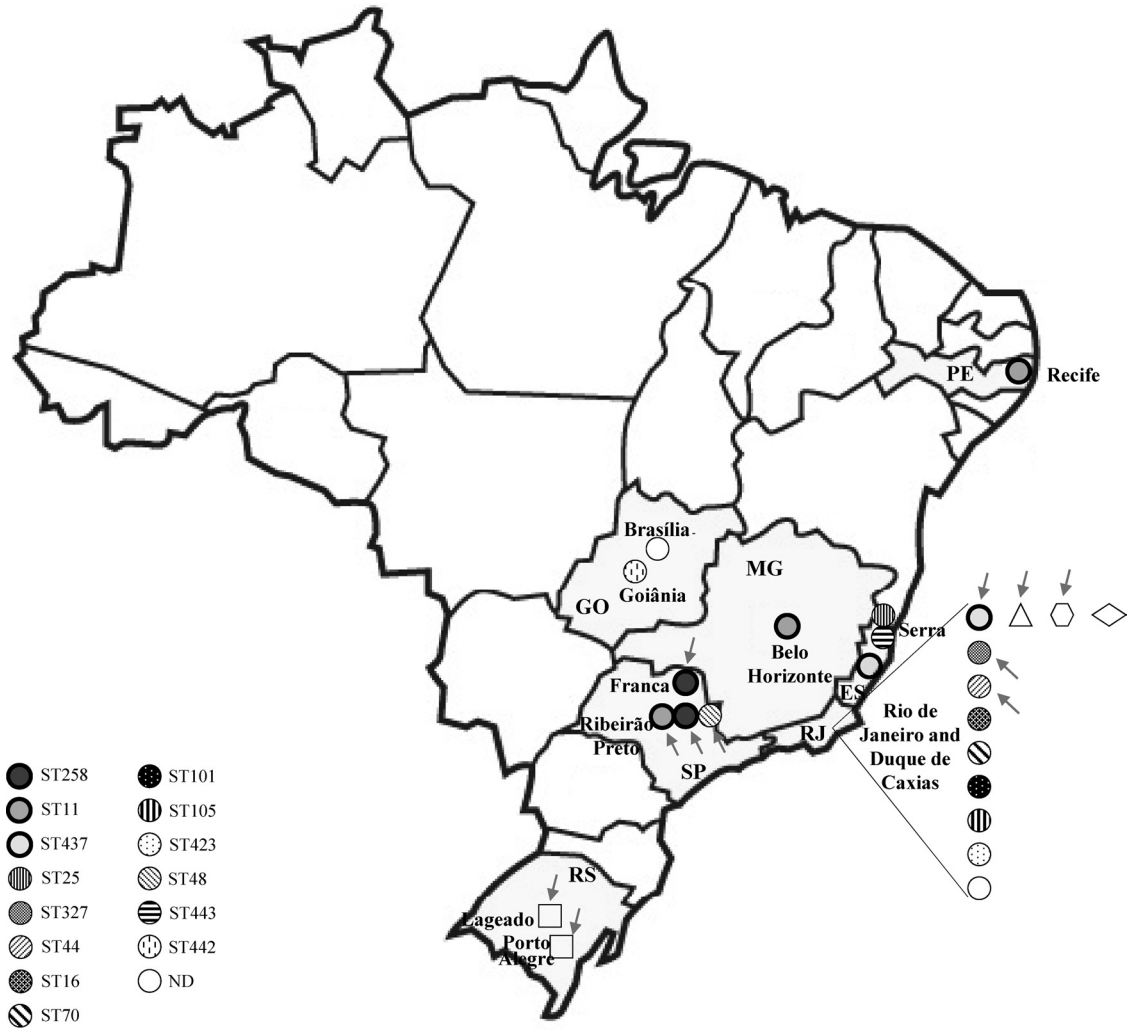

FIG. 1. Geographic distribution of KPC-2-producing *Enterobacteriaceae* in Brazil. Abbreviations: ES, Espirito Santo; GO, Goias; DF, Distrito Federal; MG, Minas Gerais; PE, Pernambuco; RJ, Rio de Janeiro; RS, Rio Grande do Sul; SP, Sao Paulo; ND, not determined. States where KPC producers were isolated appear shaded in gray. *K. pneumoniae* isolates are represented by circles, *E. cloacae* isolates by squares, *S. marcescens* by a triangle, *C. freundii* by a hexagon, and *E. coli* isolates by a rhombus. Bold circles represent STs belonging to CC258 (ST258, ST11, and ST437). Clones analyzed in this study are indicated by arrows. ST25 and ST327 are double-locus variants of each other.

distribution than that reported (9, 35) (http://www.pasteur.fr/recherche/genopole/PF8/mlst/Kpneumoniae.html) (Fig. 1). Even though only one ST437 *K. pneumoniae* isolate, recovered in Rio de Janeiro in 2009, was included in our study, one recent study by Seki et al. (35) has shown the recovery of ST437 isolates producing KPC-2 in this city from 2007 to 2009, and a degree of epidemicity similar to that reported for other CC258 members cannot be discarded. Other clones recovered in this study are not well represented in the databases, such as ST327, previously detected in Israel linked to KPC-2 (21), or ST44 and ST48, which have not previously been associated with KPC production. Although most known KPC-2 producers of *Serratia*, *Enterobacter*, and *Citrobacter* have acquired highly transmissible plasmids from *Klebsiella* isolates, the spread of selected clones of these species might also be happening (31, 38).

The presence of genes encoding carbapenemases (GES, OXA, SPM, IMP, and VIM), ESBLs (CTX-M, TEM, and SHV), and cefamicinases (CMY) was analyzed as described previously (1, 10, 12). The genes bla_{OXA-9} and bla_{TEM-1} were detected in all *K. pneumoniae* isolates, while $bla_{CTX-M-2}$ was identified in *K. pneumoniae* clones KpB, KpC, KpD, and KpE (Table 1). The frequent association of ESBLs or metallo-beta-lactamases (MBLs) with *K. pneumoniae* KPC producers in this and other studies seems to reflect acquisition of transmissible plasmids carrying bla_{KPC-2} by local endemic strains or transmissible plasmids carrying bla_{ESBL} by epidemic clones of KPC producers (8). The presence of CTX-M-2 among *K. pneumoniae* clones other than ST258 or ST11 suggests different origins, importation of globally spreading strains, and/or acquisition of KPC plasmids by endemic CTX-M-2-producing *K. pneumoniae*.

The analysis of the genetic environment of bla_{KPC} by amplification of Tn*4401*, comparison of the restriction fragment length polymorphism (RFLP) patterns obtained by digestion of amplicons with PstI, HindIII, and BamHI, and sequencing

of variants representative of distinct types revealed the presence of Tn*4401* variants known as "a" (53 *K. pneumoniae* isolates) and "b" (4 *K. pneumoniae* isolates, 1 *S. marcescens* isolate, 1 *C. freundii* isolate, and 2 *E. cloacae* isolates) and also an untypeable platform (3 *E. cloacae* isolates). They were associated with a diversity of plasmids which were identified by typing the replication region (PCR and hybridization of S1-digested DNA) and comparison of fingerprintings corresponding to XhoI and HindIII-digested plasmid DNA as described previously (4, 8). While Tn*4401*a was located on a 130-kb IncFII plasmid, Tn*4401*b was detected in plasmids belonging to the incompatibility groups IncN (40 kb), IncL/M (50 to 60 kb), and two untypeable plasmids (20 and 50 kb). Only those of IncFII were transferred by conjugation.

The IncFII plasmids from ST258 *K. pneumoniae* isolates harboring a copy of Tn*4401*a were recovered in Ribeirao Preto city for 2 years. The IncN plasmids carrying the isoform Tn*4401*b were detected in KpB-ST327, KpD-ST437, and *E. cloacae* (Eclα) isolated from unrelated patients in Rio de Janeiro, Porto Alegre, and Lageado, cities sited 1,500 km apart in the south/southwest area of Brazil. IncN plasmid replicons were identical to that of pNL194, a 70-kb plasmid widely disseminated in Greece, which carries an MBL gene (22) (GenBank accession no. GU585907). A diversity of IncN plasmids with similar backbones but slightly different replicon sequences are increasingly associated with genes encoding carbapenemases of class A (KPC) or class B (VIM), reflecting the spread of IncN evolving from a common precursor (5, 15, 22). The IncL/M plasmids that also contained Tn*4401*b were recovered from *S. marcescens* and *C. freundii*. Cuzon et al. have recently described the location of the bla_{KPC-2} gene in 12-kb IncL/M plasmids from *K. pneumoniae* isolates collected in northeast Brazil (9), and the national dissemination of highly transferable IncL/M plasmids carrying bla_{KPC-2} cannot be discarded.

This article reports the spread of bla_{KPC-2} in Sao Paulo and Rio de Janeiro states facilitated by globally spread *K. pneumoniae* CC258 clones (ST258, ST11, and ST437) and a diversity of plasmids successfully disseminated among *Enterobacteriaceae* species. It also constitutes the first description of ST258 in Brazil associated with a nosocomial outbreak in a university hospital of Ribeirao Preto city. Although only sporadic cases of KPC producers have been documented in South America (Argentina, Colombia, and Brazil) (9, 11, 24, 40), this work has pointed out the high diversity of available genetic platforms carrying bla_{KPC-2}. This might greatly amplify the dissemination of KPC genetic elements in this continent.

This study was funded by research grants from Conselho Nacional de Desenvolvimento Científico e Tecnológico in Brazil (CNPq, Projeto Universal, no. 480848/2008-4), the European Commission (LSHM-CT-2009-227258 HEALTH-F3-2008-223031), and the CIBERESP Network for Biomedical Research in Epidemiology and Public Health (Instituto Carlos III, Ministerio de Ciencia e Innovación of Spain, reference number CB06/02/0053). Initial identification and characterization of the strains were supported with laboratory equipment by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP). L.N.A. is supported by a CNPQ fellowship (Doutorado no País, no. 142736/2008-2) and CNPQ fellowship (Doutorado sanduíche, no. 201191/2009-1). T.C. is supported by a fellow research contract grant, FI09/00901, from Instituto Carlos III, Spanish Ministry of Science and Innovation.

We thank the staff of the Laboratory of Microbiology of Hospital das Clínicas of Faculty of Medicine of Ribeirão Preto, University of São Paulo (HC-FMRP-USP), for providing most of the isolates included in this study. We also thank personnel belonging to the infection control committee and to the intensive care unit (ICU) for supporting the investigation of intestinal colonization by carbapenemase-producing members of the *Enterobacteriaceae* among inpatients at the ICU of HC-FMRP-USP.

The clonal data are publicly available at http://www.pasteur.fr/mlst.

REFERENCES

1. **Andrade, L. N., et al.** 2010. Determinants of beta-lactam resistance in meningitis-causing *Enterobacteriaceae* in Brazil. Can. J. Microbiol. **56:**399–407.
2. **Baraniak, A., et al.** 2009. Emergence of *Klebsiella pneumoniae* ST258 with KPC-2 in Poland. Antimicrob. Agents Chemother. **53:**4565–4567.
3. **Bogaerts, P., et al.** 2010. Emergence of clonally related *Klebsiella pneumoniae* isolates of sequence type 258 producing KPC-2 carbapenemase in Belgium. Antimicrob. Agents Chemother. **65:**361–362.
4. **Carattoli, A., et al.** 2005. Identification of plasmids by PCR-based replicon typing. J. Microbiol. Methods **63:**219–228.
5. **Carattoli, A., et al.** 2010. Complete nucleotide sequence of the IncN plasmid pKOX105 encoding VIM-1, QnrS1and SHV-12 proteins in *Enterobacteriaceae* from Bolzano, Italy compared with IncN plasmids encoding KPC enzymes in the USA. J. Antimicrob. Chemother. **65:**2070–2075.
6. **Carvalho-Assef, A. P. D., et al.** 2010. *Escherichia coli* producing KPC-2 carbapenemase: first report in Brazil. Diagn. Microbiol. Infect. Dis. **68:**337–338.
7. **Clinical and Laboratory Standards Institute.** 2011. Performance standards for antimicrobial susceptibility testing. CLSI M100-S21. Clinical and Laboratory Standards Institute, Wayne, PA.
8. **Curiao, T., et al.** 2010. Emergence of bla_{KPC-3}-Tn*4401*a associated with a pKPN3/4-like plasmid within ST384 and ST388 *Klebsiella pneumoniae* clones in Spain. J. Antimicrob. Chemother. **65:**1608–1614.
9. **Cuzon, G., et al.** 2010. Worldwide diversity of *Klebsiella pneumoniae* that produces β-lactamase bla_{KPC-2} gene. Emerg. Infect. Dis. **16:**1349–1356.
10. **D'Andrea, M. M., et al.** 2006. CMY-16, a novel acquired AmpC-type beta-lactamase of the CMY/LAT lineage in multifocal monophyletic isolates of Proteus mirabilis from northern Italy. Antimicrob. Agents Chemother. **50:**618–624.
11. **Del Peloso, P. F., M. F. L. Barros, and F. A. Santos.** 2010. Sepse por *Serratia marcescens* KPC. J. Bras. Patol. Med. Lab. **46:**365–367.
12. **Ellington, M. J., J. Kistler, D. M. Livermore, and N. Woodford.** 2007. Multiplex PCR for rapid detection of genes encoding acquired metallo-β-lactamases. J. Antimicrob. Chemother. **59:**321–322.
13. **European Committee on Antimicrobial Susceptibility Testing.** 5 January 2011. Breakpoint tables for interpretation of MICs and zone diameters. EUCAST clinical breakpoint table v. 1.3 2011-01-05. European Committee on Antimicrobial Susceptibility Testing, Vaxjo, Sweden. http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Disk_test_documents/EUCAST_breakpoints_v1.3_pdf.pdf.
14. **Giani, T., et al.** 2009. Emergence in Italy of *Klebsiella pneumoniae* sequence type 258 producing KPC-3 carbapenemase. J. Clin. Microbiol. **47:**3793–3794.
15. **Gootz, T. D., et al.** 2009. Genetic organization of transposase regions surrounding bla_{KPC} carbapenemase genes on plasmids from *Klebsiella* strains isolated in a New York city hospital. Antimicrob. Agents Chemother. **53:**1998–2004.
16. **Kitchel, J., et al.** 2009. Molecular epidemiology of KPC-producing *Klebsiella pneumoniae* isolates in the United States: clonal expansion of multilocus sequence type 258. Antimicrob. Agents Chemother. **53:**3365–3370.
17. **Ko, K. S., et al.** 2010. Predominance of an ST11 extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* clone causing bacteraemia and urinary tract infections in Korea. J. Med. Microbiol. **59:**822–828.
18. **Kristóf, K., et al.** 2010. Identification of a bla_{VIM-4} gene in the internationally successful *Klebsiella pneumoniae* ST11 clone and in a *Klebsiella oxytoca* strain in Hungary. J. Antimicrob. Chemother. **65:**1303–1305.
19. **Leão, R. S., et al.** 2011. KPC-2 producing *Klebsiella pneumoniae* and *Escherichia coli* co-infection in a catheter related infection. Clin. Microbiol. Infect. **17:**380–382.
20. **Leavitt, A., I. Chmelnitsky, Y. Carmeli, and S. Navon-Venezia.** 2010. Complete nucleotide sequence of KPC-3-encoding plasmid pKpQIL in the epidemic *Klebsiella pneumoniae* sequence type 258. Antimicrob. Agents Chemother. **54:**4493–4496.
21. **Leavitt, A., et al.** 2010. Molecular epidemiology, sequence types, and plasmid analyses of KPC-producing *Klebsiella pneumoniae* strains in Israel. Antimicrob. Agents Chemother. **54:**3002–3006.
22. **Miriagou, V., et al.** 2010. Sequence of pNL194, a 79.3-kilobase IncN plasmid carrying the bla_{VIM-1} metallo-β-lactamase gene in *Klebsiella pneumoniae*. Antimicrob. Agents Chemother. **54:**4497–4502.
23. **Monteiro, J., A. F. Santos, M. D. Asensi, G. Peirano, and A. C. Gales.** 2009. First report of KPC-2-producing *Klebsiella pneumoniae* in Brazil. Antimicrob. Agents Chemother. **53:**333–334.

24. **Naas, T., et al.** 2008. Genetic structures at the origin of acquisition of the β-lactamase bla_{KPC} gene. Antimicrob. Agents Chemother. **52:**1257–1263.
25. **Navon-Venezia, S., et al.** 2009. First report on a hyperepidemic clone of KPC-3-producing *Klebsiella pneumoniae* in Israel genetically related to a strain causing outbreaks in the United States. Antimicrob. Agents Chemother. **53:**818–820.
26. **Nordmann, P., G. Cuzon, and T. Naas.** 2009. The real threat of *Klebsiella pneumoniae* carbapenemase-producing bacteria. Lancet Infect. Dis. **9:**228–236.
27. **Oteo, J., et al.** 2009. Emergence of CTX-M-15-producing *Klebsiella pneumoniae* of multilocus sequence types 1, 11, 14, 17, 20, 35 and 36 as pathogens and colonizers in newborns and adults. J. Antimicrob. Chemother. **64:**524–528.
28. **Peirano, G., et al.** 2009. Carbapenem hydrolysing β-lactamase KPC-2 in *Klebsiella pneumoniae* isolated in Rio de Janeiro, Brazil. J. Antimicrob. Chemother. **63:**265–568.
29. **Pournaras, S., et al.** 2010. Characteristics of meropenem heteroresistance in *Klebsiella pneumoniae* carbapenemase (KPC)-producing clinical isolates of *K. pneumoniae*. J. Clin. Microbiol. **48:**2601–2604.
30. **Qi, Y., et al.** 2011. ST11, the dominant clone of KPC-producing *Klebsiella pneumoniae* in China. J. Antimicrob. Chemother. **66:**307–312.
31. **Rasheed, J. K., et al.** 2008. Detection of the *Klebsiella pneumoniae* carbapenemase type 2 carbapenem-hydrolyzing enzyme in clinical isolates of *Citrobacter freundii* and *Klebsiella oxytoca* carrying a common plasmid. J. Clin. Microbiol. **46:**2066–2069.
32. **Rhee, J. Y., et al.** 2010. KPC-producing extreme drug-resistant *Klebsiella pneumoniae* isolate from a patient with diabetes mellitus and chronic renal failure on hemodialysis in South Korea. Antimicrob. Agents Chemother. **54:**2278–2279.
33. **Rice, L. B., et al.** 2008. The KQ element, a complex genetic region conferring transferable resistance to carbapenems, aminoglycosides, and fluoroquinolones in *Klebsiella pneumoniae*. Antimicrob. Agents Chemother. **52:**3427–3429.
34. **Samuelsen, Ø., et al.** 2009. Emergence of clonally related *Klebsiella pneumoniae* isolates of sequence type 258 producing plasmid-mediated KPC carbapenemase in Norway and Sweden. J. Antimicrob. Chemother. **63:**654–658.
35. **Seki, L. M., et al.** 10 March 2011. Molecular epidemiology of KPC-2-producing Klebsiella pneumoniae isolates in Brazil: the predominance of sequence type 437. Diagn. Microbiol. Infect. Dis. [Epub ahead of print.]
36. **Tato, M., et al.** 2010. Carbapenem heteroresistance in VIM-1-producing *Klebsiella pneumoniae* isolates belonging to the same clone: consequences for routine susceptibility testing. J. Clin. Microbiol. **48:**4089–4093.
37. **Tóth, A., et al.** 2010. Emergence of a colistin-resistant KPC-2-producing *Klebsiella pneumoniae* ST258 clone in Hungary. Eur. J. Clin. Microbiol. Infect. Dis. **29:**765–769.
38. **Tsakris, A., et al.** 2010. In vivo acquisition of a plasmid-mediated bla(KPC-2) gene among clonal isolates of *Serratia marcescens*. J. Clin. Microbiol. **48:** 2546–2549.
39. **Walsh, T. R.** 2010. Emerging carbapenemases: a global perspective. Int. J. Antimicrob. Agents **36S3:**S8–S14.
40. **Zavascki, A. P., et al.** 2009. KPC-2-producing *Enterobacter cloacae* in two cities from Southern Brazil. Int. J. Antimicrob. Agents **34:**286–298.