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KPC-Like Carbapenemase-Producing *Enterobacteriaceae* Colonizing Patients in Europe and Israel

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In a 2008-2011 survey, 17,945 patients in 18 hospital units in Europe and Israel were screened for carriage of *Klebsiella pneumoniae* carbapenemase (KPC)-producing *Enterobacteriaceae*, resulting in identification of 124 positive patients. The isolates were dominated by *Klebsiella pneumoniae* sequence type 258 (ST258) KPC-2 and ST512 KPC-3, mainly from Greece and Italy, respectively, whereas Israeli isolates were of diverse species, clones, and KPC variants. Various bla_{KPC} platforms were observed, among which $IncFII_K$-FIB_K plasmids with $bla_{KPC-2/-3}$ genes in the Tn*4401*a transposon prevailed.

Carbapenemase-producing *Enterobacteriaceae* (CPE) constitute an urgent epidemiological issue (1). One of their major, globally spread mechanisms is *Klebsiella pneumoniae* carbapenemases (KPCs), which hydrolyze most β-lactams (1, 2). KPC-2 and -3 are the most prevalent variants, while *K. pneumoniae* is their predominant host species (3, 4). KPCs have occurred in many *K. pneumoniae* clones (sequence types [STs]) (5–8), but ST258 and its close relative ST512 are key players in the pandemic spread (2–4, 6, 9–11). bla_{KPC} genes are located in Tn*4401* transposon variants (12–15) and inserted into plasmids of various replicon types and transmission potentials (5, 7, 16–20). One type of these, pKpQIL, found first in KPC-3-producing *K. pneumoniae* ST258 in Israel, has two specific replicons, FII_K and FIB_K, and low conjugation efficiency (21–23). Later, KPC-2- or -3-encoding pKpQIL-like molecules were observed in other countries, usually in *K. pneumoniae* ST258 (2, 3, 10, 24, 25).

During the European Union project MOSAR (Mastering hOSpital Antimicrobial Resistance in Europe), patients in intensive care units (ICUs) and rehabilitation units (RUs) in Europe and Israel were screened for *Enterobacteriaceae* resistant to expanded-spectrum cephalosporins (ESCs) (26). Since KPCs and metallo-β-lactamases (MBLs) confer resistance to ESCs (1), the project allowed performance of a large-scale comparative study of the KPC and MBL CPE carriage. A previous report concerned MBL CPE (27), while here we present the KPC data.

Between mid-2008 and mid-2011, all patients in 13 ICUs and five RUs in nine countries ($n = 17,945$) were screened for ESC-resistant (ESC-R) *Enterobacteriaceae* (Table 1). Rectal swabbing was performed regularly from admission until discharge. Swabs were plated onto Brilliance ESBL agar (Oxoid, Basingstoke, United Kingdom); enterobacterial colonies were stored for definite analysis. Species were identified with Vitek 2 (bioMérieux, Marcy l'Etoile, France). All isolates were tested for extended-spectrum β-lactamases (ESBLs) and AmpC-type cephalosporinases by the ESBL double-disk synergy test (DDST) without and with 250 μg/ml cloxacillin (28) and for susceptibility to ertapenem, imipenem, and meropenem. Carbapenemase screening breakpoints were from EUCAST (http://eucast.org). All suspected CPE isolates were subjected to KPC, MBL, and OXA-48 phenotypic detection, using the combined disk test with phenylboronic acid (PBA CDT) (29), the DDST with EDTA (30), and the temocillin disk (31), respectively. All nonduplicate PBA CDT-positive organisms were tested by PCR for bla_{KPC} genes (32), and this test was performed also for putative MBL producers (27).

A total of 124 patients carrying 127 unique KPC CPE organisms were identified in 6 of 18 clinical sites, located in Greece (centers AT, $n = 44$, and LA, $n = 35$), France (center RP, $n = 1$), Israel (center LH, $n = 6$, and TA, $n = 16$), and Italy (center FS, $n = 22$) (Table 1). They were 59.0% of all patients with CPE. Four Greek patients had *K. pneumoniae* strains coproducing KPC and MBL (VIM-1) and were reported previously too (27). The results for individual countries concurred with those of other reports. Since 2008, after the nationwide outbreak in 2006 and 2007, KPCs in Israel have been endemic at a lower level (2, 33, 34). Consistently, the KPC cases in the Israeli RUs were scattered during the study, being ~1% of all patients screened and ~2% of those with ESC-R organisms (Table 1). The KPC spread in Greece commenced in 2007 and was much advanced by mid-2008 (2, 34–36). Both Greek ICUs recorded KPC cases from the survey start, and their contribution to all patients screened and to ESC-R *Enterobacteriaceae* carriers was ~6% and ~35%, respectively. Italy reported the first KPC case in 2008, followed by an outbreak progressing rapidly from 2010 (2, 34, 37). The RU FS, screening patients from February 2009 to February 2011, had its first 2 cases late in 2009 and then 12 in 2010 and 8 in the first 2 months of 2011, being ~3% of all patients and ~6% of those with ESC-R organisms.

The bla_{KPC} amplicons were digested by RsaI (Fermentas, Vilnius, Lithuania), which distinguishes bla_{KPC-2} and bla_{KPC-3} (38),

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TABLE 1 Occurrence of patients colonized by KPC CPE in study centers

Country	Center	Unit type	No. of patients enrolled in the study[a]	No. (%) of patients colonized by *Enterobacteriaceae* producing acquired ESC-hydrolyzing β-lactamases[b,c,d]	No. (%) of patients colonized by CPE[b,d,e]	No. (%) of patients colonized by KPC CPE[d]
France	HM	ICU	2,373	256 (10.8)	1 (0.04)[e]	
France	RP	ICU	1,328	85 (6.4)	1 (0.08)[f]	1 (0.08)
France	SJ	ICU	1,049	51 (4.9)	4 (0.4)	
Greece	AT	ICU	796	117 (14.7)	53 (6.7)[g]	44 (5.5)
Greece	LA	ICU	558	99 (17.7)	83 (14.9)[h]	35 (6.3)
Italy	CA	ICU	788	49 (6.2)	2 (0.3)	
Latvia	RI	ICU	1,464	526 (35.9)	10 (0.7)	
Luxemburg	LU	ICU	1,823	54 (3.0)		
Portugal	PO	ICU	910	18 (2.0)		
Portugal	VR	ICU	628	24 (3.8)	1 (0.2)	
Slovenia	GO	ICU	919	32 (3.5)		
Slovenia	LJ	ICU	685	115 (16.8)		
Spain	BA	ICU	1,069	41 (3.8)		
France	BM	RU	410	76 (18.5)		
Israel	LH	RU	564	177 (31.4)	6 (1.1)[i]	6 (1.1)
Israel	TA	RU	1,650	870 (52.7)	16 (1.0)[j]	16 (1.0)
Italy	FS	RU	704	340 (48.3)	28 (4.0)	22 (2.8)
Spain	GI	RU	227	104 (45.8)	5 (2.2)	
Total			17,945	3,034 (16.9)	210 (1.2)	124 (0.7)

[a] All patients that were swabbed at least once at a clinical center, regardless of the length of hospitalization.
[b] These numbers were shown also in the report on colonization by MBL CPE in MOSAR centers (27).
[c] Acquired ESC-hydrolyzing β-lactamases include ESBLs, AmpC-type cephalosporinases, MBLs, and KPCs.
[d] Patients in this column include both those who were colonized at admission and those who were colonized due to in-hospital transmission.
[e] Carbapenemases include KPCs and MBLs except in one patient in the French ICU HM who was colonized with *E. coli* coproducing OXA-48 carbapenemase and ESBL.
[f] This patient was colonized by KPC-producing *K. pneumoniae* and MBL-producing *E. coli*.
[g] One patient was colonized by KPC-producing *E. coli* and MBL-producing *K. pneumoniae*.
[h] Four patients were colonized by *K. pneumoniae* coproducing KPC and MBL.
[i] One patient was colonized by KPC-producing *E. coli* and *K. pneumoniae*.
[j] Two patients were colonized by two different KPC producers: either *C. freundii* and *E. coli* or *E. coli* and *K. pneumoniae*.

followed by sequencing for representative isolates. KPC-producing isolates were typed by pulsed-field gel electrophoresis (PFGE) as described previously (39). PFGE types and subtypes were distinguished visually according to the method of Tenover et al. (40). Selected isolates were analyzed also by multilocus sequence typing (MLST) (41–44); databases available at http://pubmlst.org/cfreundii/ (*Citrobacter freundii*), http://pubmlst.org/ecloacae (*Enterobacter cloacae*), http://mlst.warwick.ac.uk/mlst/dbs/Ecoli (*Escherichia coli*), and http://bigsdb.web.pasteur.fr/klebsiella/klebsiella.html (*K. pneumoniae*) were used for assigning STs. *E. cloacae* STs and β-lactamases were shown previously (45).

K. pneumoniae isolates, being the predominant species (n = 110; 86.6%), were classified into 10 STs (Table 2). ST258 prevailed (n = 76; 69.1%) and was observed in all but one of the sites (FS, Italy), dominating in Greece with bla_{KPC-2} (n = 73; 93.6%). The next-most-prevalent clone, ST512 (n = 21; 19.1%), was originally identified in this study in an Israeli isolate from 2008 (http://bigsdb.web.pasteur.fr/klebsiella/klebsiella.html). This single-locus variant (SLV) of ST258 carried bla_{KPC-3} and dominated in the Italian RU FS (n = 19; 86.4%) but was sporadic in Israel. Four KPC-2- and VIM-1-positive Greek isolates belonged to ST147, the major VIM producer in Greece (27), while the remaining STs represented single isolates with KPC-2 or -3 in individual sites. *C. freundii*, *E. cloacae*, and *E. coli*, usually producing KPC-2s, were identified vastly in Israel and were clonally diverse, except for *E. coli* ST131, of which there were three KPC-2 or -3 isolates. Most of the *E. cloacae*, *E. coli*, and *K. pneumoniae* isolates represented international clones (45, 46). For *C. freundii*, the clonality data are scarce (27, 41, 47), but KPC-producing *C. freundii* ST14, originally identified in this study, was found in 2015 in Malaysia [http://pubmlst.org/cfreundii/]. In general, the clonality plus KPC type data were congruent with data in national reports. The high KPC CPE diversity in the Israeli centers corresponds to the endemicity situation following the polyclonal outbreak of KPC-2 and the clonal spread of *K. pneumoniae* ST258 KPC-3 (7, 19, 22, 48, 49), even if other studies still indicate the importance of *K. pneumoniae* ST258/ST512 (50). In contrast, the high prevalence of ST258 KPC-2 in Greece and ST512 KPC-3 in Italy reflected their clonal dissemination in real time (35–37). This study is also yet another report on KPC-producing *E. coli* ST131, which has been repeatedly identified in Israel (4, 49, 51, 52).

The location of bla_{KPC} genes within Tn*4401*-like transposons and polymorphism of these was analyzed by PCR mapping (12). For the Tn*4401*g variant (15), an additional primer was designed (5′-GTTCCACTGAGCGTCAGAC-3′) for use with primer 3781L (12) (expected product size, 370 bp). All bla_{KPC} genes were located in Tn*4401* variants (12). The main type was Tn*4401*a (12), observed in all isolates from Greece, Italy, and France and in 9/22 Israeli isolates, including most *K. pneumoniae* isolates with bla_{KPC-2} or bla_{KPC-3} (Table 2). Tn*4401*c (14) and Tn*4401*g (15)

TABLE 2 Geographic distribution, species, clones, pulsotypes, S1 plasmid profiles, plasmids and Tn*4401* transposons with bla_{KPC} genes, and other acquired β-lactamases of KPC CPE isolates[a]

Center	Species	ST (CC or CG)[b]	No. of isolates	No. of pulsotypes (no. of subtypes)	S1 profile[c]	Size of plasmid (kb); replicon(s) of plasmid with bla_{KPC} gene(s)[d]	bla_{KPC}[e]	Tn*4401* variant[f]	MBL, ESBL, and/or AmpC (no. of isolates)[g]
AT (Greece)	*E. coli*	ST10 (CC10)	1	1	Eco1	**~130; FII_K + FIB_K**	bla_{KPC-2}	Tn*4401*a	TEM-1
	K. pneumoniae	ST258 (CG258)	43	2 (18)	Kpn1	**~120; FII_K + FIB_K**	bla_{KPC-2}	Tn*4401*a	SHV-12 + TEM-1
					Kpn2	**~115; FII_K + FIB_K**	bla_{KPC-2}	Tn*4401*a	SHV-12 + TEM-1
LA (Greece)	*K. pneumoniae*	ST17 (CG17)	1	1	Kpn4	**~115; FII_K + FIB_K**	bla_{KPC-2}	Tn*4401*a	SHV-5 + TEM-1
	K. pneumoniae	ST147 (CC147)[h]	4	1 (2)	Kpn6	~115; *FII_K* + *FIB_K*	bla_{KPC-2}	Tn*4401*a	VIM-1 + TEM-1
					Kpn9	~100; *FII_K* + *FIB_K*			
	K. pneumoniae	ST258 (CG258)	30	1 (12)	Kpn2	~115; *FII_K* + *FIB_K*	bla_{KPC-2}	Tn*4401*a	SHV-12 + TEM-1
					Kpn10	**~70; NT**	bla_{KPC-2}	Tn*4401*a	SHV-12
FS (Italy)	*K. pneumoniae*	ST16 (CG17)	1	1	Kpn7	**~90; NT**	bla_{KPC-3}	Tn*4401*a	CTX-M-15
	K. pneumoniae	ST45 (CG485)	1	1	Kpn3	~115; *FII_K* + *FIB_K*	bla_{KPC-3}	Tn*4401*a	TEM-1
	K. pneumoniae	ST383 (CC42)	1	1	Kpn8	**~100; FII_K**	bla_{KPC-2}	Tn*4401*a	CMY-4 + TEM-1
	K. pneumoniae	ST512 (CG258)	19	1 (9)	Kpn2/6	**~115; FII_K + FIB_K**	bla_{KPC-3}	Tn*4401*a	TEM-1 (19); SHV-12 + CMY-2 (1); OXA-1 (1)[i]
RP (France)	*K. pneumoniae*	ST258 (CG258)	1	1	ND	ND	bla_{KPC-2}	Tn*4401*a	CTX-M-15 + SHV + TEM-1
LH (Israel)	*E. cloacae*	ST78 (CC74)[j]	1	1	Ecl1	ND	bla_{KPC-2}	Tn*4401*c	SHV-12 + TEM-1[j]
	E. coli	ST131 (CC131)	2	1 (2)	Eco2	**~75; N**	bla_{KPC-2}	Tn*4401*g	TEM-1
	E. coli	ST167 (CC10)	1	1	Eco4	**~90; FII_K + FIB_K**	bla_{KPC-3}	Tn*4401*a	SHV-12 + TEM-1
	E. coli	ST1571	1	1	Eco3	ND	bla_{KPC-2}	Tn*4401*c	SHV-12 + TEM-1
	K. pneumoniae	ST258 (CG258)	1	1	Kpn5	~115; *FII_K* + *FIB_K*	bla_{KPC-3}	Tn*4401*a	TEM-1
	K. pneumoniae	ST512 (CG258)	1	1	Kpn11	**~150; N**	bla_{KPC-3}	Tn*4401*a	-
TA (Israel)	*C. freundii*	**ST14**	1	1	Cfr1	**~80; N**	bla_{KPC-2}	Tn*4401*g	TEM-1 + OXA-1
	C. freundii	**ST12**	1	1	Cfr2	**~80; N**	bla_{KPC-2}	Tn*4401*g	CTX-M-15 + TEM-1
	C. freundii	ND	1	1	Cfr3	**~80; N**	bla_{KPC-2}	Tn*4401*g	SHV-12 + TEM-1 + OXA-1
	C. freundii	**ST10**	1	1	Cfr4	~300; ND	bla_{KPC-2}	Tn*4401*c	TEM-1 + OXA-1
	C. freundii	**ST15**	1	1	Cfr4	~300; ND	bla_{KPC-2}	Tn*4401*c	TEM-1 + OXA-1
	E. cloacae	**ST118**[j]	1	1	Ecl3	~320; ND	bla_{KPC-2}	Tn*4401*c	CTX-M-27 + SHV-12 + TEM-1[j]
	E. cloacae	**ST146**[j]	1	1	Ecl2	~300; ND	bla_{KPC-2}	Tn*4401*c	TEM-1[j]
	E. coli	ST69 (CC69)	1	1	Eco8	**~70; N**	bla_{KPC-2}	NT	TEM-1
	E. coli	ST131 (CC131)	1	1	Eco5	**~115; FII_K + FIB_K**	bla_{KPC-3}	Tn*4401*a	TEM-1
	E. coli	ST216	1	1	Eco6	**~60; N**	bla_{KPC-2}	Tn*4401*g	TEM-1 + OXA-1
	E. coli	**ST3541**	1	1	Eco7	ND	bla_{KPC-2}	Tn*4401*c	CTX-M-15 + SHV-12 + CMY-2 + TEM-1 + OXA-1
	K. pneumoniae	ST17 (CG17)	1	1	Kpn12	**~140; N**	bla_{KPC-2}	Tn*4401*g	TEM-1 + OXA-1
	K. pneumoniae	ST34 (CC34)	1	1	Kpn13	ND	bla_{KPC-2}	Tn*4401*c	CTX-M-15 + SHV-12 + TEM-1 + OXA-1
	K. pneumoniae	ST36 (CG485)	1	1	Kpn14	**~115; FII_K + FIB_K**	bla_{KPC-3}	Tn*4401*a	TEM-1
	K. pneumoniae	ST258 (CG258)	1	1	Kpn2	~115; *FII_K* + *FIB_K*	bla_{KPC-3}	Tn*4401*a	TEM-1
	K. pneumoniae	ST383 (CC42)	1	1	Kpn15	**~115; FIB_K**	bla_{KPC-2}	Tn*4401*a	CTX-M-15 + CMY-4 + TEM-1
	K. pneumoniae	**ST512** (CG258)	1	1	Kpn16	**~140; FII_K + FIB_K**	bla_{KPC-3}	Tn*4401*a	TEM-1 + OXA-1
	K. pneumoniae	ST833 (CG258)	1	1	Kpn17	**~100; FII_K + FIB_K**	bla_{KPC-2}	Tn*4401*a	SHV-12

[a] Other acquired β-lactamases include MBLs, ESBLs, AmpCs, and broad-spectrum β-lactamases. CC, clonal complex; CG, clonal group; ND, not determined; NT, nontypeable; FII_K, FIB_K, and N are plasmid replicon types.

[b] New STs are indicated in bold. Numerous reports on *K. pneumoniae* ST512 have been published since 2012 (2, 11, 34, 37); however, this ST was identified originally in this study (isolate identifier 578 in the *K. pneumoniae* MLST database [http://bigsdb.web.pasteur.fr]). In groups of four or more isolates, MLST was performed for representative isolates, based on the PFGE data.

[c] In large groups of isolates of the same ST/pulsotype (*K. pneumoniae* ST258 and ST512), the S1 analysis was performed for representative isolates. S1 plasmid profiles are numbered within species groups of isolates; profiles differed from each other by number and/or size of plasmids.

[d] Plasmids found in transformants are shown in bold. Replicons shown in italics represent the probable types of bla_{KPC} plasmids (PBRT and pKpQIL PCR mapping was performed on DNA of clinical isolates).

[e] In groups of four or more isolates of the same ST/pulsotype, bla_{KPC} sequencing was performed for representative isolates; for the remaining isolates, RsaI PCR-restriction fragment length polymorphism analysis distinguishing bla_{KPC-2} and bla_{KPC-3} sequences (38) was carried out.

[f] In groups of four or more isolates of the same ST/pulsotype, PCR mapping of Tn*4401*-like elements was performed for representative isolates.

[g] In groups of four or more isolates with the same ST/pulsotype and *bla* genes, PCR profile sequencing was performed for representative isolates.

[h] These isolates were also included in the study of MBL CPE isolates identified during the MOSAR project (27).

[i] All isolates of this group produced TEM-1; one isolate produced additionally SHV-12 and CMY-2, and another one produced OXA-1.

[j] STs and β-lactamases of the *E. cloacae* isolates from LH and TA were reported previously (45).

were found only in Israel in various species and clones, always containing bla_{KPC-2}. Tn*4401*a has been the main type of Tn*4401*, strongly associated with *K. pneumoniae* ST258 worldwide (6, 10, 18, 21, 36), while Tn*4401*c has been observed in diverse KPC-2-producing organisms in Israel (15, 49). Interestingly, Tn*4401*c-derived Tn*4401*g was identified only recently in a single *K. pneumoniae* KPC-2 isolate recovered in Israel in 2008 (15), whereas in this study, it occurred frequently in *C. freundii*, *E. coli*, and *K. pneumoniae*.

Plasmid profiling and identification of bla_{KPC}-carrying plasmids was done with nuclease S1 (New England BioLabs, Beverly, MA) analysis (53) and hybridization with the bla_{KPC} probe, using the enhanced-chemiluminescence (ECL) Random-Prime labeling and detection system (Amersham Pharmacia Biotech, Little Chalfont, United Kingdom). The analysis comprised 44 isolates of all species, STs, and pulsotypes (15 *K. pneumoniae* ST258/ST512 isolates), revealing highly varied plasmid profiles, with bla_{KPC}-carrying plasmids ranging in size from ~60 to ~320 kb (Table 2). Plasmid DNA of 27 isolates of various species, STs, and S1 profiles was purified with the Qiagen plasmid midi kit (Qiagen, Hilden, Germany) and electroporated into *E. coli* DH5α, with transformant selection with 0.5 μg/ml imipenem or 1 μg/ml cefotaxime. Subsequently, plasmids of the transformants were purified and subjected to PCR-based replicon typing (PBRT) (54–57). KPC-positive transformants were obtained for 22 isolates (Table 2). PBRT revealed that 12 of these had plasmids with FII_K and FIB_K replicons (alternating in two cases) of ~90 to ~140 kb. PCR mapping, performed as proposed by Baraniak et al. (10), showed that all these were of the pKpQIL type (21), and molecules positive in that assay were identified also in selected isolates for which no transformants were available (Table 2). The pKpQIL-like plasmids carried bla_{KPC-2} or bla_{KPC-3} (Tn*4401*a) and were hosted mainly in *K. pneumoniae* ST258 and ST512 isolates; however, these occurred also in other organisms (10, 22, 23). The other group was IncN plasmids of ~60 to ~150 kb, identified in various *C. freundii*, *E. coli*, and *K. pneumoniae* Israeli strains, usually carrying bla_{KPC-2} (Tn*4401*g). These plasmids have been observed among diverse KPC-2-producing *E. coli* and non-CG258 *K. pneumoniae* isolates in Israel (15, 49). However, some of our isolates fell beyond this pattern, like *K. pneumoniae* ST833 (SLV of ST258), with bla_{KPC-2} on a pKpQIL-like plasmid or *K. pneumoniae* ST512 with bla_{KPC-3} on an IncN molecule. Finally, the bla_{KPC-2} gene in the Tn*4401*c variant was observed in *C. freundii* and *E. cloacae* in large plasmids (~300 to ~320 kb) that could not be separated by transfer despite repeated attempts; their replicon types thus remained undetermined.

The KPC CPE isolates were analyzed for other acquired β-lactamase genes, namely, $bla_{SHV-5/SHV-12}$, bla_{CTX-M}, bla_{CMY-2}, bla_{TEM}, and bla_{OXA-1} types, by PCR and sequencing (32, 58–60). The isolates had various β-lactamase combinations, including SHV- and CTX-M-like ESBLs, AmpCs of the CMY-2 type, and broad-spectrum TEM-1 and OXA-1 enzymes (Table 2).

We assessed the KPC CPE carriage among ICU and RU patients on a large international scale, using the same time frame and methodology. Not surprisingly, KPC producers were found mainly in the countries which reported their wide spread, i.e., Greece, Italy, and Israel (2, 33–37). Considering the study period, 2008 to 2011, the rhythm of occurrence of cases in individual centers and characteristics of the organisms reflected the situation in the countries, i.e., the onset and advanced stage of nationwide outbreaks in Italy and Greece, respectively, and the postoutbreak endemicity in Israel (33, 35–37). The analysis provided a comparative snapshot of the geographic and quantitative distribution of species/clones, Tn*4401* transposon variants, and bla_{KPC}-carrying plasmids, often observed in national reports. Also, this has been one of the first studies of *C. freundii* and *E. cloacae* that included MLST data.

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REFERENCES

1. **Nordmann P, Poirel L.** 2014. The difficult-to-control spread of carbapenemase producers among Enterobacteriaceae worldwide. Clin Microbiol Infect **20:**821–830. http://dx.doi.org/10.1111/1469-0691.12719.
2. **Munoz-Price LS, Poirel L, Bonomo RA, Schwaber MJ, Daikos GL, Cormican M, Cornaglia G, Garau J, Gniadkowski M, Hayden MK, Kumarasamy K, Livermore DM, Maya JJ, Nordmann P, Patel JB, Paterson DL, Pitout J, Villegas MV, Wang H, Woodford N, Quinn JP.** 2013. Clinical epidemiology of the global expansion of *Klebsiella pneumoniae* carbapenemases. Lancet Infect Dis **13:**785–796. http://dx.doi.org/10.1016/S1473-3099(13)70190-7.
3. **Pitout JD, Nordmann P, Poirel L.** 2015. Carbapenemase-producing *Klebsiella pneumoniae*, a key pathogen set for global nosocomial dominance. Antimicrob Agents Chemother **59:**5873–5884. http://dx.doi.org/10.1128/AAC.01019-15.
4. **Mathers AJ, Peirano G, Pitout JD.** 2015. The role of epidemic resistance

plasmids and international high-risk clones in the spread of multidrug-resistant *Enterobacteriaceae*. Clin Microbiol Rev **28:**565–591. http://dx.doi.org/10.1128/CMR.00116-14.

5. **Cuzon G, Naas T, Truong H, Villegas MV, Wisell KT, Carmeli Y, Gales AC, Venezia SN, Quinn JP, Nordmann P.** 2010. Worldwide diversity of *Klebsiella pneumoniae* that produce β-lactamase bla_{KPC-2} gene. Emerg Infect Dis **16:**1349–1356. http://dx.doi.org/10.3201/eid1609.091389.
6. **Kitchel B, Rasheed JK, Patel JB, Srinivasan A, Navon-Venezia S, Carmeli Y, Brolund A, Giske CG.** 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. http://dx.doi.org/10.1128/AAC.00126-09.
7. **Leavitt A, Carmeli Y, Chmelnitsky I, Goren MG, Ofek I, Navon-Venezia S.** 2010. Molecular epidemiology, sequence types, and plasmid analyses of KPC-producing *Klebsiella pneumoniae* strains in Israel. Antimicrob Agents Chemother **54:**3002–3006. http://dx.doi.org/10.1128/AAC.01818-09.
8. **Curiao T, Morosini MI, Ruiz-Garbajosa P, Robustillo A, Baquero F, Coque TM, Canton R.** 2010. Emergence of bla_{KPC-3}-Tn*4401a* associated with a pKPN3/4-like plasmid within ST384 and ST388 *Klebsiella pneumoniae* clones in Spain. J Antimicrob Chemother **65:**1608–1614. http://dx.doi.org/10.1093/jac/dkq174.
9. **Navon-Venezia S, Leavitt A, Schwaber MJ, Rasheed JK, Srinivasan A, Patel JB, Carmeli Y.** 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. http://dx.doi.org/10.1128/AAC.00987-08.
10. **Baraniak A, Grabowska A, Izdebski R, Fiett J, Herda M, Bojarska K, Zabicka D, Kania-Pudlo M, Mlynarczyk G, Zak-Pulawska Z, Hryniewicz W, Gniadkowski M.** 2011. Molecular characteristics of KPC-producing *Enterobacteriaceae* at the early stage of their dissemination in Poland, 2008–2009. Antimicrob Agents Chemother **55:**5493–5499. http://dx.doi.org/10.1128/AAC.05118-11.
11. **Warburg G, Hidalgo-Grass C, Partridge SR, Tolmasky ME, Temper V, Moses AE, Block C, Strahilevitz J.** 2012. A carbapenem-resistant *Klebsiella pneumoniae* epidemic clone in Jerusalem: sequence type 512 carrying a plasmid encoding *aac(6′)-Ib*. J Antimicrob Chemother **67:**898–901. http://dx.doi.org/10.1093/jac/dkr552.
12. **Naas T, Cuzon G, Villegas MV, Lartigue MF, Quinn JP, Nordmann P.** 2008. Genetic structures at the origin of acquisition of the β-lactamase bla_{KPC} gene. Antimicrob Agents Chemother **52:**1257–1263. http://dx.doi.org/10.1128/AAC.01451-07.
13. **Kitchel B, Rasheed JK, Endimiani A, Hujer AM, Anderson KF, Bonomo RA, Patel JB.** 2010. Genetic factors associated with elevated carbapenem resistance in KPC-producing *Klebsiella pneumoniae*. Antimicrob Agents Chemother **54:**4201–4207. http://dx.doi.org/10.1128/AAC.00008-10.
14. **Naas T, Cuzon G, Truong HV, Nordmann P.** 2012. Role of IS*Kpn7* and deletions in bla_{KPC} gene expression. Antimicrob Agents Chemother **56:**4753–4759. http://dx.doi.org/10.1128/AAC.00334-12.
15. **Chmelnitsky I, Shklyar M, Leavitt A, Sadovsky E, Navon-Venezia S, Ben Dalak M, Edgar R, Carmeli Y.** 2014. Mix and match of KPC-2 encoding plasmids in Enterobacteriaceae-comparative genomics. Diagn Microbiol Infect Dis **79:**255–260. http://dx.doi.org/10.1016/j.diagmicrobio.2014.03.008.
16. **Andrade LN, Curiao T, Ferreira JC, Longo JM, Climaco EC, Martinez R, Bellissimo-Rodrigues F, Basile-Filho A, Evaristo MA, Del Peloso PF, Ribeiro VB, Barth AL, Paula MC, Baquero F, Canton R, Darini AL, Coque TM.** 2011. 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. Antimicrob Agents Chemother **55:**3579–3583. http://dx.doi.org/10.1128/AAC.01783-10.
17. **Gootz TD, Lescoe MK, Dib-Hajj F, Dougherty BA, He W, Della-Latta P, Huard RC.** 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. http://dx.doi.org/10.1128/AAC.01355-08.
18. **Gomez SA, Pasteran FG, Faccone D, Tijet N, Rapoport M, Lucero C, Lastovetska O, Albornoz E, Galas M, Group KPC, Melano RG, Corso A, Petroni A.** 2011. Clonal dissemination of *Klebsiella pneumoniae* ST258 harbouring KPC-2 in Argentina. Clin Microbiol Infect **17:**1520–1524. http://dx.doi.org/10.1111/j.1469-0691.2011.03600.x.
19. **Goren MG, Navon-Venezia S, Chmelnitsky I, Carmeli Y.** 2010. Carbapenem-resistant KPC-2-producing *Escherichia coli* in a Tel Aviv Medical Center, 2005 to 2008. Antimicrob Agents Chemother **54:**2687–2691. http://dx.doi.org/10.1128/AAC.01359-09.
20. **Mataseje LF, Boyd DA, Willey BM, Prayitno N, Kreiswirth N, Gelosia A, Poutanen SM, Low DE, Jenkins SG, Katz K, Mulvey MR.** 2011. Plasmid comparison and molecular analysis of *Klebsiella pneumoniae* harbouring bla_{KPC} from New York City and Toronto. J Antimicrob Chemother **66:**1273–1277. http://dx.doi.org/10.1093/jac/dkr092.
21. **Leavitt A, Chmelnitsky I, Carmeli Y, Navon-Venezia S.** 2010. Complete nucleotide sequence of KPC-3-encoding plasmid pKpQIL in the epidemic *Klebsiella pneumoniae* sequence type 258. Antimicrob Agents Chemother **54:**4493–4496. http://dx.doi.org/10.1128/AAC.00175-10.
22. **Leavitt A, Chmelnitsky I, Ofek I, Carmeli Y, Navon-Venezia S.** 2010. Plasmid pKpQIL encoding KPC-3 and TEM-1 confers carbapenem resistance in an extremely drug-resistant epidemic *Klebsiella pneumoniae* strain. J Antimicrob Chemother **65:**243–248. http://dx.doi.org/10.1093/jac/dkp417.
23. **Adler A, Shklyar M, Schwaber MJ, Navon-Venezia S, Dhaher Y, Edgar R, Solter E, Benenson S, Masarwa S, Carmeli Y.** 2011. Introduction of OXA-48-producing Enterobacteriaceae to Israeli hospitals by medical tourism. J Antimicrob Chemother **66:**2763–2766. http://dx.doi.org/10.1093/jac/dkr382.
24. **Garcia-Fernandez A, Villa L, Carta C, Venditti C, Giordano A, Venditti M, Mancini C, Carattoli A.** 2012. *Klebsiella pneumoniae* ST258 producing KPC-3 identified in Italy carries novel plasmids and OmpK36/OmpK35 porin variants. Antimicrob Agents Chemother **56:**2143–2145. http://dx.doi.org/10.1128/AAC.05308-11.
25. **Chen L, Chavda KD, Melano RG, Jacobs MR, Koll B, Hong T, Rojtman AD, Levi MH, Bonomo RA, Kreiswirth BN.** 2014. Comparative genomic analysis of KPC-encoding pKpQIL-like plasmids and their distribution in New Jersey and New York Hospitals. Antimicrob Agents Chemother **58:**2871–2877. http://dx.doi.org/10.1128/AAC.00120-14.
26. **Derde LP, Cooper BS, Goossens H, Malhotra-Kumar S, Willems RJ, Gniadkowski M, Hryniewicz W, Empel J, Dautzenberg MJ, Annane D, Aragao I, Chalfine A, Dumpis U, Esteves F, Giamarellou H, Muzlovic I, Nardi G, Petrikkos GL, Tomic V, Marti AT, Stammet P, Brun-Buisson C, Bonten MJ.** 2014. Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial. Lancet Infect Dis **14:**31–39. http://dx.doi.org/10.1016/S1473-3099(13)70295-0.
27. **Papagiannitsis CC, Izdebski R, Baraniak A, Fiett J, Herda M, Hrabak J, Derde LP, Bonten MJ, Carmeli Y, Goossens H, Hryniewicz W, Brun-Buisson C, Gniadkowski M.** 2015. Survey of metallo-β-lactamase-producing Enterobacteriaceae colonizing patients in European ICUs and rehabilitation units, 2008–11. J Antimicrob Chemother **70:**1981–1988. http://dx.doi.org/10.1093/jac/dkv055.
28. **Drieux L, Brossier F, Sougakoff W, Jarlier V.** 2008. Phenotypic detection of extended-spectrum β-lactamase production in Enterobacteriaceae: review and bench guide. Clin Microbiol Infect **14**(Suppl 1)**:**S90–S103.
29. **Doi Y, Potoski BA, Adams-Haduch JM, Sidjabat HE, Pasculle AW, Paterson DL.** 2008. Simple disk-based method for detection of *Klebsiella pneumoniae* carbapenemase-type β-lactamase by use of a boronic acid compound. J Clin Microbiol **46:**4083–4086. http://dx.doi.org/10.1128/JCM.01408-08.
30. **Lee K, Lim YS, Yong D, Yum JH, Chong Y.** 2003. Evaluation of the Hodge test and the imipenem-EDTA double-disk synergy test for differentiating metallo-β-lactamase-producing isolates of *Pseudomonas* spp. and *Acinetobacter* spp. J Clin Microbiol **41:**4623–4629. http://dx.doi.org/10.1128/JCM.41.10.4623-4629.2003.
31. **Glupczynski Y, Huang TD, Bouchahrouf W, Rezende de Castro R, Bauraing C, Gerard M, Verbruggen AM, Deplano A, Denis O, Bogaerts P.** 2012. Rapid emergence and spread of OXA-48-producing carbapenem-resistant Enterobacteriaceae isolates in Belgian hospitals. Int J Antimicrob Agents **39:**168–172. http://dx.doi.org/10.1016/j.ijantimicag.2011.10.005.
32. **Baraniak A, Izdebski R, Herda M, Fiett J, Hryniewicz W, Gniadkowski M, Kern-Zdanowicz I, Filczak K, Lopaciuk U.** 2009. Emergence of *Klebsiella pneumoniae* ST258 with KPC-2 in Poland. Antimicrob Agents Chemother **53:**4565–4567. http://dx.doi.org/10.1128/AAC.00436-09.
33. **Schwaber MJ, Lev B, Israeli A, Solter E, Smollan G, Rubinovitch B, Shalit I, Carmeli Y.** 2011. Containment of a country-wide outbreak of carbapenem-resistant *Klebsiella pneumoniae* in Israeli hospitals via a nationally implemented intervention. Clin Infect Dis **52:**848–855. http://dx.doi.org/10.1093/cid/cir025.

34. **Canton R, Akova M, Carmeli Y, Giske CG, Glupczynski Y, Gniadkowski M, Livermore DM, Miriagou V, Naas T, Rossolini GM, Samuelsen O, Seifert H, Woodford N, Nordmann P.** 2012. Rapid evolution and spread of carbapenemases among Enterobacteriaceae in Europe. Clin Microbiol Infect **18:**413–431. http://dx.doi.org/10.1111/j.1469-0691.2012.03821.x.
35. **Pournaras S, Protonotariou E, Voulgari E, Kristo I, Dimitroulia E, Vitti D, Tsalidou M, Maniatis AN, Tsakris A, Sofianou D.** 2009. Clonal spread of KPC-2 carbapenemase-producing *Klebsiella pneumoniae* strains in Greece. J Antimicrob Chemother **64:**348–352. http://dx.doi.org/10.1093/jac/dkp207.
36. **Giakkoupi P, Papagiannitsis CC, Miriagou V, Pappa O, Polemis M, Tryfinopoulou K, Tzouvelekis LS, Vatopoulos AC.** 2011. An update of the evolving epidemic of bla_{KPC-2}-carrying *Klebsiella pneumoniae* in Greece (2009–10). J Antimicrob Chemother **66:**1510–1513. http://dx.doi.org/10.1093/jac/dkr166.
37. **Giani T, Pini B, Arena F, Conte V, Bracco S, Migliavacca R, AMCLI-CRE Survey Participants, Pantosti A, Pagani L, Luzzaro F, Rossolini GM.** 2013. Epidemic diffusion of KPC carbapenemase-producing *Klebsiella pneumoniae* in Italy: results of the first countrywide survey, 15 May to 30 June 2011. Euro Surveill **18:**20489. http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20489.
38. **Lopez JA, Correa A, Navon-Venezia S, Correa AL, Torres JA, Briceno DF, Montealegre MC, Quinn JP, Carmeli Y, Villegas MV.** 2011. Intercontinental spread from Israel to Colombia of a KPC-3-producing *Klebsiella pneumoniae* strain. Clin Microbiol Infect **17:**52–56. http://dx.doi.org/10.1111/j.1469-0691.2010.03209.x.
39. **Seifert H, Dolzani L, Bressan R, van der Reijden T, van Strijen B, Stefanik D, Heersma H, Dijkshoorn L.** 2005. Standardization and interlaboratory reproducibility assessment of pulsed-field gel electrophoresis-generated fingerprints of *Acinetobacter baumannii*. J Clin Microbiol **43:**4328–4335. http://dx.doi.org/10.1128/JCM.43.9.4328-4335.2005.
40. **Tenover FC, Arbeit RD, Goering RV, Mickelsen PA, Murray BE, Persing DH, Swaminathan B.** 1995. Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol **33:**2233–2239.
41. **Bai L, Xia S, Lan R, Liu L, Ye C, Wang Y, Jin D, Cui Z, Jing H, Xiong Y, Bai X, Sun H, Zhang J, Wang L, Xu J.** 2012. Isolation and characterization of cytotoxic, aggregative *Citrobacter freundii*. PLoS One **7:**e33054. http://dx.doi.org/10.1371/journal.pone.0033054.
42. **Diancourt L, Passet V, Verhoef J, Grimont PA, Brisse S.** 2005. Multilocus sequence typing of *Klebsiella pneumoniae* nosocomial isolates. J Clin Microbiol **43:**4178–4182. http://dx.doi.org/10.1128/JCM.43.8.4178-4182.2005.
43. **Miyoshi-Akiyama T, Hayakawa K, Ohmagari N, Shimojima M, Kirikae T.** 2013. Multilocus sequence typing (MLST) for characterization of *Enterobacter cloacae*. PLoS One **8:**e66358. http://dx.doi.org/10.1371/journal.pone.0066358.
44. **Wirth T, Falush D, Lan R, Colles F, Mensa P, Wieler LH, Karch H, Reeves PR, Maiden MC, Ochman H, Achtman M.** 2006. Sex and virulence in *Escherichia coli*: an evolutionary perspective. Mol Microbiol **60:**1136–1151. http://dx.doi.org/10.1111/j.1365-2958.2006.05172.x.
45. **Izdebski R, Baraniak A, Herda M, Fiett J, Bonten MJ, Carmeli Y, Goossens H, Hryniewicz W, Brun-Buisson C, Gniadkowski M.** 2015. MLST reveals potentially high-risk international clones of *Enterobacter cloacae*. J Antimicrob Chemother **70:**48–56. http://dx.doi.org/10.1093/jac/dku359.
46. **Woodford N, Turton JF, Livermore DM.** 2011. Multiresistant Gram-negative bacteria: the role of high-risk clones in the dissemination of antibiotic resistance. FEMS Microbiol Rev **35:**736–755. http://dx.doi.org/10.1111/j.1574-6976.2011.00268.x.
47. **Gaibani P, Ambretti S, Farruggia P, Bua G, Berlingeri A, Tamburini MV, Cordovana M, Guerra L, Mazzetti M, Roncarati G, Tenace C, Moro ML, Gagliotti C, Landini MP, Sambri V.** 2013. Outbreak of *Citrobacter freundii* carrying VIM-1 in an Italian hospital, identified during the carbapenemases screening actions, June 2012. Int J Infect Dis **17:**e714–e717. http://dx.doi.org/10.1016/j.ijid.2013.02.007.
48. **Marchaim D, Navon-Venezia S, Schwaber MJ, Carmeli Y.** 2008. Isolation of imipenem-resistant *Enterobacter* species: emergence of KPC-2 carbapenemase, molecular characterization, epidemiology, and outcomes. Antimicrob Agents Chemother **52:**1413–1418. http://dx.doi.org/10.1128/AAC.01103-07.
49. **Adler A, Miller-Roll T, Assous MV, Geffen Y, Paikin S, Schwartz D, Weiner-Well Y, Hussein K, Cohen R, Carmeli Y.** 2015. A multicenter study of the clonal structure and resistance mechanism of KPC-producing *Escherichia coli* isolates in Israel. Clin Microbiol Infect **21:**230–235. http://dx.doi.org/10.1016/j.cmi.2014.10.008.
50. **Adler A, Hussein O, Ben-David D, Masarwa S, Navon-Venezia S, Schwaber MJ, Carmeli Y, Post-Acute-Care Hospital Carbapenem-Resistant Enterobacteriaceae Working Group.** 2015. Persistence of *Klebsiella pneumoniae* ST258 as the predominant clone of carbapenemase-producing Enterobacteriaceae in post-acute-care hospitals in Israel, 2008–13. J Antimicrob Chemother **70:**89–92. http://dx.doi.org/10.1093/jac/dku333.
51. **Naas T, Cuzon G, Gaillot O, Courcol R, Nordmann P.** 2011. When carbapenem-hydrolyzing β-lactamase KPC meets *Escherichia coli* ST131 in France. Antimicrob Agents Chemother **55:**4933–4934. http://dx.doi.org/10.1128/AAC.00719-11.
52. **O'Hara JA, Hu F, Ahn C, Nelson J, Rivera JI, Pasculle AW, Doi Y.** 2014. Molecular epidemiology of KPC-producing *Escherichia coli*: occurrence of ST131-*fimH30* subclone harboring pKpQIL-like IncFIIk plasmid. Antimicrob Agents Chemother **58:**4234–4237. http://dx.doi.org/10.1128/AAC.02182-13.
53. **Barton BM, Harding GP, Zuccarelli AJ.** 1995. A general method for detecting and sizing large plasmids. Anal Biochem **226:**235–240. http://dx.doi.org/10.1006/abio.1995.1220.
54. **Carattoli A, Bertini A, Villa L, Falbo V, Hopkins KL, Threlfall EJ.** 2005. Identification of plasmids by PCR-based replicon typing. J Microbiol Methods **63:**219–228. http://dx.doi.org/10.1016/j.mimet.2005.03.018.
55. **Villa L, Garcia-Fernandez A, Fortini D, Carattoli A.** 2010. Replicon sequence typing of IncF plasmids carrying virulence and resistance determinants. J Antimicrob Chemother **65:**2518–2529. http://dx.doi.org/10.1093/jac/dkq347.
56. **Garcia-Fernandez A, Fortini D, Veldman K, Mevius D, Carattoli A.** 2009. Characterization of plasmids harbouring *qnrS1*, *qnrB2* and *qnrB19* genes in *Salmonella*. J Antimicrob Chemother **63:**274–281. http://dx.doi.org/10.1093/jac/dkn470.
57. **Johnson TJ, Bielak EM, Fortini D, Hansen LH, Hasman H, Debroy C, Nolan LK, Carattoli A.** 2012. Expansion of the IncX plasmid family for improved identification and typing of novel plasmids in drug-resistant *Enterobacteriaceae*. Plasmid **68:**43–50. http://dx.doi.org/10.1016/j.plasmid.2012.03.001.
58. **Woodford N, Fagan EJ, Ellington MJ.** 2006. Multiplex PCR for rapid detection of genes encoding CTX-M extended-spectrum β-lactamases. J Antimicrob Chemother **57:**154–155.
59. **Empel J, Baraniak A, Literacka E, Mrowka A, Fiett J, Sadowy E, Hryniewicz W, Gniadkowski M.** 2008. Molecular survey of β-lactamases conferring resistance to newer β-lactams in *Enterobacteriaceae* isolates from Polish hospitals. Antimicrob Agents Chemother **52:**2449–2454. http://dx.doi.org/10.1128/AAC.00043-08.
60. **Izdebski R, Baraniak A, Fiett J, Adler A, Kazma M, Salomon J, Lawrence C, Rossini A, Salvia A, Vidal Samso J, Fierro J, Paul M, Lerman Y, Malhotra-Kumar S, Lammens C, Goossens H, Hryniewicz W, Brun-Buisson C, Carmeli Y, Gniadkowski M.** 2013. Clonal structure, extended-spectrum β-lactamases, and acquired AmpC-type cephalosporinases of *Escherichia coli* populations colonizing patients in rehabilitation centers in four countries. Antimicrob Agents Chemother **57:**309–316. http://dx.doi.org/10.1128/AAC.01656-12.