Supplemental methods

Genome sequencing

Total DNA was extracted by the phenol-chloroform method. Libraries were constructed using Nextera technology and sequenced on an Illumina's HiSeq-2000 using a 2 x 100 nucleotides (nt) paired-end strategy. All reads were processed to remove low quality or artefactual nucleotides, using sequentially sickle (github.com/najoshi/sickle), AlienTrimmer (1), and fqDuplicate (ftp.pasteur.fr/pub/gensoft/projects/fqtools). Read pairs were assembled using clc_novo_assemble (www.clcbio.com/products/clc-genomics-workbench) with a minimum contig size of 500 nt.

Strict core genome subset construction

Because few rearrangements are observed at the short evolutionary distances that separate strains within species, and because horizontal gene transfer is frequent, genes outside conserved blocks of synteny are likely to be xenologs or paralogs. Hence, we combined homology analysis with synteny analysis to define gene loci to be compared for strain genotyping purposes. The protein-coding genes of reference strain NTUH-K2044 chromosome (GenBank accession no. NC_012731) were used to identify 2,088 orthologous gene clusters by reciprocal tblastn using as cutoff 90% amino acid similarity and 80% length coverage. Clusters were sorted according to their order on the reference and only those that belonged to groups of five or more clusters that showed the same order for all genomes were retained. Amino acid sequences were aligned with Muscle (2, 3) and back-translated into codon-level multiple sequence alignments. Each alignment was subsequently inspected visually in order to select character regions that were aligned without ambiguity and did not involve too many gaps, including gaps resulting from gene location near the end of contigs.

Following this stringent approach, and after eliminating MLST and ribosomal MLST (rMLST) genes (4), a final set of 634 genes defined as the strict core genome MLST (scgMLST) set was obtained.

Phylogenetic reconstruction from core genome MLST genes

For each of the 694 genes of the core genome MLST scheme, amino acid sequences were aligned with MUSCLE (2, 3) and back-translated to obtain a multiple codon sequence alignment. For each pair of taxa ij, the p-distance was computed for each corresponding aligned codon sequence, therefore obtaining up to k evolutionary pairwise distance estimates d_{ij}. Assuming that the observed values d_{ij} are distributed according to a Gamma distribution $\Gamma(\alpha_{ij}, \beta_{ij})$, a first Maximum Likelihood (ML) estimate of the two parameters α_{ij} and β_{ij} was performed from all evolutionary distances d_{ij}. Second, considering extreme d_{ij} values as outliers, i.e. $\min[P(d \leq d_{ij}), P(d_{ij} \leq d)] < 1\%$, every outlier d_{ij} was discarded and the ML estimate of α_{ij} and β_{ij} was performed another time from the remaining d_{ij} values. This procedure was reiterated until a subset of observed values d_{ij} with no outlier was reached, and a final evolutionary distance Δ_{ij} was estimated by averaging these remaining d_{ij} values. Detecting and discarding outlier distance estimates d_{ij} was performed because unexpectedly small or large d_{ij} values are often caused by non-clonal evolutionary events, such as homologous recombination, therefore biasing average Δ_{ij}. Finally, a phylogenetic tree was inferred from the distance matrix (Δ_{ij}) with the program FastME (5). Confidence values at branches were inferred following a locus-by-locus bootstrapping procedure with 1,000 replicates.

Inclusion of virulence and heavy metal resistance genes in the BIGSdb-Kp virulence gene set

Virulence associated genome features included in the virulence scheme in the BIGSdb-Kp database were *rmpA* (regulator of mucoid phenotype) (6, 7) and *rmpA2* (7, 8), the *kvgAS* two-component system (9), the mannose-resistant *Klebsiella*-like (type III) fimbriae cluster (*mrkABCDF*) (10), the ferric uptake system *kfuABC* (11), the allantoinase cluster including gene *allS* (12), as well as the aerobactin (*iucABCDiutA*) (7, 13), yersiniabactin (*ybt*) (14), microcin E492 (*mcc*) (15) and colibactin (*clb*) (16) gene clusters. The sequences of the heavy metal resistance clusters *pbrABCR*, *pcoABCDERS*, *silCERS*, and *terWXY*, located on the large virulence plasmid of *K. pneumoniae* (7), were also included in the BIGSdb-Kp database.

Inclusion of antimicrobial resistance genes in the BIGSdb-Kp resistance gene set

Currently described variants of major antimicrobial resistance determinants, namely beta-lactamases (www.lahey.org/Studies/), aminoglycoside resistance conferring enzymes (17-19) and fluoroquinolone resistance loci (20-23) (www.lahey.org/qnrStudies/) were included. The reference nomenclature of OKP and LEN enzyme variants previously hosted at Institut Pasteur was integrated into the BIGSdb-Kp database, where newly detected variants were defined.

Antimicrobial susceptibility testing

For antimicrobial susceptibility testing, we selected at least one isolate to represent each clonal group (CG), as well as all isolates representing distinct resistance genotypes (specific combinations of resistance genes) when different genotypes were found for a given CG. Moreover, reference strains MGH 78578 (ST38) and NTUH-K2044 (CG23) were included. Susceptibility to beta-lactams (amoxicillin, ceftriaxone, ceftazidime, imipenem, and cefoxitin), aminoglycosides (streptomycin, spectinomycin, kanamycin, tobramycin, netilmicin, gentamicin, amikacin, and isepamicin), and quinolones (nalidixic acid, ofloxacin, and ciprofloxacin) was determined by the agar disk diffusion method and interpreted according to the guidelines of the French Antibiogram Committee (http://www.sfm-microbiologie.org/UserFiles/file/CASFM/CASFM_2013.pdf). In case of resistance to extended-spectrum cephalosporins, imipenem and/or quinolones, minimum inhibitory concentrations (MICs) of some of these antimicrobial agents were determined using strip tests (BioMérieux, la Balme, France) following the manufacturer's instructions.

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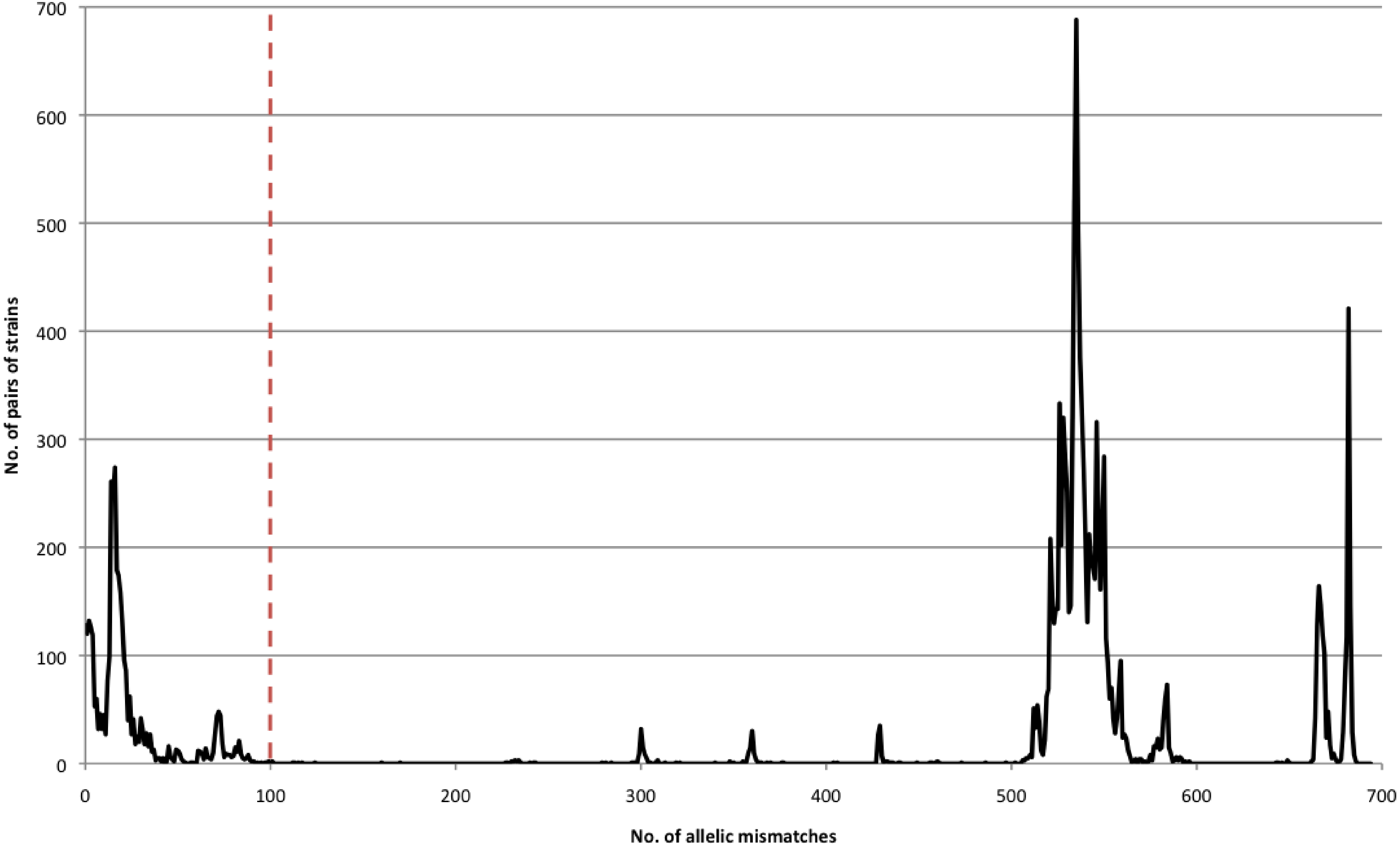
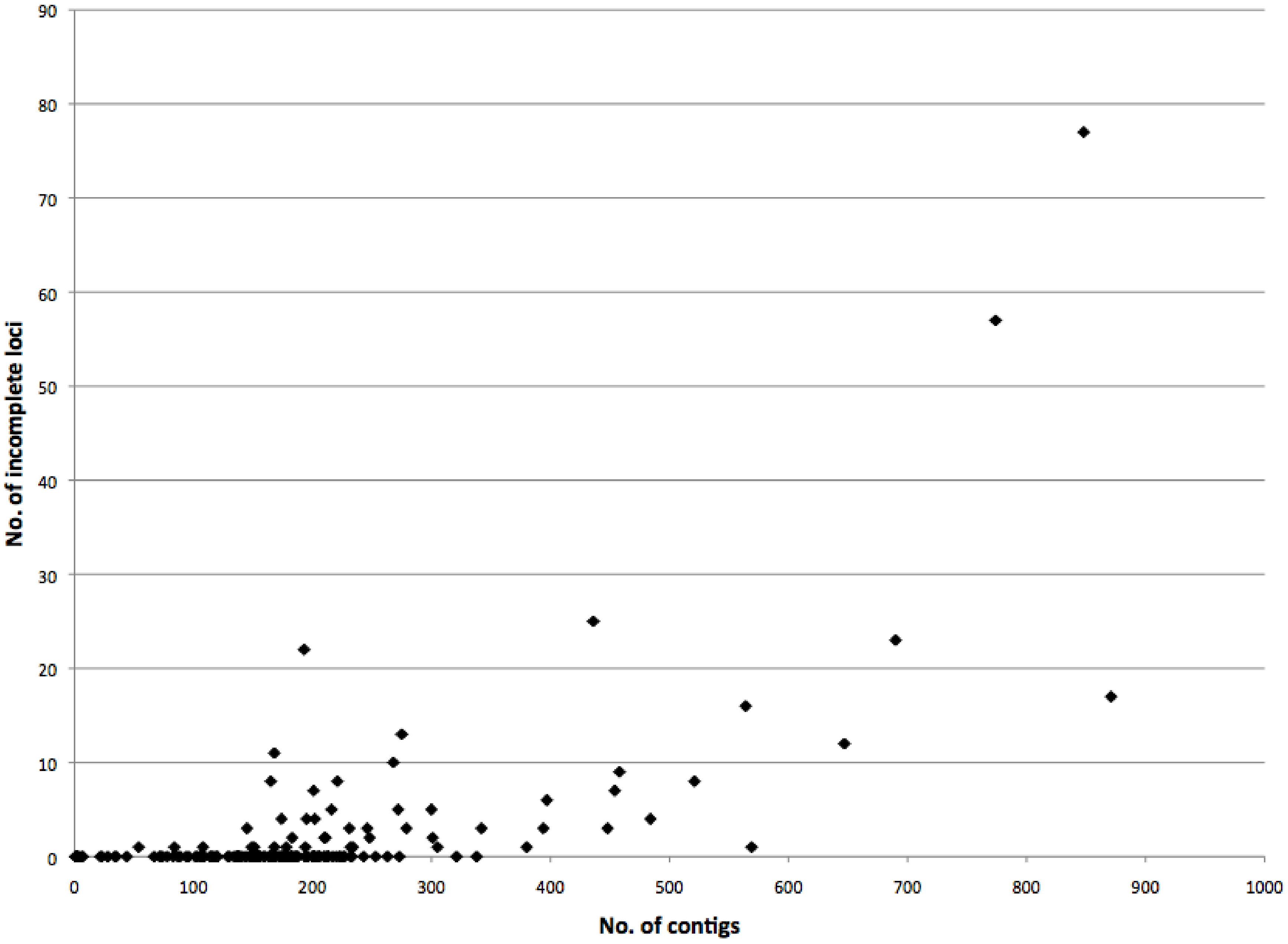


Technical Appendix Figure S1. Distribution of the number of pairwise allelic mismatches (i.e. number of loci at which sequences of a given pair of strains differ). The 100 allelic mismatches cut-off, proposed for clonal group definition, is represented in red.



Technical Appendix Figure S2. Impact of genome fragmentation on the number of incomplete cgMLST loci (loci for which an allele number could not be assigned, because of truncation resulting from contig end proximity). The x-axis represents the number of contigs of the assembly for each of the 167 genomes.

Technical appendix Table S1.

Characteristics of the 167 *Klebsiella pneumoniae* isolates

Data source	Strain	Strain Bank ID	Taxonomic designation	Isolation year	Country	City	Host	Source	Infection	Capsular serotype	ST (MLST)	Clonal group	GenBank accession number(s)	Reference[§]	No. of contigs or scaffolds	No. of bases assembled	Contig N50	Coverage[#]
This study	SA2	SB4384	*K. pneumoniae*	2008	France	Paris	Human	Blood	Liver abscess	K1	23	CG23			223	5719746	50483	407
This study	SA12	SB4385	*K. pneumoniae*	2008	France	Paris	Human	Liver pus	Liver abscess	K1	23	CG23			454	5531648	27726	23
This study	A18970	SB4446	*K. pneumoniae*	2009	France	Paris	Human		Liver abscess	K1	23	CG23			279	5465519	36673	414
This study	BJ-LI	SB4448	*K. pneumoniae*	2010	France	Clichy	Human	Blood	Tibial abscess	K1	23	CG23			151	5450162	79293	313
This study	BP1011625	SB4467	*K. pneumoniae*	2011	France	Bobigny	Human		Sepsis	K1	23	CG23			89	5580373	113951	429
This study	20479	SB4698	*K. pneumoniae*	2012	France	Bordeaux	Human		Liver abscess	K1	23	CG23			145	5460502	89369	593
This study	02A029	SB14	*K. pneumoniae*	1997	Belgium	Brussels	Human	Blood		K1	23	CG23		Diancourt et al., 2005; Brisse et al., 2009	84	5330811	111115	701
This study	12A041	SB42	*K. pneumoniae*	1997	The Netherlands	Utrecht	Human	Blood		K1	23	CG23		Diancourt et al., 2005; Brisse et al., 2009	108	5679147	102706	788
This study	16A151	SB53	*K. pneumoniae*	1997	Spain	Sevilla	Human	Blood		K1	23	CG23		Diancourt et al., 2005; Brisse et al., 2009	149	5490608	79037	623
This study	IPEUC-1037	SB3308	*K. pneumoniae*	1985	France	Pont l Eveque	Horse			K1	23	CG23		Brisse et al., 2009	102	5612893	115252	747
This study	IPEUC-1056	SB3309	*K. pneumoniae*	1985	France	Caen	Horse			K1	23	CG23		Brisse et al., 2009	202	5504853	52517	594
This study	IPEUC-1570	SB3310	*K. pneumoniae*	1988	France	Paris	Horse (mare)		Metritis	K1	23	CG23		Brisse et al., 2009	106	5583646	114796	492
This study	A3021	SB3926	*K. pneumoniae*		Taiwan	Taiwan	Human	Liver pus	Liver abscess	K1	23	CG23		Brisse et al., 2009	848	5478137	10408	446
This study	A5011	SB3927	*K. pneumoniae*		Taiwan	Taiwan	Human	Liver pus	Liver abscess	K1	23	CG23		Brisse et al., 2009	436	5406580	22496	482
This study	MET1_63/88063	SB3380	*K. pneumoniae*	2004	France	Nantes	Horse (mare)		Metritis	K1	23	CG23			275	5550735	39310	625
This study	BG094	SB4720	*K. pneumoniae*	2007	Madagascar	Antananarivo	Human	Pus		K1	23	CG23			108	5623047	170436	324
This study	BG130	SB4721	*K. pneumoniae*	2008	Vietnam	Ha Noi	Human	Post-operative fluid		K1	23	CG23			120	5865999	176018	319
This study	BG141	SB4722	*K. pneumoniae*	2007	Madagascar	Antananarivo	Human	Pus		K1	23	CG23			106	5672875	147983	71
This study	Zaire1	SB3431	*K. pneumoniae*	After 2005	France	Paris	Human	Liver pus	Liver abscess	K1	57	CG23		Brisse et al., 2009	397	5491004	28486	325
This study	BD-DU	SB4565	*K. pneumoniae*	2011	France	Bordeaux	Human	Liver pus	Liver abscess	K1	57	CG23			774	5542863	11826	383
This study	cur15505	SB2390	*K. pneumoniae*	2002	Curacao	Curacao	Human	Urinary tract		K2	14	CG14	CCBO01	Van Westreenen et al., 2003; Diancourt et al., 2005; Brisse et al., 2009	72	5623305	135002	109
This study	KpS13	SB3434	*K. pneumoniae*	2004	France	Villejuif	Human	Blood	Sepsis	K2	14	CG14			248	6198683	70382	434
This study	T69	SB4536	*K. pneumoniae*	2010	France	Paris	Human	Liver pus	Liver abscess	K2	375	CG375	CBTV01	Bialek-Davenet et al., 2013	234	5463228	39422	140
This study	T6	SB4537	*K. pneumoniae*	2008	France	Paris	Human	Ascitic fluid	Post-perforation peritonitis	K2	375	CG375			647	5154585	15989	47
This study	BJ1-GA	SB4496	*K. pneumoniae*	2011	France	Clichy	Human	Liver pus	Liver abscess	K2	380	CG380	CBTU01	Bialek-Davenet et al., 2013	114	5421195	133474	478
This study	SA17	SB4386	*K. pneumoniae*	2008	France	Paris	Human	Blood	Pneumonia	K2	380	CG380		Decré et al., 2011	180	5479532	70979	789
This study	SA25	SB4533	*K. pneumoniae*	2010	France	Paris	Human	Blood	Severe Sepsis	K2	380	CG380		Decré et al., 2011	342	5445137	37610	179
This study	SA26	SB4534	*K. pneumoniae*	2010	France	Paris	Human	Blood	Pneumonia	K2	380	CG380		Decré et al., 2011	305	5386073	38752	104
This study	L8	SB4539	*K. pneumoniae*	2008	France	Paris	Human	Blood	Severe pneumonia	K2	380	CG380			226	5398330	57797	100
This study	BJ2-KE	SB4449	*K. pneumoniae*	2010	France	Clichy	Human	Liver pus	Liver abscess	K2	679	CG380			253	5448698	47772	172
This study	03-9138	SB3332	*K. pneumoniae*	2003	Martinique		Human	Anal pus	Anal abscess	K2	65	CG65		Brisse et al., 2009	380	5281893	27143	502
This study	IPEUC-1279	SB4472	*K. pneumoniae*	1987	France	Mulhouse	Maki vari lemur	Liver	Generalized infection	K2	65	CG65		Richard, 1989	243	5293344	40350	99
This study	SA1	SB4021	*K. pneumoniae*	2008	France	Paris	Human	Blood	Pneumonia	K2	86	CG86	CBTW01	Decré et al., 2011	67	5492681	250254	469
This study	100519185	SB4360	*K. pneumoniae*	2010	France	Pau	Human	Blood	Severe Sepsis	K2	86	CG86			201	5356115	48568	554
This study	T88	SB4447	*K. pneumoniae*	2009	France	Paris	Human	Cerebrospinal fluid	Meningitis	K2	86	CG86		Decré et al., 2011	273	5369378	41350	717
This study	CIP 52.204	SB3197	*K. pneumoniae*		Unknown		Unknown			K2	86	CG86		Brisse et al., 2009	211	5083391	47151	303
This study	CG43	SB4454	*K. pneumoniae*		Taiwan		Human		Liver abscess	K2	86	CG86		Chang et al., 1996	448	5275614	24902	517
This study	IPEUC-340	SB4501	*K. pneumoniae*	1975	France	Lyon	Human (infant)		Septicemia and meningitis	K2	86	CG86			221	5378320	45163	504
This study	L3	SB4538	*K. pneumoniae*	2008	France	Paris	Human	Blood	Pneumonia and septic shock	K2	25				94	5393699	129948	226
This study	KpS12	SB4523	*K. pneumoniae*		France	Paris	Human		Nosocomial infection	K2	520				263	5579666	44955	140
This study	IPEUC-1106	SB4519	*K. pneumoniae*		France	Paris	Human	Broncho-alveolar lavage		K2	559				74	5386709	208221	402
This study	CIP 52.145 (= B5055)	SB3341	*K. pneumoniae*	<1935	Indonesia	Java	Human			K2	66		FO834904, FO834905, FO834906	Nassif et al., 1986; Brisse et al., 2009	3	5656097	5439142	202
This study	LM21	SB4762	*K. pneumoniae*	1992	France	Clermont-Ferrand	Human	Skin lesion	Nosocomial infection	K35	12			Favre-Bonté et al., 1999	156	5509751	104592	191
This study	VI9C3	SB2803	*K. pneumoniae*	1999	The Netherlands	Mastenbroek	Horse	Abdomen	Peritonitis	K35	163			Brisse et al., 2009	78	5676136	135471	498
This study	BJ-CH1	SB4450	*K. pneumoniae*	2009	France	Clichy	Human	Urine	Nosocomial urinary tract infection		340	CG258			134	5380985	109678	645
This study	CH1031	SB4763	*K. pneumoniae*	2012	France	Clermont-Ferrand	Human	Urine (catheter)	Nosocomial infection		35	CG35-A			154	5543779	145318	76
This study	610356538	SB4312	*K. pneumoniae*	2009	France	Paris	Human		Liver abscess		382				83	5410617	222505	560
This study	CH137	SB3464	*K. pneumoniae* subsp. *ozaenae*	1999	France	Reims	Human	Nasal and pharyngeal swabs	Laryngeal scleroma		90			De Champs et al., 2005	564	5419179	28034	20 (Illumina and 454)
NCBI	DSM 30104T (= ATCC 13883T)	SB132	*K. pneumoniae*		Unknown		Human	Blood			3		AJJI01	Skerman, 1980; Lee et al., 2012	22	5234536	459638	
NCBI	HS11286		*K. pneumoniae*	2011	China	Shanghai	Human	Sputum			11	CG258	NC_016838, NC_016839, NC_016840, NC_016841, NC_016845, NC_016846, NC_016847	Liu et al., 2012	7	5682322	5333942	
NCBI	ATCC BAA-2146		*K. pneumoniae*	2010	USA		Human	Urine			11	CG258	AOCV01	Leski et al., 2012; Broberg et al., 2013	109	5680367	270044	
NCBI	ATCC BAA-2146		*K. pneumoniae*	2010	USA		Human				11	CG258	APNN01	Leski et al., 2012	690	5644669	17409	
NCBI	WGLW2		*K. pneumoniae*		USA		Human				14		AMLM01		32	5745996	528699	
NCBI	JHCK1		*K. pneumoniae*	2012	Argentina	Buenos Aires	Human (newborn)	Cerebrospinal fluid	Meningitis		14	CG14	ANGH01	Xie et al., 2013	227	6015282	129981	
NCBI	UHKPC57		*K. pneumoniae*		USA		Human				15	CG15	ARPR01		246	5671251	69489	
NCBI	UHKPC179		*K. pneumoniae*		USA		Human				15	CG15	ARSM01		174	5515994	83960	
NCBI	NTUH-K2044	SB3928	*K. pneumoniae*		Taiwan	Taiwan	Human	Liver pus	Liver abscess	K1	23	CG23	NC_012731, NC_006625	Wu et al., 2009	2	5472672	5248520	
NCBI	1084		*K. pneumoniae*	2002	Taiwan		Human			K1	23	CG23	NC_018522	Lin et al., 2012	1	5386705	5386705	
NCBI	RYC492		*K. pneumoniae*	1984	Spain	Madrid	Human	Feces	Carriage		35	CG35-A	APGM01	de Lorenzo, 1984; Marcoleta et al., 2013	159	5383782	5095761	
NCBI	HSL4		*K. pneumoniae*		China	Guangzhou	Environment	Mangrove sediment slurry			35	CG35-B	APFG01	Zhou et al., 2013	210	5221198	49655	
NCBI	KpQ3		*K. pneumoniae*	2008	Spain	Madrid	Human	Blood			37		AMSU01	Tobes et al., 2013	54	5466672	368134	
NCBI	MGH 78578	SB107	*K. pneumoniae*	1994	Unknown		Human	Blood	Pneumonia	K52	38		NC_009648, NC_009649, NC_009650, NC_009651, NC_009652, NC_009653	Ogawa et al., 2005	6	5694894	5315120	
NCBI	MS 92-3		*K. pneumoniae*		USA		Human	Gut			45		AFBO01		871	5576613	11156	
NCBI	DMC0799		*K. pneumoniae*		USA		Human				45		ARRZ01		120	5431615	104940	
NCBI	WGLW1		*K. pneumoniae*		USA		Human				48		AMLL01		23	5548332	673632	

NCBI	LCT-KP214	*K. pneumoniae*		China		Human		Pneumonia	48		AJHE01		484	5573211	31717
NCBI	WGLW3	*K. pneumoniae*		Unknown		Unknown			48		AMLN01		23	5518063	405884
NCBI	ATCC 13884T	*K. pneumoniae* subsp. *rhinoscleromatis*		USA		Unknown			67		ACZD01		268	5280675	41286
NCBI	hvKP1	*K. pneumoniae*		USA	Buffalo	Human	Blood	Liver abscess	86	CG86	AOIZ01	Russo et al., 2013	272	5368567	43309
NCBI	1162281	*K. pneumoniae*		USA		Human			133		AFQL01	Kumar et al., 2011	116	5535020	161835
NCBI	WGLW5	*K. pneumoniae*		USA		Human			134		AMLO01		34	5821816	363305
NCBI	JH1	*K. pneumoniae*		USA		Human			134		AFQK01	Kumar et al., 2011	118	5534249	141130
NCBI	342	*K. variicola*		USA		Maize			146		NC_011281, NC_011282, NC_011283	Fouts et al., 2008	3	5920257	5641239
NCBI	UHKPC81	*K. pneumoniae*		USA		Human			234		APVQ01		231	5532328	70624
NCBI	KPNIH2	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Wound	Bacteremia	258	CG258	AJZV01	Snitkin et al., 2012	147	5724800	154879
NCBI	KPNIH1	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Skin lesion (groin)	Colonization	258	CG258	AJZU01	Snitkin et al., 2012	130	5723756	158289
NCBI	KPNIH5	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Peritoneal fluid	Bacteremia	258	CG258	AJZX01	Snitkin et al., 2012	168	5716297	126254
NCBI	KPNIH6	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Peritoneal fluid	Bacteremia	258	CG258	AJZY01	Snitkin et al., 2012	149	5714943	130041
NCBI	KPNIH4	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Peritoneal fluid	Bacteremia	258	CG258	AJZW01	Snitkin et al., 2012	173	5718058	120800
NCBI	KPNIH7	*K. pneumoniae*	2011	USA	Bethesda, MD	Environment	Ventilator		258	CG258	AJZZ01	Snitkin et al., 2012	160	5723848	158114
NCBI	KPNIH8	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Rectal swab	Bacteremia	258	CG258	AKAA01	Snitkin et al., 2012	182	5714705	158021
NCBI	KPNIH9	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Rectal swab	Bacteremia	258	CG258	AKAB01	Snitkin et al., 2012	115	5720331	178365
NCBI	KPNIH10	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Groin	Colonization	258	CG258	AKAC01	Snitkin et al., 2012	182	5716118	158000
NCBI	KPNIH11	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Rectal swab	Colonization	258	CG258	AKAD01	Snitkin et al., 2012	185	5714016	150495
NCBI	KPNIH12	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Rectal swab	Colonization	258	CG258	AKAE01	Snitkin et al., 2012	164	5719358	149661
NCBI	KPNIH14	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Rectal swab	Bacteremia	258	CG258	AKAF01	Snitkin et al., 2012	165	5723355	147593
NCBI	KPNIH16	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Throat	Colonization	258	CG258	AKAG01	Snitkin et al., 2012	178	5715478	158009
NCBI	KPNIH17	*K. pneumoniae*	2011	USA	Bethesda, MD	Human		Colonization	258	CG258	AKAH01	Snitkin et al., 2012	137	5715795	158097
NCBI	KPNIH18	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Rectal swab	Colonization	258	CG258	AKAI01	Snitkin et al., 2012	167	5769474	153222
NCBI	KPNIH19	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Rectal swab	Colonization	258	CG258	AKAJ01	Snitkin et al., 2012	201	5715894	98646
NCBI	KPNIH20	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Throat	Colonization	258	CG258	AKAK01	Snitkin et al., 2012	155	5724448	167325
NCBI	KPNIH21	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Rectal swab	Bacteremia	258	CG258	AKAL01	Snitkin et al., 2012	178	5757750	117020
NCBI	KPNIH22	*K. pneumoniae*	2011	USA	Bethesda, MD	Human	Rectal swab	Bacteremia	258	CG258	AKAM01	Snitkin et al., 2012	165	5749696	131068
NCBI	KPNIH23	*K. pneumoniae*	2011	USA	Bethesda, MD	Human		Colonization	258	CG258	AKAN01	Snitkin et al., 2012	338	5740386	47638
NCBI	VA360	*K. pneumoniae*	2007	USA	Cleveland, OH	Human			258	CG258	ANGI01	Xie et al., 2013	210	5578970	142055
NCBI	ATCC BAA-1705	*K. pneumoniae*		USA		Human			258	CG258	AOGQ01	Broberg et al., 2013	169	5662914	203714
NCBI	361_1301	*K. pneumoniae*		USA		Human			258	CG258	APWF01		148	5389421	85283
NCBI	440_1540	*K. pneumoniae*		USA		Human			258	CG258	APWG01		213	5488293	89550
NCBI	500_1420	*K. pneumoniae*		USA		Human			258	CG258	APWH01		149	5388717	85427
NCBI	540_1460	*K. pneumoniae*		USA		Human			258	CG258	APWI01		213	5558834	89801
NCBI	646_1568	*K. pneumoniae*		USA		Human			258	CG258	APWJ01		139	5398867	100339
NCBI	UHKPC52	*K. pneumoniae*		USA		Human			258	CG258	ARVN01		154	5424339	97690
NCBI	UHKPC01	*K. pneumoniae*		USA		Human			258	CG258	APVP01		223	5575547	96149
NCBI	UHKPC04	*K. pneumoniae*		USA		Human			258	CG258	APVV01		232	5550266	85429
NCBI	UHKPC05	*K. pneumoniae*		USA		Human			258	CG258	ARVM01		187	5502006	95429
NCBI	UHKPC09	*K. pneumoniae*		USA		Human			258	CG258	APVO01		205	5501391	89783
NCBI	UHKPC22	*K. pneumoniae*		USA		Human			258	CG258	APVU01		200	5603708	85436
NCBI	UHKPC23	*K. pneumoniae*		USA		Human			258	CG258	AQQA01		195	5503448	96146
NCBI	UHKPC24	*K. pneumoniae*		USA		Human			258	CG258	APVS01		129	5396453	105332
NCBI	UHKPC26	*K. pneumoniae*		USA		Human			258	CG258	APVT01		202	5502788	86762
NCBI	UHKPC27	*K. pneumoniae*		USA		Human			258	CG258	APVR01		220	5571683	89639
NCBI	UHKPC29	*K. pneumoniae*		USA		Human			258	CG258	ARVQ01		176	5421295	99234
NCBI	UHKPC32	*K. pneumoniae*		USA		Human			258	CG258	ARPQ01		202	5621477	98006
NCBI	UHKPC40	*K. pneumoniae*		USA		Human			258	CG258	AQOT01		155	5490156	95435
NCBI	UHKPC45	*K. pneumoniae*		USA		Human			258	CG258	ARVO01		210	5620790	95425
NCBI	UHKPC48	*K. pneumoniae*		USA		Human			258	CG258	ARPP01		194	5620362	99169
NCBI	VAKPC252	*K. pneumoniae*		USA		Human			258	CG258	APVW01		175	5476814	80360
NCBI	VAKPC254	*K. pneumoniae*		USA		Human			258	CG258	APVX01		175	5531658	85430
NCBI	VAKPC269	*K. pneumoniae*		USA		Human			258	CG258	APVY01		155	5354224	86762
NCBI	VAKPC270	*K. pneumoniae*		USA		Human			258	CG258	APWA01		200	5472934	99231
NCBI	VAKPC276	*K. pneumoniae*		USA		Human			258	CG258	APWB01		205	5468994	97690
NCBI	VAKPC278	*K. pneumoniae*		USA		Human			258	CG258	ARVP01		151	5355272	98004
NCBI	VAKPC280	*K. pneumoniae*		USA		Human			258	CG258	APVZ01		164	5366546	90580
NCBI	VAKPC297	*K. pneumoniae*		USA		Human			258	CG258	APWC01		216	5624526	85432
NCBI	VAKPC309	*K. pneumoniae*		USA		Human			258	CG258	APWD01		217	5473881	82613
NCBI	KpMDU1	*K. pneumoniae*	2012	Australia		Human			258	CG258	AMWO01		521	5698251	19243
NCBI	DMC0526	*K. pneumoniae*		USA		Human			258	CG258	ARPO01		167	5555255	99235
NCBI	ST258-490	*K. pneumoniae*	2006	Israel	Tel Aviv	Human	Urine		258	CG258	ALIS01	Chmelnitsky et al., 2012	569	5707592	59798
NCBI	ST258-K26BO	*K. pneumoniae*		Italy		Human			258	CG258	CANR01	Comandatore, Sassera et al., 2013	193	5526679	65094
NCBI	ST258-K28BO	*K. pneumoniae*		Italy		Human			258	CG258	CANS01	Comandatore, Sassera et al., 2013	168	5663706	69464
NCBI	120_1020	*K. pneumoniae*		USA		Human			258	CG258	ARSO01		232	5542623	89329
NCBI	140_1040	*K. pneumoniae*		USA		Human			258	CG258	ARSP01		206	5498752	96146
NCBI	160_1080	*K. pneumoniae*		USA		Human			258	CG258	ARSN01		144	5390028	98001
NCBI	280_1220	*K. pneumoniae*		USA		Human			258	CG258	ARSQ01		153	5406392	90406
NCBI	DMC1097	*K. pneumoniae*		USA		Human			258	CG258	ARSA01		166	5556076	99230
NCBI	DMC1316	*K. pneumoniae*		USA		Human			258	CG258	ARSB01		168	5450966	95435
NCBI	UHKPC02	*K. pneumoniae*		USA		Human			258	CG258	ARSK01		233	5681241	104468
NCBI	UHKPC06	*K. pneumoniae*		USA		Human			258	CG258	ARSJ01		141	5407973	97588
NCBI	UHKPC07	*K. pneumoniae*		USA		Human			258	CG258	ARSF01		172	5473249	89334
NCBI	UHKPC17	*K. pneumoniae*		USA		Human			258	CG258	ARSG01		186	5616818	104468
NCBI	UHKPC18	*K. pneumoniae*		USA		Human			258	CG258	ARSH01		194	5617463	99231

NCBI	UHKPC28	*K. pneumoniae*		USA		Human			258	CG258	ARRU01		137	5398963	96146
NCBI	UHKPC31	*K. pneumoniae*		USA		Human			258	CG258	ARSI01		136	5390751	112903
NCBI	UHKPC33	*K. pneumoniae*		USA		Human			258	CG258	ARSD01		183	5502001	104467
NCBI	UHKPC47	*K. pneumoniae*		USA		Human			258	CG258	ARRV01		195	5498288	97796
NCBI	UHKPC59	*K. pneumoniae*		USA		Human			258	CG258	ARSE01		213	5667894	100349
NCBI	UHKPC61	*K. pneumoniae*		USA		Human			258	CG258	ARSC01		138	5397800	95436
NCBI	UHKPC67	*K. pneumoniae*		USA		Human			258	CG258	ARSL01		151	5541667	97796
NCBI	UHKPC69	*K. pneumoniae*		USA		Human			258	CG258	ARRW01		194	5606925	95790
NCBI	UHKPC77	*K. pneumoniae*		USA		Human			258	CG258	ARRX01		194	5622301	104468
NCBI	UHKPC96	*K. pneumoniae*		USA		Human			258	CG258	ARRY01		188	5610303	105805
NCBI	KCTC 2242	*K. pneumoniae*		South Korea		Unknown			375		NC_017540, NC_017541	Shin et al., 2012	2	5462423	5259571
NCBI	Ecl8	*K. pneumoniae*		United Kingdom		Unknown			375	CG375	CANH01		54	5500661	279996
NCBI	1191100241	*K. pneumoniae*	2011	The Netherlands		Human			395		AFXH01		394	5687314	34170
NCBI	12-3578	*K. pneumoniae*	2012	China	Beijing	Human	Blood	Pneumonia	421		AQOC01		183	5742061	136195
NCBI	ATCC 700603	*K. pneumoniae*	1994	USA	Richmond, VA	Human			489		AOGO01	Broberg et al., 2013	103	5461663	226688
NCBI	ST512-K30BO	*K. pneumoniae*		Italy	Milan	Human			512	CG258	CAJM01	Comandatore, Gaibani et al., 2013	458	5362417	25551
NCBI	1_1_55	*K. variicola*		Canada		Unknown			848		ACXA01		96	5417477	110877
NCBI	At-22	*K. variicola*		Unknown		Environment	Atta cephalotes fungus garden		1220		NC_013850	Pinto-Tomas et al., 2009	1	5458505	5458505
NCBI	4_1_44FAA	*K. pneumoniae*		Canada		Unknown			1221		ACWO01		195	5478883	84371
NCBI	LZ	*K. pneumoniae*		China		Environment (soil)	Soil		1222		AJVY01	Tao et al., 2012	196	5431750	118550
NCBI	ATCC 25955	*K. pneumoniae*		China		Unknown			1271		AQQH01	Wang et al., 2013	87	5292468	203308
NCBI	G5-2	*K. pneumoniae*		China	Shanghai	Environment (soil)	Soil		1271		AQQI01		107	5292693	153688
NCBI	KP-11	*K. pneumoniae*		USA		Human			1272		APWE01		301	5718845	62507
NCBI	KP-7	*K. pneumoniae*		USA		Human			1272		AQQD01		321	5672685	70423
NCBI	KTE92	*K. variicola*		USA		Unknown			1273		ASQN01		34	5433481	344789
NCBI	PR04	*K. pneumoniae*	2009	Malaysia	Putrajaya	Human	Blood	Sepsis	1402		AOPN01		300	5285449	42754

[#] Unless otherwise stated, sequencing was performed using Illumina technology and a 2 x 100 nucleotides paired-end strategy.

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Technical appendix Table S2.

Characteristics of the 167 genomes and level of detection of the seven MLST, 53 rMLST and 634 strict core genome loci.

Parameter	Public genomes		Genomes from this study	Total
	Draft	Complete		
Uploaded genomes	112	7	48	167
Average no. of contigs per strain	195.6	3.1	238.0	199.7
N50	188 728	5 377 657	153 261	396 034
MLST				
Genomes with all alleles identified	112 (100%)	7 (100%)	48 (100%)	167 (100%)
Average complete genes per genome	7 (100%)	7 (100%)	7 (100%)	7 (100%)
Average partial genes per genome	0 (0%)	0 (0%)	0 (0%)	0 (0%)
rMLST				
Genomes with all alleles identified	106 (94.6%)	7 (100%)	46 (95.2%)	159 (95.2%)
Average complete genes per genome	52.95 (99.9%)	53 (100%)	52.94 (99.9%)	52.95 (99.9%)
Average partial genes per genome	0.05 (0.1%)	0 (0%)	0.06 (0.1%)	0.05 (0.1%)
scgMLST				
Genomes with all alleles identified	87 (77.7%)	7 (100%)	24 (50.0%)	118 (70.7%)
Average complete genes per genome	632.7 (99.8%)	634 (100%)	628.7 (99.2%)	631.6 (99.6%)
Average partial genes per genome	1.3 (0.2%)	0 (0%)	5.3 (0.8%)	2.4 (0.4%)

Technical appendix Table S3.

Klebsiella pneumoniae virulence and heavy metal resistance-associated loci included in the BIGSdb-Kp database and their detection in the 167 genomes.

Locus/cluster	**Function**	**Reference**[§]	**No. (%) of genomes within a clonal group (CG) harbouring the locus or cluster**							
			Total	CG258	CG23	CG380	CG86	CG375	CG14	Other
			n = 167	n = 82	n = 22	n = 6	n = 7	n = 4	n = 4	n = 42
Virulence-associated										
Allantoinase cluster	Metabolism of allantoin	Chou et al., 2004	24 (14.4)	0 (0)	22 (100)	0 (0)	0 (0)	0 (0)	1 (25)	1 (2.4)
Yersiniabactin cluster	Iron acquisition system	Lawlor et al., 2007	47 (28.1)	2 (2.4)	20 (90.9)	6 (100)	4 (57.1)	1 (25)	2 (50)	12 (28.6)
Aerobactin *iucABCDiutA* cluster	Iron acquisition system	Chen et al., 2004	40 (24.0)	0 (0)	17 (77.3)	6 (100)	6 (85.7)	2 (50)	1 (25)	8 (19.0)
Ferric uptake *kfuABC* cluster	Iron acquisition system	Ma et al., 2005	48 (28.7)	0 (0)	22 (100)	6 (100)	0 (0)	0 (0)	4 (100)	16 (38.1)
kvgAS cluster	Two-component regulatory system involved in capsular polysaccharide synthesis and iron acquisition	Lai et al., 2003 (FEMS)	22 (13.2)	0 (0)	0 (0)	6 (100)	7 (100)[a]	3 (75)	0 (0)	6 (14.3)
mrkABCDF cluster	Mannose-resistant *Klebsiella*-like fimbriae	Jagnow et al., 2003	161 (96.4)	80 (97.6)	22 (100)	6 (100)	7 (100)	4 (100)	4 (100)	38 (90.5)
rmpA	Regulator of mucoid phenotype	Cheng et al., 2010	42 (25.1)	0 (0)	19 (86.4)	6 (100)	6 (85.7)	2 (50)	1 (25)	8 (19.0)
rmpA2	Regulator of mucoid phenotype	Lai et al., 2003 (J Bacteriol)	22 (13.2)	0 (0)	14 (63.6)	0 (0)	5 (71.4)	2 (50)	0 (0)	1 (2.4)
Microcin E492 *mceABCDEGHIJ* cluster	Bacteriocin production	Hetz et al., 2002	26 (15.6)	0 (0)	17 (77.3)[b]	6 (100)	0 (0)	0 (0)	0 (0)	3 (7.1)
Colibactin *clbABCDEFGHIJKLMNOPQR* cluster	Toxin production	Nougayrede et al., 2006	30 (18.0)	0 (0)	17 (77.3)	6 (100)	0 (0)	0 (0)	0 (0)	7 (16.7)[c]
Heavy metal resistance-associated										
pbrABCR cluster	Lead resistance	Chen et al., 2004; Tang et al., 2010	29 (17.4)	0 (0)	17 (77.3)	0 (0)	6 (85.7)	2 (50)	1 (25)	3 (7.1)
pcoABCDERS cluster	Copper resistance	Chen et al., 2004; Tang et al., 2010	100 (59.9)	45 (54.9)	18 (81.8)[d]	0 (0)	6 (85.7)	2 (50)	4 (100)	25 (59.5)[e]
silCERS cluster	Silver resistance	Chen et al., 2004; Tang et al., 2010	100 (59.9)	45 (54.9)[f]	18 (81.8)[g]	0 (0)	6 (85.7)	2 (50)	4 (100)	25 (59.5)
terABCDEWXYZ cluster	Tellurite resistance	Chen et al., 2004; Tang et al., 2010	34 (20.4)	0 (0)	19 (86.4)	0 (0)	6 (85.7)	0 (0)	3 (75)	6 (14.3)

[a] *kvgA* missing/not detected in 1 strain

[b] *mceEGHIJ* missing/not detected in 1 strain

[c] *clbKLMNOPQ* missing/not detected in 1 strain

[d] only locus *pcoE* detected in 1 strain

[e] *pcoS* missing/not detected in 2 strains

[f] *silE* missing/not detected in 2 strains

[g] *silE* missing/not detected in 1 strain

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Technical appendix Table S4.

Klebsiella pneumoniae beta-lactam resistance-associated loci included in the BIGSdb-Kp database and their detection in the 167 genomes.

Locus	**Reference**[§]	**No. (%) of genomes within a clonal group (CG) harbouring the locus**								**Variants detected**
		Total n = 167	CG258 n = 82	CG23 n = 22	CG380 n = 6	CG86 n = 7	CG375 n = 4	CG14 n = 4	Other n = 42	
Serine beta-lactamases (molecular class A)										
bla$_{\text{BEL}}$	Lahey	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
bla$_{\text{CARB}}$	Lahey	1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.4)	CARB-2
bla$_{\text{CTX-M}}$	Lahey	9 (5.4)	3 (3.7)	2 (9.1)	0 (0)	0 (0)	0 (0)	0 (0)	4 (9.5)	CTX-M-14 and 15
bla$_{\text{GES}}$	Lahey	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
bla$_{\text{KPC}}$	Lahey	82 (49.1)	77 (93.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (11.9)	KPC-2, 3, 7 and a potential new variant
bla$_{\text{LEN}}$	Pasteur	4 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (9.5)	3 new variants
bla$_{\text{OKP-A}}$	Pasteur	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
bla$_{\text{OKP-B}}$	Pasteur	2 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4.8)	OKP-B-6 and 8
bla$_{\text{PER}}$	Lahey	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
bla$_{\text{SHV}}$	Lahey	160 (95.8)	82 (100)	22 (100)	6 (100)	7 (100)	4 (100)	4 (100)	35 (83.3)	SHV-1, 2, 7, 11, 12, 18, 28, 33, 38, 60, 75 and 5 new variants
bla$_{\text{SME}}$	Lahey	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
bla$_{\text{TEM}}$	Lahey	45 (26.9)	32 (39.0)	2 (9.1)	0 (0)	0 (0)	0 (0)	1 (25)	10 (23.8)	TEM-1 and 10
bla$_{\text{VEB}}$	Lahey	0 (0)	0 (0)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Metallo-beta-lactamases (molecular class B)										
bla$_{\text{IMP}}$	Lahey	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
bla$_{\text{IND}}$	Lahey	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
bla$_{\text{NDM}}$	Lahey	2 (1.2)	2 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NDM-1
bla$_{\text{VIM}}$	Lahey	1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	VIM-1
Cephalosporinases (molecular class C)										
bla$_{\text{AmpC}}$	Lahey	3 (1.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (7.1)	DHA-1
bla$_{\text{CMY}}$	Lahey	2 (1.2)	2 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	CMY-6
Oxacillinases (molecular class D)										
bla$_{\text{OXA}}$	Lahey	80 (47.9)[a]	67 (81.7)	2 (9.1)	0 (0)	0 (0)	0 (0)	1 (25)	10 (23.8)	OXA-1, 2, 9, 10, 48 and a potential new variant

[§] Protein variants are defined on the following reference beta-lactamase nomenclature web sites:
Lahey: http://www.lahey.org/Studies/
Pasteur: http://www.pasteur.fr/ip/easysite/pasteur/en/research/plates-formes-technologiques/pasteur-genopole-ile-de-france/genotyping-of-pathogens-and-public-health-pf8/beta-lactamase-enzyme-variants/beta-lactamase-enzyme-variants

[a] including 48 (28.7%) with an internal stop codon

Technical appendix Table S5.

Klebsiella pneumoniae quinolone resistance-associated loci included in the BIGSdb-Kp database and their detection in the 167 genomes.

Locus	Reference[§]	No. (%) of genomes within a clonal group (CG) harbouring the locus								Variants detected
		Total n = 167	CG258 n = 82	CG23 n = 22	CG380 n = 6	CG86 n = 7	CG375 n = 4	CG14 n = 4	Other n = 42	
DNA gyrase										
gyrA mutation in QRDR region (Ala67-Gln106)	Hopkins et al., 2005; Jacoby et al., 2005	90 (53.9)	82 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	7 (16.7)	
gyrB mutation in QRDR region (Asp426-Lys447)	Hopkins et al., 2005; Jacoby et al., 2005	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Topoisomerase IV										
parC mutation in QRDR region (Ala64-Gln103)	Hopkins et al., 2005; Jacoby et al., 2005	87 (52.1)	82 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	4 (9.5)	
parE mutation in QRDR region (Asp420-Lys441)	Hopkins et al., 2005; Jacoby et al., 2005	1 (0.6)	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
Efflux pump										
oqxA	Hansen et al., 2004	163 (97.6)	81 (98.8)	22 (100)	6 (100)	7 (100)	4 (100)	4 (100)	39 (92.9)	
oqxB	Hansen et al., 2004	163 (97.6)	81 (98.8)	22 (100)	6 (100)	7 (100)	4 (100)	4 (100)	39 (92.9)	
Plasmid-mediated quinolone resistance										
qnrA	Lahey; Jacoby et al., 2008	1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.4)	A1
qnrB	Lahey; Jacoby et al., 2008	5 (3.0)	2 (2.4)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4.8)	B1, B4, B9
qnrC	Lahey; Jacoby et al., 2008	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
qnrD	Lahey; Jacoby et al., 2008	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
qnrS	Lahey; Jacoby et al., 2008	5 (3.0)	1 (1.2)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)	3 (7.1)	S1
qnrVC	Lahey; Jacoby et al., 2008	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
aac(6')-Ib-cr	Robicsek et al., 2006	6 (3.6)	2 (2.4)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)	3 (7.1)	

[§] References:

Hopkins KL, Davies RH, Threlfall EJ. Mechanisms of quinolone resistance in *Escherichia coli* and *Salmonella*: recent developments. Int J Antimicrob Agents. 2005 May;25(5):358-73.

Jacoby GA. Mechanisms of resistance to quinolones. Clin Infect Dis. 2005 Jul 15;41 Suppl 2:S120-6.

Hansen LH, Johannesen E, Burmolle M, Sorensen AH, Sorensen SJ. Plasmid-encoded multidrug efflux pump conferring resistance to olaquindox in *Escherichia coli*. Antimicrob Agents Chemother. 2004 Sep;48(9):3332-7.

Lahey: http://www.lahey.org/qnrStudies/

Jacoby G, Cattoir V, Hooper D, Martinez-Martinez L, Nordmann P, Pascual A, et al. *qnr* Gene nomenclature. Antimicrob Agents Chemother. 2008 Jul;52(7):2297-9.

Robicsek A, Strahilevitz J, Jacoby GA, Macielag M, Abbanat D, Park CH, et al. Fluoroquinolone-modifying enzyme: a new adaptation of a common aminoglycoside acetyltransferase. Nat Med. 2006 Jan;12(1):83-8.

Technical appendix Table S6.

Klebsiella pneumoniae aminoglycoside resistance-associated loci included in the BIGSdb-Kp database and their detection in the 167 genomes.

Family	Reference[§]	Subgroup	Locus	Alternative names	Variants	No. (%) of genomes within a clonal group (CG) harbouring the locus								Variants detected
						Total	CG258	CG23	CG380	CG86	CG375	CG14	Other	
						n = 167	n = 82	n = 22	n = 6	n = 7	n = 4	n = 4	n = 42	
Aminoglycoside N-acetyltransferases	Ramirez et al., 2010	AAC(3)-I	*aac3_Ia*	*aac(3)-Ia, aacC1*		1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	new variant
			aac3_Ib	*aac(3)-Ib*		-	-	-	-	-	-	-	-	
			aac3_Ic	*aac(3)-Ic*		-	-	-	-	-	-	-	-	
			aac3_Id	*aac(3)-Id, aac(3)-Ie*, *aacCA5*		-	-	-	-	-	-	-	-	
		AAC(3)-II	*aac3_IIa*	*aac(3)-IIa, aaC3, aacC5, aacC2, aac(3)-Va*	*aac(3)-IIc*	9 (5.4)	3 (3.7)	2 (9.1)	0 (0)	0 (0)	0 (0)	1 (25)	3 (7.1)	1 new variant similar to *aac(3)-IIc*
			aac3_IIb	*aac(3)-IIb, aac(3)-Vb*		-	-	-	-	-	-	-	-	
		AAC(3)-III	*aac3_IIIa*	*aac(3)-IIIa, aacC3*		-	-	-	-	-	-	-	-	
			aac3_IIIb	*aac(3)-IIIb*		-	-	-	-	-	-	-	-	
			aac3_IIIc	*aac(3)-IIIc, ant(2")-Ib*		-	-	-	-	-	-	-	-	
		AAC(3)-IV	*aac3_IVa*	*aac(3)-IVa*		21 (12.6)	21 (25.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 new variants
		AAC(3)-VI	*aac3_VIa*	*aac(3)-VIa*		-	-	-	-	-	-	-	-	
		AAC(3)-VII	*aac3_VIIa*	*aac(3)-VIIa, aacC7*		-	-	-	-	-	-	-	-	
		AAC(3)-VIII	*aac3_VIIIa*	*aac(3)-VIIIa, aacC8*		-	-	-	-	-	-	-	-	
		AAC(3)-IX	*aac3_IXa*	*aac(3)-IXa, aacC9*		-	-	-	-	-	-	-	-	
		AAC(3)-X	*aac3_Xa*	*aac(3)-Xa*		-	-	-	-	-	-	-	-	
		AAC(2')-I	*aac2p_Ia*	*aac(2')-Ia*		-	-	-	-	-	-	-	-	
			aac2p_Ib	*aac(2')-Ib*		-	-	-	-	-	-	-	-	
			aac2p_Ic	*aac(2')-Ic*		-	-	-	-	-	-	-	-	
			aac2p_Id	*aac(2')-Id*		-	-	-	-	-	-	-	-	
			aac2p_Ie	*aac(2')-Ie*		-	-	-	-	-	-	-	-	
		AAC(6')-I	*aac6p_Ia*	*aac(6')-Ia, aacA1*		-	-	-	-	-	-	-	-	
	Robicsek et al., 2006		*aac6p_Ib*	*aac(6')-Ib, aac(6')-4, aacA4*	*aac(6')-Ib', Ib3-4, Ib7-11, 31-32, Ib-Suzhou, Ib-Hangzhou, Ib-cr,* fusion variants *aac(6')-30/aac(6')-Ib'* and *aac(3)-Ib/aac(6')-Ib"*	69 (41.3)	61 (74.4)	1 (4.5)	0 (0)	0 (0)	0 (0)	2 (50)	5 (11.9)	*aac(6')-Ib, Ib3, Ib-cr,* and 2 new variants
			aac6p_Ic	*aac(6')-Ic*		-	-	-	-	-	-	-	-	
			aac6p_If	*aac(6')-If*		-	-	-	-	-	-	-	-	
			aac6p_Ig	*aac(6')-Ig*	*aac(6')-Ik*	-	-	-	-	-	-	-	-	
			aac6p_Ih	*aac(6')-Ih*	*aac(6')-Ij, aac(6')-Ir, aac(6')-Is, aac(6')-It, aac(6')-Iu, aac(6')-Iv, aac(6')-Iw, aac(6')-Ix*	-	-	-	-	-	-	-	-	
			aac6p_Ii	*aac(6')-Ii*		-	-	-	-	-	-	-	-	
			aac6p_Il	*aac(6')-Il, aacA7*		2 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (50)	0 (0)	
			aac6p_Im	*aac(6')-Im*		1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	
			aac6p_Ip	*aac(6')-Ip*		-	-	-	-	-	-	-	-	
			aac6p_Iq	*aac(6')-Iq*	*aac(6')-Iaf*	-	-	-	-	-	-	-	-	
			aac6p_Isa	*aac(6')-Isa*		-	-	-	-	-	-	-	-	
			aac6p_Iy	*aac(6')-Iy*	*aac(6')-Iaa*	-	-	-	-	-	-	-	-	
			aac6p_Iz	*aac(6')-Iz*		-	-	-	-	-	-	-	-	
			aac6p_Iad	*aac(6')-Iad*		-	-	-	-	-	-	-	-	
			aac6p_Iae	*aac(6')-Iae*	*aac(6')-Iai*	-	-	-	-	-	-	-	-	
			aac6p_29	*aac(6')-29*	*aac(6')-29a* and *aac(6')-29b*	-	-	-	-	-	-	-	-	
			aac6p_I30	*aac(6')-I30*	*aac(6')-33*	-	-	-	-	-	-	-	-	
			aac6p_Iid	*aac(6')-Iid*	*aac(6')-Iih*	-	-	-	-	-	-	-	-	
			aac6p_SK	*aac(6')-SK*		-	-	-	-	-	-	-	-	
		AAC(6')-II	*aac6p_IIa*	*aac(6')-IIa*		-	-	-	-	-	-	-	-	
			aac6p_IIb	*aac(6')-IIb*		-	-	-	-	-	-	-	-	
			aac6p_IIc	*aac(6')-IIc*		-	-	-	-	-	-	-	-	

Aminoglycoside O-nucleotidyltransferases	Ramirez et al., 2010	ANT(6)-Ia	*ant6_Ia*	*ant(6)-Ia, ant6, aadE*	*aadK, aad(6)*	-	-	-	-	-	-	-	-	
		ANT(6)-Ib	*ant6_Ib*	*ant(6)-Ib*		-	-	-	-	-	-	-	-	
		ANT(9)-Ia	*ant9_Ia*	*ant(9)-Ia, aad(9), spc*		-	-	-	-	-	-	-	-	
		ANT(9)-Ib	*ant9_Ib*	*ant(9)-Ib, aad(9), spc*		-	-	-	-	-	-	-	-	
		ANT(4')-Ia	*ant4p_Ia*	*ant(4')-Ia, aadD, aadD2, ant(4',4")-I*		-	-	-	-	-	-	-	-	
		ANT(4')-IIa	*ant4p_IIa*	*ant(4')-IIa*		-	-	-	-	-	-	-	-	
		ANT(4')-IIb	*ant4p_IIb*	*ant(4')-IIb*		-	-	-	-	-	-	-	-	
		ANT(2")-Ia	*ant2pp_Ia*	*ant(2")-Ia, aadB*		8 (4.8)	0 (0)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)	7 (16.7)	old and 1 new variant
		ANT(3")-Ia	*ant3pp_Ia*	*ant(3")-Ia, aadA, aadA1, aad(3")(9)*	*aadA2-17, 21-24*	100 (59.9)	80 (97.6)	4 (18.2)	0 (0)	0 (0)	0 (0)	3 (75)	13 (31.0)	*aadA1*, *aadA2*, *aadA5*, *aadA23*, and 6 new variants
Aminoglycoside O-phosphotransferases	Ramirez et al., 2010	APH(4)-I	*aph4_Ia*	*aph(4)-Ia, hph*		22 (13.2)	21 (25.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.4)	
			aph4_Ib	*aph(4)-Ib, hyg*		-	-	-	-	-	-	-	-	
		APH(6)-I	*aph6_Ia*	*aph(6)-Ia, aphD, strA*		-	-	-	-	-	-	-	-	
			aph6_Ib	*aph(6)-Ib, sph*		-	-	-	-	-	-	-	-	
			aph6_Ic	*aph(6)-Ic, str*		-	-	-	-	-	-	-	-	
			aph6_Id	*aph(6)-Id, strB, orfI*		15 (9.0)	6 (7.3)	1 (4.5)	0 (0)	0 (0)	0 (0)	2 (50)	6 (14.3)	old and 2 new variants
		APH(9)-I	*aph9_Ia*	*aph(9)-Ia*		-	-	-	-	-	-	-	-	
			aph9_Ib	*aph(9)-Ib, spcN*		-	-	-	-	-	-	-	-	
		APH(3')-I	*aph3p_Ia*	*aph(3')-Ia, aphA-1*	*aph(3')-Ic* (= *apha1-1AB*, *apha7*)	41 (24.6)	31 (37.8)	3 (13.6)	0 (0)	1 (14.3)	0 (0)	1 (25)	5 (11.9)	*aph(3')-Ia*, *aph(3')-Ia*, and 1 new variant
			aph3p_Ib	*aph(3')-Ib, aphA-like*		-	-	-	-	-	-	-	-	
		APH(3')-II	*aph3p_IIa*	*aph(3')-IIa, aphA-2*		-	-	-	-	-	-	-	-	
			aph3p_IIb	*aph(3')-IIb*		-	-	-	-	-	-	-	-	
			aph3p_IIc	*aph(3')-IIc*		-	-	-	-	-	-	-	-	
		APH(3')-III	*aph3p_IIIa*	*aph(3')-IIIa*		-	-	-	-	-	-	-	-	
		APH(3')-IV	*aph3p_IVa*	*aph(3')-IVa, aphA-4*		-	-	-	-	-	-	-	-	
		APH(3')-V	*aph3p_Va*	*aph(3')-Va, aphA-5a*		-	-	-	-	-	-	-	-	
			aph3p_Vb	*aph(3')-Vb, aphA-5b, rph*		-	-	-	-	-	-	-	-	
			aph3p_Vc	*aph(3')-Vc, aphA-5c*		-	-	-	-	-	-	-	-	
		APH(3')-VI	*aph3p_VIa*	*aph(3')-VIa, aphA-6*		-	-	-	-	-	-	-	-	
		APH(3')-VII	*aph3p_VIIa*	*aph(3')-VIIa, aphA-7*		-	-	-	-	-	-	-	-	
		APH(2")-II	*aph2pp_IIa*	*aph(2")-IIa, aph(2')-Ib*		1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (25)	0 (0)	
		APH(2")-III	*aph2pp_IIIa*	*aph(2")-IIIa, aph(2')-Ic*		-	-	-	-	-	-	-	-	
		APH(2")-IV	*aph2pp_IVa*	*aph(2")-IVa, aph(2")-Id*	*aph(2")-Ie*	-	-	-	-	-	-	-	-	
		APH(3')-I	*aph3pp_Ia*	*aph(3")-Ia, aphE, aphD2*		-	-	-	-	-	-	-	-	
			aph3pp_Ib	*aph(3")-Ib, strA, orfH*		14 (8.4)	3 (3.7)	2 (9.1)	0 (0)	0 (0)	0 (0)	2 (50)	7 (16.7)	2 new variants
			aph3pp_Ic	*aph(3")-Ic*		-	-	-	-	-	-	-	-	
Fusion variants	Ramirez et al., 2010		*aac6p_aph2pp*	*aac(6')-aph(2")*	*aac(6')-Ie-aph(2")-Ia*	-	-	-	-	-	-	-	-	
rRNA methylases	Doi et al., 2007		*apmA*			-	-	-	-	-	-	-	-	
			armA			1 (0.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2.4)	
			npmA			-	-	-	-	-	-	-	-	
			rmtA			-	-	-	-	-	-	-	-	
			rmtB			2 (1.2)	1 (1.2)	1 (4.5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
			rmtC			2 (1.2)	2 (2.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
			rmtD			-	-	-	-	-	-	-	-	

- not found

§ References:

Ramirez MS, Tolmasky ME. Aminoglycoside modifying enzymes. Drug resistance updates : reviews and commentaries in antimicrobial and anticancer chemotherapy. 2010 Dec;13(6):151-71.

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Doi Y, Arakawa Y. 16S ribosomal RNA methylation: emerging resistance mechanism against aminoglycosides. Clin Infect Dis. 2007 Jul 1;45(1):88-94.

Technical appendix Table S7.

Susceptibility towards beta-lactams, aminoglycosides and quinolones of selected *Klebsiella pneumoniae* isolates

Strain	ST (MLST)	Clonal group	Susceptibility categorization[#]																MIC[§] (mg/l)								ESBL[*]
			AMX	CRO	CAZ	IMP	FOX	STR	SPE	KAN	TOB	NET	GM	AMK	ISE	NAL	OFX	CIP	CRO	CAZ	CTX	IMP	MEM	ERT	NAL	CIP	
SA17	380	CG380	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
SA1	86	CG86	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
T69	375	CG375	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
L3	25		R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
610356538	382		R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
IPEUC-1037	23	CG23	R	S	S	S	S	R	R	S	S	S	S	S	S	S	S	S									no
IPEUC-1056	23	CG23	R	S	S	S	S	R	R	R	S	S	S	S	S	S	S	S									no
IPEUC-1570	23	CG23	R	S	S	S	S	R	S	R	S	S	S	S	S	S	S	S									no
MET1_63/88063	23	CG23	R	S	S	S	S	R	R	R	S	S	S	S	S	S	S	S									no
BG094	23	CG23	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
BG130	23	CG23	R	R	I	S	S	R	R	R	R	R	R	R	R	R	R	R	>256	3	>16				>256	16	yes
BG141	23	CG23	R	R	R	S	S	R	S	R	R	R	R	S	S	R	R	R	128	16	>16				16	3	yes
cur15505	14	CG14	R	R	R	S	S	R	R	R	R	R	S	I	I	S	S	S	6	>32	4						yes
KpS13	14	CG14	R	R	R	R	R	S	S	R	R	R	I	R	I	R	R	R	>256	>32	>16	>32	12	12	>256	4	no
03-9138	65	CG65	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
CIP 52.145 (= B5055)	66		S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
VI9C3	163		R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
KpS12	520		R	I	R	S	R	R	S	S	S	S	S	S	S	S	S	S	4	6	4						no
IPEUC-1106	559		R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
LM21	12		R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
CH1031	35	CG35-A	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
CH137	90		R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
BJ-CH1	340	CG258	R	R	R	S	S	R	S	R	R	R	R	S	S	R	R	R	>256	>32	>16				>256	>32	yes
NTUH-K2044	23	CG23	R	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S									no
MGH 78578	38		R	S	R	S	S	R	R	R	R	R	R	S	S	R	R	S	12	>32	4				>256	0.5	yes

[#] Susceptibility categorization according to the French Antibiogram Committee: S, susceptible; I, intermediate; R, resistant.

[§] MIC, minimum inhibitory concentration

[*] ESBL, extended-spectrum beta-lactamase

AMX, amoxicillin; CRO, ceftriaxone; CAZ, ceftazidime; IMP, imipenem; FOX, cefoxitine; STR, streptomycin; SPE, spectinomycin; KAN, kanamycin; TOB, tobramycin; NET, netilmicin; GM, gentamicin; AMK, amikacin; ISE, isepamicin; NAL, nalidixic acid; OFX, ofloxacin; CIP, ciprofloxacin; CTX, cefotaxime; MEM, meropenem; ERT, ertapenem.