

Table S1: List of primers used for polymerase chain reaction

Gene	Primer	Sequence (5'-3')	T _a	Product (bp)	Reference
<i>cas1</i> form A (I-E)	Cas1A-F	CGAAACGCTACGGTGTGAAA	60 °C	341	(Li et al., 2018)
	Cas1A-R	CGGAATCAATTTGCCTGTCA			
<i>cas1</i> form B (I-E*)	Cas1B-F	CGGCTGGAAATTGATGACAG		309	
	Cas1B-R	ATCCGGAAAGCGTTTAGCAA			
<i>cas3</i> form A (I-E)	Cas3A-F	GCCGCTTTGCCTTTTATGAC	66 °C	362	
	Cas3A-R	GCCGTGATCGGGATAGACAT			
<i>cas3</i> form B (I-E*)	Cas3B-F	AGTCTGGAGGTCTGGCAAGC		407	
	Cas3B-R	CGCACCAGCTGCTGATTAAG			
<i>acc (6')-Ib</i>	<i>aac(6')-Ib-F</i>	CTTGCGATGCTCTATGAGTGG	60 °C	480	(Hamed et al., 2018)
	<i>aac(6')-Ib-R</i>	GAATGCCTGGCGTGTGTTGAA			
<i>qnrS</i>	<i>qnrS-F</i>	TCGGCACCACAACCTTTTCAC		255	
	<i>qnrS-R</i>	TCACACGCACGGAACCTCTAT			
<i>qnrB</i>	<i>qnrB-F</i>	TATGGCTCTGGCACTCGTT		193	
	<i>qnrB-R</i>	GCATCTTTCAGCATCGCAC			
<i>bla</i> _{CTX-M}	<i>CTX-M-F</i>	TTTGCGATGTGCAGTACCAGTAA	47 °C	544	(Edelstein et al., 2003)
	<i>CTX-M-R</i>	CGATATCGTTGGTGGTGCCATA			
<i>bla</i> _{SHV}	<i>SHV-F</i>	AAGATCCACTATCGCCAGCAG	64 °C	234	(Poirel et al., 2004)
	<i>SHV-R</i>	ATTCAGTTCGTTTCCCAGCGG			
<i>bla</i> _{NDM}	<i>NDM-F</i>	GGTTTGGCGATCTGGTTTTC	53 °C	621	(Poirel et al., 2011)
	<i>NDM-R</i>	CGGAATGGCTCATCACGATC			
<i>armA</i>	<i>armA-F</i>	TATGGGGGTCTTACTATTCTGCCTAT	58 °C	518	(Fritsche et al., 2008)
	<i>armA-R</i>	TCTTCCATTCCCTTCTCCTTT			

T_a, annealing temperature.

Table S2: Relationship between the CRISPR-Cas system and the antibiotic resistance profile in *K. pneumoniae* clinical isolates

Antimicrobial agents	No. of resistant isolates		P-value*
	Cas-positive (n=46)	Cas-negative (n=135)	
Amoxicillin/Clavulanic acid	45 (97.8%)	135 (100%)	0.066
Cefepime	46 (100%)	135 (100%)	NA
Cefotaxime	44 (95.6%)	129 (95.6%)	0.697
Ceftriaxone	44 (95.6%)	128 (94.8%)	0.720
Cefoxitin	38 (82.6%)	116 (86%)	0.406
Ceftazidime	44 (95.6%)	132 (97.8%)	0.179
Aztreonam	42 (91.3%)	127 (94.1%)	0.325
Imipenem	35 (76.1%)	110 (81.5%)	0.304
Gentamicin	38 (82.6%)	93 (68.9%)	0.116
Amikacin	32 (69.6%)	95 (70.4%)	0.769
Tetracycline	28 (60.9%)	72 (53.3%)	0.459
Ciprofloxacin	41 (89.1%)	127 (94.1%)	0.199
Trimethoprim-Sulfamethoxazole	40 (87%)	120 (88.9%)	0.493
Chloramphenicol	30 (65.2%)	76 (56.3%)	0.367
Nitrofurantoin	41(89.1%)	126 (93.3%)	0.220
Tigecycline	8 (17.4%)	19 (14%)	0.624
Colistin	3 (6.5%)	1 (0.7%)	0.054

*P-values were calculated by Chi Square or Fisher's Exact tests where appropriate

Table S3: Features of CRISPR/Cas loci identified in K57 and 117

Features	K57	117
No. of CRISPR arrays	1	2
Repeat Consensus:	gtgtccccgcgcagcggggataaacg	gaaacacccccacgtgcgtggggaagac gaaacacccccacgcatgtggggaagac
Repeat Length:	29 bp	28 bp
Total No. of Spacers	50	21
Mean size Spacers:	31.94 bp	33 bp
Spacers sequences:	>spacer1 gcgatcatgccgtagtcttcgatcacgtaac >spacer2 ttgcttctgtctgcagaggcgcgacagg >spacer3 cgtagctaaaattaactgcattcggcgcacct >spacer4 ccagctcaatttcgcctgtccgccagcgcc >spacer5 aatgcagcaaccggcaaatatcgccggtaa >spacer6 ccgcaatacaaaaataaatgagggttaaagt >spacer7 gtaaatgggaatgagtagaagagcgtcattg g >spacer8 attaaattttcgggtaaagagaaattgcgaa >spacer9 ctgcgagctaccctgaatttcagcgacagggg >spacer10 tagtgccatatattatcctctgcggtatgact >spacer11 gagactattatgcgaaaaactattactccga >spacer12 ccccgcgacatgcttaaacgcgctatcacg >spacer13 ggcactgttgtgaatgttgagtttttca >spacer14 cagggtaaacatgtaaaaaatgaccgtgccg >spacer15 cacattgccggtctgaaaagtatttgaaaat >spacer16 ccggaacaccaccagtaacagctactgtaggc >spacer17 tgaccctgtgattttgttacaggtaatacgt >spacer18 ttaacctcgtcgttctggttccgccaggat >spacer19 gaacctgaattcgaagggtgggtcatccttc >spacer20 ttgagtacagagagattgaccgcctgtttt >spacer21	<u>CRISPR1:</u> >spacer1 agaacgaatgccgcgctggtacggcgcgctcg tggattcca >spacer2 tgccggatatcatcaccgcgattaaacggcgga >spacer3 cacacggcgcgctgttggccactccgaaata >spacer4 tcttgccgatattgatatacacgccttttgca >spacer5 actcactcaatagtgtctctatctccgcatgg >spacer6 cgacacaatgagccgctccggcgactattg >spacer7 gcggtgaaccttggggcgctctcctcggaacta >spacer8 gctaaccagtggatagagcactatgtgacgaca >spacer9 gccagggccgcgacgcggtccaggtgctcct g >spacer10 cggcagcagaacggcatgatgacgcggatttt a >spacer11 aataaccccggtttgaagtcattcagcccata >spacer12 ccagacaaagctttgcgtcggcgaacgacgac a >spacer13 caggctttaactgatccgcatagatcacctga >spacer14 ctccccgtcttcggctccggccactcgcgttg <u>CRISPR2:</u> >spacer1 aggatagagtcaaatccgctcacacgtgatgaa >spacer2 ccggcatccgtcagctcgacggccagctgcag g >spacer3 acccgcagcgctatcccgccgagatgatggaa

Features	K57	117
	gtcagatcacgtcaaccacgcttgattttacc >spacer22 ctcactaacgccgttgctgcgatagctgatg >spacer23 gtgatcgcccggaatgcgtgagctaataca >spacer24 ttgagtgcagagagattgaccgccttgttt >spacer25 aactgaatgttccaaatccggttgacgacca >spacer26 ttcagcagcgctctgtccctctgtcgga >spacer27 ctctactacgataacggatccacgcgggctg >spacer28 gctgccagccattccgtaattgcctgttca >spacer29 gcgaatataggcattaatgctttaataatat >spacer30 ctccgtcaccagttctgtctatccggcaca >spacer31 tcacgtttgcagaactcgcgaggagaaga a >spacer32 gatcccccgaggagactgatcaaaccactc g >spacer33 cgctggtaatgggcttccggaagggtggg c >spacer34 tctatcgcaaccacgctgaggcgctgattga >spacer35 ccgctccacggtgagcggtgttaatgtagt >spacer36 catcacgcgtggccaatgtgttaaccaa >spacer37 ggcatcattctctcgctactccgccgatca >spacer38 cggaaatttgattagttgaatctgtgccatt >spacer39 ccgacttgggacgaggatccggcggaatg g >spacer40 taatggcaaaacatgacctgatccgggcgtc >spacer41 cctgaatctcacttcgtcgatcattctgcgc >spacer42 gggtcaaaagggttcattcgagcatcgagttgca >spacer43 gtaacgcagacggcgaaacgtcggatccattg g	>spacer4 ccgcatgcggaagtcgaaataccacaccgacg a >spacer5 tcaatgaggctatgagagaggttgaggcgctc a >spacer6 tgtccccacttggcgccggggtaaagttgtcag >spacer7 actattcgcaaaaatccggtttaccggcggtta

Features	K57	117
	>spacer44 gaccagaaagcctgggcattgttcgctcatt >spacer45 ccccgccgcgtggccgattgccattaccgc >spacer46 ttaataccagggggcaggttcagcaggtccc >spacer47 ccgctttaaccgctccggcagatccgggtga >spacer48 cgcgctgcgaattgttggtcgattcgatct >spacer49 cagacagacagcaggcagcaaacagggaagac >spacer50 gggttcacttgggtgaaactgaactaact	

Spacers written in red match plasmid sequences, while spacers written in blue have no similarity in the nt/nr NCBI database. Other spacers match chromosomal sequences.

Table S4: Features of the CRISPR-positive plasmids

Strain	Plasmid-Accession No	Replicon type	Antibiotic resistance genes (By R.G.I)	No of Spacers
PittNDM01	NZ_CP006799.1	IncHI1B, IncFIB	<i>aac</i> (6')-Ib-cr6, <i>bla</i> _{NDM-1} , <i>aph</i> (3')-VI, <i>mphE</i> , <i>msrE</i> , <i>armA</i> , <i>sul1</i> , <i>qacEdelta1</i> , <i>aadA2</i> , <i>dfrA12</i> , <i>dfrA14</i> , <i>bla</i> _{OXA1} , <i>qnrB</i>	12
KP617	NZ_CP012754.1	IncHI1B, IncFIB	<i>mphE</i> , <i>msrE</i> , <i>armA</i> , <i>sul1</i> , <i>qacEdelta1</i> , <i>aadA2</i> , <i>dfrA12</i> , <i>qnrB1</i> , <i>bla</i> _{NDM-1} , <i>aph</i> (3')-VI	12
11	NZ_CP016921.1	IncHI1B, IncFIB	<i>qnrB1</i> , <i>bla</i> _{OXA1} , <i>dfrA14</i> , <i>dfrA12</i> , <i>aadA2</i> , <i>qacEdelta1</i> , <i>sul1</i> , <i>armA</i> , <i>msrE</i> , <i>mphE</i> , <i>aph</i> (3')-VI, <i>bla</i> _{NDM-1} , <i>acc</i> (6')-Ib-cr6	12
825795-1	NZ_CP017986.1	IncHI1B, IncFIB	None	17
AR_0068	NZ_CP020068.1	IncHI1B, IncFIB	<i>dfrA12</i> , <i>aadA2</i> , <i>qacEdelta1</i> , <i>sul1</i> , <i>armA</i> , <i>msrE</i> , <i>mphE</i> , <i>aph</i> (3')-VI, <i>bla</i> _{NDM-1} , <i>aac</i> (3)-Iid, <i>bla</i> _{SHV-11} , <i>sul2</i> , <i>aph</i> (6)-Id, <i>aph</i> (3'')-Ib	12
KPN528	NZ_CP020854.1	IncHI1B, IncFIB	<i>qnrB1</i> , <i>bla</i> _{OXA-1} , <i>dfrA12</i> , <i>aadA2</i> , <i>qacEdelta1</i> , <i>sul1</i> , <i>armA</i> , <i>msrE</i> , <i>mphE</i> , <i>aph</i> (3')-VI, <i>bla</i> _{NDM-1} , <i>aac</i> (6')-Ib-cr6, <i>dfrA14</i>	12
AR_0153	NZ_CP028929.1	IncHI1B, IncFIB	<i>dfrA12</i> , <i>aadA2</i> , <i>qacEdelta1</i> , <i>sul1</i> , <i>armA</i> , <i>msrE</i> , <i>mphE</i> , <i>aph</i> (3')-VI, <i>bla</i> _{NDM-1} , <i>qnrB1</i> , <i>bla</i> _{OXA-1} , <i>dfrA14</i> , <i>aac</i> (6')-Ib-cr6	12
CDC 0106	NZ_CP022612.1	IncFIA, IncR, IncFIB, IncHI1B	<i>sul2</i> , <i>cmlA5</i> , <i>arr-2</i> , <i>bla</i> _{SHV-11} , <i>aac</i> (3)-Iid, <i>bla</i> _{CTX-M-15} , <i>bla</i> _{OXA-9} , <i>bla</i> _{TEM-1} , <i>bla</i> _{NDM-1} , <i>aph</i> (3')-VI, <i>mphE</i> , <i>msrE</i> , <i>armA</i> , <i>sul1</i> , <i>qacEdelta1</i> , <i>aadA2</i> , <i>dfrA12</i> , <i>aph</i> (3'')-Ib, <i>aph</i> (6)-Id, <i>sul1</i> , <i>ereA2</i> , <i>aac</i> (6')-Ib10, <i>aadA</i>	12
KP33	NZ_AP018748.1	IncHI1B, IncFIB	<i>bla</i> _{OXA-1} , <i>qnrB1</i> , <i>dfrA14</i> , <i>tet</i> (D), <i>bla</i> _{TEM-1} , <i>bla</i> _{CTX-M-15} , <i>dfrA12</i> , <i>aadA2</i> , <i>qacEdelta1</i> , <i>sul1</i> , <i>armA</i> , <i>msrE</i> , <i>mphE</i> , <i>aph</i> (3')-VI, <i>aac</i> (6')-Ib-cr6, <i>aac</i> (6')-Ib10, <i>bla</i> _{NDM-28}	11
M5	CP031735.1	IncFIB(K), IncFII(K)	<i>bla</i> _{TEM-1} , <i>bla</i> _{CTX-M-15} , <i>catI</i> , <i>dfrA14</i> , <i>aac</i> (6')-Ib10	9
AR_0046	NZ_CP032223.1	IncHI1B, IncFIB	None	13
NH34	NZ_CP034406.1	IncHI1B, IncFIB	<i>bla</i> _{OXA-1} , <i>aph</i> (3')-VI, <i>mphE</i> , <i>msrE</i> , <i>armA</i> , <i>sul1</i> , <i>qacEdelta1</i> , <i>aadA2</i> , <i>dfrA12</i> , <i>bla</i> _{CTX-M-15} , <i>bla</i> _{TEM-1} , <i>qnrB1</i> , <i>aac</i> (6')-Ib10, <i>tet</i> (D), <i>dfrA14</i> , <i>aac</i> (6')-Ib-cr6	12
BP327	NZ_CP036336.1	IncHI1B	<i>sul2</i> , <i>bla</i> _{TEM-1} , <i>bla</i> _{CTX-M-15} , <i>dfrA12</i> , <i>qacEdelta1</i> , <i>sul1</i> , <i>armA</i> , <i>msrE</i> , <i>mphE</i> , <i>aph</i> (3'')-Ib, <i>aph</i> (6)-Id, <i>aadA2</i>	7
2018S07-013	CP044381.1	IncHI1B, IncFIB, IncN	<i>sul1</i> , <i>bla</i> _{TEM-1} , <i>sul3</i> , <i>bla</i> _{DHA-1} , <i>qnrB4</i> , <i>aac</i> (3)-Iic, <i>aph</i> (3'')-Ib, <i>aph</i> (6)-Id, <i>qacI</i> , <i>aadA2</i>	22
BP3636	NZ_CP053772.1	IncHI1B, IncFIB	<i>dfrA12</i> , <i>aadA2</i> , <i>qacEdelta1</i> , <i>sul1</i> , <i>armA</i> , <i>msrE</i> , <i>mphE</i> , <i>dfrA14</i> , <i>tet</i> (D), <i>bla</i> _{TEM-1} , <i>bla</i> _{CTX-M-15} , <i>aac</i> (6')-Ib-cr6, <i>bla</i> _{OXA-1}	12
IR5065	NZ_CP061949.1	IncHI1B, IncFIB	<i>aph</i> (3')-Ia, <i>sul1</i> , <i>tetR</i> , <i>qacEdelta1</i> , <i>ant</i> (3'')-Iia, <i>tet</i> (B)	19

COL17	NZ_CP072906 .1	IncHI1B, IncFIB	<i>catI</i> , <i>bla</i> _{OXA-1} , <i>catB3</i> , <i>arr-3</i> , <i>qacEdelta1</i> , <i>sul1</i> , <i>bla</i> _{NDM-1} , <i>bla</i> _{TEM-26} , <i>qnrE2</i> , <i>aac</i> (6')-Ib-cr6, <i>aac</i> (3)-Iie, <i>adeF</i>	14
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Table S5: Association between resistance genes and CRISPR/Cas systems in *K. pneumoniae* published genomes

Gene	Affected antimicrobial class	Resistance mechanism	CRISPR/Cas-positive (n=206)	CRISPR/Cas-negative (n=682)	P-value
<i>aac(6')-Ib/aac(3)</i>	Aminoglycosides	Antibiotic inactivation	78 (37.9%)	254 (37.2%)	0.872
<i>acc(6')-Ib-cr6</i>	Aminoglycosides and fluoroquinolones	Antibiotic inactivation	51 (24.8%)	144 (21.1%)	0.268
<i>aph(6)-Id</i>	Aminoglycosides	Antibiotic inactivation	77 (37.4%)	267 (39.1%)	0.647
<i>ant(3'')</i>	Aminoglycosides	Antibiotic inactivation	11 (5.3%)	38 (5.6%)	0.898
<i>bla_{CTX-M}</i>	B-lactams	Antibiotic inactivation	81 (39.3%)	291 (42.7%)	0.393
<i>bla_{DHA-1}</i>	B-lactams	Antibiotic inactivation	5 (2.4%)	35 (5.1%)	0.101
<i>bla_{CMY-4}</i>	B-lactams	Antibiotic inactivation	8 (3.9%)	15 (2.2%)	0.182
<i>bla_{SHV}</i>	B-lactams	Antibiotic inactivation	24 (11.7%)	103 (15.1%)	0.215
<i>bla_{OXA}</i>	B-lactams	Antibiotic inactivation	57 (27.7%)	175 (25.7%)	0.565
<i>bla_{NDM}</i>	B-lactams	Antibiotic inactivation	40 (19.4%)	45 (6.6%)	0.000
<i>bla_{VIM}</i>	B-lactams	Antibiotic inactivation	6 (2.9%)	5 (0.7%)	0.023
<i>bla_{TEM}</i>	B-lactams	Antibiotic inactivation	74 (35.9%)	360 (52.8%)	0.000
<i>bla_{LAP-2}</i>	B-lactams	Antibiotic inactivation	2 (1%)	59 (8.7%)	0.000
<i>bla_{KPC}</i>	B-lactams	Antibiotic inactivation	18 (8.7%)	213 (31.2%)	0.000
<i>bla_{FOX-5}</i>	B-lactams	Antibiotic inactivation	1 (0.5%)	0 (0%)	0.232
<i>bla_{FONA-6}</i>	B-lactams	Antibiotic inactivation	1 (0.5%)	1 (0.1%)	0.410
<i>bla_{IMP}</i>	B-lactams	Antibiotic inactivation	2 (1%)	9 (1.3%)	1.000
<i>bla_{VEB}</i>	B-lactams	Antibiotic inactivation	2 (1%)	4 (0.6%)	0.627
<i>bla_{SCO-1}</i>	B-lactams	Antibiotic inactivation	0 (0%)	1 (0.1%)	1.000
<i>armA</i>	Aminoglycosides	Antibiotic target alteration	23 (11.2%)	23 (3.4%)	0.000
<i>rmtB</i>	Aminoglycosides	Antibiotic target alteration	5 (2.4%)	98 (14.4%)	0.000

Gene	Affected antimicrobial class	Resistance mechanism	CRISPR/Cas-positive (n=206)	CRISPR/Cas-negative (n=682)	P-value
<i>rmtC</i>	Aminoglycosides	Antibiotic target alteration	2 (1%)	5 (0.7%)	0.666
<i>rmtF</i>	Aminoglycosides	Antibiotic target alteration	5 (2.4%)	21 (3.1%)	0.627
<i>rmtG</i>	Aminoglycosides	Antibiotic target alteration	0 (0%)	2 (0.3%)	1.000
<i>floR</i>	Phenicol antibiotic	Antibiotic efflux	9 (4.4%)	12 (1.8%)	0.038
<i>ereA2</i>	Macrolides	Antibiotic inactivation	8 (3.9%)	3 (0.4%)	0.001
<i>msrE</i>	Macrolides	Antibiotic target protection	26 (12.6%)	27 (4%)	0.000
<i>catA3</i>	Phenicol antibiotic	Antibiotic inactivation	35 (17%)	189 (27.7%)	0.002
<i>fosA</i>	Phosphonic acid antibiotic	Antibiotic inactivation	1 (0.5%)	44 (6.5%)	0.001
<i>ICR-Mo</i>	Peptide antibiotic	Antibiotic target alteration	0 (0%)	1 (0.1%)	1.000
<i>oqxA</i>	Fluoroquinolone antibiotic, glycylcycline	Antibiotic efflux	0 (0%)	1 (0.1%)	1.000
<i>aadA</i>	Aminoglycoside antibiotic	Antibiotic inactivation	55 (26.7%)	207 (30.4%)	0.314
<i>tet(A)</i>	Tetracycline antibiotic	Antibiotic efflux	46 (22.3%)	189 (27.7)	0.125
<i>tet(B)</i>	Tetracycline antibiotic	Antibiotic efflux	4 (1.9%)	2 (0.3%)	0.028
<i>tet(D)</i>	Tetracycline antibiotic	Antibiotic efflux	18 (8.7%)	63 (9.2%)	0.827
<i>cmlA</i>	Phenicol antibiotic	Antibiotic efflux	11 (5.3%)	51 (7.5%)	0.291
<i>mphE</i>	Macrolide antibiotic	Antibiotic inactivation	59 (28.6%)	188 (27.6%)	0.763
<i>mefB</i>	Macrolide antibiotic	Antibiotic efflux	1 (0.5%)	7 (1%)	0.689
<i>sat-2</i>	Nucleoside antibiotic	Antibiotic inactivation	1 (0.5%)	3 (0.4%)	1.000
<i>mcr-1</i>	Peptide antibiotic	Antibiotic target alteration	0 (0%)	5 (0.7%)	0.595

Gene	Affected antimicrobial class	Resistance mechanism	CRISPR/Cas-positive (n=206)	CRISPR/Cas-negative (n=682)	P-value
<i>mcr-3</i>	Peptide antibiotic	Antibiotic target alteration	3 (1.5%)	1 (0.1%)	0.041
<i>mcr-3.5</i>	Peptide antibiotic	Antibiotic target alteration	1 (0.5%)	2 (0.3%)	0.547
<i>mcr-8</i>	Peptide antibiotic	Antibiotic target alteration	2 (1%)	9 (1.3%)	0.692
<i>mcr-9</i>	Peptide antibiotic	Antibiotic target alteration	0 (0%)	1 (0.1%)	1.000
<i>dfrA</i>	Diaminopyrimidine antibiotic	Antibiotic target replacement	89 (43.2%)	308 (45.2%)	0.620
<i>qnrA</i>	Fluoroquinolone antibiotic	Antibiotic target protection	1 (0.5%)	9 (1.3%)	0.320
<i>qnrB</i>	Fluoroquinolone antibiotic	Antibiotic target protection	40 (19.4%)	133 (19.5%)	0.979
<i>qnrE</i>	Fluoroquinolone antibiotic	Antibiotic target protection	1 (0.5%)	1(0.1%)	0.410
<i>qnrS</i>	Fluoroquinolone antibiotic	Antibiotic target protection	27 (13.1%)	99 (14.5%)	0.611
<i>qacI</i>	Disinfecting agents and antiseptics	Antibiotic efflux	3 (1.5%)	26 (3.8%)	0.095
<i>qacEdelta</i>	Disinfecting agents and antiseptics	Antibiotic efflux	68 (33%)	205 (30.1%)	0.421
<i>sul</i>	Sulfonamide antibiotic	Antibiotic target replacement	105 (51%)	371 (54.4%)	0.387
<i>erm</i>	Macrolides	Antibiotic efflux	9 (4.4%)	21(3.1%)	0369

Statistically significant P-values are written in red.

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