Send Orders for Reprints to reprints@benthamscience.ae

The Open Microbiology Journal, 2018, 12, 195-199



Whole Genome Sequencing of *Klebsiella pneumoniae* Strain Unravels a New Model for the Development of Extensive Drug Resistance in Enterobacteriaceae

Mubarak Alfaresi^{*}

College of Medicine, University of Sharjah, Sharjah, UAE

| Received: March 15, 2018 | Revised: June 5, 2018 | Accepted: June 6, 2018 |
|--------------------------|-----------------------|------------------------|
| | | |

Abstract:

Introduction:

Increased incidence of carbapenem-resistant Enterobacteriaceae (CRE) has been reported worldwide. The WHO warns about the imminent risk to global health if the spread of resistant bacteria is not contained.

Materials and Methods:

Here, single molecule real time sequencing was used to analyse the whole genome and resistome of SKGH01, a strain of *Klebsiella* pneumoniae.

Results and Discussions:

The data showed that SKGH01 was resistant to all commercially available antibiotics. A complete account of extensively drugresistant (XDR) CRE at a genomic level and the entire location map of all antibiotic resistance components are here presented. Additionally, this work proposes a model of XDR acquisition in Enterobacteriaceae.

Keywords: Klebsiella pneumoniae, Extensive drug resistance (XDR), Whole genome sequencing, Antibiotics, WHO, Enterobacteriaceae.

1. INTRODUCTION

Klebsiella pneumoniae of the Enterobacteriaceae family is a non-motile, rod-shaped, Gram-negative bacterium and it is one of the primary causes of hospital-acquired infections globally [1]. *K. pneumoniae* genomes have a strong virulence and a wide array of resistance factors that make them a major source of antimicrobial resistance genes [2]. The *K. pneumoniae* that produce carbapenemase (KPC-KP) are the most challenging pathogens. They exhibit extensive drug-resistant phenotypes and high potential for rapid spread having an overwhelming impact on morbidity and mortality rates [3]. Colistin and polymyxin B are antimicrobial agents that, for the most part, are still active against KPC-KP [4]. However, the emergence of polymyxin-resistant KPC-KP has recurrently been reported [5]. In *K. pneumoniae*, resistance to cationic antimicrobial agents is facilitated via lipopolysaccharide (LPS) sequence alterations driven by the pbgPE operon products, which are highly conserved among Enterobacteriaceae [6, 7]. The PhoQ/PhoP and PmrAB signalling systems positively regulate the pbgPE operon [7]. Activation of the PhoQ/PhoP signalling system induces production of a transmembrane regulatory protein called MgrB. The protein acts as a negative feedback loop on this signalling system by interacting with the PhoQ sensor kinase [8]. The MgrB protein has been shown to have this regulatory function in *Salmonella enterica, Escherichia coli* as well as *Yersinia pestis* and thus might also be conserved in other species, including *K. pneumoniae* [8].

195

^{*} Address correspondence to this author at the College of Medicine, University of Sharjah, Sharjah, UAE; E-mail: uaenow@eim.ae

2. MATERIAL AND METHODS

The Hospital Medical Executive Committee approved the study. The SKGH01 strain was isolated from an 80-yearold man with urinary tract infection. The species was characterised with the VITEK II compact GN system (bioM'erieux, France). For the antimicrobial susceptibility testing the VITEK II N211 system (bioM'erieux) and the Etest method were used. Breakpoints published by the Clinical and Laboratory Standards Institute were applied to determine the susceptibility to the tested antibiotics and the European Committee for Antibiotic Susceptibility Testing breakpoints in the E-test were used to determine the minimum inhibitory concentration of colistin. K. pneumoniae SKGH01 genome was sequenced with the Pacific Biosciences (PacBio, Inc., CA) RS II Single-Molecule Real Time (SMRT) kit. Bell template libraries were prepared using the Template Preparation Kit (PacBio). A single, streamlined protocol was used to create libraries of varying insert lengths, from 250 bp to 20,000 bp. The PacBio SMRT analysis software suite (v. 3.0) and hierarchical genome assembly process were used for *de novo* genome assembly. For the gene calling and automatic functional annotation of SKGH01 chromosome and plasmids the Prokka v1.12b (Vicbioinformatics, Australia) software was used. ResFinder and PlasmidFinder with data from the Center for Genomic Epidemiology (CGE) were employed to analyse the antimicrobial resistance genes and plasmid types. The Antibiotic Resistance Genes Database [9] and the Comprehensive Antimicrobial Resistance Database [10] were compared to all the predicted coding regions in order to screen the outstanding antimicrobial resistance genes. The insertion sequences (IS) in the genome were identified with the online tool, ISfinder 2 (version 2016-05-27). Closely related bacterial genomes were identified with the Microbial Nucleotide BLAST program. The search set consisted of complete genomes of K. pneumoniae (taxid: 573) available in the NCBI database. The BLAST search produced 48 significant hits, with overall similarities between 95% and 99%, and coverages between 85% and 98%. A genome tree was built, which comprised SKGH01 and 40 related strains from NCBI database (accession date: 10/05/16).

3. RESULTS AND DISCUSSION

The data showed that SKGH01 is a true extensively Drug-Resistant (XDR) strain to ampicillin, ampicillinclavulanic acid, piperacillin-tazobactam, cefotaxime, ceftazidime, cefepime, aztreonam, meropenem, cotrimoxazole, amikacin, gentamicin, and colistin. A total of 6 contigs representing 6,088,457 bases (GC content 56.54%, N50=10,230) were obtained from assembled sequences of strain SKGH01 (Table S1). 6,034 genes (total), 5,907 CDS (total), 5,777 genes (coding), and 127 tRNAs genes were annotated for final contigs. The complete genome of K. pneumoniae SKGH01 consists of a circular chromosome 5,490,611 base-pairs in length with an average G-C content of 56.4%, four circular plasmids. The complete genome of strain SKGH01 consisted of a circular chromosome (5,490,611 base-pairs long) with an average G-C content of 56.4%, and four circular plasmids. Most of the genes for acquired resistance to antibiotics were positioned on the chromosome. The complete resistomes of strain SKGH01 are presented in Table 1. The insertion sequence, ISEcp1 (synonym, ISEc9) was found in four and blaOXA-181 in three places on the SKGH01 chromosome. The search for the (partial) protein sequence encoded by mgrB was performed. The most significant tblast match was a 42-amino acid, 5' partial sequence of mgrB, which corresponded to the first ISEcp1 position identified on the SKGH01 chromosome. The remaining 3' partial sequence of mgrB was identified with a manual search. Another manual search identified left- and right-flanking, inverted repeats (IRL and IRR, respectively) located at the first ISEcp1 position on the chromosome. We also found two alternative IRRs (IRRalts), which produced the insertions ISEcp1-blaOXA-181-IRRalt1 and ISEcp1-blaOXA-181-IRRalt2. One of these insertions led to the inactivation of the mgrB gene (Fig. S1). ISEcp1-like insertion sequences are the most common genetic element associated with blaCTX-M, blaCMY and blaACC genes and have more recently been associated with blaOXA-181 [11].

| START | STOP | Gene | Identity %* | Associated Resistance | |
|---------|---------|--------|-------------|---|--|
| 2637986 | 2638846 | shv-11 | 100 | beta-lactam resistance gene | |
| 1544531 | 1545253 | baeR | 91 | aminocoumarin resistance gene; aminoglycoside resistance gene; | |
| 2009887 | 2010294 | h-ns | 94 | macrolide resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene; beta-lactam resistance gene | |
| 253419 | 254558 | acrE | 75 | beta-lactam resistance gene; fluoroquinolone resistance gene | |
| 489403 | 490224 | bacA | 89 | peptide antibiotic resistance gene | |
| 1546725 | 1548140 | mdtD | 84 | efflux pump conferring antibiotic resistance | |
| 95184 | 95666 | dfrA14 | 99 | trimethoprim resistance gene | |

| Table 1. | Resistome | analysis for | r the SKGH01 | strain of K. | pneumoniae. |
|----------|-----------|--------------|--------------|--------------|-------------|
| | | | | | |

| 2011B 201750 cp 99 macrolide resistance gene: beta-lactam resistance gene: fluoroquinolone resistance gene 59699 60490 aadA25 99 antibiotic inagt protection protein, fluoroquinolone resistance gene 2392102 2392854 arr.2 100 infimpin resistance gene 2392102 2392854 arr.2 100 infimpin resistance gene 2389792 239047 au(6)/169 90 aminoglycoid crisitance gene 2389792 239047 au(6)/169 90 aminoglycoid crisitance gene 2343782 434358 4347751 fluor bata-factam resistance gene 2343782 3448715 fluor bata-factam resistance gene fluoroquinolone resistance gene 3448775 3489415 pmc7 70 polymyxin resistance gene fluoroquinolone resistance gene 35485 316735 maxb 81 effluoroquinolone resistance gene fluoroquinolone resistance gene 314847 516745 parC 94 fluoroquinolone resistance gene 314848 516745 parC <td< th=""><th>(Table 1) cor</th><th></th><th></th><th></th><th></th></td<> | (Table 1) cor | | | | |
|---|------------------|------------------|--------------|-------------|---|
| 9999 64900 and 25 99 antibiotic inget protection protein, flooroquinolone resistance gene 98949 99593 quibii 100 antibiotic target protection protein, flooroquinolone resistance gene 920202 225242 225242 225242 225242 225242 252771 452817 mdM 75 efflux pump conferring ambiotic resistance gene 289793 2390347 anc(67)-109 99 antionoglycoside resistance gene 243652 443555 robat based based 25654 1857691 oxa-181 100 beta-lactam resistance gene 25645 based 100 chloramphenicol resistance gene chloramphenicol resistance gene 25646 8451 arnA 77 polymyxin resistance gene chloramphenicol resistance gene 254183 523013 mdL 75 efflux pump conferring ambiotic resistance gene 254147 florAdation robat lactam resistance gene chloramphenicol resistance gene 254145 gene sarnacolde resistance gene chloramphenicol resista | START | STOP | Gene | Identity %* | Associated Resistance |
| 99993 quality 100 antibility target potection protein, flooroquinolone resistance gene 2392402 2392844 arr.2 100 riftmap resistance gene 2302402 2392844 mdfA 85 efftux pump conferring ambiotic resistance 2387978 2390447 anc()-169 aminoglycostic resistance gene efftux pump conferring ambiotic resistance gene 443658 443751 roA 82 chloramphenicol resistance gene infampi resistance gene 1856844 1857601 oxa-181 100 beta-factam resistance gene 1848775 3489415 roA 81 efflux pump conferring ambiotic resistance gene 184875 3489415 cntA 81 efflux pump conferring ambiotic resistance gene 194381 516745 parC 94 fluoroquinolone resistance gene 194387 196757 119370 mecD 91 chloramphenicol resistance gene 201487 516745 parC 94 fluoroquinolone resistance gene 214387 516745 parC 94 fl | | | | | |
| 2192402 2192524 air-2 100 rifampin resistance gent 2410534 9411766 md/A 85 efflux pump conferring milbiotic resistance 2389793 2390347 acc/s10150 99 aminoglycoside resistance gent 238973 2390347 acc/s10150 99 aminoglycoside resistance gent 238973 2390347 acc/s10150 99 aminoglycoside resistance gent 155684 1857691 oxa-181 100 bela-lactan resistance gent 53618 54255 oat 100 chloramphenicol resistance gent 53618 54255 oat 100 chloramphenicol resistance gent 53618 54255 oat 100 chloramphenicol resistance gent 53618 54255 oat 110075 119370 mcAD 91 chloramphenicol resistance gent fluoroquinolone resistance gent 531435 523035 52306 oat.18 100 bela-lactan resistance gent 5231435 52306 oat.18 100 bela-lactan resistance gent 52348 523406 oat.18 100 | | | | | |
| 5410534 5411766 mdfA 85 efflux pump conferring antibiotic resistance 542767 1425091 mdtM 75 efflux pump conferring antibiotic resistance 5430552 542705 20071 20071 20071 5430552 4437451 robA 82 ehforamphenicol resistance gene. Host-lactam resistance gene 543075 543074 543074 543074 543074 544775 543041 100 beta-lactam resistance gene 55368 54318 54256 cat 100 chloramphenicol resistance gene 56318 54318 54256 max 77 polymyxin resistance gene 514475 514487 516745 parC 94 fluoroquinolone resistance gene 514487 5144421 516745 parC 94 fluoroquinolone re | | | qnrB1 | | |
| 4527671 4528072 2300347 acc(6)-Lby 99 aninoglycoside (resistance gane) 436582 437451 robA 82 chloramphenicol resistance gene, beta-lactam resistance gene 436582 437451 robA 82 chloramphenicol resistance gene, beta-lactam resistance gene 53618 54256 cat 100 chloramphenicol resistance gene 190757 193870 mexD 91 chloramphenicol resistance gene 14847 516745 parC 54 efflux pump conferring antibiotic resistance gene 5203015 300086 ovar-181 100 batarne statance gene 520302 523406 ovar-18 100 batarne statance gene 520302 524421 5353008 polymyxin resistance gene 1254421 523426 5142420 <td></td> <td></td> <td></td> <td></td> <td></td> | | | | | |
| 289793 290047 aac(6)-lb9 99 aminoglycoside resistance gene 443682 4437451 robA 82 chloramphenicol resistance (nucoquinolone resistance gene 1856994 185799 0xa-181 100 beta-lactam resistance gene 348775 3484775 348471 rifampine resistance gene 0 53618 54256 cat 100 chloramphenicol resistance gene 53618 54256 cat 100 chloramphenicol resistance gene 54646 58431 arnA 7 polymyxin resistance gene 190757 193870 mexD 91 chloramphenicol resistance gene; macrolide resistance gene 250346 mexD 91 chloramphenicol resistance gene; macrolide resistance gene 250346 mexD 86 chloramphenicol resistance gene; macrolide resistance gene 251442 1555580 mdA 79 aminocournair resistance gene; 251252 1626455 quarka 92 fluoroquinolone resistance gene; 251252 174652 17822 marn | | | | | |
| 443658 4437451 robA 82 chloramphenicol resistance gene; fluoroquinolone resistance gene 1856894 1857691 oxa-181 100 beta-lactam resistance gene 348773 3489415 pmrC 70 polymyxin resistance gene 348773 3489415 pmrC 70 polymyxin resistance gene 945981 947153 emrA 81 efflux pump conferring antibiotic resistance gene 947981 947153 emrA 81 efflux pump conferring antibiotic resistance gene 947873 Ins75 efflux pump conferring antibiotic resistance gene fluoroquinolone resistance gene 231835 5233013 mdL 75 efflux pump conferring antibiotic resistance gene 2448769 4049566 oxa-181 100 beta-lactam resistance gene 245342 555580 mdA 79 antinocounnarin resistance gene 244874 4040566 oxa-181 100 beta-lactam resistance gene 245342 555580 mdA 79 antinocounnarin resistance gene 245429 <t< td=""><td></td><td></td><td></td><td></td><td></td></t<> | | | | | |
| 143052rifampin resistance gene161-actam resistance gene1566841857691oxa-181100beta-lactam resistance gene1561841857691oxa-181100beta-lactam resistance gene15618514256cat100chloramphenicol resistance gene156184187763184915pmC70polymyxin resistance gene15908147153cmrA81efflux pump conferring antibiotic resistance gene11907271193870mexD91ehloramphenicol resistance gene; macrolide resistance gene11907271193870mexD94ehloramphenicol resistance gene; macrolide resistance gene1290726121487116745parC94202082253406mexD86ehloramphenicol resistance gene; macrolide resistance gene1543421555580mdA79aminocoumarin resistance gene1543431555580mdA79aminocoumarin resistance gene2617502617882marA92Chloramphenicol resistance gene; macrolide resistance gene213232512609epxA94aminocoumarin resistance gene; macrolide resistance gene21324279180991polymyxin resistance gene; macrolide resistance gene213242918069mrA87fluoroquinolone resistance gene2132421220883mdK87fluoroquinolone resistance gene2132421220843mdK87fluoroquinolone resistance gene21324271220883mdK | 2389793 | 2390347 | aac(6')-Ib9 | 99 | |
| 3487775 3489415 pmrC 70 polymyxin resistance gene 35618 54256 cat 100 chloramphenicol resistance gene 35618 54256 cat 100 chloramphenicol resistance gene 36646 88451 amA 77 polymyxin resistance gene 1190757 119870 meXD 91 chloramphenicol resistance gene; macrolide resistance gene 5231835 5233013 mdL 75 efflux pump conferring antibiotic resistance 5231835 5233003 mdA 79 antinocoumarin resistance gene; 5234821 555550 mdA 79 antinocoumarin resistance gene; 544725 94720 94720 94720 q4720 947270 94720 mdA 79 antinocoumarin resistance gene; 2417505 2617882 marA 92 chloramphenicol resistance gene; macrolide resistance gene; 24123 94956 erristance gene; macrolide resistance gene; gene; 2124627 512562 cpxA 94 aminocoumarin | 4436582 | 4437451 | robA | 82 | |
| 3518 54256 cat 100 chloramphenicol resistance gene 94598 947153 emrA 81 efflux pump conferring antibiotic resistance gene 94598 947153 emrA 81 efflux pump conferring antibiotic resistance gene 1190757 1193870 mexD 91 chloramphenicol resistance gene, macrolide resistance gene 231835 523303 mdil. 75 efflux pump conferring antibiotic resistance 2484769 4449566 oxa-181 100 beta-lactam resistance gene 253046 mexD 86 chloramphenicol resistance gene, macrolide resistance gene; 1000rupinyin resistance gene; 947279 947809 emrR 92 chloramphenicol resistance gene; 1000rupinyin resistance gene; 212322 124299 phoN 92 echloramphenicol resistance gene; 112322 212325 124299 phoN 92 echloramphenicol resistance gene; macrolide resistance gene; 212326 124299 phoN 91 polymyxin resistance gene; 1124258 1242627 124299 <td>1856894</td> <td>1857691</td> <td>oxa-181</td> <td>100</td> <td>beta-lactam resistance gene</td> | 1856894 | 1857691 | oxa-181 | 100 | beta-lactam resistance gene |
| 945981 947153 emrA 81 efflux pump conferring antibiotic resistance; fluoroquinolone resistance gene 945981 9471 973 Ti377 Ti37 | 3487775 | 3489415 | pmrC | 70 | polymyxin resistance gene |
| 86466 88451 amA 77 polymyxin resistance gene 1190757 1193870 mexD 91 chloramphenicol resistance gene, macrolide resistance gene 5231835 523013 mdL 75 cfllux pump conferring antibiotic resistance 5231835 523013 mdL 75 cfllux pump conferring antibiotic resistance 520206 253406 maxL 75 cfllux pump conferring antibiotic resistance 520206 253406 maxL 79 antinocourantir resistance gene 154342 1555580 mdA 79 antinocourantir resistance gene 3438415 340006 pmrA 78 polymyxin resistance gene 512522 126605 cpxA 94 antinocourantir resistance gene 512522 126605 cpxA 94 antinocourantir resistance gene 512452 126605 cmrY 94 efflux pump conferring antibiotic resistance gene 5124627 512525 cpxR 94 efflux pump conferring antibiotic resistance gene 5126605 cmrV | 53618 | 54256 | cat | 100 | |
| 1190757 1193870 mex.D 91 chloramplenicol resistance gene, macrolide resistance gene, fluoroquinolone resistance gene 231835 5233013 mdt. 75 efflux punp conferring antibiotic resistance 250246 253406 mex.D 86 chloramplenicol resistance gene, macrolide resistance gene 250246 253406 mex.D 86 chloramplenicol resistance gene, macrolide resistance gene 250246 polymyxin resistance gene macrolide resistance gene 1544321 1555580 mdt. 79 2617505 2617882 mar.A 92 fluoroquinolone resistance gene 2617505 2617882 mar.A 92 chloramplenicol resistance gene, etert-lactam resistance gene 2123228 2126095 cpx.A 94 aminocoumarin resistance gene, etert-sycline resistance gene 2123228 2126095 cmx.A 94 efflux pump conferring antibiotic resistance gene, etertagene 2124627 5125325 cpx.R 94 efflux pump conferring antibiotic resistance gene, etertagene 2124627 5125325 cpx.R 94 efflux pump conferring antibiotic resistance gene, etertagene 2124627 5125325 cpx.R 94 efflux pump conferring antibiotic resistance gene 278711 309852 <td>945981</td> <td>947153</td> <td>emrA</td> <td>81</td> <td>efflux pump conferring antibiotic resistance; fluoroquinolone resistance gene</td> | 945981 | 947153 | emrA | 81 | efflux pump conferring antibiotic resistance; fluoroquinolone resistance gene |
| 514487 516745 parC 94 fluoroquinolone resistance gene 5231835 5233013 mdt 75 efflux pump conferring antibiotic resistance gene 648769 4049566 coxa-181 100 beta-lactam resistance gene 5231835 5233013 mdt 79 aminocoumarin resistance gene 154342 1555580 mdtA 79 aminocoumarin resistance gene 247279 947809 emrA 78 polymyxin resistance gene 2617505 2617882 marA 92 chloramphenicol resistance gene; fluoroquinolone resistance gene 512522 5126695 cpxA 94 aminocoumarin resistance gene; macrolide resistance gene 2123628 3124299 phoP 91 polymyxin resistance gene; macrolide resistance gene 2124627 945956 cmrY 94 efflux pump conferring antibiotic resistance; transcline resistance gene 2124627 5125325 cpxR 94 efflux pump conferring antibiotic resistance gene; mairolyzo 79584 orX581 oxa-181 100 anthiotic inactivation | 86466 | 88451 | arnA | 77 | polymyxin resistance gene |
| 5231835 5233013 mdtl. 75 efflux pump conferring antibiotic resistance 520296 523406 mexD 86 chloramphenicol resistance gene; macrolide resistance gene 553432 1555580 mdtA 79 aminocoumarin resistance gene; 3489415 3490086 purA 78 polymyxin resistance gene; 947229 947809 emrR 92 floaroquinolone resistance gene; 2617505 2617882 marA 92 chloramphenicol resistance gene; flacoroquinolone resistance gene; 3123263 8124229 phoP 91 polymyxin resistance gene; macrolide resistance gene 3123263 8124229 phoP 91 polymyxin resistance gene; mainoglycoide resistance gene 3124263 8124229 phoP 91 polymyxin resistance gene; mainocumarin resistance gene 3124263 8124227 s125325 cpxR 94 efflux pump conferring antibiotic resistance; aminocumarin resistance gene 3124263 812427 812525 cpxR 94 efflux pump conferring antibiotic resistance gene 312428 812427 s125325 cpxR 94 efflux pump conferr | 1190757 | 1193870 | mexD | 91 | chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene |
| 4048769 4049566 oxa-181 100 beta-lactam resistance gene 250296 2533406 mexD 86 chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene 1554342 155580 mdtA 79 aminocoumarin resistance gene 947279 947809 emrR 92 fluoroquinolone resistance gene; 947279 947809 emrR 92 chloramphenicol resistance gene; macrolide resistance gene; 947279 947809 emrR 92 chloramphenicol resistance gene; beta-lactam resistance gene; 947279 947809 emrR 92 chloramphenicol resistance gene; macrolide resistance gene; 94125322 \$1256695 cpxA 94 efflux pump conferring antibiotic resistance; tertracycline resistance gene 91215010 2220883 mdtK 87 fluoroquinolone resistance gene; 912667 \$125322 cpxR 94 efflux pump conferring antibiotic resistance; aminocoumarin resistance gene \$124627 \$125322 cpxR 94 etflux pump conferring antibiotic resistance gene; \$1254627 | 514487 | 516745 | parC | 94 | fluoroquinolone resistance gene |
| 250296253406mexD86chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene3489415155580mdA79aminocoumarin resistance gene34894153490086pmrA78polymyxin resistance gene;26175052617882marA92chloramphenicol resistance gene; heta-lactan resistance gene31232251512695cpxA94aminocoumarin resistance gene; heta-lactan resistance gene31232681324299phoP91polymyxin resistance gene; macrolide resistance gene2147505cmrY94efflux pump conferring antibiotic resistance gene;312325s124299phoP91polymyxin resistance gene;3124290pack84fluoroquinolone resistance gene31242912220883mdK87fluoroquinolone resistance gene;3124292ploP94efflux pump conferring antibiotic resistance gene;3124293s2325cpxR94efflux pump conferring antibiotic resistance gene;3124293sava86chloramphenicol resistance gene;fluoroquinolone resistance gene;3124293sava86chloramphenicol resistance gene;fluoroquinolone resistance gene;3124293sava86chloramphenicol resistance gene;fluoroquinolone resistance gene;3124293sava86chloramphenicol resistance gene;fluoroquinolone resistance gene;3124294fluoroquinolonefluoroquinolone resistance gene;fluoroquinolone resistance gene;< | 5231835 | 5233013 | mdtL | 75 | efflux pump conferring antibiotic resistance |
| 1554342155580mdtA79aminocoumarin resistance gene34894153490086pmrA78polymyxin resistance gene947279947809emrR92fluoroquinolone resistance gene;26175052617882marA92ehloramphenicol resistance gene; fluoroquinolone resistance gene;31232283124299phOP91polymyxin resistance gene; marrolide resistance gene212427945965emrY94efflux pump conferring antibiotic resistance gene;2124283124299phOP91polymyxin resistance gene;2124283124299phOP94efflux pump conferring antibiotic resistance; tetracycline resistance gene21242675125325cpxR94efflux pump conferring antibiotic resistance; tetracycline resistance gene;31308773309852ctx-M-15100antibiotic institunce gene; infampin resistance gene;3308977309852ctx-M-15100beta-lactam resistance gene2434323453453453453fs43345fs433452578571227975emrD99efflux pump conferring antibiotic resistance gene2386032389382rmtF100aminoglycoside resistance gene23864886469pmrF83polymyxin resistance gene; beta-lactam resistance gene3797172377513ramA92chloramphenicol resistance gene; gene altering cell wall charge conferring antibiotic resistance gene3124299and(6)100antibiotic aresistance gene11412712 </td <td>4048769</td> <td>4049566</td> <td>oxa-181</td> <td>100</td> <td>beta-lactam resistance gene</td> | 4048769 | 4049566 | oxa-181 | 100 | beta-lactam resistance gene |
| 34894153490086pmrA78polymyxin resistance gene947279947809emrR92fluoroquinolone resistance gene;26175052617882marA92chloramphenicol resistance gene; fluoroquinolone resistance gene;31236283124299phoP91polymyxin resistance gene; beta-lactam resistance gene944427945965emrY94efflux pump conferring antibiotic resistance; tetracycline resistance gene944427945965emrY94efflux pump conferring antibiotic resistance; tetracycline resistance gene94427945965emrY94efflux pump conferring antibiotic resistance; tetracycline resistance gene9124627\$125325cpxR94efflux pump conferring antibiotic resistance; gene; efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene3089778acerA86chloramphenicol resistance gene; fluoroquinolone resistance gene; fluoroquinolone resistance gene2785715279755emrD99efflux pump conferring antibiotic resistance gene2886032389382rmtF100amtibiotic inacitivation enzyme; beta-lactam resistance gene2386032389382rmtF83polymyxin resistance gene; gene altering cell wall charge conferring antibiotic resistance37571723757513ramA92fluoroquinolone resistance gene37451723157513ramA92fluoramphenicol resistance gene <t< td=""><td>250296</td><td>253406</td><td>mexD</td><td>86</td><td>chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene</td></t<> | 250296 | 253406 | mexD | 86 | chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene |
| 947279947809emrR92fluoroquinolone resistance gene;26175052617882marA92chloramphenicol resistance gene; fluoroquinolone resistance gene;51253225126695cpxA94aminocoumarin resistance gene; beta-lactam resistance gene31236283124299phoP91polymyxin resistance gene; macrolide resistance gene2195102220883mdK87fluoroquinolone resistance; tetracycline resistance gene51246275125325cpxR94efflux pump conferring antibiotic resistance; tetracycline resistance gene;38926963893781acrA86chloramphenicol resistance gene; gene modulating antibiotic efflux38926963893781acrA86chloramphenicol resistance gene; fluoroquinolone resistance gene; beta-lactam resistance gene50750845075881oxa-181100beta-lactam resistance gene5075084507581oxa-181100beta-lactam resistance gene288603283802rmtF100aminoglycoide resistance gene2876031877152straft92chloramphenicol resistance gene; gene altering cell wall charge conferring antibiotic resistance3108085gyrA92chloramphenicol resistance gene; fluoroquinolone resistance gene31127123157513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene31286032138053rmtF100aminoglycoside resistance gene318603319203mtF83polymyxin resistance gene; fluoroquinolone re | | | mdtA | 79 | |
| 26175052617882marA92chloramphenicol resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene5123225126695cpxA94aminocoumarin resistance gene; aminoglycoside resistance gene91236283124299phoP91polymyxin resistance gene; marcolide resistance gene944427945965emrY94efflux pump conferring antibiotic resistance; tetracycline resistance gene22195102220883mdK87fluoroquinolone resistance; gene51246275125325cpxR94efflux pump conferring antibiotic resistance; gene; macrolide resistance gene; gene modulating antibiotic efflux38926963893781acrA86chloramphenicol resistance gene; fluoroquinolone resistance gene; beta-lactam resistance gene30389773309852etx-M-15100antibiotic inactivation enzyme; beta-lactam resistance gene50750845075881oxa-181100beta-lactam resistance gene52785715279755emrD99efflux pump conferring antinoglycoside resistance gene2386032389382rmtF100aminoglycoside resistance gene3771723757513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene31028533127093dtf1x12100antibiotic resistance gene3172173757513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene3172173757513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene3190855< | 3489415 | 3490086 | pmrA | 78 | polymyxin resistance gene |
| 20173032017862mark92rifampin resistance gene; beta-lactam resistance gene51253225126695cpxA94aminocoumarin resistance gene; amarolide resistance gene31236283124299phoP91polymyxin resistance gene; amarolide resistance gene21219510220883mdK87fluoroquinolone resistance; tetracycline resistance gene51246275125325cpxR94efflux pump conferring antibiotic resistance; aminogoumarin resistance gene; aminogoumarin resistance gene; gene modulating antibiotic efflux38926963893781acrA86chloramphenicol resistance gene; infampin resistance gene; beta-lactam resistance gene5075084oxa-181100beta-lactam resistance gene5075084sox-181100beta-lactam resistance gene23886032389382rmtF100aminoglycoside resistance gene23886032389382rmtF100aminoglycoside resistance gene37571723757513rmA92chloramphenicol resistance gene; gene altering cell wall charge conferring antibiotic resistance gene31236281395difA12100aminoglycoside resistance gene31236292389382rmtF100aminoglycoside resistance gene23860532389382rmtF100aminoglycoside resistance gene33886032389382rmtF100aminoglycoside resistance gene3445686469pmrF83polymyxin resistance gene; fluoroquinolone resistance gene31242993125755fm | 947279 | 947809 | emrR | 92 | fluoroquinolone resistance gene; |
| 3123628 3124299 phoP 91 polymyxin resistance gene; macrolide resistance gene 944427 945965 emrY 94 efflux pump conferring antibiotic resistance; tetracycline resistance gene 2219510 2220883 mdK 87 fluoroquinolone resistance gene 5124627 5125325 cpxR 94 efflux pump conferring antibiotic resistance; aminogycom resistance gene; gene modulating antibiotic efflux 3892696 3893781 acrA 86 chloramphenicol resistance gene; fluoroquinolone resistance gene; beta-lactam resistance gene 5075084 5075881 oxa-181 100 beta-lactam resistance gene 5075884 5075881 oxa-181 100 beta-lactam resistance gene 5278571 5279755 emrD 99 efflux pump conferring antinoglycoid resistance gene 238603 2389382 rmtF 100 aminoglycoid resistance gene 3757172 3757513 ramA 92 chloramphenicol resistance gene; fluoroquinolone resistance gene 387548 887014 rosB 73 polymyxin resistance gene; fluoroquinolone resistance gene; 3112121 1415345 gyrA 92 fluor | 2617505 | 2617882 | marA | 92 | chloramphenicol resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene; rifampin resistance gene; beta-lactam resistance gene |
| 944427945965emrY94efflux pump conferring antibiotic resistance; tetracycline resistance gene22195102220883mdtK87fluoroquinolone resistance gene51246275125325cpxR94efflux pump conferring antibiotic resistance; aminocoumarin resistance gene; aminoglyco resistance gene; fluoroquinolone resistance gene; flux pump conferring antibiotic resistance gene; efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene; flux pump conferring antibiotic inactivation enzyme; beta-lactam resistance gene3089773309852ctx-M-15100antibiotic inactivation enzyme; beta-lactam resistance gene50750845075881oxa-181100beta-lactam resistance gene52785715279755emrD99efflux pump conferring antibiotic resistance23880022389382rmtF100aminoglycoside resistance gene8548686469pmrF83polymyxin resistance gene; fluoroquinolone resistance gene85751723757513ramA92fluoroquinolone resistance gene8754388877114rosB73polymyxin resistance gene; beta-lactam resistance gene81543613290fluoroquinolone resistance gene14127121415345gyrA92fluoroquinolone resistance gene8154353132093mdtH85efflux pump conferring antibiotic resistance gene14127121415345gyrA92fluoroquinolone resistance gene8154353132093mdtH85efflux pump conferring antibiotic resistance gene< | 5125322 | 5126695 | cpxA | 94 | aminocoumarin resistance gene; aminoglycoside resistance gene |
| 2219510 2220883 mdtK 87 fluoroquinolone resistance gene 5124627 5125325 cpxR 94 efflux pump conferring antibiotic resistance; aminocoumarin resistance gene; aminoglyco resistance gene; gene modulating antibiotic efflux 3892696 3893781 acrA 86 chloramphenicol resistance gene; flampin resistance gene; demus dualting antibiotic efflux 3308977 3309852 ctx-M-15 100 antibiotic inactivation enzyme; beta-lactam resistance gene 5075084 5075881 oxa-181 100 beta-lactam resistance gene 5075084 5075881 oxa-181 100 beta-lactam resistance gene 5278571 5279755 emrD 99 efflux pump conferring antibiotic resistance 2388603 2389382 rmtF 100 aminoglycosid resistance gene 85486 86469 pmrF 83 polymyxin resistance gene; gene altering cell wall charge conferring antibiotic resistance gene 1412712 1415345 gyrA 92 fluoroquinolone resistance gene 1412712 1415345 gyrA 92 fluoroquinolone resistance gene 385481 861395 flu12 100 antibiotic | 3123628 | 3124299 | phoP | 91 | polymyxin resistance gene; macrolide resistance gene |
| 51246275125325cpxR94efflux pump conferring antibiotic resistance; aminocoumarin resistance gene; aminoglyco resistance gene; gene modulating antibiotic efflux38926963893781acrA86chloramphenicol resistance gene; fluoroquinolone resistance gene; efflux pump conferring an resistance; tetracycline resistance gene; rifampin resistance gene; beta-lactam resistance gene3089773309852ctx-M-15100antibiotic inactivation enzyme; beta-lactam resistance gene50750845075881oxa-181100beta-lactam resistance gene52785715279755emrD99efflux pump conferring antibiotic resistance gene2386032389382rmtF100aminoglycoside resistance gene8548686469pmrF83polymyxin resistance gene; fluoroquinolone resistance gene1127121415345gyrA92fluoroquinolone resistance gene; tetracycline resistance gene1127121415345gyrA92fluoroquinolone resistance gene1127121415345gyrA92fluoroquinolone resistance gene1127121415345gyrA92fluoroquinolone resistance gene1127121415345gyrA92fluoroquinolone resistance gene1382493172386955cat100antibiotic target replacement protein; trimethoprim resistance gene13928683192093mdtH85efflux pump conferring antibiotic resistance gene131242993125765phoQ81polymyxin resistance gene; macrolide resistance gene13124299< | 944427 | 945965 | emrY | 94 | efflux pump conferring antibiotic resistance; tetracycline resistance gene |
| 312402 312323 cpxk 94 resistance gene; gene modulating antibiotic efflux 3892696 3893781 acrA 86 chloramphenicol resistance gene; fluoroquinolone resistance gene; efflux pump conferring antibiotic factory in antibiotic inactivation enzyme; beta-lactam resistance gene 308977 3309852 ctx-M-15 100 antibiotic inactivation enzyme; beta-lactam resistance gene 5075084 5075881 oxa-181 100 beta-lactam resistance gene 5278571 5279755 emrD 99 efflux pump conferring antibiotic resistance 388603 2389382 rmtF 100 aminoglycoside resistance gene 375717 23757513 ramA 92 chloramphenicol resistance gene; gene altering cell wall charge conferring antibiotic resistance 3757172 3757513 ramA 92 fluoroquinolone resistance gene; beta-lactam resistance gene 38486 8469 pmrF 83 polymyxin resistance gene; beta-lactam resistance gene 375712 3757513 ramA 92 fluoroquinolone resistance gene; beta-lactam resistance gene 38486 8469 pmrF 83 polymyxin resistance gene; beta-lactam resistance gene 3875438 | 2219510 | 2220883 | mdtK | 87 | fluoroquinolone resistance gene |
| 38926963893781acrA86resistance; tetracycline resistance gene; rifampin resistance gene; beta-lactam resistance gene30089773309852ctx-M-15100antibiotic inactivation enzyme; beta-lactam resistance gene50750845075881oxa-181100beta-lactam resistance gene52785715279755emrD99efflux pump conferring antibiotic resistance2386032389382rmtF100aminoglycoside resistance gene2386032389382rmtF100aminoglycoside resistance gene3757513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene14127121415345gyrA92fluoroquinolone resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; fluoroquinolone resistance gene503638505116tolC83antibiotic inactivation enzyme; aminoglycoside resistance gene; beta-lactam51982831599449pmrE82polymyxin resistance gene; fluoroquinolone resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene; macrolide resistance gene; macrolide resistance gene; fluoroquin | 5124627 | 5125325 | cpxR | 94 | efflux pump conferring antibiotic resistance; aminocoumarin resistance gene; aminoglycoside resistance gene; gene modulating antibiotic efflux |
| 50750845075881oxa-181100beta-lactam resistance gene52785715279755emrD99efflux pump conferring antibiotic resistance45435234543945fosA597fosfomycin resistance gene23886032389382rmtF100aminoglycoside resistance gene8548686469pmrF83polymyxin resistance gene; gene altering cell wall charge conferring antibiotic resistance gene37571723757513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene14127121415345gyrA92fluoroquinolone resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; teriacycline resistance gene3198868319921mdtG84efflux pump conferring antibiotic resistance3198868319921mdtG84efflux pump conferring antibiotic resistance38938043896950mexD92efflux pump conferring antibiotic resistance gene; macrolide resistance gene; macrolide resistance gene | 3892696 | 3893781 | acrA | 86 | chloramphenicol resistance gene; fluoroquinolone resistance gene; efflux pump conferring antibiotic resistance; tetracycline resistance gene; rifampin resistance gene; beta-lactam resistance gene |
| 52785715279755emrD99efflux pump conferring antibiotic resistance45435234543945fosA597fosfomycin resistance gene23886032389382rmtF100aminoglycoside resistance gene8548686469pmrF83polymyxin resistance gene; gene altering cell wall charge conferring antibiotic resistance37571723757513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene14127121415345gyrA92fluoroquinolone resistance gene85754383877114rosB73polymyxin resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene;503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; resistance gene; tetracycline resistance gene;3198868319921mdtG84efflux pump conferring antibiotic resistance gene;31988643896950mexD92efflux pump conferring antibiotic resistance gene;31988043896950mexD92efflux pump conferring antibiotic resistance gene; | 3308977 | 3309852 | ctx-M-15 | 100 | antibiotic inactivation enzyme; beta-lactam resistance gene |
| 45435234543945fosA597fosfomycin resistance gene23886032389382rmtF100aminoglycoside resistance gene8548686469pmrF83polymyxin resistance gene; gene altering cell wall charge conferring antibiotic resistance37571723757513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene14127121415345gyrA92fluoroquinolone resistance gene88754383877114rosB73polymyxin resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene503638505116tolC83aminocoumarin resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene; beta-lactar resistance gene; fluoroquinolone resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene; fluoroquinolone resistance gene; fluoroquinolone resistance gene; fluoroquinolone resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene31988643896950mexD92efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene; beta-resistance gene31988643896950mexD92efflux pump conferring antibiotic resistance gene< | 5075084 | 5075881 | oxa-181 | 100 | beta-lactam resistance gene |
| 23886032389382rmtF100aminoglycoside resistance gene8548686469pmrF83polymyxin resistance gene; gene altering cell wall charge conferring antibiotic resistance37571723757513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene14127121415345gyrA92fluoroquinolone resistance gene38754383877114rosB73polymyxin resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene5709557649aac(6')-Ib999antibiotic resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; beta-31988683199821mdtG84efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene | 5278571 | 5279755 | emrD | 99 | efflux pump conferring antibiotic resistance |
| 8548686469pmrF83polymyxin resistance gene; gene altering cell wall charge conferring antibiotic resistance37571723757513ramA92chloramphenicol resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene14127121415345gyrA92fluoroquinolone resistance gene38754383877114rosB73polymyxin resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; fluoroquinolone resistance gene; fluoroquinolone resistance gene; macrolide resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene; beta-resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene; beta-resistance gene31988683199849pmrE82polymyxin resistance gene31988643896950mexD92efflux pump conferring antibiotic resistance gene | 4543523 | 4543945 | fosA5 | 97 | fosfomycin resistance gene |
| 37571723757513ramA92Chloramphenicol resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene14127121415345gyrA92fluoroquinolone resistance gene38754383877114rosB73polymyxin resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; beta-31988683199821mdtG84efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene; macrolide resistance gene; fluoroquinolone resistance gene31988683199821 </td <td>2388603</td> <td>2389382</td> <td>rmtF</td> <td>100</td> <td>aminoglycoside resistance gene</td> | 2388603 | 2389382 | rmtF | 100 | aminoglycoside resistance gene |
| 375/1/2375/513ramA92rifampin resistance gene; beta-lactam resistance gene14127121415345gyrA92fluoroquinolone resistance gene38754383877114rosB73polymyxin resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance23863172386955cat100chloramphenicol resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene5709557649aac(6')-Ib999antibiotic inactivation enzyme; aminoglycoside resistance gene503638505116tolC83chloramphenicol resistance gene; fluoroquinolone resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene; macrolide resistance gene | 85486 | 86469 | pmrF | 83 | polymyxin resistance gene; gene altering cell wall charge conferring antibiotic resistance |
| 38754383877114rosB73polymyxin resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene3190885319203mdtH85efflux pump conferring antibiotic resistance23863172386955cat100chloramphenicol resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene5709557649aac(6')-Ib999antibiotic inactivation enzyme; aminoglycoside resistance gene503638505116toIC83chloramphenicol resistance gene; fluoroquinolone resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance15982831599449pmrE82polymyxin resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene | 3757172 | 3757513 | ramA | 92 | chloramphenicol resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene; rifampin resistance gene; beta-lactam resistance gene |
| 38754383877114rosB73polymyxin resistance gene6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance23863172386955cat100chloramphenicol resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene5709557649aac(6')-Ib999antibiotic inactivation enzyme; aminoglycoside resistance gene503638505116toIC83chloramphenicol resistance gene; fluoroquinolone resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance15982831599449pmrE82polymyxin resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene; fluoroquinolone resistance gene | 1412712 | 1415345 | gyrA | 92 | |
| 6089861395dfrA12100antibiotic target replacement protein; trimethoprim resistance gene31908853192093mdtH85efflux pump conferring antibiotic resistance23863172386955cat100chloramphenicol resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene5709557649aac(6')-Ib999antibiotic inactivation enzyme; aminoglycoside resistance gene503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; aminocoumarin resistance gene; tetracycline resistance gene; rifampin resistance gene; beta-resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance15982831599449pmrE82polymyxin resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene; macrolide resistance gene | | | | | |
| 31908853192093mdtH85efflux pump conferring antibiotic resistance23863172386955cat100chloramphenicol resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene5709557649aac(6')-Ib999antibiotic inactivation enzyme; aminoglycoside resistance gene503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene; rifampin resistance gene; beta-resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene; macrolide resistance gene | | | | | |
| 23863172386955cat100chloramphenicol resistance gene31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene5709557649aac(6')-Ib999antibiotic inactivation enzyme; aminoglycoside resistance gene503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene; rifampin resistance gene; beta-resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene15982831599449pmrE82polymyxin resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene; macrolide resistance gene | | | | | |
| 31242993125765phoQ81polymyxin resistance gene; macrolide resistance gene5709557649aac(6')-Ib999antibiotic inactivation enzyme; aminoglycoside resistance gene503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; tetracycline resistance gene; rifampin resistance gene; beta-resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene15982831599449pmrE82polymyxin resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene; macrolide resistance gene | | | | | |
| 5709557649aac(6')-Ib999antibiotic inactivation enzyme; aminoglycoside resistance gene503638505116tolC83chloramphenicol resistance gene; macrolide resistance gene; rifampin resistance gene; tetracycline resistance gene; rifampin resistance gene; beta-resistance gene31988683199821mdtG84efflux pump conferring antibiotic resistance gene15982831599449pmrE82polymyxin resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance gene; macrolide resistance gene | | | | | |
| 503638 505116 tolC 83 chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; beta-resistance gene 3198868 3199821 mdtG 84 efflux pump conferring antibiotic resistance gene 1598283 1599449 pmrE 82 polymyxin resistance gene 3893804 3896950 mexD 92 efflux pump conferring antibiotic resistance gene; macrolide resistance gene | | | · · | | |
| 31988683199821mdtG84efflux pump conferring antibiotic resistance15982831599449pmrE82polymyxin resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance; chloramphenicol resistance gene; macrolide resigne; fluoroquinolone resistance gene | | | | | chloramphenicol resistance gene; macrolide resistance gene; fluoroquinolone resistance gene; aminocoumarin resistance gene; tetracycline resistance gene; rifampin resistance gene; beta-lactam |
| 15982831599449pmrE82polymyxin resistance gene38938043896950mexD92efflux pump conferring antibiotic resistance; chloramphenicol resistance gene; macrolide res gene; fluoroquinolone resistance gene | 3198868 | 3199821 | mdtG | 84 | |
| 3893804 3896950 mexD 92 efflux pump conferring antibiotic resistance; chloramphenicol resistance gene; macrolide res gene; fluoroquinolone resistance gene 92 efflux pump conferring antibiotic resistance; chloramphenicol resistance gene; macrolide res | | | | | |
| | | | | | efflux pump conferring antibiotic resistance; chloramphenicol resistance gene; macrolide resistance |
| 55905 56684 rmtF 100 aminoglycoside resistance gene | 55905 | 56684 | rmtF | 100 | |
| 1545250 1546728 baeS 77 aminocoumarin resistance gene; aminoglycoside resistance gene | | | | | |
| | 3893804 55905 | 3896950 56684 | mexD rmtF | 92 100 | efflux pump conferring antibiotic resistance; chloramphenicol resistance gene; macrolide resista gene; fluoroquinolone resistance gene aminoglycoside resistance gene |

198 The Open Microbiology Journal, 2018, Volume 12

(Table 1) contd.....

| START | STOP | Gene | Identity %* | Associated Resistance |
|--------|--------|------|-------------|-----------------------|
| 987867 | 991019 | oqxB | 98.5 | Quinolone resistance |
| 991043 | 992218 | oqxA | 99.5 | Quinolone resistance |

* Percentage given by the Antibiotic Resistance Genes Database (ARDB) and the Comprehensive Antimicrobial Resistance Database (CARD) when compared with known resistance genes database.

CONCLUSION

Here, using the long-read sequencing technology multiple, identical, carbapenem-resistance elements in the *K. pneumoniae* strain SKGH01 genome were identified. Based on the data, a new model explaining how XDR in this *K. pneumoniae* isolate developed via colistin resistance by mgrB gene disruption by ISEcp1. In this model, new resistance was driven by the existing mobile resistance determinants. Additionally, the data showed that ISEcp1 sequence interrupted the negative feedback regulator of the PhoQ-PhoP signalling system, namely the *mgrB* gene. Interestingly, this disruption was previously shown to drive the KPC-KPs acquired colistin resistance. Indeed, interruption of the *mgrB* gene caused upregulation of PhoQ-PhoP signalling; in turn, this upregulation activated the Pmr system, which was responsible for modifying the LPS target of polymyxin [12].

NUCLEOTIDE SEQUENCE ACCESSION NUMBER

The nucleotide sequence data are available in the GenBank nucleotide database, under accession numbers CP015500.1 to CP015505.1.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the hospital Medical executive committee.

HUMAN AND ANIMAL RIGHTS

Animals did not participate in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2008.

CONSENT FOR PUBLICATION

Consent for publication is obtained.

CONFLICT OF INTEREST

The author declare that they have no competing interests.

ACKNOWLEDGMENTS

Part of the Bioinformatics work was provided by omics2view.consulting GbR, Kiel (Germany).

SUPPLEMENTARY MATERIAL

Supplementary material is available on the publishers Web site along with the published article.

REFERENCES

- Podschun R, Ullmann U. Klebsiella spp. as nosocomial pathogens: Epidemiology, taxonomy, typing methods, and pathogenicity factors. Clin Microbiol Rev 1998; 11(4): 589-603.
 [PMID: 9767057]
- [2] Centres for Disease Control & Prevention. Antibiotic Resistance Threats in the United States 2013.
- [3] Munoz-Price LS, Poirel L, Bonomo RA, et al. Clinical epidemiology of the global expansion of *Klebsiella pneumoniae* carbapenemases. Lancet Infect Dis 2013; 13(9): 785-96.
 [http://dx.doi.org/10.1016/S1473-3099(13)70190-7] [PMID: 23969216]

- Petrosillo N, Giannella M, Lewis R, Viale P. Treatment of carbapenem-resistant *Klebsiella pneumoniae*: the state of the art. Expert Rev Anti Infect Ther 2013; 11(2): 159-77.
 [http://dx.doi.org/10.1586/eri.12.162] [PMID: 23409822]
- [5] Bogdanovich T, Adams-Haduch JM, Tian GB, et al. Colistin-resistant, Klebsiella pneumoniae carbapenemase (KPC)-producing Klebsiella pneumoniae belonging to the international epidemic clone ST258. Clin Infect Dis 2011; 53(4): 373-6. [http://dx.doi.org/10.1093/cid/cir401] [PMID: 21810751]
- Helander IM, Kato Y, Kilpeläinen I, et al. Characterization of lipopolysaccharides of polymyxin-resistant and polymyxin-sensitive Klebsiella pneumoniae O3. Eur J Biochem 1996; 237(1): 272-8.
 [http://dx.doi.org/10.1111/j.1432-1033.1996.0272n.x] [PMID: 8620884]
- [7] Cheng HY, Chen YF, Peng HL. Molecular characterization of the PhoPQ-PmrD-PmrAB mediated pathway regulating polymyxin B resistance in *Klebsiella pneumoniae* CG43. J Biomed Sci 2010; 17: 60.
 [http://dx.doi.org/10.1186/1423-0127-17-60] [PMID: 20653976]
- [8] Lippa AM, Goulian M. Feedback inhibition in the PhoQ/PhoP signaling system by a membrane peptide. PLoS Genet 2009; 5(12): e1000788. [http://dx.doi.org/10.1371/journal.pgen.1000788] [PMID: 20041203]
- Liu B, Pop M. ARDB-Antibiotic resistance genes database. Nucleic Acids Res 2009; 37(Database issue): D443-7. [http://dx.doi.org/10.1093/nar/gkn656] [PMID: 18832362]
- [10] McArthur AG, Waglechner N, Nizam F, et al. The comprehensive antibiotic resistance database. Antimicrob Agents Chemother 2013; 57(7): 3348-57.

[http://dx.doi.org/10.1128/AAC.00419-13] [PMID: 23650175]

- Zowawi HM, Forde BM, Alfaresi M, et al. Stepwise evolution of pandrug-resistance in Klebsiella pneumoniae. Sci Rep 2015; 5: 15082. [http://dx.doi.org/10.1038/srep15082] [PMID: 26478520]
- [12] Cannatelli A, Di Pilato V, Giani T, et al. In vivo evolution to colistin resistance by PmrB sensor kinase mutation in KPC-producing Klebsiella pneumoniae is associated with low-dosage colistin treatment. Antimicrob Agents Chemother 2014; 58(8): 4399-403. [http://dx.doi.org/10.1128/AAC.02555-14] [PMID: 24841267]

© 2018 Mubarak Alfaresi.

This is an open access article distributed under the terms of the Creative Commons Attribution 4.0 International Public License (CC-BY 4.0), a copy of which is available at: (https://creativecommons.org/licenses/by/4.0/legalcode). This license permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.