

# Characterization of a NDM-7 carbapenemase-producing *Escherichia coli* ST410 clinical strain isolated from a urinary tract infection in China

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**Purpose:** The emergence of New Delhi metallo-beta-lactamase (NDM) carbapenemase-producing *Escherichia coli* leaves few therapeutic options. Infections due to NDM-7 carbapenemase-producing *E. coli* are infrequent. In this study, we report the whole-genome sequence of an NDM-7 carbapenemase-producing *E. coli* belonging to sequence type (ST) 410 isolated from a patient with a urinary tract infection in China.

**Patients and methods:** The NDM-7 producing *E. coli* strain EC25 was isolated from a urine sample of a male patient hospitalized in a tertiary hospital in Zhejiang Province of China. Susceptibility assay of antibiotics was performed according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI). The whole genome of the strain was sequenced, and the *bla*<sub>NDM-7</sub>-harboring plasmid was analyzed. The genomic characterization and molecular epidemiology of the strain were further elucidated.

**Results:** *E. coli* EC25 was resistant to all antimicrobials tested, except tigecycline and colistin. The whole genome of *E. coli* EC25 was composed of one chromosomal DNA and five plasmids. Four virulence factors and twenty-five antimicrobial resistance genes, including *bla*<sub>NDM-7</sub>, were identified. Resistance genes were all located in an IncF-type plasmid (pEC25-1), except *bla*<sub>NDM-7</sub>, which was located in an individual IncX3-type plasmid (pEC25\_NDM-7). Twenty-one phylogenetically related strains were identified. The phylogenetically related *E. coli* ST410 strains exist globally. The closest relative strain of EC25 was a strain isolated from Sichuan province of China in 2016, with a similar IncX3-type plasmid that encoded *bla*<sub>NDM-5</sub>.

**Conclusion:** Our study reports the emergence of an *E. coli* ST410 strain harboring *bla*<sub>NDM-7</sub> in China. This strain may evolve as a successful epidemic clone of NDM-producing *E. coli* in China, and the *bla*<sub>NDM</sub> gene is prone to mutate during its dissemination.

**Keywords:** *Escherichia coli*, *bla*<sub>NDM-7</sub>, IncX3 type plasmid, carbapenem resistant, ST410

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## Introduction

*Escherichia coli* is a member of Enterobacteriaceae, and it is an important opportunistic pathogen. *E. coli* is the leading cause of urinary tract infections and the cause of a variety of other infections, including liver abscesses and bacteremia. *E. coli* that carry extended-spectrum  $\beta$ -lactamase (ESBL) are very common.<sup>1</sup> Besides tigecycline and colistin, carbapenems are often the last resort for treating infections due to ESBL-producing *E. coli*. However, the emergence of carbapenemase has

contributed to resistance to all  $\beta$ -lactams including carbapenems. New Delhi metallo-beta-lactamase (NDM) is one of the most important carbapenemases. Since the first report of *bla*<sub>NDM-1</sub> in 2009,<sup>2</sup> 24 NDM variants (NDM-1 to NDM-24) were identified.<sup>3</sup> NDM spread among Enterobacteriaceae and other Gram-negative bacteria, such as *Pseudomonas aeruginosa* and *Acinetobacter baumannii*,<sup>4,5</sup> and *E. coli* is the predominant carrier of *bla*<sub>NDM</sub>.

NDM-7 differs from NDM-1 by the substitution of two amino acids at positions 130 (Asp→Asn) and 154 (Met→Leu). NDM-7 was first described in an *E. coli* strain in Germany in 2013, and it exhibited higher carbapenemase activity compared to NDM-1.<sup>6</sup> NDM-7 was reported sporadically in many countries.<sup>7–13</sup> NDM-7-producing *E. coli* was first reported in 2016 in China. *bla*<sub>NDM-7</sub> was located on a conjugative IncX3-type plasmid in five clinically isolated *E. coli* strains of sequence types ST131 and ST650 in the Jiangxi Province.<sup>14</sup> Yingying Hao et al recently reported an NDM-7-producing *E. coli* ST167 strain isolated from a urine sample in the Shandong Province of China, and *bla*<sub>NDM-7</sub> was also located on a conjugative IncX3-type plasmid.<sup>15</sup> IncX3-type plasmids likely play an important role in the distribution of *bla*<sub>NDM-7</sub> in China. Considering the global emergence of NDM-7, an epidemiological survey and analysis of *bla*<sub>NDM-7</sub>-harboring strains are urgently needed to prevent its future prevalence.

The present study isolated an NDM-7-producing *E. coli* strain from a male patient hospitalized in a tertiary hospital in the Zhejiang Province of China. The entire genome of the strain was sequenced, and the *bla*<sub>NDM-7</sub>-harboring plasmid was analyzed. Genomic characterization and molecular epidemiology of the strain were further elucidated.

## Material and methods

### Patient and isolate

A 57-year-old male patient diagnosed with pulmonary infection was hospitalized in a tertiary hospital in the Zhejiang Province of China on August 14, 2017. The patient had a pulmonary infection and comorbidities, including hypoxic-ischemic encephalopathy, hypertension, and hypertensive heart disease. During his hospitalization, the patient received an indwelling urinary catheter. Routine urine tests suggested a urinary tract infection, and carbapenem-resistant *E. coli* was isolated from a urine sample on August 17, 2017. The strain was preliminarily identified using the VITEK MS

system (bioMérieux, France) and further confirmed using 16S rRNA gene sequencing.

### Antimicrobial susceptibility test

A susceptibility assay to antibiotics was performed according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI). The minimum inhibitory concentrations (MICs) of tigecycline and colistin (Sigma-Aldrich, St. Louis, MO, USA) were determined using standard broth microdilution tests with fresh Mueller-Hinton broth (Cation-adjusted, Oxoid LTD, England). The MICs of other antimicrobial agents were determined using the Etest method. Antimicrobial susceptibility was determined using the breakpoints approved by the CLSI, and the US Food and Drug Administration (FDA) breakpoints were used for tigecycline.

### Whole-genome sequencing

Genomic DNA of the isolate was extracted using a QIAamp DNA MiniKit (Qiagen, USA) and subjected to whole-genome sequencing (WGS) using the Illumina HiSeqTM 4000 platform (Illumina, San Diego, CA, USA). The short reads generated were *de novo* assembled into contigs using SPAdes. To obtain the complete sequence, EC25 was subjected to sequencing using the long-read MinION Sequencer (Nanopore, Oxford, UK). The MinION sequencing libraries were prepared using the rapid barcoding kit and loaded onto a single MinION R9.4 flow cell. The MinION reads were base-called with Albacore v2.0.2 and generated 2.4 Gbp of data. Raw and trimmed Illumina reads were assessed using FastQC v0.11.7, and quality trimming was performed using Trimmomatic v0.32. The MinION reads were demultiplexed and quality-trimmed using Porechop v0.2.3 with the default settings. The *de novo* hybrid assembly of short Illumina reads and long MinION reads was performed using Unicycler (v0.4.7; parameters: -min\_component\_size 500-min\_dead\_end\_size 500-verbosity 1-mode conservative) under conservative mode for increased accuracy. Complete circular contigs generated were corrected using Pilon with Illumina reads for several rounds until no change was detected. We obtained one circular contig, which was represented by a complete chromosome with a size of 4,782,653 bp and five plasmids of 227,349 bp, 46,161 bp, 5,167 bp, 4,991 bp, and 3,373 bp. The whole-genome sequence was annotated in the NCBI Prokaryotic Genomes Annotation Pipeline (PGAP) server.

**Table 1** MICs of the antibiotics tested in *E. coli* EC25

Antibiotics	MIC(mg/L)
Cefazolin <sup>a</sup>	>256
Ceftriaxone <sup>a</sup>	>256
Cefotaxime <sup>a</sup>	>256
Cefepime <sup>a</sup>	>256
Imipenem <sup>a</sup>	>32
Meropenem <sup>a</sup>	>32
Aztreonam <sup>a</sup>	>32
Amoxicillin/clavulanate <sup>a</sup>	>256
Cefoperazone/sulbactam <sup>a</sup>	>256
Ciprofloxacin <sup>a</sup>	>32
Gentamicin <sup>a</sup>	>256
Tetracycline <sup>a</sup>	>256
Tigecycline <sup>b</sup>	0.25
Colistin <sup>b</sup>	0.25

**Notes:** <sup>a</sup>Tested by Etest method. <sup>b</sup>Tested by standard broth microdilution tests.

## Identification of antimicrobial resistance genes

Acquired antimicrobial resistance genes were identified using ResFinder 3.0 with a 99% threshold for gene identification and a 100% minimum length via depositing of the entire genome sequence into the database.<sup>16</sup> The carbapenem-resistant gene *bla*<sub>NDM-7</sub> was confirmed using PCR and Sanger sequencing.

## Genomic characterization

Multilocus sequence typing (MLST) of the isolate was analyzed using the BacWGSTdb server of the entire genome sequence.<sup>17</sup> Virulence genes and plasmid replicon type were analyzed using VirulenceFinder 1.5 and PlasmidFinder 1.3.<sup>16</sup> Further bioinformatics analysis, such as identification of insertion elements (IS), clustered regularly interspaced short palindromic repeat (CRISPR) sequences and secondary metabolite gene clusters, were predicted using applications of ISfinder, CRISPRfinder, and antiSMASH tools, respectively.<sup>18,19</sup>

**Table 2** Virulence genes in strain *E. coli* EC25

Virulence factor	Identity	Query/template length	Contig	Position in contig	Protein function	Accession number
gad	100	1401/1401	EC25	251,983..253,383	Glutamate decarboxylase	AP010953
gad	99.79	1401/1401	EC25	2,444,792..2,446,192	Glutamate decarboxylase	CP002967
iss	98.64	294/294	EC25	3,714,038..3,714,331	Increased serum survival	CP004009
lpfA	100	573/573	EC25	4,749,714..4,750,286	Long polar fimbriae	AY646923

## Plasmid analysis

The plasmid sequences were annotated in the NCBI Prokaryotic Genomes Annotation Pipeline (PGAP) server. A graphical map of the *bla*<sub>NDM-7</sub>-carrying plasmid was converted in the CGView Server and completed with labels and footnotes.<sup>20</sup>

## Phylogenetic relationship analysis

The phylogenetic relationship between EC25 and other *E. coli* strains was analyzed using the BacWGSTdb server and the entire genome sequence.<sup>17</sup> The BacWGSTdb server offers SNP and genome MLST approaches to investigate the phylogenetic relationship of the uploaded genome sequence with sequences deposited in the BacWGSTdb. The database currently contains 10,545 *E. coli* strains, including 77 strains of ST410. Scheme cgMLST was used with a 200 threshold for phylogenetic analysis.

## Nucleotide sequence accession numbers

The complete sequence of strain *E. coli* EC25 and plasmids were submitted to GenBank under accession number CP035123-CP035128.

## Ethical approval

The urine sample and clinical isolate of *E. coli* EC25 were generated as part of routine hospital laboratory procedures. This study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Zhejiang Provincial People's Hospital, China. Written informed consent was obtained from the patient, which included publication of the case details.

## Results and discussion

The MICs of strain EC25 to different antibiotics are presented in Table 1. The strain was resistant to all antimicrobials tested except tigecycline and colistin.

**Table 3** Distribution of resistance genes in *E. coli* strain EC25

Resistance gene	%identity	HSP length/query	Contig	Position in contig	Predicted phenotype	Accession number
<b>Aminoglycoside</b>						
<i>aph(3'')-Ib</i>	100	804/804	pEC25-1	94,244..95,047	Aminoglycoside resistance	AF321551
<i>aph(6)-Id</i>	100	837/837	pEC25-1	95,047..95,883	Aminoglycoside resistance	M28829
<i>aac(3)-IId</i>	99.88	861/861	pEC25-1	97,435..98,295	Aminoglycoside resistance	EU022314
<i>aadA16</i>	99.65	846/846	pEC25-1	111,488..112,333	Aminoglycoside resistance	EU675686
<i>aac(6)-Ib-cr</i>	100	600/600	pEC25-1	113,669..114,268	Fluoroquinolone and aminoglycoside resistance	DQ303918
<i>aadA5</i>	100	789/789	pEC25-1	204,055..204,843	Aminoglycoside resistance	AF137361
<i>aac(6)-Ib-cr</i>	100	600/600	pEC25-1	208,288..208,887	Fluoroquinolone and aminoglycoside resistance	DQ303918
<b>Beta-lactam</b>						
<i>bla<sub>NDM-7</sub></i>	100	813/813	pEC25_NDM-7	44,052..44,864	Beta-lactam resistance	JX262694
<i>bla<sub>OXA-1</sub></i>	100	831/831	pEC25-1	209,018..209,848	Beta-lactam resistance	HQ170510
<i>bla<sub>TEM-1B</sub></i>	100	861/861	pEC25-1	214,606..215,466	Beta-lactam resistance	AY458016
<i>bla<sub>CTX-M-3</sub></i>	100	876/876	pEC25-1	216,248..217,123	Beta-lactam resistance	Y10278
<b>Fluoroquinolone</b>						
<i>qnrB2</i>	99.84	645/645	pEC25-1	105,800..106,444	Fluoroquinolone resistance	DQ351242
<i>aac(6)-Ib-cr</i>	100	600/600	pEC25-1	113,669..114,268	Fluoroquinolone and aminoglycoside resistance	DQ303918
<i>aac(6)-Ib-cr</i>	100	600/600	pEC25-1	208,288..208,887	Fluoroquinolone and aminoglycoside resistance	DQ303918
<i>qnrS1</i>	100	657/657	pEC25-1	221,088..221,744	Fluoroquinolone resistance	AB187515
<b>Rifampicin</b>						
<i>arr-3</i>	100	453/453	pEC25-1	113,120..113,572	Rifampicin resistance	JF806499
<b>MLS - Macrolide, Lincosamide and Streptogramin B</b>						
<i>mph(A)</i>	100	906/906	pEC25-1	99,354..100,259	Macrolide resistance	D16251
<i>mph(A)</i>	100	906/906	pEC25-1	196,453..197,358	Macrolide resistance	D16251
<b>Sulphonamide</b>						
<i>sul2</i>	100	816/816	pEC25-1	93,368..94,183	Sulphonamide resistance	HQ840942
<i>sul1</i>	100	840/840	pEC25-1	104,470..105,309	Sulphonamide resistance	U12338
<i>sul1</i>	100	840/840	pEC25-1	110,191..111,030	Sulphonamide resistance	U12338
<i>sul1</i>	100	840/840	pEC25-1	202,669..203,508	Sulphonamide resistance	U12338

(Continued)

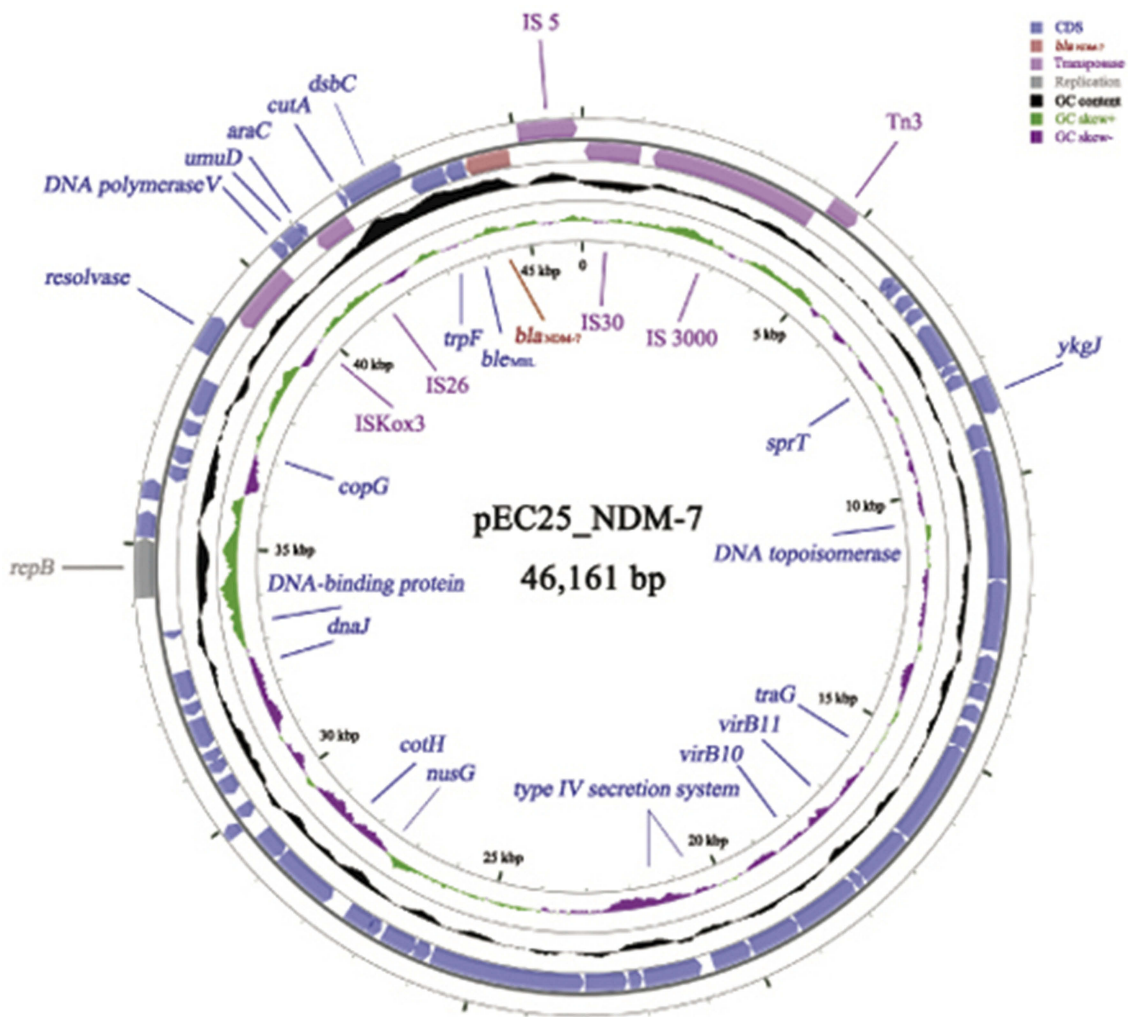
Table 3 (Continued).

Resistance gene	%identity	HSP length/query	Contig	Position in contig	Predicted phenotype	Accession number
Tetracycline						
<i>tet(A)</i>	100	1200/1200	pEC25-1	118,110..119,309	Tetracycline resistance	AJ517790
Trimethoprim						
<i>dfrA27</i>	100	474/474	pEC25-1	112,514..112,987	Trimethoprim resistance	FJ459817
<i>dfrA17</i>	100	474/474	pEC25-1	204,974..205,447	Trimethoprim resistance	FJ460238

The whole-genome sequence of *E. coli* EC25 was composed of one chromosomal DNA that comprised 4,782,653 bp and five plasmids of 227,349 bp, 46,161 bp, 5,167 bp, 4,991 bp, and 3,373 bp. The chromosomal DNA contained 88 tRNA genes, 3 rRNA operons, and 4,707 protein-coding sequences, which were identified using the PGAP server. The MLST scheme revealed that EC25 belonged to sequence type ST410. The genome contained two confirmed CRISPRs (CRISPR1 start position and end position: 1,042,955–1,043,471, CRISPR length: 516; CRISPR2 start position and end position: 1,065,855–1,066,433, CRISPR length: 578). Several IS elements were found in the genome, and most belonged to the IS3 and IS5 families. Four secondary metabolite regions, *nrps-t1pks*, thiopeptide, NRPS, and siderophore, were also identified.

Four virulence factors were found in the genome (Table 2), which were two copies of *gad* (glutamate decarboxylase), a single copy of *iss* (increased serum survival) and *lpfA* (long polar fimbriae). The distribution of the resistance genes in the genome of the strain EC25 is presented in Table 3. We identified the aminoglycoside resistance genes *aph(3'')-Ib*, *aph(6)-Id*, *aac(3)-IId*, *aadA16*, *aac(6)-Ib-cr*, and *aadA5*, the beta-lactam resistance genes *bla<sub>NDM-7</sub>*, *bla<sub>OXA-1</sub>*, *bla<sub>TEM-1B</sub>*, and *bla<sub>CTX-M-3</sub>*, the fluoroquinolone resistance genes *qnrB2*, *aac(6)-Ib-cr* and *qnrS1*, the rifampicin resistance gene *arr-3*, the macrolide, lincosamide and streptogramin B resistance gene *mph(A)*, the sulfonamide resistance genes *sul1* and *sul2*, the tetracycline resistance gene *tet(A)*, and the trimethoprim resistance genes *dfrA27* and *dfrA17*. Except for *bla<sub>NDM-7</sub>*, all of the resistance genes were located in the IncF-type plasmid pEC25-1, including two copies of *aac(6)-Ib-cr* and *mph(A)* and three copies of *sul1*. The carbapenem-resistant gene *bla<sub>NDM-7</sub>* was located in an individual plasmid, pEC25\_NDM-7.

The plasmid profile of pEC25\_NDM-7 is presented in Figure 1. It is an IncX3-type plasmid composed of 46,161 bp. The carbapenem-resistant gene *bla<sub>NDM-7</sub>* was preceded by Tn3-IS3000-IS30-IS5 in the upstream region and followed by *ble<sub>MBL</sub>-trpF-dsbC-cutA-IS26* in the downstream region. The similarity of pEC25\_NDM-7 to other *bla<sub>NDM</sub>*-harboring plasmids was analyzed using Basic Local Alignment Search Tool (BLAST). pEC25\_NDM-7 was 99% identical to several previously reported plasmids, namely, pJN05NDM7 (Accession No. MH523639), pAD-19R (Accession No. KX833071), pNDM-20 (Accession No. MF458176), pM216\_X3 (Accession No. AP018146), and pKW53T-NDM (Accession No. KX214669). Plasmid



**Figure 1** Profile of the *bla*<sub>NDM-7</sub>-encoding plasmid pEC25\_NDM-7.

pJN05NDM7 (carrying *bla*<sub>NDM-7</sub>) was identified in an *E. coli* ST167 clinical strain isolated from a patient with a urinary tract infection at a teaching hospital in the Shandong Province of China in 2015.<sup>15</sup> Plasmid pAD-19R (carrying *bla*<sub>NDM-17</sub>) was identified in an *E. coli* ST48 strain isolated from a chicken at a commercial poultry farm in the Shandong Province of China in 2015.<sup>21</sup> Plasmid pNDM-20 (carrying *bla*<sub>NDM-20</sub>) was identified in an *E. coli* ST1114 strain isolated from a swine faecal swab collected from a commercial pig farm in the Shandong province of China in 2016.<sup>22</sup> Plasmid pM216\_X3 (carrying *bla*<sub>NDM-4</sub>) was identified in an *E. coli* ST101 clinical strain isolated from a urine specimen at a tertiary care hospital in Yangon, Myanmar, in 2015.<sup>23</sup> Plasmid pKW53T-NDM (carrying *bla*<sub>NDM-7</sub>) was identified in an *E. coli* ST448 clinical strain isolated from a urine sample in Kuwait in 2012.<sup>12</sup> These plasmids encode distinct *bla*<sub>NDM</sub> variants, and it is likely that *bla*<sub>NDM</sub> mutates from

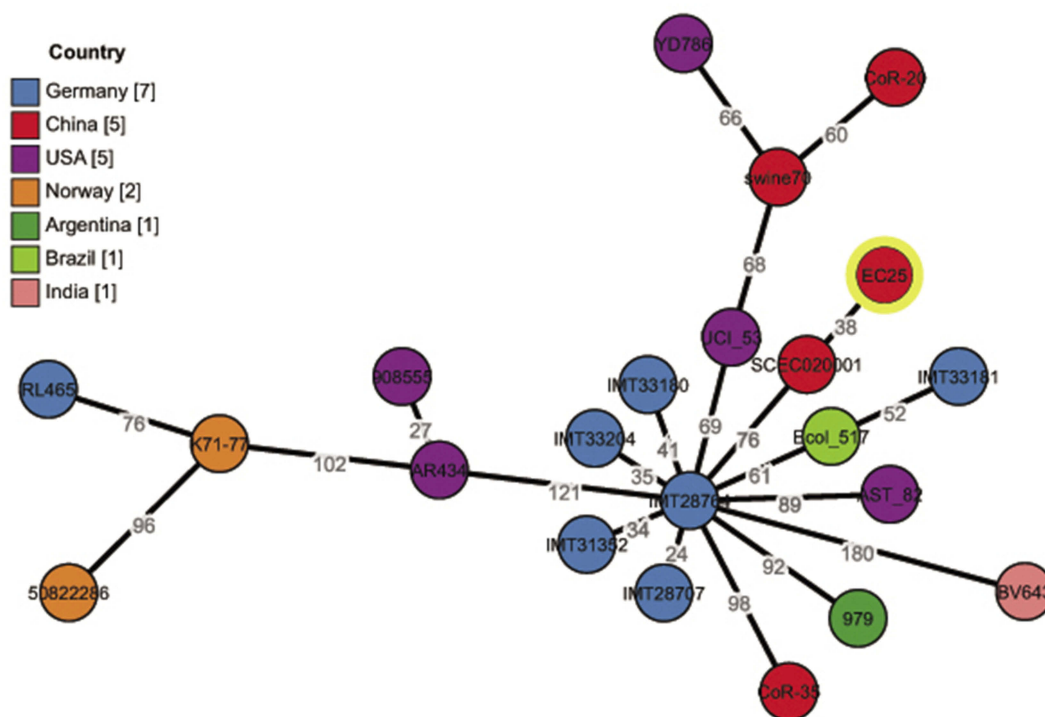
*bla*<sub>NDM-1</sub> to other *bla*<sub>NDM</sub> variants via nucleic acid replication in the 46,161 bp IncX3-type plasmid to evolve higher carbapenemase activity. Notably, the 46,161 bp IncX3-type plasmid does not carry antimicrobial resistance genes other than *bla*<sub>NDM</sub>, and the plasmid appeared in different ST type of *E. coli* strain across different countries in humans and animals. It seems the structure of the 46,161 bp plasmid is stable and suitable for the horizontal transfer of *bla*<sub>NDM</sub>, which plays an important role in horizontal transmission of NDM carbapenemase worldwide.

The phylogenetic relationship between *E. coli* EC25 and other *E. coli* strains is presented in Table 4 and Figure 2. Twenty-one phylogenetically related strains were identified in the database, all of which belong to ST410. Most of these strains produce ESBL, and only six strains produced carbapenemase, including one KPC-2-producing strain, one VIM-4-producing strain, and four NDM-producing strains. The phylogenetically related *E. coli* ST410 strains are spread

**Table 4** Information of close isolates (based on cgMLST strategy) to strain *E. coli* EC25

Isolate	Accession number	ST	Host	Isolation source	Country state	Collection year	Major resistance genotype	Different alleles	Reference
EC25	CP035123	410	Homo sapiens	Urine	China: Zhejiang	2017	<i>bla</i> <sub>NDM-7</sub>	0	This study
SCEC020001	CP032426	410	Homo sapiens	N/A <sup>a</sup>	China: Sichuan	2016	<i>bla</i> <sub>NDM-5</sub>	38	Unpublished
IMT31352	LJGF01	410	Dog	Feces	Germany	2013	ESBL	96	<sup>25</sup>
IMT28764	LJGC01	410	Mute swan	Feces	Germany	2012	ESBL	97	<sup>25</sup>
IMT33180	LJGI01	410	Homo sapiens	Blood	Germany	2009	ESBL	99	<sup>25</sup>
IMT28707	LJGB01	410	Mute swan	Feces	Germany	2012	ESBL	99	<sup>25</sup>
IMT33204	LJGK01	410	Homo sapiens	Blood	Germany	2010	ESBL	103	<sup>25</sup>
IMT33181	LJGJ01	410	Homo sapiens	Blood	Germany	2009	ESBL	118	<sup>25</sup>
Ecol_517	CP018965	410	Homo sapiens	N/A <sup>a</sup>	Brazil:	2011	<i>bla</i> <sub>KPC-2</sub>	119	<sup>26</sup>
UCI_53	JMVS01	410	Homo sapiens	Biliary drain	USA	2013	ESBL	127	<sup>27</sup>
Swine70	LVOT01	410	Suscrofa	Rectum	China: Jiangsu	2012	- <sup>b</sup>	135	Unpublished
YD786	CP013112	410	Homo sapiens	Urine	USA	2012	ESBL	138	<sup>28</sup>
CoR-20	MKFO01	410	Homo sapiens	Sputum	China: Zhejiang	2014	ESBL	145	Unpublished
AST_82	LLXC01	410	N/A <sup>a</sup>	N/A <sup>a</sup>	USA	2015	AmpC	147	Unpublished
979	PIJB01	410	Homo sapiens	Urine	Argentina	2016	ESBL	150	Unpublished
CoR-35	NISA01	410	Homo sapiens	Ascites	China: Zhejiang	2015	ESBL	153	Unpublished
K71-77	LNGY01	410	Homo sapiens	Blood	Norway	2010	<i>bla</i> <sub>NDM-1</sub>	164	<sup>29</sup>
RL465	FLKU01	410	N/A <sup>a</sup>	N/A <sup>a</sup>	Germany	N/A <sup>a</sup>	ESBL	174	<sup>30</sup>
AR434	CP029122	410	N/A <sup>a</sup>	N/A <sup>a</sup>	USA	N/A <sup>a</sup>	- <sup>b</sup>	176	Unpublished
50,822,286	LNJK01	410	Homo sapiens	Rectal swab	Norway	2014	<i>bla</i> <sub>VIM-4</sub>	185	<sup>31</sup>
908,555	AXTR01	410	Homo sapiens	N/A <sup>a</sup>	USA	N/A <sup>a</sup>	- <sup>b</sup>	193	Unpublished
BV643	PVPJ01	410	Homo sapiens	Blood	India	2016	<i>bla</i> <sub>NDM-5</sub>	194	Unpublished

**Notes:** <sup>a</sup>Data not available. <sup>b</sup>No carbapenemase, ESBL, and AmpC-type β-Lactamases can be found in the genome.



**Figure 2** Phylogenetic relationship between *E. coli* ST410 strain EC25 and other *E. coli* strains. Twenty-one phylogenetically related strains were identified in the BacWGSTdb server. All of these strains belonged to ST410. Seven strains were isolated from Germany, five from the USA, four from China, two from Norway, and one each from Argentina, Brazil, and India.

globally. Seven strains were isolated from Germany, five strains from the USA, four strains from China, two strains from Norway, and one strain each from Argentina, Brazil, and India. Of the four strains from China, two of the strains were isolated from the Zhejiang province, one strain was from the Jiangsu province, and one strain was from the Sichuan province. The strain closest to EC25 was *E. coli* SCEC020001, which was isolated from the Sichuan province of China in 2016. There are only 38 different alleles between *E. coli* EC25 and *E. coli* SCEC020001. *E. coli* SCEC020001 also harbors a 46,161 bp IncX3-type plasmid (pNDM5\_020001, Accession No. CP032424) that encodes *bla*<sub>NDM-5</sub>. pNDM5\_020001 was 99% identical to pEC25\_NDM-7. The main difference between the two plasmids was the subtype of *bla*<sub>NDM</sub>; pNDM5\_020001 encoded *bla*<sub>NDM-5</sub> and pEC25\_NDM-7 encoded *bla*<sub>NDM-7</sub>. There is a geographic distinction between the Zhejiang province and Sichuan province, and the patient did not have a travel history out of Zhejiang province in recent years, which suggests that the NDM-positive *E. coli* ST410 strain EC25 was locally acquired, and the *bla*<sub>NDM-7</sub> subtype may evolve during local dissemination.

A variety of STs were found in NDM-positive *E. coli* strains worldwide, and there are no predominant STs. The number of large-scale studies examining the clonal

background of NDM-positive *E. coli* strains is limited in China. Zhang R et al suggested that ST167 and ST410 were two of the most common sequence types of NDM-positive *E. coli* strains in China.<sup>24</sup> We report the whole-genome sequence of a clinically isolated *E. coli* ST410 strain harboring *bla*<sub>NDM-7</sub>. Our study is the first report on fully sequenced *E. coli* ST410 strain carrying *bla*<sub>NDM-7</sub> isolated from China because *bla*<sub>NDM-7</sub> is rare. A similar NDM-positive *E. coli* ST410 strain was found in the BacWGSTdb server in other provinces of China. ST410 is more likely to emerge as a successful epidemic clone of NDM-producing *E. coli* in China, and the *bla*<sub>NDM</sub> gene is prone to mutate during its dissemination. Therefore, more studies are required to illuminate the epidemic clones of NDM-positive *E. coli* in China.

### Conclusion

In summary, our study reports the first identification of a clinical carbapenem-resistant *E. coli* ST410 strain carrying *bla*<sub>NDM-7</sub> recovered from a urinary tract infection in China. Our study highlights the potential transmission opportunity of carbapenem-resistant plasmid carriage in *E. coli*. Further studies involving more NDM-producing isolates are warranted to identify reservoirs and monitor the transmission dynamics of *bla*<sub>NDM</sub> genes in China.



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## Disclosure

The authors report no conflicts of interest in this work.

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