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RAPID COMMUNICATION

Global Emergence and Genomic Epidemiology of *bla*$_{NDM}$-Carrying *Klebsiella variicola*

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Purpose: *Klebsiella variicola* has emerged as a human pathogen in the past decade. Here, we present findings related to a *K. variicola* strain carrying the *bla*$_{NDM-1}$ gene, which was isolated from a urinary tract infection in China. Global transmission dynamics and genomic epidemiology of *bla*$_{NDM}$-carrying *K. variicola* were further investigated.

Material and Methods: The complete genome sequence of the strain was determined using the Illumina NovaSeq 6000 and Nanopore MinION sequencer. Genomic features and resistance mechanisms were analyzed through diverse bioinformatics approaches. Additionally, genome sequences of *K. variicola* strains carrying *bla*$_{NDM}$ were retrieved from the NCBI database, and a comprehensive analysis of the global dissemination trends of these strains was conducted.

Results: *K. variicola* strain 353 demonstrated resistance to multiple antimicrobials, including carbapenems. Within its genome, we identified fourteen antimicrobial resistance genes associated with β-lactam, aminoglycoside, fosfomycin, quinolone, trimethoprim, rifamycin, and sulfonamide resistance. The carbapenem-resistant gene *bla*$_{NDM-1}$ was located on an IncU-type plasmid spanning 294,608 bp and flanked by IS*CR1* and IS*26*. Downstream of *bla*$_{NDM-1}$, we identified an *Intl1* element housing numerous antibiotic resistance genes. A comprehensive search of the NCBI database revealed 72 *K. variicola* strains carrying *bla*$_{NDM}$ from twelve different countries, predominantly from clinical sources, with the highest prevalence observed in the USA and China. A total of 28 distinct sequence types (STs) were identified, with ST115 being the most prevalent, followed by ST60.

Conclusion: In summary, this study presents the genomic characterization of a *K. variicola* strain carrying *bla*$_{NDM-1}$ on an IncU-type plasmid. The research highlights the global dissemination of *bla*$_{NDM}$-carrying *K. variicola*, observed in both healthcare settings and natural environments. Our data have revealed a diverse array of antimicrobial resistance determinants in *K. variicola*, providing valuable insights that could aid in the development of strategies for the prevention, diagnosis, and treatment of *K. variicola* infections.

Keywords: *Klebsiella variicola*, *bla*$_{NDM-1}$, whole-genome sequencing, IncU type plasmid, urinary tract infection

Introduction

Klebsiella variicola is a gram-negative, facultative anaerobe, nonsporogenic, and nonmotile rod-shaped bacterium that forms round, convex, and smooth colonies.[1] Initially discovered in bananas in 2004, *K. variicola* is commonly present in agriculturally sourced soils, plants, freshwater, and sewage.[2] It frequently contributes to nitrogen fixation and promotes plant growth. Moreover, it is recognized as a commensal of insects and can act as a pathogen for both plants and animals.[3–5] Belonging to the *Klebsiella* genus, *K. variicola* has historically been prone to misidentification as *Klebsiella pneumoniae* through traditional biochemical methods. This challenge persisted until the adoption of advanced techniques such as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) and whole-genome sequencing for accurate species identification.[6,7] The past misidentification, particularly within the *K. pneumoniae* complex, has hindered comprehensive research on *K. variicola* within the healthcare system.

K. variicola has emerged as a noteworthy human pathogen, witnessing a consistent rise in clinical infections in recent years.[8] Reports have extensively documented infections involving isolates from various sources, including

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fecal, blood, sputum, vaginal, and urine samples.[9,10] Notably, hypermucoviscous strains of *K. variicola* were initially identified in 2015, intensifying the concerns surrounding its clinical impact.[11,12] Adding to these apprehensions, a study highlighted that among hospitalized adults with bloodstream infections, the mortality rate associated with *K. variicola* exceeded that linked to *K. pneumoniae*.[13] This underscores the increasing significance of *K. variicola* as a clinically relevant pathogen, prompting a closer examination of its implications in healthcare settings.

In this investigation, the *K. variicola* strain 353, which carries the $bla_{\text{NDM-1}}$ gene, was isolated from a urinary tract infection in a male patient hospitalized in the department of rehabilitation of a teaching hospital in China. The isolate was preliminarily identified using the VITEK MS system (bioMérieux, France) and was further confirmed by whole-genome sequencing. Bioinformatics analysis was undertaken to delve into the genetic characteristics of both the strain and the plasmid carrying the $bla_{\text{NDM-1}}$ gene. The global transmission dynamics and genomic epidemiology of bla_{NDM}-carrying *K. variicola* were further investigated.

Materials and Methods

Antimicrobial Susceptibility Test

Antimicrobial susceptibility testing was performed using the VITEK 2 system (bioMérieux, France) with Gram-negative antimicrobial susceptibility testing cards (AST-GN13) and the Etest method. The testing procedures adhered to the guidelines established by the Clinical and Laboratory Standards Institute (CLSI) M100, 33rd edition. Breakpoints were interpreted in accordance with the recommendations outlined in the CLSI guidelines. In cases where CLSI breakpoints were unavailable for colistin and tigecycline, interpretations for colistin minimum inhibitory concentration (MIC) followed the guidelines of the European Committee on Antimicrobial Susceptibility Testing (EUCAST), while standards set by the US Food and Drug Administration (FDA) were utilized for tigecycline.

Whole-Genome Sequencing

Whole-genome sequence of the strain was determined utilizing the Illumina NovaSeq 6000 platform (Illumina Inc., San Diego, CA, USA) in the 150-bp paired-end sequencing mode, with an average sequencing depth of ≥100×. Additionally, long-read sequencing was performed using a Nanopore MinION sequencer (Nanopore, Oxford, UK). Both short Illumina reads and long MinION reads underwent hybrid assembly using Unicycler (v0.4.7) in the conservative mode. This process resulted in complete circular contigs, which underwent further refinement and correction using Pilon with Illumina reads through multiple rounds of iteration until no further changes were detected. The resultant complete genome sequence was subsequently automatically annotated using the NCBI Prokaryotic Genome Annotation Pipeline (PGAP) server.

Genomic Features and Plasmid Characterization

The investigation into the antimicrobial resistance genes and plasmid replicons of the strain was carried out using the BacWGSTdb server.[14,15] MLST (Multi Locus Sequence Typing) analysis was conducted utilizing the database available at http://mlstkv.insp.mx/.[16] Circular comparisons, represented by concentric rings, were performed to examine the $bla_{\text{NDM-1}}$-carrying plasmid and its similarity to analogous plasmids. This comparative analysis was visualized using the BLAST Ring Image Generator (BRIG).[17]

Phylogenetic Analysis

The phylogenetic relationship between *K. variicola* 353 and other *K. variicola* strains obtained from the NCBI GenBank database was assessed using the BacWGSTdb server.[14,15] This server employs single nucleotide polymorphism (SNP) approaches to analyze the phylogenetic relationship of the uploaded genome sequence with sequences available in the database. The resulting phylogenetic tree was enhanced for visual clarity using iTOL.[18]

Nucleotide Sequence Accession Numbers

The complete genome sequence of *K.variicola* 353 has been submitted to the NCBI GenBank database and is assigned the accession number CP141632-CP141634.

Ethical Approval

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Zhejiang Provincial People's Hospital (Ethics approval number 2019KY244).

Results and Discussion

K. variicola strain 353 was isolated from a urine sample obtained from a male patient who was admitted to a tertiary hospital in China following a cerebral hemorrhage. The genome of the *K. variicola* strain 353 is composed of three contigs, totaling 6,213,895 bp. Notably, one of these contigs, designated as contig 1 and spanning 5,727,068 bp, is associated with the chromosome, while the remaining two contigs correspond to plasmids (contig pCRKP353-NDM1: 294,608 bp and contig 3: 192,219 bp). The genome harbors two distinct plasmid replicons: one on plasmid pCRKP353-NDM1 (IncU) and another on contig 3 (IncFIB(K)). Analysis conducted through the PGAP server yielded predictions for 6001 protein-coding sequences, 88 tRNA genes, and 25 rRNA operons.

The antibiotic susceptibility profiles, as depicted in Table S1, reveal that *K. variicola* 353 exhibited resistance to a broad spectrum of antibiotics, including ceftazidime, ceftriaxone, cefotetan, cefazolin, cefepime, ciprofloxacin, levofloxacin, ertapenem, imipenem, meropenem, ampicillin/sulbactam, and sulfamethoxazole/trimethoprim. However, it demonstrated susceptibility to amikacin, gentamicin, aztreonam, tigecycline, and colistin. Table 1 outlines the resistance genes identified in the genome of the isolate. Notably, β-lactam resistance genes $bla_{\text{LEN-16}}$ and $bla_{\text{NDM-1}}$ were identified, along with aminoglycoside resistance genes *aph(3')-Ia, aadA16, aadA2* and *aac (6')-Ib-cr*, fosfomycin resistance gene *fosA*, quinolone resistance genes *oqxB, oqxA*, and *qnrS1*, trimethoprim resistance gene *dfrA27*, rifamycin resistance gene *arr-3*, and sulfonamide resistance gene *sul1*. Except for *oqxA, oqxB,* $bla_{\text{LEN-16}}$, and *fosA*, which are located on the chromosome, all other resistance genes, including $bla_{\text{NDM-1}}$, are situated on plasmid pCRKP353-NDM1.

The plasmid pCRKP353-NDM1, carrying the bla_{NDM} gene, was identified as an IncU-type plasmid. Two copies of IS*26* are situated upstream of $bla_{\text{NDM-1}}$, while two IS*CR1* (insertion sequence common region 1) elements flank $bla_{\text{NDM-1}}$. Downstream of $bla_{\text{NDM-1}}$, an *Intl1* (Class 1 Integron) is present, housing numerous

Table 1 Antimicrobial Resistance Genes in Klebsiella Variicola 353

Antimicrobial Resistance Gene	Contig	Identity (%)	Position	Antimicrobial Resistance Category
oqxB	Contig1	97.56	1,267,999.1271151	Quinolone
oqxA	Contig1	96	1,271,175.1272350	Quinolone
$bla_{\text{LEN-16}}$	Contig1	99.88	2,841,905.2842765	Beta-lactam
fosA	Contig1	94.05	5,008,144.5008563	Fosfomycin
qnrS1	pCRKP353-NDM1	100.00	2947.3603	Quinolone
dfrA27	pCRKP353-NDM1	100.00	289,664.290137	Trimethoprim
arr-3	pCRKP353-NDM1	90.79	290,270.290762	Rifamycin
$bla_{\text{NDM-1}}$	pCRKP353-NDM1	100.00	282,492.283304	Beta-lactam
sul1	pCRKP353-NDM1	100.00	258,029.258895	Sulfonamide
sul1	pCRKP353-NDM1	100.00	287,341.288207	Sulfonamide
aph(3')-Ia	pCRKP353-NDM1	100.00	265,918.266733	Aminoglycoside
aadA16	pCRKP353-NDM1	100.00	288,638.289483	Aminoglycoside
aac(6')-Ib-cr	pCRKP353-NDM1	100.00	290,819.291418	Aminoglycoside
aadA2	pCRKP353-NDM1	99.27	256,739.257551	Aminoglycoside

antibiotic resistance genes such as *sul1, aadA16, dfrA27, arr-3* and *aac(6')-Ib-cr*. IS*26* typically plays a pivotal role in disseminating antibiotic resistance genes within Gram-negative bacteria, contributing to their widespread distribution.[19–21] Additionally, IS*CR1* is closely associated with various antibiotic resistance determinants, underscoring its significance in this context.[22] This implies that both IS*26* and IS*CR1* are crucial players in the propagation of bla_{NDM}. The presence of *Intl1* (Class 1 Integron) downstream of bla_{NDM-1} enables the plasmid to harbor multiple drug-resistant genes, transforming it into a multi-drug-resistant plasmid. This emphasizes the role of *Intl1* in facilitating the accumulation of diverse drug resistance determinants within the plasmid.

Comparative analysis of pCRKP353-NDM1 with similar plasmids obtained from the NCBI database was performed using the Basic Local Alignment Search Tool (Figure 1). These plasmids, all falling under the IncU type, include three that harbor the bla_{NDM} gene (Table S2). IncU plasmids are distinguished for their extensive

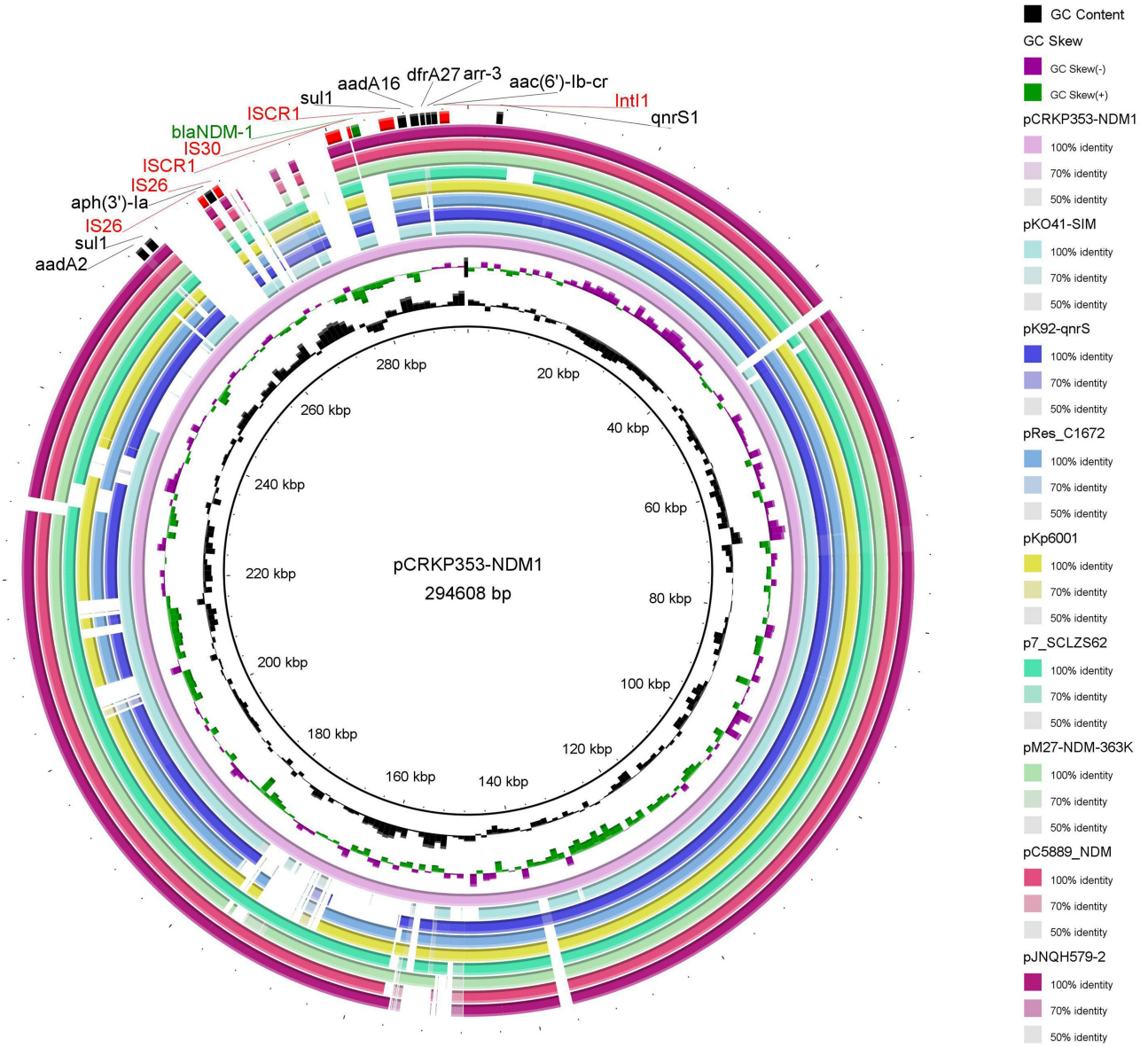

Figure 1 Circular comparative analysis plasmid pCRKP353-NDM1 with similar plasmids retrieved from the NCBI database, including pKO41-SIM (*Klebsiella michiganensis* strain KM41, accession no. CP090080), pK92-qnrS (*Klebsiella michiganensis* strain K92, accession no. OL828743), pRes_C1672 (*Klebsiella pneumoniae* strain C1672, accession no. CP073918), pKp6001 (*Klebsiella pneumoniae* strain Kp6, accession no. CP082291), p7_SCLZS62 (*Raoultella planticola* strain SCLZS62, accession no. CP082175), pM27-NDM-363K (*Raoultella ornithinolytica* strain RoM27LC23, accession no. CP130154), pC5889_NDM (*Enterobacter cloacae* strain C5889, accession no. MZ532978), and pJNQH579-2 (*Klebsiella variicola* strain JNQH579, accession no. CP078148).

host ranges, enabling the efficient transmission of antibiotic resistance genes owing to their robust binding and mobility features.[23] Notably, characterized by their high binding and mobility attributes, IncU plasmids demonstrate resilience and adept replication capabilities across diverse bacterial species. Consequently, they serve as crucial vectors in the dissemination of antibiotic resistance genes. It is noteworthy that IncU plasmids carrying $bla_{\text{NDM-1}}$ genes have begun to proliferate across diverse genera, encompassing *Raoultella ornithinolytica, Enterobacter cloacae*, and *K. variicola*.

In order to gain a more profound understanding of global transmission dynamics and genomic epidemiology of bla_{NDM}-carrying *K. variicola*, an extensive search was conducted within the NCBI pathogen database for strains harboring the bla_{NDM} gene until December 1, 2023. A total of 72 bla_{NDM}-carrying *K. variicola* strains were identified from the NCBI database (Table 2). These strains were discovered in 12 countries worldwide, with the highest prevalence observed in the USA (32 strains), followed by China (18 strains), Bangladesh (4 strains), and three strains each from the United Kingdom, Switzerland, and South Korea. Additionally, two strains each were found in Australia and Brazil, as well as one strain each from Lebanon, Germany and Canada. This global distribution highlights the widespread dissemination of bla_{NDM}-carrying *K. variicola*. Among these strains, five sub-types of bla_{NDM} were identified: 38 strains carried $bla_{\text{NDM-1}}$, 13 strains carried $bla_{\text{NDM-5}}$, 11 strains carried $bla_{\text{NDM-4}}$, 3 strains carried $bla_{\text{NDM-9}}$, and 1 strain carried $bla_{\text{NDM-18}}$. According to the MLST (Multi Locus Sequence Typing) results available at http://mlstkv.insp.mx/,[16] KV353 is assigned to a newly identified, unnamed sequence type (ST) distinguished by *leuS*60, *pgi*39, *pgk*1, *phoE*29, *pyrG*1, *rpoB*1 and *fusA*4. Among the 72 bla_{NDM}-carrying *K. variicola* strains, excluding 20 strains with unclassified sequence types, a total of 28 distinct ST types were identified (Figure 2). ST115 was the most prevalent, comprising 12 strains, followed by ST60 (4 strains), ST10 (3 strains), ST20 (3 strains), ST64 (3 strains), and ST277 (3 strains). Phylogenetic analysis revealed that *K. variicola* 353 belongs to a distinct clone. Furthermore, eleven strains originating from the United States were identified to be part of a single clone, exhibiting single nucleotide polymorphism (SNP) differences of ≤20. This observation suggests that clonal transmission, possibly associated with nosocomial infection, could be contributing to the epidemic of bla_{NDM}-carrying *K. variicola*.

Relevant analyses were conducted on the bla_{NDM}-carrying plasmid. Subsequent investigation into these bla_{NDM}-carrying strains, among which 34 had complete genome sequences, revealed that all bla_{NDM}-carrying plasmids were located on plasmids. Specifically, 13 were classified as IncX3 type, 10 as IncA/C2 type, 5 as IncFII type, 3 strains as IncHI1B type, with one each belonging to IncFIA, IncFIB, and IncN types. The occurrence of IncU type bla_{NDM}-carrying plasmid in *K. variicola* is uncommon.

Remarkably, seven strains from distinct regions were identified to carry multiple carbapenemases, with three strains co-harboring bla_{NDM} and bla_{IMP}, and four strains co-harboring bla_{NDM} and bla_{KPC}. Over the past decade, there has been a substantial increase in the proportion of *K. pneumoniae* strains carrying multiple-carbapenemase genes, presenting an elevated threat to public health.[24] The current study suggests that *K. variicola* strains carrying multiple-carbapenemase genes are also undergoing global dissemination. The existence and prevalence of *K. variicola* with multiple carbapenemases pose formidable challenges for clinical treatment.

Among the 72 strains of *K. variicola* obtained from NCBI, there was a notably higher prevalence in urine (18/72), blood (10/72), and sputum (6/72) samples. Additionally, *K. variicola* strains were detected in environmental sewage and fields. It is noteworthy, that one strain carrying the $bla_{\text{NDM-1}}$ gene was detected in hospital wastewater in China, and three strains carrying the $bla_{\text{NDM-9}}$ gene from South Korea were found in river water, while the remaining strains were of clinical origin. This implies that bacteria carrying the bla_{NDM} gene have transferred between clinical settings and the natural environment.

In summary, our findings reveal the global dissemination of *K. variicola* carrying the bla_{NDM} gene in both healthcare settings and natural environments. These data have unveiled a diverse array of antimicrobial resistance determinants in *K. variicola*, offering valuable insights that may contribute to the development of strategies for the prevention, diagnosis, and treatment of *K. variicola* infections.

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Table 2 Clinical Metadata for 72 Klebsiella Variicola Strains Carrying bla_{NDM} Retrieved from the NCBI Database

Assembly	Strain	Country	Collection Date	Isolation Source	Carbapenemase Genes	Replicon of bla_{NDM}-Carrying Plasmids	ST
GCA_001989495.1	GJ1	South Korea	2014	river water	bla_{NDM-9}	IncFII	64
GCA_001989515.1	GJ2	South Korea	Unknown	river water	bla_{NDM-9}	IncFII	64
GCA_001989535.1	GJ3	South Korea	Unknown	river water	bla_{NDM-9}	IncFII	64
GCA_002156765.1	KPN1481	USA	2014	urine	bla_{NDM-1}	IncHI1B	76
GCA_002740885.1	1TM	Romania	2015	fecal screen	bla_{NDM-1}	IncFII	271
GCA_002740845.1	6TM	Romania	2015	fecal screen	bla_{NDM-1}	IncFII	194
GCA_002853275.1	SCKV020148	China	2017	-	bla_{NDM-5}	-	93
GCA_002855465.1	BD.DM.165	Bangladesh	2016	blood	bla_{NDM-1}	-	60
GCA_003384975.1	BD_DM_166	Bangladesh	2016	blood	bla_{NDM-1}	-	60
GCA_003386925.1	BD_DM_97	Bangladesh	2016	blood	bla_{NDM-1}	-	60
GCA_003386995.1	BD_DM_169	Bangladesh	2016	blood	bla_{NDM-1}	-	60
GCA_900607545.1	ERS2735096	Switzerland	2016	-	bla_{NDM-1}	IncFIA	277
GCA_009497715.1	13,450	China	2013	-	bla_{IMP-4}, bla_{NDM-1}	IncX3	10
GCA_011075275.1	20-X3	China	2016	-	bla_{NDM-5}	IncX3	229
GCA_014595775.1	CRE135	USA	2018	surveillance swab	bla_{NDM-5}	-	14
GCA_022049985.1	SRS7259695	China	2017	bile	bla_{NDM-5}	IncX3	100
GCA_021971215.1	2020GO-0202	USA	2021	sputum	bla_{NDM-5}	IncX3	-
GCA_018420335.1	ur19078501	Germany	2019	urine	bla_{NDM-5}	-	78
GCA_021938995.2	2021LY00003	USA	2021	blood	bla_{NDM-7}	-	94
GCA_019222805.1	JNQH579	China	2021	sputum	bla_{NDM-1}	IncHI1B	-
GCA_020119435.1	403,773–16	Switzerland	2016	-	bla_{NDM-1}	-	277
GCA_021897435.1	KPN2043	Australia	2020	urine	bla_{NDM-1}	-	183
GCA_020857895.1	KCJ3K605	USA	2019	-	bla_{NDM-1}	-	-
GCA_020857955.1	KCJ3K606	USA	2019	-	bla_{NDM-1}	-	-
GCA_021837705.1	N1538	Switzerland	2020	-	bla_{NDM-1}	-	-
GCA_021727155.1	DY1825	China	2018	sputum	bla_{NDM-1}	-	32
GCA_021727475.1	DY1750	China	2017	blood	bla_{NDM-1}	-	-
GCA_021727535.1	DY1744	China	2017	blood	bla_{NDM-1}	-	-
GCA_022100855.1	253,839	United Kingdom	2016	-	bla_{NDM-1}	-	-
GCA_022156125.1	243,761	United Kingdom	Unknown	-	bla_{NDM-18}	-	-
GCA_022099875.1	249,330	United Kingdom	2016	-	bla_{NDM-1}	IncX3	61
GCA_022474435.2	2020HL-01140	USA	2020	wound	bla_{KPC-3}, bla_{NDM-1}	-	10
GCA_022818945.1	KV214	Lebanon	2018	urine	bla_{NDM-1}	-	-
GCA_022857045.1	KP100195	China	2019	-	bla_{NDM-1}	IncX3	-
GCA_022860305.1	83,799	China	2018	-	bla_{NDM-1}	-	-
GCA_022861645.1	75,401	China	2018	-	bla_{NDM-5}	IncX3	54

GCA_022861705.1	75,260	China	2018	-	*bla*$_{NDM-1}$	IncX3	20
GCA_031039815.1	2022LY00014	USA	2022	-	*bla*$_{NDM-1}$	-	69
GCA_024418895.2	2022DK-00076	USA	2022	rectal swab	*bla*$_{NDM-1}$	IncX3	101
GCA_024855165.2	2022SY-00046	USA	2022	sputum	*bla*$_{KPC-3}$, *bla*$_{NDM-5}$	-	-
GCA_024855125.2	2022SY-00043	USA	2022	urine	*bla*$_{NDM-7}$	IncX3	-
GCA_026222775.1	605_17	Brazil	2017	Infective secretion	*bla*$_{NDM-1}$	-	-
GCA_026222995.1	463_20	Brazil	2020	surveillance swab	*bla*$_{NDM-1}$	-	78
GCA_026372215.2	2022HL-01877	USA	2022	urine	*bla*$_{NDM-5}$	-	10
GCA_026459905.1	CHS117	China	2022	sputum	*bla*$_{NDM-5}$	-	183
GCA_026611755.2	2022KU-00273	USA	2022	urine	*bla*$_{NDM-7}$	IncX3	-
GCA_026967735.1	2022CK-00564	USA	2022	urine	*bla*$_{NDM-4}$	IncA/C2	115
GCA_026967755.1	2022CK-00565	USA	2022	urine	*bla*$_{NDM-4}$	IncA/C2	115
GCA_025579445.2	2022CK-00500	USA	2022	urine	*bla*$_{NDM-4}$	IncA/C2	115
GCA_025676585.2	2022CK-00501	USA	2022	urine	*bla*$_{NDM-4}$	IncA/C2	115
GCA_025579405.2	2022CK-00502	USA	2022	urine	*bla*$_{NDM-4}$	IncA/C2	115
GCA_025579525.2	2022CK-00503	USA	2022	urine	*bla*$_{NDM-4}$	IncA/C2	115
GCA_025579425.2	2022CK-00504	USA	2022	urine	*bla*$_{NDM-4}$	IncA/C2	115
GCA_025676845.2	2022CK-00505	USA	2022	urine	*bla*$_{NDM-4}$	IncA/C2	115
GCA_026069065.2	2022CK-00567	USA	2022	wound/abscess	*bla*$_{NDM-4}$	IncA/C2	115
GCA_026069095.2	2022CK-00568	USA	2022	blood	*bla*$_{NDM-4}$	IncA/C2	115
GCA_028114685.1	2023EP-00006	USA	2023	urine	*bla*$_{NDM-7}$	-	172
GCA_028871695.1	SHET-01	China	2018	-	*bla*$_{IMP-4}$, *bla*$_{NDM-1}$	IncHI1B	-
GCA_029617685.1	2023LY00015	USA	2023	-	*bla*$_{NDM-5}$	-	-
GCA_031047475.1	2023CB-00243	USA	2023	urine	*bla*$_{NDM-4}$	-	115
GCA_030294325.1	CPO293	Australia	2019	wound	*bla*$_{NDM-1}$	IncN	95
GCA_031013925.1	2023LY00040	USA	2023	-	*bla*$_{NDM-1}$	-	166
GCA_030972385.1	JXR172	China	2015	-	*bla*$_{IMP-4}$, *bla*$_{NDM-1}$	-	115
GCA_031056435.1	2023BV-00125	USA	2023	blood	*bla*$_{NDM-7}$	-	1
GCA_031435165.1	2023SY-00164	USA	2023	urine	*bla*$_{NDM-5}$	IncX3	41
GCA_032149985.1	2023GO-0326	USA	2023	-	*bla*$_{NDM-7}$	-	1
GCA_032744875.1	23-C-YW-22	China	2023	hospital sewage	*bla*$_{NDM-1}$	-	370
GCA_032984365.1	01A19CPO019	Canada	2019	stool/rectal swab	*bla*$_{KPC-3}$, *bla*$_{NDM-1}$	IncFIB	20
GCA_033195215.1	2023LY00062	USA	2023	-	*bla*$_{NDM-1}$	-	20
GCA_033278505.1	PS00263.3	USA	2018	blood	*bla*$_{KPC-5}$, *bla*$_{NDM-1}$	-	277
GCA_034363275.1	CHN10012	China	2018	shunt fluid	*bla*$_{NDM-5}$	IncX3	-
GCA_034394215.1	CHN22083	China	2019	sputum	*bla*$_{NDM-1}$	-	-

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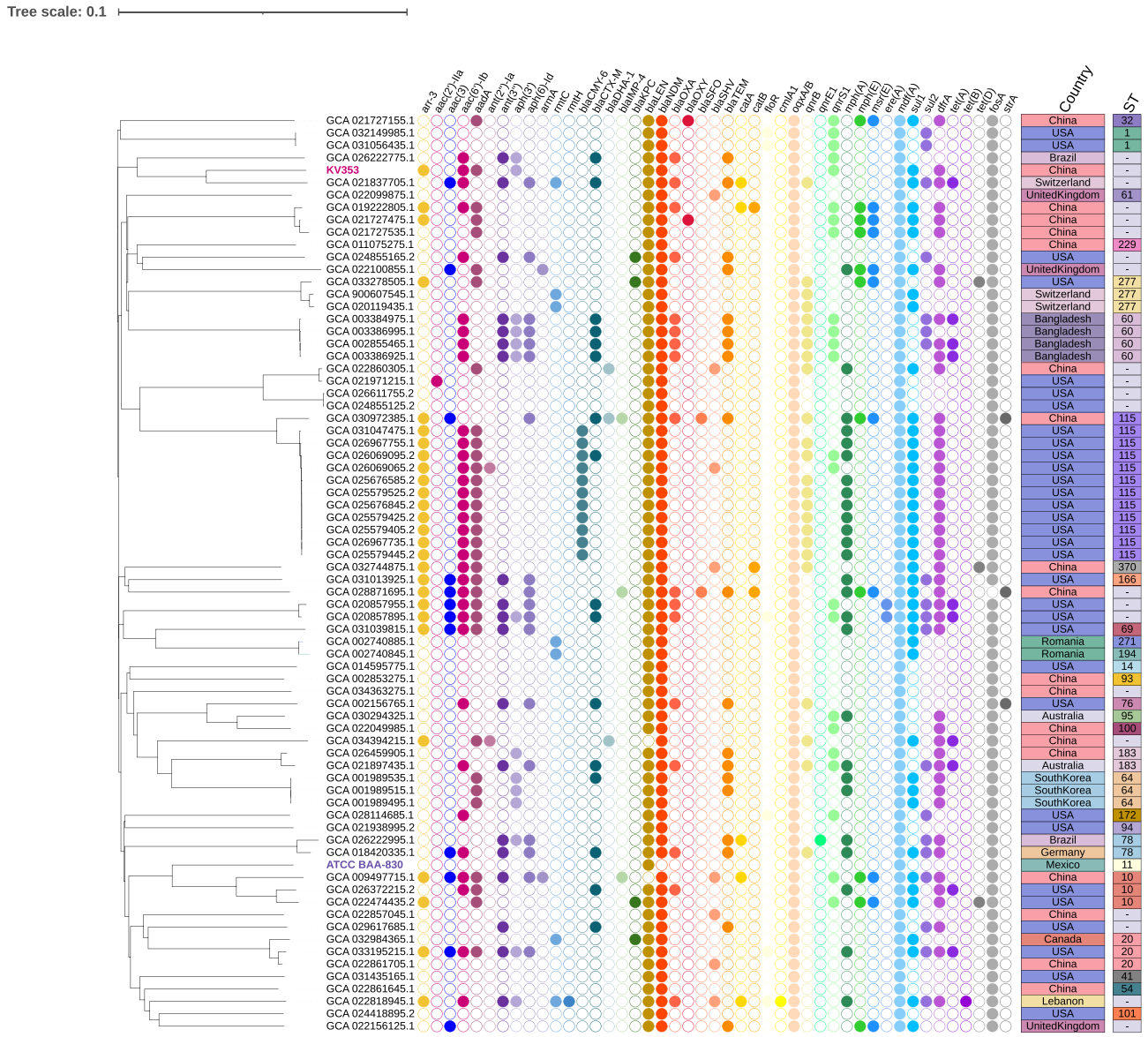

Figure 2 Phylogenetic tree of *K. variicola* 353, *K. variicola* ATCC BAA-830 and other bla_{NDM}-carrying *K. variicola* strains retrieved from the NCBI database. Cells with different colors indicate the presence of different antimicrobial resistance genes, whereas blank cells indicate the absence of the gene. The color of each rectangular indicates a specific country.

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Disclosure

The authors report no conflicts of interest in this work.

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