Letter to the Editor

Isolation of *Leclercia adecarboxylata* Producing Carbapenemases in A Newborn Female*

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Leclercia adecarboxylata is a Gram-negative bacterium belonging to the Enterobacteriaceae family. To our knowledge, this is the first report of a carbapenem-resistant *L. adecarboxylata* strain isolated from a healthy newborn. The *L. adecarboxylata* strain isolated in this study carried four plasmids that may serve as reservoirs for antibiotic resistance genes. Plasmids 2 and 4 did not harbor any antimicrobial resistance genes. Plasmid 3 is a novel plasmid containing three resistance genes. The bla_{IMP} gene harbored in the strain was most similar to bla_{IMP-79} at the nucleotide level, with a similarity of 99.4% (737/741). This case highlights the importance of considering *L. adecarboxylata* as a potential cause of infections in children.

Key words: *Leclercia adecarboxylata*; Carbapenem-resistant; Newborn

Leclercia adecarboxylata is a motile, facultatively anaerobic, Gram-negative bacterium first identified by Leclerc in 1962[1]. *L. adecarboxylata* has been isolated from water, food, and other environmental sources, and is now recognized as a pathogenic organism[2]. Previous studies have reported the presence of this bacterium in immunocompromised patients; however, several recent cases of *L. adecarboxylata* have been reported in immunocompetent patients, particularly children[3-5].

Carbapenems are first-line antibiotics used to treat multidrug-resistant Gram-negative bacterial infections. However, carbapenem-resistant Enterobacteriaceae have become a major public health threat, leading to severe infections, limited treatment options, and mortality rates of 26%–44%. The prevalence of carbapenem resistance in Enterobacteriaceae is mediated by the rapid emergence of carbapenemase genes[6,7]. Although most cases of *L. adecarboxylata* infection are susceptible to common antibiotics, some drug-resistant strains have recently been detected[8-10]. A review of cases of *L. adecarboxylata* infection in humans revealed 82 publications describing clinical cases of *L. adecarboxylata* infection in 148 patients (104 adults and 44 children) since the first report in 1991[11-14]. Among the documented cases of pediatric infection, one case occurred in 1991, two in 2000–2004, six in 2011–2014, four in 2015–2019, and 31 in 2020–2022. *L. adecarboxylata* infection remains relatively rare; however, the number of reported cases in children has recently increased[15]. Here, we present a case of a carbapenem-resistant *L. adecarboxylata* strain in a newborn female to increase awareness of *L. adecarboxylata* as an emerging infection in children.

L. adecarboxylata 17YN198 was isolated in 2017 from the feces of a healthy 5-day-old female newborn with no relevant medical history in Yunnan, China. The strain was preliminarily identified using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) (Bruker Daltonics, Billerica, MA, USA)[16]. Identification was confirmed by 16S rRNA gene sequencing. Antimicrobial susceptibility was determined using the broth microdilution method, according to the Clinical Laboratory Standards Institute (CLSI) guidelines[17]. Twenty-nine common antimicrobial agents were used to evaluate antimicrobial susceptibility. The isolated strain exhibited resistance to ceftriaxone, ceftazidime, cefazolin, amoxicillin-clavulanate, trimethoprim-sulfamethoxazole, ertapenem, and meropenem

doi: 10.3967/bes2023.104

*This study was supported by Chinese Field Epidemiology Training Program; the National Natural Science Foundation of China [81861138053].

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(Table 1) according to the CLSI guidelines, and was susceptible to amikacin, gentamicin, aztreonam, chloramphenicol, norfloxacin, piperacillin-tazobactam, and minocycline.

Whole-genome sequencing was performed using the Illumina NovaSeq PE150 platform (Illumina, https://www.illumina.com) and PacBio single-molecule real-time sequencing[18]. Resistance genes were analyzed using ResFinder 2.1, and mobile elements were determined using bioinformatics tools provided by IS Finder. The entire *L. adecarboxylata* 17YN198 genome sequence was deposited in the GenBank database under the accession number CP106959-CP106963. *L. adecarboxylata* 17YN198 contained a single circular chromosome with a length of 4,725,550 base pairs (bp) and a GC content of 55.69%. The chromosome carried 4,305 protein-coding genes, 86 tRNA genes,

Table 1. The MIC profile of 29 common antimicrobial agents for Leclercia adecarboxylata strain 17YN198

Drug classes	Antibiotics	MIC (μg/mL)
Aminoglycosides	Amikacin	≤ 8
Aminoglycosides	Gentamicin	≤ 2
Aminoglycosides	Tobramycin	8
β-lactam combination agents	Amoxicillin – clavulanate	32/16
β-lactam combination agents	Amoxicillin – sulbactam	> 16/8
β-lactam combination agents	Piperacillin – tazobactam	≤ 4/4
Monobactams	Aztreonam	≤ 2
Cephems	Cefazolin	> 16
Cephems	Cefepime	4
Cephems	Cefoperazone – sulbactam	> 32/8
Cephems	Cefoxitin	> 16
Cephems	Ceftazidime	> 32
Cephems	Ceftriaxone	16
Cephems	Cefuroxime	> 16
Phenicols	Chloramphenicol	≤ 4
Quinolones	Ciprofloxacin	≤ 0.5
Quinolones	Levofloxacin	≤ 1
Quinolones	Moxifloxacin	≤ 0.5
Quinolones	Norfloxacin	≤ 2
Lipopeptides	Colistin	2
Carbapenems	Ertapenem	> 2
Carbapenems	Imipenem	1
Carbapenems	Meropenem	4
Fosfomycins	Fosfomycin/G6P	128
Tetracyclines	Minocycline	2
Tetracyclines	Tetracycline	> 8
Tetracyclines	Tigecycline	≤ 1
Nitrofurans	Macrodantin	32
Folate pathway antagonists	Trimethoprim – sulfamethoxazole	> 4/76

Note. MIC, minimum inhibitory concentration.

and 25 rRNA genes (Figure 1).

Analysis of acquired resistance genes using ResFinder 2.1 showed that *L. adecarboxylata* 17YN198 harbored 33 antimicrobial resistance genes encoding resistance to tetracyclines (*tetA* and *tetR*), carbapenems (bla_{IMP}), aminoglycosides [*aph(3')-Ia*, *aadA6*, *(AGly)aacA4*, *aadA1*], fluoroquinolones (*qnrB5*), and folate pathway antagonists (*sul1*) (Table 2). According to the assembly results, the *L. adecarboxylata* 17YN198 isolate carried four plasmids. These included the 42,504-bp *sul1*-bearing plasmid pIMP-1 (CP106960), 155,030-bp plasmid 2 (CP106961), 115,001-bp bla_{IMP}-harboring plasmid 3 (CP106962), and 52,474-bp plasmid 4 (CP106963). Plasmids 2 and 4 did not harbor any antimicrobial resistance genes. The results showed a susceptibility pattern consistent with the presence of bla_{IMP} and *sul1*, that is, resistance to meropenem, ertapenem, and trimethoprim-sulfamethoxazole. The bla_{IMP} gene harbored in the strain was most similar to bla_{IMP-79} at the nucleotide level, with a similarity of 99.40% (737/741). The carbapenemase IMP encoded by the bla_{IMP} gene had 100% amino acid identity with carbapenemase IMP-1.

The bla_{IMP}-harboring plasmid, designated as plasmid 3, had a length of 42,504 bp and an average GC content of 51.70%. Plasmid 3 belonged to the IncN3-incompatible group and contained three resistance genes [bla_{IMP-1}, *aadA6*, and (*AGly*)*aacA4*] (Figure 2). Plasmid comparison using BLASTn and the NCBI plasmid database (ftp.ncbi.nlm.nih.gov:/refseq/release/plasmid/) revealed that plasmid 3 is a novel plasmid. Although plasmid 3 did not carry ISs elements, it carried a type IV secretion system (*virB1*, *virB3–virB6*, and *virB8–virB11*). This suggests that the transfer of resistance genes may be related to T4SS binding. Since *L. adecarboxylata* 17YN198 was isolated from a newborn female, bla_{IMP-1}-harboring plasmid 3 may represent a newly emerging risk factor for the spread of carbapenemase resistance.

Infections caused by *L. adecarboxylata* have likely been underestimated for several decades because of the difficulty in correctly identifying the bacterium, leading to underreporting in the medical literature[19]. *L. adecarboxylata* was previously considered an opportunistic pathogen. However, this

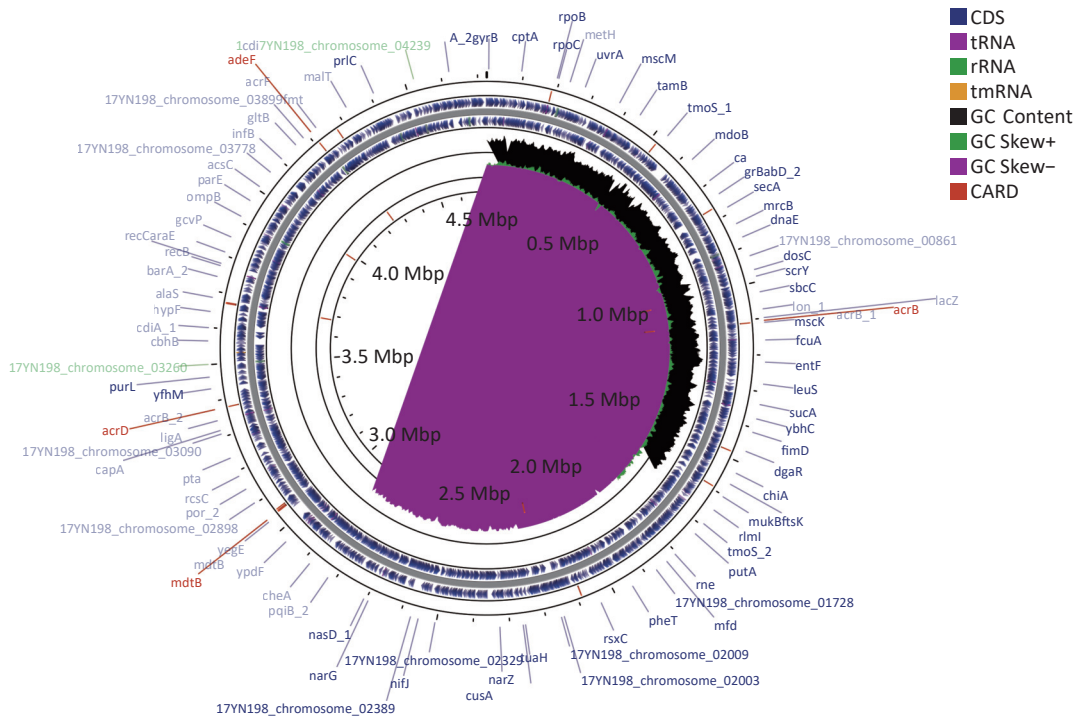

Figure 1. Circular map of the *L. adecarboxylata* 17YN198 genome was designed using CGView. The gene marked in red in the outermost circle is the drug resistance gene obtained from card database comparison. The outer ring denotes the ORFs on the positive strand. The next ring illustrates ORFs on the complementary strand. The black circle presents GC content. The inner rings show G+C content and G+C skew, where peaks represent the positive (outward) and negative (inward) deviation from the mean G+C content and G+C skew, respectively.

may be due to misdiagnosis because this organism shares several biochemical characteristics with *Escherichia coli*. *L. adecarboxylata* is now considered a pathogenic organism due, in part, to the use of modern identification techniques such as API 20E (bioMérieux, Craponne, France) and MALDI-TOF MS, which have been used to accurately identify and isolate *L. adecarboxylata* from *E. coli*.

To the best of our knowledge, this is the first report of carbapenem-resistant *L. adecarboxylata* isolated from a healthy newborn. The *L. adecarboxylata* strain isolated in this study carried four plasmids that may serve as reservoirs for antibiotic resistance genes. This case highlights the importance of considering *L. adecarboxylata* as a potential cause of infections in children. These

Table 2. Thirty-three resistance genes harbored in the *L. adecarboxylata* 17YN198

Chromosome	Start	End	ARGs
17YN198_chromosome_1	1009446	1010621	*(Bla)ampH*
17YN198_chromosome_1	1104447	1107587	*acrB*
17YN198_chromosome_1	1107610	1108803	*Enterobacter_cloacae_acrA*
17YN198_chromosome_1	1177961	1178302	*ramA*
17YN198_chromosome_1	1271921	1273822	*(Bla)Penicillin_Binding_Protein_Ecoli*
17YN198_chromosome_1	1480168	1481403	*mdf(A)*
17YN198_chromosome_1	1591372	1593120	*msbA*
17YN198_chromosome_1	1784331	1785539	*mdtH*
17YN198_chromosome_1	2191719	2192102	*marA*
17YN198_chromosome_1	2680813	2681226	*H-NS*
17YN198_chromosome_1	2968917	2970359	*mdtK*
17YN198_chromosome_1	3042283	3043515	*mdtA*
17YN198_chromosome_1	3043515	3046640	*mdtB*
17YN198_chromosome_1	3051130	3052533	*baeS*
17YN198_chromosome_1	3052530	3053255	*baeR*
17YN198_chromosome_1	3173857	3175500	*yojI*
17YN198_chromosome_1	3375652	3378765	*acrD*
17YN198_chromosome_1	3671973	3672503	*emrR*
17YN198_chromosome_1	3672629	3673804	*Klebsiella_pneumoniae_KpnG*
17YN198_chromosome_1	3673821	3675368	*emrB*
17YN198_chromosome_1	3987117	3987935	*bacA*
17YN198_chromosome_1	4274088	4274720	*CRP*
17YN198_chromosome_1	4587843	4589216	*cpxA*
17YN198_plasmid1_1	70246	71445	*(Tet)tetA*
17YN198_plasmid1_1	71524	72201	*(Tet)tetR*
17YN198_plasmid1_1	80428	81243	*aph(3')-Ia*
17YN198_plasmid1_1	83245	83925	*QnrB5*
17YN198_plasmid1_1	86408	87247	*sul1*
17YN198_plasmid1_1	87752	88543	*aadA1*
17YN198_plasmid1_1	88636	89109	*dfrA1*
17YN198_plasmid3_1	30895	31740	*aadA6*
17YN198_plasmid3_1	31810	32307	*(AGly)aacA4*
17YN198_plasmid3_1	32826	33566	*blaIMP-79*

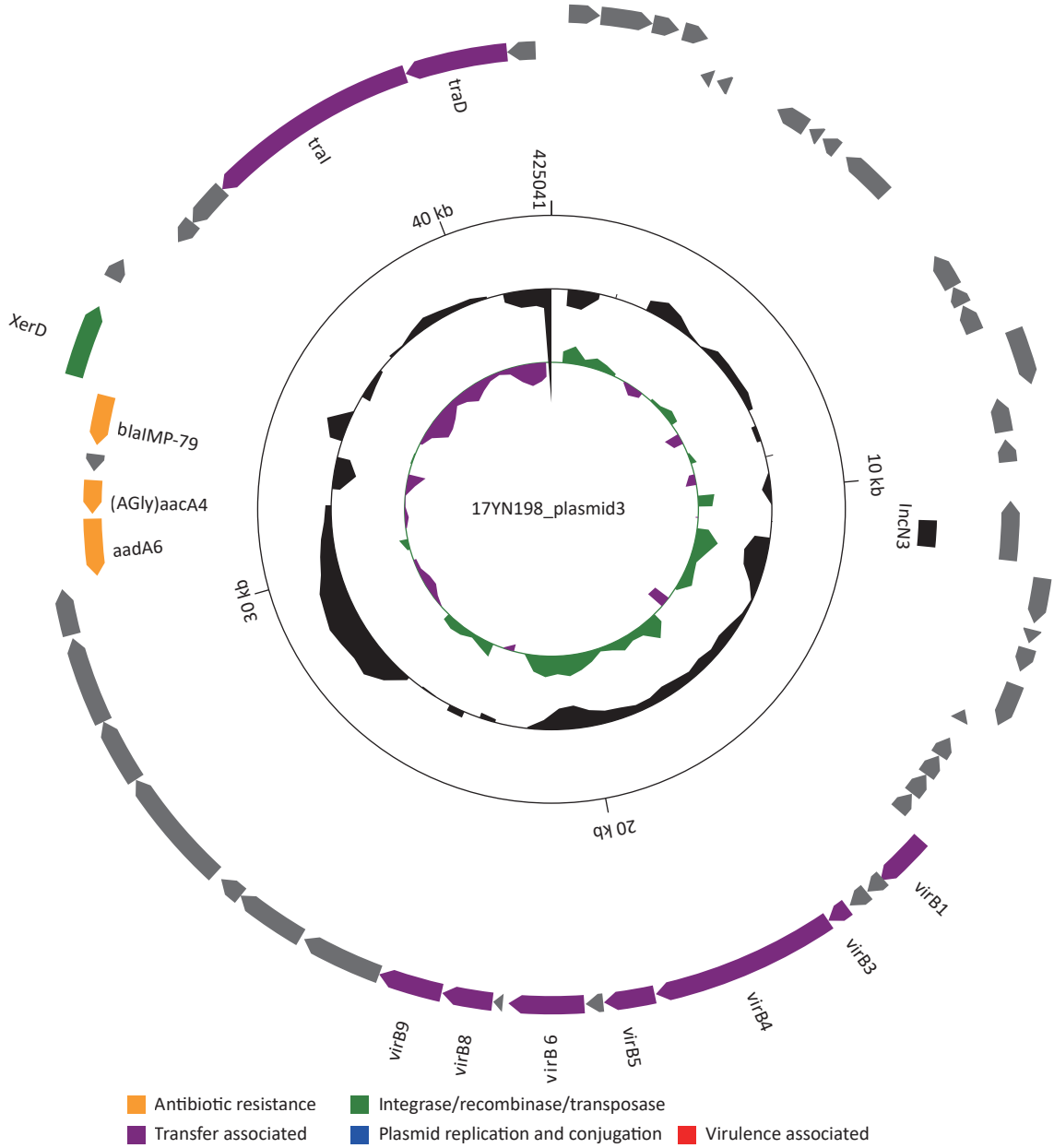

Figure 2. Schematic map of plasmid 3. Genes are denoted by arrows and colored based on gene function classification. The innermost circle presents GC-Skew (G-C/G+C) with a window size of 1,000 and step size of 500. The black circle presents GC content. Backbone and accessory module regions are also shown.

findings suggest that close monitoring of resistant strains in the human gut microbiota should become routine clinical practice to prevent the occurrence of infections.

Data Availability Statement The datasets generated in this study are available in GenBank: SAMN31079621 and CP106959-CP106963.

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Received: January 3, 2023;

Accepted: April 18, 2023

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