Genomic characterisation of *Klebsiella michiganensis* co-producing OXA-181 and NDM-1 carbapenemases isolated from a cancer patient in uMgungundlovu District, KwaZulu-Natal Province, South Africa

To the Editor: The emergence and spread of carbapenem-resistant Enterobacteriaceae (CRE) is a serious public health concern worldwide, especially for hospitalised patients.[1-3] *Klebsiella* spp. are recognised as significant pathogens responsible for serious difficult-to-treat nosocomial infections.[1,4] Several reports have identified *Klebsiella* spp. co-producing New Delhi metallo-beta-lactamase (NDM) and other carbapenemases worldwide.[1,4-7] Although NDM-1-producing *K. michiganensis* was reported in clinical samples from the private sector in KwaZulu-Natal Province, South Africa (SA),[8] this is the first detection of $bla_{\text{NDM-1}}$ and $bla_{\text{OXA-181}}$ in a carriage isolate of *K. michiganensis* A202R3B6 (accession no. QKWV00000000). A 59-year-old cancer patient was screened at admission and discharge in a surgical ward in a district hospital in SA. The patient received cloxacillin 250 mg twice daily for 5 days until discharge. Faecal culture was negative at admission but revealed carriage of carbapenemase-producing *K. michiganensis* ST 29 (A202R3B6) at discharge.

This isolate was initially identified as *K. oxytoca*, but genomic identification confirmed it to be *K. michiganensis*. *K. michiganensis* formed part of a bigger study investigating antibiotic-resistant bacteria in clinical and carriage samples from patients admitted to a district and tertiary hospital in uMgungundlovu District, KwaZulu-Natal, SA. The isolate was identified using biochemical tests (Rosco Diagnostica, Denmark). Antimicrobial susceptibility testing was performed by broth microdilution, and results were interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST). *Escherichia coli* ATCC 25922, *K. pneumoniae* ATCC 700603 and *K. pneumoniae* ATCC 51503 were used as controls.

Whole-genome sequencing (WGS) analysis was performed on a MiSeq platform (Illumina, USA) with 100× coverage. The bacterial analysis pipeline of GoSeqIt tools was used to annotate and identify known acquired antibiotic-resistant genes via ResFinder,[9] virulence factors using VirulenceFinder[10] and mobile genetic elements through PlasmidFinder.[11] The multi-locus sequence type was determined from WGS data.

The final assembly of *K. michiganensis* ST 29 A202R3B6 contained 6 499 557 base pairs with 60.87% G+C content. Analysis of WGS data revealed that the *K. michiganensis* harboured several antibiotic resistance genes and multidrug resistance efflux pumps (Table 1). PlasmidFinder revealed that the genome of *K. michiganenesis* ST 29 (A202R3B6) harboured 12 plasmids, and genomic analysis revealed that the IncX3 plasmid harboured $bla_{\text{NDM-1}}$ (Table 1).

To the best of our knowledge, the detection of these carbapenemases along with several resistance genes in a carriage sample is the first reported from SA and suggests that the intestinal tract serves as reservoir of resistant bacteria. $bla_{\text{OXA-181}}$ and $bla_{\text{NDM-1}}$ are commonly detected in *E. coli* and *K. pneumoniae* worldwide,[4,7] and as such, the concomitant presence of these carbapenemase genes in *K. michiganensis* ST 29 suggests that horizontal gene transfer occurs within and between bacterial species. In addition, this isolate was not detected on screening at admission but only at discharge, suggesting a lack of infection prevention and control (IPC) measures at the hospital. Our findings therefore underline the importance of routine screening for extended-spectrum beta-lactamases and/or carbapenemase bacteria upon admission and the

Table 1. Antibiotic resistance profiles of the carbapenemase-producing *Klebsiella michiganensis* isolate

Isolate ID	Antibiotic resistance genes and MDR efflux pumps	Plasmid types	MIC values (µg/mL)									
			Ampicillin	Cefoxitin	Cefotaxime	Ceftazidime	Imipenem	Meropenem	Gentamicin	Amikacin	Ciprofloxacin	Ofloxacin	Trimethoprim
A105R1B5	*aph*(6)-1d, *AadA*1, *AadA*2, *rmtC*, *strA*, *aph*(3')-1a, *aac*(6') Ib-cr, $bla_{\text{NDM-1}}$, $bla_{\text{OXY-5-1}}$, $bla_{\text{SHV-12}}$, $bla_{\text{OXA-181}}$, *oqxA*, *oqxB*, *QnrS1*, aac(6') Ib-cr, *fosA*, *catA*2, *ARR-3*, *sul1*, *sul2*, *dfrA14*, MATE, MFS, EmrA, EmrB, MacA, MacB	ColRNAI, ColKP3, IncFIB[(K); K17:A-:B36], IncFIB(pB171), IncFII, IncFII(Yp), IncH12 (ST-1), IncHI2A (ST-1), IncN (ST-7), IncU, IncX3, RepA	≥512	≥512	≥512	≥512	≥512	256	≥512	≥512	256	128	≥512

MIC = minimum inhibitory concentration; MDR = multidrug resistance.

need for IPC to be strictly implemented to reduce the dissemination of CRE in SA.

Author contributions. RCF co-conceptualised the study, undertook sample collection and microbiological laboratory and data analyses, prepared tables, interpreted results, contributed to bioinformatics analysis, and drafted the manuscript. LLF undertook sample collection and microbiological laboratory analyses, contributed to bioinformatics analysis and vetted the results. MA undertook bioinformatics analysis. AI performed whole-genome sequencing analysis. SYE co-conceptualised the study and undertook critical revision of the manuscript. All authors read and approved the final manuscript.

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