Genomic characterisation of Klebsiella michiganensis co-producing OXA-181 and NDM-1 carbapenemases isolated from a cancer patient in uMngungundlovu 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.\(^1\)\(^-\)\(^4\) 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.\(^1\)\(^-\)\(^7\) 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 \(\text{bla}_{\text{NDM-1}}\) and \(\text{bla}_{\text{OXA-181}}\) in a carriage isolate of K. michiganensis A202R3B6 (accession no. KQWV00000000). 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 cefoxitin 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 uMngungundlovu 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,\(^9\) and mobile genetic elements through PlasmidFinder.\(^9\) 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. michiganensis ST 29 (A202R3B6) harboured 12 plasmids, and genomic analysis revealed that the IncX3 plasmid harboured \(\text{bla}_{\text{NDM-1}}\) (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. \(\text{bla}_{\text{OXA-181}}\) and \(\text{bla}_{\text{OXA-181}}\) are commonly detected in E. coli and K. pneumoniae worldwide,\(^1\)\(^-\)\(^4\) 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. Antimicrobial resistance profiles of the carbapenemase-producing Klebsiella michiganensis isolate

<table>
<thead>
<tr>
<th>Isolate ID</th>
<th>Antibiotic resistance genotype</th>
<th>Plasmid types</th>
<th>MDR efflux</th>
<th>MIC values (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A105R1B5</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td><strong>Trimetoprim</strong></td>
<td>2512</td>
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<td></td>
<td><strong>Ofloxacin</strong></td>
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<td></td>
<td><strong>Ciprofloxacin</strong></td>
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<td></td>
<td><strong>Amikacin</strong></td>
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<tr>
<td></td>
<td><strong>Gentamicin</strong></td>
<td>2512</td>
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<tr>
<td></td>
<td><strong>Meropenem</strong></td>
<td>2512</td>
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<td>2.56</td>
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<tr>
<td></td>
<td><strong>Imipenem</strong></td>
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<td></td>
<td><strong>Cefotaxime</strong></td>
<td>2512</td>
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<tr>
<td></td>
<td><strong>Cefoxitin</strong></td>
<td>2512</td>
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<td>2.56</td>
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<tr>
<td></td>
<td><strong>Ampicillin</strong></td>
<td>2512</td>
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<td>2.56</td>
</tr>
</tbody>
</table>

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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