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Genomic analysis of a multidrug-resistant clinical *Providencia rettgeri* (PR002) strain with the novel integron *In*1483 and an A/C plasmid replicon

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Whole-genome sequence analysis was performed on a multidrug-resistant *Providencia rettgeri* PR002 clinical strain isolated from the urine of a hospitalized patient in Pretoria, South Africa, in 2013. The resistome, mobilome, pathogenicity island(s), as well as virulence and heavy-metal resistance genes of the isolate, were characterized using whole-genome sequencing and bioinformatic analysis. PR002 had a genome assembly size of 4,832,624 bp with a GC content of 40.7%, an A/C_2 plasmid replicase gene, four integrons/gene cassettes, 17 resistance genes, and several virulence and heavy metal resistance genes, confirming PR002 as a human pathogen. A novel integron, *In*1483, harboring the gene bla_{OXA-2}, was identified, with other uncharacterized class 1 integrons harboring *aacA4cr* and *dfrA1*. *Aac(3′)-IIa* and bla_{SCO-1}, as well as bla_{PER-7}, *sul2*, and *tet*(B), were found bracketed by composite Tn*3* transposons, and IS*91*, IS*91*, and IS*4* family insertion sequences, respectively. PR002 was resistant to all antibiotics tested except amikacin, carbapenems, cefotaxime-clavulanate, ceftazidime-clavulanate, cefoxitin, and fosfomycin. PR002 was closely related to PR1 (USA), PRET_2032 (SPAIN), DSM_1131, and NCTC7477 clinical *P. rettgeri* strains, but not close enough to suggest it was imported into South Africa from other countries. Multidrug resistance in *P. rettgeri* is rare, particularly in clinical settings, making this case an important incident requiring urgent attention. This is also the first report of an A/C plasmid in *P. rettgeri*. The array, multiplicity, and diversity of resistance and virulence genes in this strain are concerning, necessitating stringent infection control, antibiotic stewardship, and periodic resistance surveillance/monitoring policies to preempt further horizontal and vertical spread of these resistance genes.

Keywords: *Providencia rettgeri*; IncA/C2 plasmid; resistome; mobilome; virulence; South Africa

Introduction

Providencia rettgeri is a Gram-negative opportunistic human pathogenic bacterium that belongs to Proteae bacteria, which comprises the Morganella and Proteus genera. It is found in hospital settings and is mainly associated with urinary tract infections (UTI).[1] *P. rettgeri* has also been reported to cause other infections, such as bacteremia, eye infections, meningitis, endocarditis, pneumonia, UTI, and diarrhea.[2,3] *P. rettgeri* is intrinsically resistant to colistin and tigecycline,[4] which can be transferred horizontally to *Escherichia coli,* and generally resistant to gentamycin, tobramycin, aminopenicillins, and first-generation cephalosporins.[3] It is known to harbor various virulence and resistance genes, which could easily be mobilized owing to their locations on mobile genetic elements (MGEs). These MGEs, specifically plasmids, integrons, insertion sequences (ISs), and transposons, contribute significantly to its pathogenicity and resistance.[3,5]

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Supporting information

Additional supporting information may be found in the online version of this article.

Figure S1. Prophages of *P. rettgeri* PR002 were identified using the PHAge Search Tool (PHAST). PR002 contained four intact prophages (red color), one incomplete prophage (gray color), and one questionable prophage (green color).

Table S1. Metadata (biosample data) of all sequenced *P. rettgeri* isolates from NCBI GenBank database

Table S2. Genes associated with general COG functional categories in the genome of *P. rettgeri* PR002.

Table S3. Pathogenicity islands (PAIs) predicted for PR002 from VFDB (http://www.paidb.re.kr/about_paidb.php).

Table S5. Diversity of metal resistance gene determinants found in PR002 genome.

File S1. Metadata of isolates used in phylogenomics.

Competing interests

The authors declare no competing interests.

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