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Genome Note

Draft genome sequence of a multidrug-resistant KPC-2 and SRT-2 co-producing *Serratia marcescens* strain isolated from a hospitalised patient in Chile

Mario Quezada-Aguiluz[a,b,c], Nilton Lincopan[d,e], Louise Cerdeira[d], Bruna Fuga[d,e], Francisco Silva[f], Boris Barrera[f], Marcela Cifuentes[g], Helia Bello-Toledo[a,c], Andrés Opazo-Capurro[a,c,*], Gerardo González-Rocha[a,c]

[a] *Laboratorio de Investigación en Agentes Antibacterianos (LIAA-UdeC), Facultad de Ciencias Biológicas, Universidad de Concepción, Concepción, Chile*
[b] *Departamento de Medicina Interna, Facultad de Medicina, Universidad de Concepción, Concepción, Chile*
[c] *Millennium Nucleus for Collaborative Research on Bacterial Resistance (MICROB-R), Chile*
[d] *Department of Clinical Analysis, School of Pharmacy, University of São Paulo, São Paulo, Brazil*
[e] *Department of Microbiology, Institute of Biomedical Sciences, University of São Paulo, São Paulo, Brazil*
[f] *Servicio de Laboratorio Clínico, Hospital Clínico Universidad de Chile, Santiago, Chile*
[g] *Comité de Prevención y Control de Infecciones Asociadas a la Atención de Salud y Epidemiología Hospitalaria, Hospital Clínico Universidad de Chile, Santiago, Chile*

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ABSTRACT

Objectives: Serratia marcescens is a neglected opportunistic pathogen of public-health concern, especially due to its antimicrobial resistance features. Here we report the draft genome sequence of the first KPC-2 and SRT-2 co-producing *S. marcescens* strain (UCO-366) recovered from a catheter tip culture of a hospitalised patient in Santiago, Chile, in 2014.

Methods: Whole genomic DNA of strain UCO-366 was extracted and was sequenced using an Illumina NextSeq platform. De novo genome assembly was performed using Unicycler v.0.4.0 and the genome was annotated by the NCBI Prokaryotic Genome Annotation Pipeline (PGAP) v.4.8. Genomic features were analysed using bioinformatic tools available at the Center for Genomic Epidemiology, the Comprehensive Antibiotic Resistance Database (CARD) and Pathosystems Resource Integration Center (PATRIC).

Results: The genome size of strain UCO-366 was 5 267 357 bp, with a G+C content of 59.7% and comprising 5299 coding sequences (CDS), 42 tRNAs and 115 pseudogenes. The genome of UCO-366 also included an IncL/M plasmid. The resistome comprised various antimicrobial resistance genes (ARGs) conferring resistance to carbapenems, cephalosporins, aminoglycosides, sulfonamides, chloramphenicol, rifampicin and fluoroquinolones. Importantly, *S. marcescens* UCO-366 harboured bla_{KPC-2} and bla_{SRT-2}, representing the first description of these β-lactamase genes in this species in Chile.

Conclusion: Here we report the genome of the first KPC-positive multidrug-resistant *S. marcescens* strain identified in Chile, which co-harboured several ARGs. The genome sequence of *S. marcescens* UCO-366 provides an insight into the antimicrobial resistance characteristics of this species in this country and offers important data for further genomic studies on this critical priority pathogen.

Serratia marcescens is a Gram-negative bacillus belonging to the Enterobacteriaceae family. This species is classified as an opportunistic bacterial pathogen, which causes nosocomial infections in immunocompromised or critically ill patients, mostly in neonatal intensive care units [1]. The most effective drugs to treat infections caused by multidrug-resistant (MDR) Gram-negative bacteria are carbapenems; however, there has been an increase in resistance rates to these antibiotics in the last years within this group [1]. Accordingly, the World Health Organization (WHO) has classified carbapenem-resistant and extended-spectrum β-lactamase-producing Enterobacteriaceae as critical pathogens for which new research is urgently needed [2].

* Corresponding author. Present address: Laboratorio de Investigación en Agentes Antibacterianos (LIAA-UdeC), Departamento de Microbiología, Facultad de Ciencias Biológicas, Universidad de Concepción, Concepción, Chile.
E-mail address: andopazo@udec.cl (A. Opazo-Capurro).

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Among the Enterobacteriaceae family, *Klebsiella pneumoniae* and *Escherichia coli* are the predominant species involved in hospital-acquired infections. Nevertheless, reports of carbapenem-resistant isolates in neglected members of the Enterobacteriaceae, such as *Proteus mirabilis* and *S. marcescens*, have been increasing recently [3]. *Serratia marcescens* strains involved in outbreaks are normally MDR owing to the remarkable ability of this species to acquire antimicrobial resistance genes (ARGs) via horizontal gene transfer [1,4]. This is particularly worrying since *S. marcescens* is intrinsically resistant to polymyxins (i.e. colistin), which are the last-resort antibiotics to treat serious infections caused by carbapenem-resistant micro-organisms [3]. In Chile, the main Enterobacteriaceae species involved in hospital-acquired infections are *E. coli* and *K. pneumoniae*; however, *S. marcescens* was the fourth major aetiological agent of ventilator-associated pneumonia in neonates in 2017 [5].

Although *S. marcescens* has emerged as an important nosocomial pathogen globally, whole-genome sequencing (WGS) data are scarce [1]. Therefore, genomic analyses are necessary to understand the evolution of this pathogen and to study its epidemiology in order to implement rapid infection control protocols. Accordingly, this study describes the draft genome sequence of *S. marcescens* strain UCO-366 isolated from an inpatient in Chile in 2014, which was reported as resistant to carbapenems and cephalosporins.

Serratia marcescens UCO-366 was originally identified by matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF/MS). Antimicrobial susceptibility testing was performed by the disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) 2018 guidelines (M100-S28). Strain UCO-366 was then subjected to WGS using an Illumina NextSeq platform (150-bp paired-end reads) with libraries prepared using a Nextera DNA Flex Kit (Illumina Inc., San Diego, CA, USA). De novo genome assembly was performed using Unicycler v.0.4.0 and the genome was subsequently annotated using the NCBI Prokaryotic Genome Annotation Pipeline (PGAP) v.4.8. Species identification was corroborated using SpeciesFinder v.2.0 (https://cge.cbs.dtu.dk/services/SpeciesFinder/). Subsequently, the genetic features of *S. marcescens* UCO-366 were analysed using a set of bioinformatic tools. Specifically, the resistome and virulence factors were characterised by ResFinder v.3.2 (https://cge.cbs.dtu.dk/services/ResFinder/), the Comprehensive Antibiotic Resistance Database (CARD) (https://card.mcmaster.ca/) and the Pathosystems Resource Integration Center (PATRIC) server (https://www.patricbrc.org).

Moreover, the plasmid content was analysed using the PlasmidFinder v.2.1 (https://cge.cbs.dtu.dk/services/PlasmidFinder/), whilst clustered regularly interspaced short palindromic repeat (CRISPR) sequences were predicted by CRISPRFinder (https://crisprcas.i2bc.paris-saclay.fr/).

The draft genome of *S. marcescens* UCO-366 is 5 267 357 bp with a G+C content of 59.7%. The assembled genome comprises 173 contigs, with a N_{50} value of 112 359 bp. Moreover, the genome of strain UCO-366 contains 5299 coding sequences (CDS), 115 pseudogenes, 42 tRNAs, 3 rRNAs and 7 non-coding RNAs. Species identification was confirmed from WGS analysis. Moreover, several ARGs were identified, including $bla_{\text{SRT-2}}$,$bla_{\text{OXA-1}}$, $bla_{\text{TEM-1}}$, $bla_{\text{KPC-2}}$, *sul1*, *catB3*, *aac(6′)-Ib*-cr, *aac(6′)-Ic*, *arr-3*, *adeF* and *qnrB20*, conferring resistance to carbapenems, cephalosporins, aminoglycosides, sulfonamides, chloramphenicol, rifampicin and fluoroquinolones. These genes are concordant with the observed MDR phenotype, including resistance to imipenem and meropenem. In addition, the PlasmidFinder tool detected a plasmid belonging to the IncL/M incompatibility group, and 58 virulence determinants were identified by PATRIC. The genome of strain UCO-366 had no CRISPR sequences.

Considering the relevance of carbapenem- and cephalosporin-resistant Enterobacteriaceae according to the WHO [2], the current report corresponds to the first identification of a carbapenemase (KPC-2) and AmpC (SRT-2) co-producing *S. marcescens* isolate in Chile. These findings confirm the importance of surveillance of resistance against 'last-line' antibiotics in bacterial species that are normally neglected in the human clinical setting. Although *S. marcescens* infections in Chile are less prevalent than infections caused by other Enterobacteriaceae such as *K. pneumoniae* and *E. coli*, it is important to emphasise its potential role as a reservoir of ARGs. In the case of *S. marcescens* UCO-366, the strain co-harboured the carbapenemase- and AmpC-encoding genes $bla_{\text{KPC-2}}$ and $bla_{\text{SRT-2}}$ mediating resistance to carbapenems (imipenem and meropenem) and cephalosporins (i.e. cefotaxime), respectively, which are important options to treat serious infections caused by Gram-negative bacteria [2].

In conclusion, these findings represent the first genomic characterisation of a carbapenem- and cephalosporin-resistant *S. marcescens* isolate in Chile and provide a baseline for future genomic studies on the epidemiology of this bacterial pathogen.

This Whole Genome Shotgun project has been deposited at DDBJ/ENA/GenBank under accession no. **VHJH00000000.1**. The version described in this paper is version **VHJH00000000.1**.

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Competing interest

None declared.

Ethical approval

Not required.

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