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Genome Note

# Panton-Valentine leukocidin-positive sequence type 88 methicillin-resistant *Staphylococcus aureus* emerging as nosocomial pathogen in Brazil

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ABSTRACT

*Objectives:* This study describes the genomic and phenotypic characteristics of a Panton-Valentine Leukocidin (PVL)-positive methicillin-resistant *Staphylococcus aureus* (MRSA)-ST88, causing ventilator-associated pneumonia (VAP) in Brazil.

*Methods:* The MRSA-ST88 isolate (SQ684) was recovered from a tracheal aspirate of a patient with VAP. Identification and antimicrobial susceptibility testing were performed using the BD Phoenix automated system, with vancomycin susceptibility and MICs for daptomycin and tigecycline confirmed by broth microdilution. Whole-genome sequencing (WGS) was conducted on the Illumina NextSeq 550 platform, followed by genomic analyses including MLST, SCC*mec* typing, resistome and virulome profiling, and core-genome SNP phylogeny incorporating international MRSA isolates.

*Results:* WGS classified SQ684 as ST88 carrying SCC*mec* IVc (2B). Phenotypically, the isolate was resistant to oxacillin and azithromycin, and harboured multiple resistance genes, including *mecA*, *blaZ*, aminoglycoside and macrolide resistance determinants, as well as genes linked to efflux pumps, plasmid replication, and virulence factors such as PVL. Core-genome phylogeny revealed substantial divergence from 169 international MRSA-ST88 isolates (243–293 SNPs), consistent with long-term, geographically independent evolution within the ST88 lineage.

*Conclusion:* With only one previous clinical report of MRSA-ST88 in Brazil, the identification of an SCC*mec* IVc- and PVL-positive ST88 strain underscores the potential for CA-MRSA clones to infiltrate hospital settings. Continued genomic surveillance is critical to clarify its epidemiological dynamics and assess public health implications in Brazil.



## 1. Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a successful pathogen, responsible for infections ranging from mild to life-threatening. Healthcare-associated MRSA (HA-MRSA) strains are typically multidrug-resistant (MDR), contributing to infections

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associated with prolonged hospitalisation and high mortality [1]. In contrast, community-associated MRSA (CA-MRSA) tends to exhibit greater virulence than HA-MRSA and primarily affects individuals without prior healthcare exposure [2], although they also cause hospital-acquired infections [3].

In South America, MRSA lineages are mainly associated with clonal complexes (CCs) 5, 8, and 30 [4]. In Brazil, CC5 is the most prevalent, particularly sequence types (STs) 5 and 105. Other clones have been detected at lower frequencies [5]. Here, we report a Panton-Valentine (PVL)-positive MRSA-ST88 isolate causing hospital-acquired pneumonia in a patient admitted to a tertiary hospital in Brazil. This finding is significant as ST88 is a CA-MRSA clone primarily reported in Africa and Asia [6] with only rare reports from Latin America - two isolates from Colombia [6], one from Chile [7], and a single one previously described in Brazil [8]. Continuous monitoring is essential to track epidemiological dynamics and assess the potential public health impact of MRSA-ST88 in Brazil.

## 2. Materials and methods

Identification and antimicrobial susceptibility testing (AST) were performed using the BD Phoenix automated system (BD Diagnostics) against oxacillin, azithromycin, ciprofloxacin, levofloxacin, clindamycin, gentamicin, linezolid, rifampicin, trimethoprim-sulfamethoxazole, teicoplanin, and vancomycin. Vancomycin susceptibility and MICs for daptomycin and tigecycline were confirmed by manual broth microdilution (see Supplementary Methods S1).

Genomic DNA was extracted with the PureLink Genomic DNA Mini Kit (Thermo Fisher Scientific). DNA purity and concentration were assessed using a NanoDrop spectrophotometer (Thermo Scientific) and Qubit 2.0 fluorometer (Life Technologies). A genomic library was prepared with the Nextera DNA Flex kit (Illumina) and sequenced on the Illumina NextSeq 550 platform (paired-end 2 × 75 bp). Reads were quality-trimmed with Trimmomatic v0.39 and assembled using CLC Genomics Workbench v12.0.3.

Multilocus sequence typing (MLST), SCC*mec* type, spa type, species identification, resistome, virulome and plasmids were predicted using MLST v2.0, SCCmecFinder v1.2, spaTyper v1.0, SpeciesFinder 2.0, ResFinder v4.7.2, VirulenceFinder v2.0, and PlasmidFinder v2.1, respectively, available at the Center for Genomic Epidemiology (https://genomicepidemiology.org/). Efflux pumps were predicted using the Comprehensive Antibiotic Resistance Database (CARD) via ABRicate v1.0.1.

A coregenome phylogeny was constructed using SQ684 and 169 publicly available international MRSA-ST88 genomes from Pathogenwatch (https://pathogen.watch) (see Supplementary Methods S2). Genomes were annotated with Prokka v1.14.6, and the pangenome was inferred with Roary v3.13.0, which also generated core gene identification and alignment. Core genome single-nucleotide polymorphisms (SNPs) were called using SNP-sites v2.5.1, and pairwise SNP distances were calculated with SNP-dists v0.8.2. An approximately maximum-likelihood tree was inferred with IQ-TREE v3.0.1 and visualised in iTOL v6, with metadata (date, country, source) retrieved from NCBI BioSamples.

## 3. Results and discussion

On 20 February 2021, a 47-year-old man presented to a tertiary hospital in Brazil with dyspnea, bilateral pulmonary crackles, and an oxygen saturation of 92% on 10 L/min via face mask (Fig. S1). He was conscious, afebrile, blood pressure was 140/90 mmHg, and his heart rate was 90 bpm. After a positive SARS-CoV-2 RT-PCR, he was admitted to an intensive care unit (ICU) for acute respiratory distress. Chest computed tomography revealed diffuse, bilateral ground-glass opacities with peripheral and subpleural distribution, areas of consolidation, and interlobular septal thickening, involving more than 50% of the lung parenchyma, consistent with viral pneumonia.

On 22 February, the patient was intubated and started on empirical piperacillin-tazobactam. Procalcitonin levels ranged from 0.23 ng/mL to 0.52 ng/mL between 20 and 26 February. He was extubated on 28 February but developed a fever within 24 h and was reintubated on 1 March. A tracheal aspirate was collected, and therapy was switched to meropenem and linezolid. Procalcitonin rose to 3.01 ng/mL, indicating bacterial infection. Due to continued deterioration, polymyxin E was added on 2 March.

Culture of the tracheal aspirate grew *S. aureus* and *Klebsiella pneumoniae*. Antimicrobial susceptibility testing confirmed the *S. aureus* isolate as MRSA, resistant to oxacillin and azithromycin, but susceptible to all other tested agents. By 4 March, the patient improved clinically and was transferred to a semi-intensive care unit, with oxygen support gradually reduced. He was discharged in stable condition on 12 March for outpatient follow-up.

The SQ684 draft genome assembly generated a 2,816,058 bp genome with 139 contigs, 2,649 protein-coding genes, 14 tRNAs, 2 rRNAs, and a GC content of 32.7%. The strain belonged to sequence type ST88 and carried the *mecA* gene and the SCC*mec* IVc (2B). The *spa* type could not be determined due to incomplete locus coverage.

Resistome analysis predicted genes encoding resistance to beta-lactams (*mecA* and *blaZ*) and macrolides [msr(A) and mph(C)], consistent with the AST profile. Aminoglycoside resistance genes aph(3′)-III and *ant(6)-Ia* were also detected, despite phenotypic susceptibility, likely due to loss of functionality in aminoglycosidemodifying enzyme genes or minimal inhibitory concentration (MIC) below EUCAST breakpoints [9]. Additional determinants included efflux pump regulators and components (*arlS, arlR, mgrA, mepA, mepR, sdrM, lmrS, norA, norC, sepA*), and plasmid replication genes (rep21, rep10b, rep16) (Table S1). Virulence factors included genes encoding serine proteases (*splAB*), aureolysin (*aur*), staphylokinase (*sak*), staphylococcal complement inhibitor (*scn*), gamma-hemolysin (*hlgABC*), leukocidinDE (*lukD, lukE)* and Panton-Valentine Leukocidin (PVL) (*lukF-PV, lukS-PV*) (Table S1).

Although SQ684 showed resistance only to oxacillin and azithromycin, MRSA-ST88 isolates from China and other regions have exhibited broader resistance profiles, including trimethoprim-sulfamethoxazole and clindamycin [6,7]. Virulence genes and SCC*mec* diversity have also been reported among ST88 lineages. For example, one study found *hlgABC* in most ST88 genomes [6] while another reported widespread PVL and immune evasion genes such as *splAB, sak*, and *scn*, but absence of *aur* and *hlgABC* [7]. In SQ684, the presence of PVL genes is notable, as PVL is a pore-forming toxin targeting neutrophils and associated with severe necrotising pneumonia and skin infections [10]. Regarding SCC*mec*, most human-associated MRSA-ST88 strains carry type IVa, whereas food-associated strains often harbour type IVc [6]. Both SQ684 and the only previously reported Brazilian clinical ST88 isolate carried SCC*mec* IVc [8]. In Latin America, SCC*mec* IVc is prevalent across MRSA from food, livestock, and clinical sources, suggesting cross-sector dissemination [11,12]. Its efficient transfer is linked to a smaller size and lower fitness cost [12].

Comparative coregenome phylogeny revealed seven major MRSA-ST88 clades. SQ684 clustered with isolates from Australia, Italy, Germany, the United States of America, and the United Kingdom, but pairwise distances (243–293 SNPs) indicate substantial genetic divergence. Given the estimated *S. aureus* mutation rate of ~1 SNP per 6 weeks [13] and the >40 SNP threshold to exclude recent transmission, SQ684 is unlikely to be directly related to any international isolates. Instead, this divergence suggests long-term,

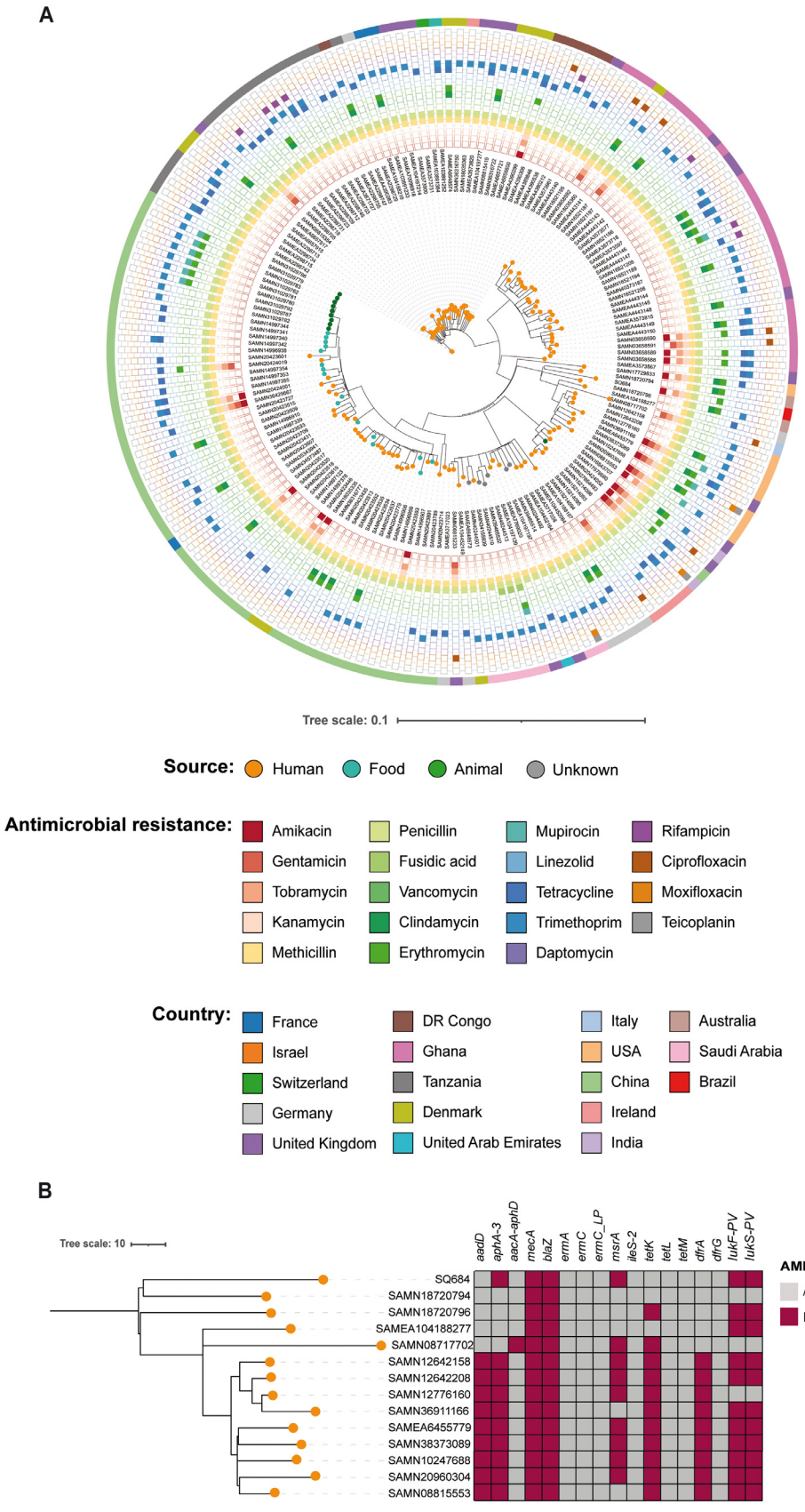


**Fig. 1.** Comparative genome phylogeny. (A) Maximum likelihood phylogeny of the 170 MRSA-ST88 was inferred from aligned core genomes by Roary and visualized using iTOL; (B) Resistome and presence of PVL genes of strains that showed the greatest phylogenetic relationship with the study isolate. SQ684, isolate; AMR, antimicrobial resistance; PVL, Panton-Valentine Leukocidin.

geographically independent evolution within the ST88 lineage [14] (Fig. 1A and B, Table S2).

The close temporal association between symptom onset, rising procalcitonin levels, and SQ684 isolation, following exposure to invasive mechanical ventilation and broad-spectrum antibiotic exposure, supports classifying the infection as hospital-acquired. This case underscores the role of genomic surveillance for detecting emerging MRSA clones and illustrates how a CA-MRSA clone can infiltrate hospital settings. Continuous monitoring is essential to track epidemiological dynamics and assess the potential public health impact of MRSA-ST88 in Brazil.

The Whole Genome Shotgun project of PRJNA1108341 has been deposited at DDBJ/ENA/GenBank under accession no. SAMN41239092.

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**Declaration of competing interest**: None declared.

**Ethical approval**: This study was approved by the Research Ethics Committee of the São José do Rio Preto Medical School – FAMERP (CAAE: 52,157,921.3.0000.5415).

**Data availability**: Supplementary Fig. S1, Methods S1 and S2, and Tables S1 and S2 are available in Supplementary Materials.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jgar.2026.02.009.

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