

Draft Genome Sequence of Strain SA_ST125_MupR of Methicillin-Resistant *Staphylococcus aureus* ST125, a Major Clone in Spain

Laura Barrado,^a Esther Viedma,^a Ana Vindel,^b Joaquín R. Otero,^a Fernando Chaves^a

Servicio de Microbiología Clínica, Hospital Universitario 12 de Octubre, Madrid, Spain^a; Nosocomial Infectious Diseases Laboratory, Servicio de Bacteriología, Instituto de Salud Carlos III, Centro Nacional de Microbiología, Majadahonda, Madrid, Spain^b

Here, we report the draft genome sequence of a methicillin-resistant *Staphylococcus aureus* (MRSA) strain with high-level mupirocin resistance (SA_ST125_MupR), isolated from a patient with recurrent bacteremia. This strain belonged to sequence type ST125, which was responsible for more than 50% of the health care-associated infections caused by MRSA in Spain.

Received 3 July 2013 Accepted 11 July 2013 Published 8 August 2013

Citation Barrado L, Viedma E, Vindel A, Otero JR, Chaves F. 2013. Draft genome sequence of strain SA_ST125_MupR of methicillin-resistant *Staphylococcus aureus* ST125, a major clone in Spain. Genome Announc. 1(4):e00588-13. doi:10.1128/genomeA.00588-13.

Copyright © 2013 Barrado et al. This is an open-access article distributed under the terms of the Creative Commons Attribution 3.0 Unported license.

Address correspondence to Fernando Chaves, fernando.chaves@salud.madrid.org.

W ethicillin-resistant *Staphylococcus aureus* (MRSA) is among the most frequently identified antimicrobial drug-resistant pathogens worldwide. It has been demonstrated that some lineages are ecologically highly successful and that most isolates belong to pandemic clones (1). In Spain, *S. aureus* sequence type ST125 continues to be responsible for more than half of the nosocomial MRSA infections (2). With increasing pressure to prevent MRSA infection, it is possible that there will be increased use of mupirocin for nasal decolonization of MRSA (3), which will be reflected in increased rates of resistance (4). High-level mupirocin resistance (Hi-Mup^R) (MICs of \geq 512 µg/ml) is mediated by acquisition of a novel isoleucyl-tRNA synthetase gene (*mupA* or *ileS2*) on a transferable plasmid, which could carry multiple resistance determinants for other classes of antimicrobial agents (3).

S. aureus ST125 was the most prevalent MRSA strain (83.3%) in our institution. We detected 8.8% Hi-Mup^R among MRSA isolates, and most of this resistance was focused on the ST125 clone (5). The *S. aureus* SA_ST125_MupR strain was isolated from an adult patient with recurrent bacteremia. This strain was characterized as pulsed-field gel electrophoresis pattern type E8, *spa* type t1399, *agr* type II, and staphylococcal cassette chromosome *mec* element (SCC*mec*) type IVc (6).

Genomic DNA was extracted from an overnight culture using the DNeasy blood and tissue kit (Qiagen) after addition of lysostaphin (100 μ g/ml) and incubation at 37°C for 2 h. The *S. aureus* SA_ST125_MupR genome was sequenced by using the 454 GS-Junior platform (Roche), generating 196,055 reads, for a total of 91,441,914 bp, with 29-fold average coverage. With the Newbler Assembler v2.7 (Roche), the obtained sequences were *de novo* assembled into 49 contigs with an N_{50} contig size of 192,317 nucleotides and a total length of 2,852,031 bp. The average G+C content was 32.7%. Sequences were annotated using the NCBI Prokaryotic Genomes Automatic Annotation Pipeline (PGGAP) (http://www.ncbi.nlm.nih .gov/genome/annotation_prok/), yielding a total of 2,757 genes, 2,664 coding DNA sequence (CDS) genes, 26 pseudogenes, 58 tRNAs, and 9 rRNAs. Furthermore, the Rapid Annotations using Subsystems Technology (RAST) (http://rast.nmpdr.org) server

(7) and Comprehensive Antibiotic Resistance Database (CARD) (http://arpcard.mcmaster.ca) (8) were used. There were genes related to antibiotic resistance and toxic compounds. These included efflux pumps (ATP-binding cassette [ABC] transporter, major facilitator superfamily, small multidrug resistance) potentially carrying resistance to a wide range of antimicrobials (fluoroquinolones, tetracyclines, and macrolides), and genes associated with specific resistance to β -lactams (mecA, mecR1, mprF, blaZ, blaI, and blaR), aminoglycosides (phosphotransferases, adenvltransferases, and nucleotidyltransferases), macrolides/lincosamides/streptogramins (mph, macB), fosfomycin (fosB), tetracycline (tetM), rifampin (dnaA), glycopeptides (bleO), and mupirocin (ileS, ileS2), as well as resistance determinants to arsenic, cadmium, cobalt, mercury, and zinc. The ileS2 gene was located on a plasmid which was partially sequenced, giving a final size of ~58 kb, and it harbored other genes associated with resistance to β -lactams and macrolides. Overall, the availability of the present genome sequences facilitates further comparative genomic and bioinformatic analysis in S. aureus populations and may also provide insights into the genetic background for the success of this nosocomial lineage.

Nucleotide sequence accession number. This whole-genome shotgun project has been deposited at GenBank under the accession number ASTH00000000.

ACKNOWLEDGMENTS

This work was supported by the Plan Nacional de i+D+i 2008-2011 and the Instituto de Salud Carlos III, Subdirección General de Redes y Centros de Investigación Cooperativa, Ministerio de Economía y Competitividad (Spanish Network for Research in Infectious Diseases REIPI RD12/0015), and cofinanced by the European Development Regional Fund (ERDF), "A way to achieve Europe," and by the Spanish Ministry of Health (FIS PI08/ 1520 and PI12/01205).

REFERENCES

1. Enright MC, Robinson DA, Randle G, Feil EJ, Grundmann H, Spratt BG. 2002. The evolutionary history of methicillin-resistant *Staphylococcus aureus* (MRSA). Proc. Natl. Acad. Sci. U. S. A. **99**:7687–7692.

- 2. Vindel A, Trincado P, Gómez E, Cabrera R, Boquete T, Solá C, Valdezate S, Saez-Nieto JA. 2006. Prevalence and evolution of methicillin-resistant *Staphylococcus aureus* in Spanish hospitals between 1996 and 2002. J. Clin. Microbiol. 44:266–270.
- 3. Patel JB, Gorwitz RJ, Jernigan JA. 2009. Mupirocin resistance. Clin. Infect. Dis. 49:935–941.
- 4. Desroches M, Potier J, Laurent F, Bourrel AS, Doucet-Populaire F, Decousser JW; on behalf of the Microbs Study Group. 2013. Prevalence of mupirocin resistance among invasive coagulase-negative staphylococci and methicillin-resistant *Staphylococcus aureus* (MRSA) in France: emergence of a mupirocin-resistant MRSA clone harbouring *mup*A. J. Antimicrob. Chemother. [Epub ahead of print.] doi:10.1093/jac/dkt085.
- Daskalaki M, Otero JR, Chaves F. 2009. Molecular characterization of resistance to mupirocin in methicillin-resistant *Staphylococcus aureus* isolates in a tertiary hospital in Spain. J. Antimicrob. Chemother. 63:826–828.
- 6. Vindel A, Cuevas O, Cercenado E, Marcos C, Bautista V, Castellares C,

Trincado P, Boquete T, Pérez-Vázquez M, Marín M, Bouza E, Spanish Group for the Study of Staphylococcus. 2009. Methicillin-resistant *Staphylococcus aureus* in Spain: molecular epidemiology and utility of different typing methods. J. Clin. Microbiol. 47:1620–1627.

- Aziz RK, Bartels D, Best AA, DeJongh M, Disz T, Edwards RA, Formsma K, Gerdes S, Glass EM, Kubal M, Meyer F, Olsen GJ, Olson R, Osterman AL, Overbeek RA, McNeil LK, Paarmann D, Paczian T, Parrello B, Pusch GD, Reich C, Stevens R, Vassieva O, Vonstein V, Wilke A, Zagnitko O. 2008. The RAST server: rapid annotations using subsystems technology. BMC Genomics 9:75. doi:10.1186/1471-2164-9-75.
- McArthur AG, Waglechner N, Nizam F, Yan A, Azad MA, Baylay AJ, Bhullar K, Canova MJ, De Pascale G, Ejim L, Kalan L, King AM, Koteva K, Morar M, Mulvey MR, O'Brien JS, Pawlowski AC, Piddock LJ, Spanogiannopoulos P, Sutherland AD, Tang I, Taylor PL, Thaker M, Wang W, Yan M, Yu T, Wright GD. 2013. The comprehensive antibiotic resistance database. Antimicrob. Agents Chemother. 57:3348–3357.