JB Journals.ASM.org

GENOME ANNOUNCEMENT

Draft Genome Sequences of *Staphylococcus aureus* Sequence Type 34 (ST34) and ST42 Hybrids

Jonathan C. Thomas,[a] Paul A. Godfrey,[b] Michael Feldgarden,[b] and D. Ashley Robinson[a]

Department of Microbiology, University of Mississippi Medical Center, Jackson, Mississippi, USA,[a] and Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA[b]

***Staphylococcus aureus* is a major cause of antimicrobial-resistant infections of humans. Hybrids of *S. aureus*, which originate from large-scale chromosomal recombinations between parents of distinct genetic backgrounds, are of interest from clinical and evolutionary perspectives. We present draft genome sequences of two *S. aureus* hybrids of sequence type 34 (ST34) and ST42.**

Staphylococcus aureus, a premier human pathogen, possesses an arsenal of virulence and antimicrobial resistance genes that are subject to horizontal genetic transfer and recombination (2, 8). Some entire *S. aureus* genetic backgrounds are hybrids that originated from recombinations of large, contiguous portions of the chromosomes of genetically distinct parent backgrounds (14). The first described bacterial hybrid of this sort from nature was the *S. aureus* sequence type 239 (ST239). ST239 strains are resistant to multiple antimicrobials and cause epidemics of hospital-associated infections (5, 16). Genome sequencing has confirmed the ST239 hybrid genome structure (7). *S. aureus* ST34 and ST42 backgrounds have also been suggested to be of hybrid origin based on multilocus sequencing (14), but these two backgrounds have not been studied previously through genome sequencing. ST42 is relatively rare, whereas ST34 has spread to multiple continents and can cause community-associated skin and soft tissue infections (1, 4, 18).

Genome sequences were determined for ST34 (strain C160) and ST42 (strain C427), using 454 FLX pyrosequencing (Roche). Sequencing, assembly, and annotation were performed as described previously (17). The ST34 genome was assembled into 26 scaffolds and 63 contigs, whereas the ST42 genome was assembled into 18 scaffolds and 54 contigs; >50% of each genome was assembled into contigs of >95.66 kb and scaffolds of >974.96 kb. The average coverage was >25×. The ST34 and ST42 genomes were 2.82 and 2.86 Mb in length, with 32.69 and 32.70% G+C ratios, and comprised 2,750 and 2,781 open reading frames (ORFs), respectively, with 56 tRNAs each, but only 10 and 4 rRNAs, respectively, were detected.

The genomes of the two putative hybrids and the previously sequenced parent-like backgrounds ST145 (strain D139), ST10 (strain H19), ST36 (strain MRSA252), and ST30 (strain WW2703/97) (6, 17) were aligned using the progressiveMauve algorithm of Mauve v2.3.1 (3) with default parameters. Putative recombination events were detected using the Chimaera (13), Geneconv (15), MaxChi (12), and RDP (10) methods, implemented by RDP v.3.44 (11). Statistical significance was based at a P value of < 0.05, and a Bonferroni correction for multiple tests was applied. Events detected by three of the four methods were further examined by manual inspection and confirmed using the genetic algorithm for recombination detection (GARD) method (9).

The previously identified breakpoints of the two recombination events that resulted in ST34 and ST42 (14), including a common breakpoint 3′ of the origin of replication in ORFs SFAG_00636/SASG_01570 and unique breakpoints 5′ of the origin in ORFs SFAG_00460 and SASG_01367, respectively, were confirmed. For ST34 and ST42, respectively, at least 199,596 and 230,662 bp of contiguous sequence was inherited from their ST10/ST145-like parent, and at least 2,623,050 and 2,631,028 bp of contiguous sequence was inherited from their ST30/ST36-like parent. One additional recombination event of at least 164 bp was identified in ORF SASG_01774 for ST42. Four other potential recombination events were rejected as analysis artifacts that occurred in repeat regions and other regions of poor alignment quality. Further analyses of these two genome sequences, in addition to those of other *S. aureus* hybrids, may provide insight into the mechanisms by which bacterial hybrids form and diversify.

Nucleotide sequence accession numbers. Draft genome sequences of *S. aureus* strains C160 and C427 were deposited in GenBank under accession numbers ACUV00000000 and ACSQ00000000, respectively.

ACKNOWLEDGMENTS

This project has been funded in part with federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH), Department of Health and Human Services, under contract no. HHSN272200900018C, and by grant number GM080602 (to D.A.R.) from the National Institute of General Medical Sciences, National Institutes of Health.

REFERENCES

1. **Aires de Sousa M, Conceição T, Simas C, de Lencastre H.** 2005. Comparion of genetic backgrounds of methicillin-resistant and -susceptible *Staphylococcus aureus* isolates from Portuguese hospitals and the community. J. Clin. Microbiol. **43**:5150–5157.
2. **Chan CX, Beiko RG, Ragan MA.** 2011. Lateral transfer of genes and gene fragments in *Staphylococcus* extends beyond mobile elements. J. Bacteriol. **193**:3964–3977.
3. **Darling AE, Mau B, Perna NT.** 2010. progressiveMauve: multiple genome alignment with gene gain, loss and rearrangement. PLoS One **5**:e11147.
4. **Daskalaki M, et al.** 2010. Panton-Valentine leukocidin-positive *Staphylococcus aureus* skin and soft tissue infections among children in an emergency department in Madrid, Spain. Clin. Microbiol. Infect. **16**:74–77.

Received 16 February 2012 **Accepted** 2 March 2012

Address correspondence to D. Ashley Robinson, darobinson@umc.edu.

doi:10.1128/JB.00248-12

5. **Harris SR, et al.** 2010. Evolution of MRSA during hospital transmission and intercontinental spread. Science **327**:469–474.
6. **Holden MT, et al.** 2004. Complete genomes of two clinical *Staphylococcus aureus* strains: evidence for the rapid evolution of virulence and drug resistance. Proc. Natl. Acad. Sci. U. S. A. **101**:9786–9791.
7. **Holden MT, et al.** 2010. Genome sequence of a recently emerged, highly transmissible, multi-antibiotic- and antiseptic-resistant variant of methicillin-resistant *Staphylococcus aureus*, sequence type 239 (TW). J. Bacteriol. **192**:888–892.
8. **Hughes AL, Friedman R.** 2005. Nucleotide substitution and recombination at orthologous loci in *Staphylococcus aureus*. J. Bacteriol. **187**:2698–2704.
9. **Kosakovsky Pond SL, Posada D, Gravenor MB, Woelk CH, Frost SD.** 2006. Automated phylogenetic detection of recombination using a genetic algorithm. Mol. Biol. Evol. **23**:1891–1901.
10. **Martin D, Rybicki E.** 2000. RDP: detection of recombination amongst aligned sequences. Bioinformatics **16**:562–563.
11. **Martin DP, et al.** 2010. RDP3: a flexible and fast computer program for analyzing recombination. Bioinformatics **26**:2462–2463.
12. **Maynard Smith J.** 1992. Analyzing the mosaic structure of genes. J. Mol. Evol. **34**:126–129.
13. **Posada D, Crandall KA.** 2001. Evaluation of methods for detecting recombination from DNA sequences: computer simulations. Proc. Natl. Acad. Sci. U. S. A. **98**:13757–13762.
14. **Robinson DA, Enright MC.** 2004. Evolution of *Staphylococcus aureus* by large chromosomal replacements. J. Bacteriol. **186**:1060–1064.
15. **Sawyer SA.** 1989. Statistical tests for detecting gene conversion. Mol. Biol. Evol. **6**:526–538.
16. **Smyth DS, et al.** 2010. Population structure of a hybrid clonal group of methicillin-resistant *Staphylococcus aureus*, ST239-MRSA-III. PLoS One **5**:e8582.
17. **Thomas JC, Godfrey PA, Feldgarden M, Robinson DA.** 2012. Candidate targets of balancing selection in the genome of *Staphylococcus aureus*. Mol. Biol. Evol. **29**:1175–1186.
18. **Wehrhahn MC, et al.** 2010. Clinical and laboratory features of invasive community-onset methicillin-resistant *Staphylococcus aureus* infection: a prospective case-control study. Eur. J. Clin. Microbiol. Infect. Dis. **29**:1025–1033.