Supplemental Methods

Institutional Review Board Approval

This Investigation was carried out according to a no-subject-contact study protocol approved by the UCSF Institutional Review Board (IRB# 17-24056) which permitted analysis of de-identified leftover clinical microbiology samples and subsequent review of study subject electronic medical records.

Bacterial Culture

Bacterial cultures were inoculated into BD BACETC Plus Aerobic and Lytic Anaerobic blood culture bottles (Becton Dickinson) using standard clinical protocols. Species identification was performed using MALDI Biotyper CA mass spectrometry system and Revision D reference library (Bruker). Notably, this database does not differentiate *S. argenteus* from *S. aureus* (1).

Whole Genome Sequencing

10-25 nanograms of DNA were extracted from the cultured isolates using the Zymo Duet DNA/RNA kit or the Zymo Bacterial/Fungal kit (Zymo Research) according to the manufacturer's protocol. The NEBNext Ultra II FS DNA Sequencing kit (New England Biolabs) was used for library preparation according to the manufacturer's protocol and incorporating custom TruSeq dual unique indexing primers. Paired-end 150 base pair sequencing was performed using an Illumina NextSeq 550 instrument.

Bioinformatics Analysis

Raw reads (NCBI BioProject PRJNA562563) were adaptor-trimmed and quality filtered using fastp (2). *De novo* genome assembly using the filtered reads was performed using Unicycler with default parameters (3). The resulting contigs (n=43) were aligned against the NCBI nr/nt database using BLAST with default parameters to identify the best reference

genomes for each sample. SNP analysis was performed with Snippy v4.3.0 using the reference genome *S. argenteus* strain BN75 (NZ_CP015758.1) (4. Unique SNPs and the associated genes were manually inspected using Bowtie2 (5). Phylogenetic analysis based on protein families are shared across all examined genomes was performed using PATRIC with a previously described pipeline consisting of BLAST, MCL, Muscle, hmmbuild, hmmsearch, Gblocks, FastTree and RAxML (6).

Supplemental References

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3. Wick RR, Judd LM, Gorrie CL, Holt KE. Unicycler: Resolving bacterial genome assemblies from short and long sequencing reads. PLoS computational biology. 2017 Jun;13(6):e1005595.

4. Seemann T. Snippy: Rapid haploid variant calling and core genome alignment. 2015.

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