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P2686 Evaluation of the *Staphylococcus aureus* Analysis "1928D" Pipeline to determine the epidemiological threshold using whole-genome sequence data

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Background: Numerous tools are available for typing *Staphylococcus aureus*, including pulsed-field gel electrophoresis (PFGE), multilocus sequencing typing (MLST), *agr*- and *spa*-typing, and most recently, whole genome sequencing (WGS). PFGE has long been the benchmark method; however, it has many challenges. A pipeline platform (1928D) that provides resistance mechanism predictions and core-genome (cg) epidemiological analysis for *S. aureus* has been developed. This study evaluated and compared the typing data provided by 1928D against standard typing information utilized to differentiate persistent infection from re-infection among patients enrolled in a nosocomial pneumonia clinical trial.

Materials/methods: Initially, 40 oxacillin-resistant *S. aureus* (MRSA) clinical trial isolates, 2 strains per patient (pre- and post-pneumonia course treatment) were characterized by standard PFGE, SCC*mec*, *spa* and *agr* typing methods. WGS data were obtained using MiSeq (Illumina) and FASTQ files were fed into the 1928D pipeline for generation of cgMLST, allelic variants, and single nucleotide polymorphisms (cgSNP). Additionally, 8 surveillance MRSA isolates genetically related based on MLST data, but epidemiologically unrelated to the clinical trial isolate pairs, were included as a control set.

Results: MLST and SCC*mec* (I, II, and IV) information obtained by standard methods matched those generated by 1928D in 27/30 isolates while most (8/10) SCC*mec* III isolates were unassigned. Pre- and post-treatment isolate pairs characterized as persistent strains and epidemiologically related (genetically identical or similar) by standard methods showed the fewest allelic and cgSNP differences (≤22 or ≤32, respectively; Table). Isolate pairs characterized as re-infections (genetically different isolate pairs) demonstrated >200 differences. When the clinical isolate pairs were compared to the respective MLST-matched and epidemiologically unrelated control, allele and cgSNP differences of 45-244 and 46-277 were observed, respectively (Table).

Conclusions: 1928D is a robust platform for relatedness analysis of *S. aureus*. This tool provided high-resolution typing information able to distinguish between isolates causing persistent infection (epidemiologically/genetically related) and re-infection cases (unrelated isolates). The data suggest that, when combined with metadata, a threshold of approximately 35 (alleles and cgSNP differences) may be used for defining persistent infections in a clinical trial set. Additional studies with a greater number of isolates are needed to refine this cutoff value.

1928D analysis (difference in)	Analysis of each pair of isolates by PFGE			Analysis against an epidemiologically unrelated control set			
	Identical (n=11)	Similar (n=4)	Different (n=5)	CC22	CC5	CC72	CC8/239
No. alleles	0-21	1-31	202-1268	57-65	45-244	114-119	66-230
No. cgSNP	0-22	1-32	219-9203	58-66	46-277	120-125	68-266