

Supplemental materials descriptions

Figure S1: Phylogenetic tree estimated by kSNP3. Strains predicted to be MRSA are shown in red typeface, while those predicted to be MSSA are shown in black typeface. The three strains in which there is a conflict between the predicted phenotype and the experimentally determined phenotype are enclosed in boxes. Branches along which the predicted phenotype changed from MSSA to MRSA are shown in red, while those in which the predicted phenotype changed from MRSA to MSSA are shown in blue.

PPFS2 algorithm: Brief description of PPFS2 algorithm.

Table S1: Predicted antibiotic susceptibilities of *S. aureus* isolates based on genotype.

Table S2: MLST sequence types of *S. aureus* isolates.

Table S3: *S. aureus* isolate information. Accession number is a unique identifier for each isolate. SampleID is a unique identifier for each genome sequence. PatientNo identifies the patient from which the isolate was obtained, with letter suffixes indicating isolates taken at different times from the same patient. Blocks of samples from the same patient are shaded in blue. Samples from the same patient and with the same accession number (shown in red) are replicate sequences of the same isolate and have PatientNo such as Patient021A1 and 021A2. MRSA = methicillin resistant, MSSA =- methicillin sensitive. **Obs MRMS** is Observed MRSA or MSSA phenotype. **Predic MRMS** is the MRSA or MSSA phenotype predicted by the program PPFS2.

Table S4: Number of SNP difference for all pairs of CF genomes with pairs being listed in increasing order of number of SNP difference.

Table S5: Number of SNP difference for all pairs of CF genomes which shows the presence of unrelated isolates in single patients.

Table S6: Identities and IDs of proteins containing non-synonymous causal SNPs.

Table S7: Number of differences accumulated per week for pairs of the same strain from the same patient.

Table S8: GenBank accession numbers for all *S. aureus* isolates.