Staphylococcus argenteus

Taxonomy and Background

The *S. aureus complex* consists of 3 species: *S. aureus, S. argenteus* and *S. schweitzeri*. *S. aureus* can be further divided into the two subspecies *aureus* and *anaerobius*

- *S. argenteus* was first discovered in remote Indigenous communities in the Northern Territory in 2006 (then designated CC75, an MRSA strain). Delineated into a separate species by WGS in 2015. Considered to be an ancestral lineage of *S. aureus,* due to the very small accessory genome and lower genomic plasticity (due to the presence of a CRISPR/cas system, rarely found in *aureus* isolates). 16s rRNA gene is identical to *S. aureus*: differences exist in the *soda, rpoB, tuf* and *hsp60*
- *S. schweitzeri* – first detected in African bats and monkeys in 2011. Possess mutations in the thermostable nuclease gene (*nuc1 -> nucM)*.

Epidemiology

S. argenteus: world-wide distribution, but 'hot spots' exist in South-East Asia, remote Australia, and the Amazon. Accounts for 71% of CA-MRSA in Australian aboriginal communities. In one multicentre study in Thailand comparing *S. aureus* and *S. argenteus* sepsis, 19% were infected with the latter – postulated bovine reservoir in this population.

S. schweitzeri – restricted to the African continent, particularly West and Central Africa. Has been isolated from bats and non-human primates, but has not been associated with infection in either animals or humans.

Clinical Manifestations

S. argenteus: early reports assumed a lower virulence compared to *S. aureus*, however it is now known that it has a similar ability to produce a wide spectrum of invasive infections and produce similar toxin mediated syndromes. Comparative genomics of 15 *S. argenteus* genomes demonstrated 76% of the 111 virulence genes associated with *S.aureus* were detected. PVL was found in isolates from skin and soft-tissue infection, however this has not been demonstrated in Australian isolates. Carries a variety of resistance genes, including haemolysin, capsule polysaccharides, adhesins and other leucocidins.

S. schweitzeri: despite lack of described infections in humans, this species does not differ substantially from *S. aureus* in possession of virulence factors, including toxic shock syndrome toxin-1 gene (tst). However, it appears to be missing genes carried on a prophage associated with human adaption and evasion of the immune response.

Identification

Microscopy, colony appearance and phenotypic tests cannot distinguish members of the *Staphylococcus aureus complex*.
S. argenteus classically has creamy white colonies without pigmentation, however regular *S. aureus* can also produce this picture. No commercially available DNA based assays can reliably differentiate them either - *S. schweitzeri* may be identified by identification of the *nucM* mutation, and targeting variations in *nuc1* may be a method for identifying *S. argenteus*. 16srRNA sequencing fails.
The most practical way is MALDI-TOF: several specific MS signals allow differentiation. WGS provides a definitive allocation, and MLST can help identify genotypes associated with either *S. argenteus* or *S. schweitzeri*.

Table 2
Utility of diagnostic approaches to differentiate within the *Staphylococcus aureus* complex

Diagnostic approach	Differentiation between *S. aureus* subsp. *aureus* and		Reference
	S. argenteus	*S. schweitzeri*	
Microscopy	Not possible	Not possible	[3]
Colony morphology	Uncertain	Not possible	[3,10,12,44]
Chemotaxonomy:			
- Fatty acid composition	Not possible	Not possible	[3]
- Menaquinone composition	Not possible	Not possible	[3]
- Peptidoglycan composition	Possible	Possible	[3]
Tube coagulase assay	Not possible	Not possible	[3]
Biochemistry	Not definitively	Not definitively	[3]
DNA-based methods:			
- 16S rRNA gene targeting	Not possible	Possible (1 bp difference)	[3]
- *nuc* gene targeting	Possible[a]	Possible[a]	[4]
- Whole genome sequencing	Possible	Possible	[3]
Genotyping:			
- MLST	Indicative	Indicative	[3,9,36]
- *spa* typing	Probably indicative (unstudied)	Indicative	[36]
MALDI-TOF MS	Possible[b]	Possible[b]	[3,17,53]

MLST, multilocus sequence typing; MALDI-TOF MS, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry.
[a] Dependent on the annealing sites and nucleotide composition of primers and probes used (widely used *nuc* PCR as described by Brakstad et al. [50] results in amplification products for *S. argenteus* isolates despite some mismatches, but not for *S. schweitzeri*).
[b] Dependent on the database entries.

Antimicrobial Susceptibility

Rates of resistance appear to be lower for *S. argenteus:* penicillin resistant (*blaZ positive)* isolates are common, other resistance phenotypes are rare (with the exception of Australian isolates from remote communities, which are frequently methicillin-resistant). Methicillin resistance is *mecA* based, and they possess SCC*mec* type IV elements.
S. schweitzeri are usually susceptible to all antibiotics – penicillin resistance is rare.

Reporting and Post-analytical issues

There is potential for confusion of *S. argenteus* and *S. schweitzeri* with other, less pathogenic staphylococci. No significant differences concerning morbidity, mortality and transmission has been found between *S. argenteus* and *S. aureus*. Conventional MRSA guidelines should be followed if methicillin resistance detected.
The ESCMID Study Group for Staphylococci and Staphylococcal Diseases recommend that the need to distinguish between members of the complex is questionable, and if *S. argenteus*/ *S. schweitzeri* are explicitly reported, the comment " member of the *S. aureus complex* ' should be added.

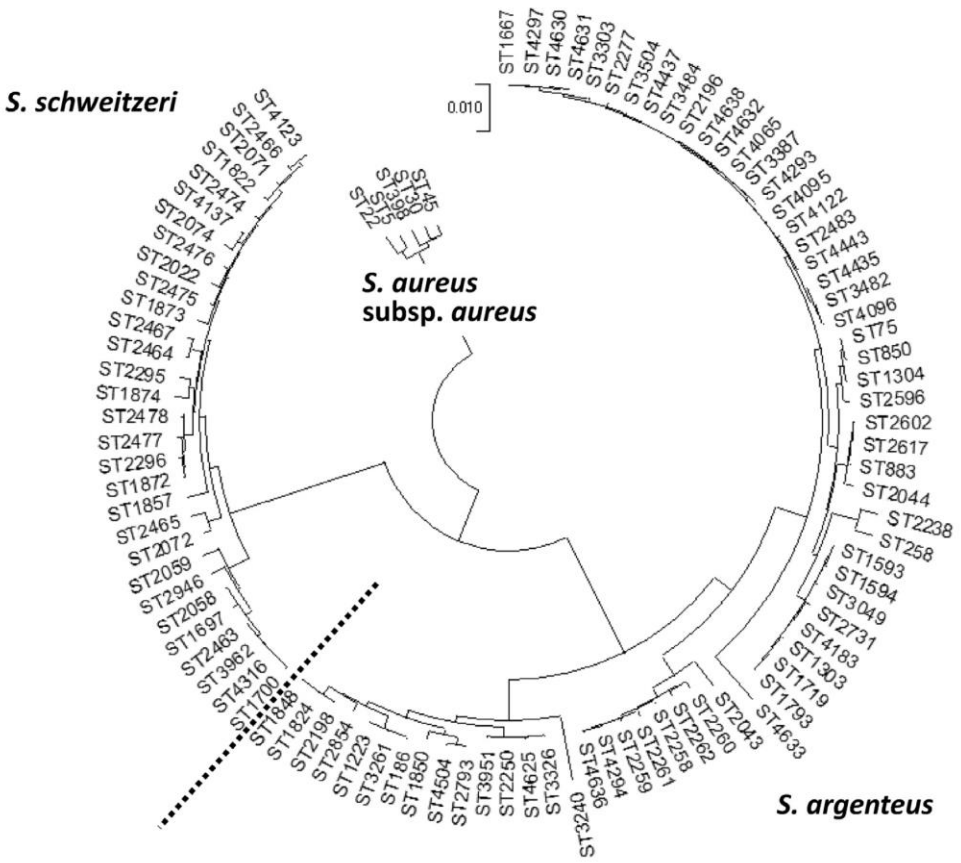

Fig. 1. Phylogenetic tree of *Staphylococcus aureus*, *Staphylococcus schweitzeri* and *Staphylococcus argenteus*. A neighbour-joining tree was constructed using the concatenated sequences of the seven multilocus sequence typing (MLST) loci. The sequences of the most common *S. aureus* lineages (ST5, ST22, ST30, ST45 and ST398) were used for rooting. All published MLST sequence types (ST) of *S. schweitzeri* and *S. argenteus* were included. Additional related ST were identified in the MLST database (accessed 9 October 2018, https://pubmlst.org/saureus/) using eBURST.