Epidemiology and genetic characterization of CC398 and non-CC398 *S. aureus* strains isolated from bloodstream infections

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Objectives

- Invasive infections due to CC398 isolates are increasingly detected in humans in animal-free environments, in relation with the emergence of isolates that easily colonize and spread between humans.
- To gain understanding about the recent evolution within the CC398 lineage, (i) we studied the molecular characteristics of the *S. aureus* isolates recovered from 129 bloodstream infections detected during a 3-month period, and including eight CC398- and 121 non-CC398 isolates, and (ii) we compared the epidemiological data of the CC398-associated- and the non-CC398-associated bloodstream infections.

Methods

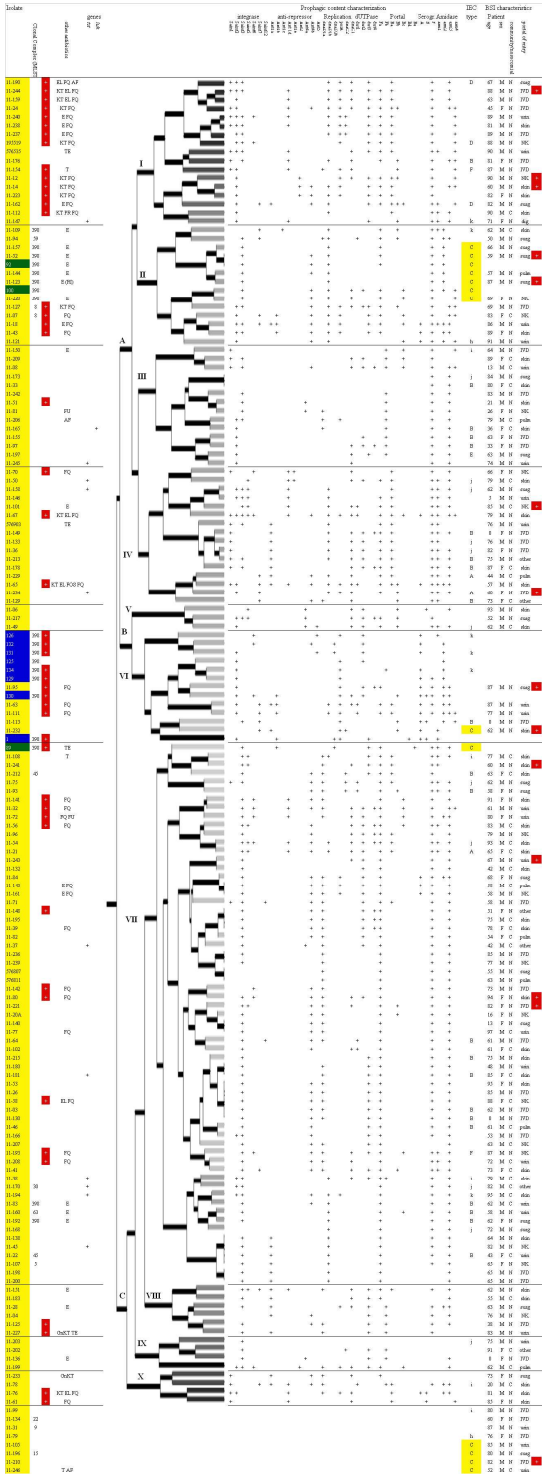
- During an epidemiological survey carried out in 2011 and covering 413,985 patient days (PD) in 30 French hospitals of Centre region (2.5 million inhabitants), 129 *S. aureus* strains were isolated from bloodstream infections.
- The variables studied included patient age and sex, portal of entry (skin, surgical site, pulmonary, urine, intravascular devices, or digestive) and death within 7 days of bloodstream infections diagnosis.
- The *S. aureus* isolates were tested for antibiotic susceptibility and characterized using *Sma*I PFGE, MLST, prophage profiling and IEC-typing.

Results

- *S. aureus* BSI incidence was 0.31/1000 PD.
- The frequency of MRSA was 26 %. Seven isolates, all MSSA, belonged to CC398 (7.4 % of MSSA).
- CC398 and non-CC398 BSI cases did not differ according to patient age or sex. By contrast, CC398 bloodstream infections cases were significantly associated with a surgical site (57.1 % *vs* 13.1 % for non CC398, p=0.011) and a higher rate of death within 7 days of bloodstream infections diagnosis (28.6 % *vs* 4.1 % for non CC398, p=0.047).
- Using MLST, PFGE and prophage profiling, the 129 isolates were distributed into 10 divisions, one of which (division II) clustering 6 of the 8 CC398 isolates and 5 of the 121 non-CC398 isolates (75 % *vs* 4.1 %, p<0.001).
- IEC-typing demonstrated that the IEC-C carrying two human-specific virulence genes *chp* and *scn* genes was rare among bloodstream infections strains (6.2 %) and significantly associated with CC398 strains (71.4 % *vs* 2.4 % for non CC398, p<0.001).

Conclusion

- Our findings bring evidences of genetic specificities and virulence traits of the human-adapted CC398 clone.
- The CC398 isolates harbour a β-converting prophage carrying two virulences genes, *chp* and *scn*.
- The β-converting prophage carried by the CC398 isolates is a rare prophage among non-CC398 BSI human isolates, suggesting a non-human origin of this prophage.
- The high rate of CC398 bloodstream infections associated with a surgical site suggests an endogenous cutaneous portal of entry. The chemotaxis inhibitory protein (CHIPS), and the staphylococcal complement inhibitor (SCIN), encoded by *chp* and *scn*, are immune-modulating proteins that facilitate long-term colonization of *S. aureus* in humans and may contribute to bacterial pathogenesis at the time of infection. We should pay attention for efficient skin desinfection before surgery to prevent such CC398 invasive infections.
- The high rate of mortality associated with the CC398 bloodstream infections needs to be further investigated, and alerts us over the need to prevent the spread of this human-adapted clone into the hospital setting.



Figure

Distribution of the studied isolates

The 129 BSI isolates

CC398 human ref. isolates

CC398 pig-borne ref. isolates