



**HAL**  
open science

# Novel staphylococcal cassette chromosome composite island (SCC-CI) with a new subtype of SCCmecVI cassette found in ST5 methicillin-resistant *Staphylococcus aureus* in France

Olivier Barraud, Frederic Laurent, Virginie Dyon-Tafani, Celine Dupieux-Chabert, Michele Bes, Marie-Cecile Ploy, Fabien Garnier, Patricia Martins Simoes

## ► To cite this version:

Olivier Barraud, Frederic Laurent, Virginie Dyon-Tafani, Celine Dupieux-Chabert, Michele Bes, et al.. Novel staphylococcal cassette chromosome composite island (SCC-CI) with a new subtype of SCCmecVI cassette found in ST5 methicillin-resistant *Staphylococcus aureus* in France. *International Journal of Antimicrobial Agents*, 2019, 53, pp.694 - 697. 10.1016/j.ijantimicag.2019.03.015 . hal-03485042

**HAL Id: hal-03485042**

**<https://hal.science/hal-03485042>**

Submitted on 20 Dec 2021

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

1 **Title: Novel Staphylococcal Cassette Chromosome composite island (SCC-CI)**  
2 **with a new subtype of *SCCmecVI* cassette found in ST5 MRSA in France**

3

4 Olivier Barraud (a,b,c), Frederic Laurent (d,e,f), Virginie Dyon-Tafani (d), Celine  
5 Dupieux-Chabert (d,e), Michele Bes (d,e), Marie-Cecile Ploy (a,b,c), Fabien Garnier  
6 (a,b,c), Patricia Martins Simoes #(d,e,f)

7

8 (a) CHU de Limoges, Laboratoire de Bactériologie-Virologie-Hygiène, Limoges,  
9 France

10 (b) Inserm, U1092, Limoges, France

11 (c) University of Limoges, UMR-S1092, Limoges, France

12 (d) National Reference Center for Staphylococci, Hospices Civils de Lyon, Lyon,  
13 France

14 (e) Department of Clinical Microbiology, Northern Hospital Group, Hospices Civils de  
15 Lyon, Lyon, France

16 (f) International Centre for Research in Infectious diseases, INSERM U1111, University  
17 of Lyon, Lyon, France

18

19 **#corresponding author** : [patricia.martins-simoes01@chu-lyon.fr](mailto:patricia.martins-simoes01@chu-lyon.fr)

20

21

22

23

24

25 **Abstract**

26 An emergent kanamycin-susceptible ST5-MRSA lineage has been identified in France.  
27 Whole genome sequencing revealed a 40 kb SCC composite island with a mosaic  
28 structure including 3 SCC elements: a  $\Psi$ SCC<sub>cop/ars</sub>, a SCC<sub>Lim88A</sub> with a *ccrC*  
29 recombinase, and a novel subtype of SCC*mec* type VI (VIb). This mosaic structure  
30 suggests a high recombination rate of SCC elements from distinct staphylococci  
31 species.

32

33 **Keywords:** *Staphylococcus aureus*, Antimicrobial resistance, MRSA, *mecA*, novel  
34 SCC*mec*

35

36 **1. Introduction**

37 Methicillin resistance in *Staphylococcus aureus* (MRSA) is due to the acquisition of an  
38 alternative penicillin-binding protein PBP2a which has a low affinity for  $\beta$ -lactam  
39 antibiotics [1]. This enzyme, encoded by the *mecA* gene, is horizontally transferred  
40 within staphylococci by a large mobile genetic element named the “staphylococcal  
41 cassette chromosome *mec*” (SCC*mec*) [2]. SCC*mec* elements integrate into the  
42 genome of *S. aureus* within the *orfX/rlmH* gene, via recombination events mediated by  
43 the site-specific recombinases (*ccr* complex) encoded by the SCC*mec* element itself  
44 [3]. Majority of MRSA clones detected worldwide belongs to a few common clonal  
45 complexes (CCs): 1, 5, 8, 22, 30 and 45 [4,5]. The CC5 is one of the CCs clustering  
46 the higher number of MRSA clones that have a worldwide distribution. Each of these  
47 MRSA clones harbors distinct SCC*mec* elements such as the ones found in the  
48 pandemic ST5-MRSA type II (New York/Japan clone), ST5-MRSA type IV (Paediatrics

49 clone), ST5-MRSA type VI (the New Paediatrics clone), ST5-MRSA type I (EMRSA-3)  
50 and ST5-MRSA type I (Geraldine clone) [6–9].

## 51 **2. Materials and Methods**

52 In July 2014, a 90 year-old man was admitted at the Limoges University Hospital  
53 Center, France, for a sepsis whose origin was a heel bed sore. Blood cultures were  
54 positive with Gram-positive cocci in clusters. They were directly tested for the presence  
55 of *S. aureus*/MRSA with the Xpert® MRSA/SA Blood Culture kit (Cepheid), as  
56 recommended by the manufacturer. The presence of *S. aureus* was confirmed by *spa*  
57 gene detection, but the presence of a MRSA was not retained as positive, despite a  
58 positive *mecA* PCR result, due to the absence of amplification for the *orfX-SCCmec*  
59 junction. The day after, antimicrobial susceptibility testing revealed a MRSA profile  
60 (strain LIM88). Whole-genome sequencing (WGS) of LIM88 was performed using the  
61 Ion Proton™ system (ThermoFisher Scientific), according to the manufacturer's  
62 instructions. The reads were assembled using MIRA (Mimicking Intelligent Read  
63 Assembly). WGS analysis, using both the SRST2 v0.2.0 [10] and RidomsStaphType  
64 v2.0 (Ridom GmbH), revealed that LIM88 belonged to the ST5 genetic background  
65 and that it had a *spa*-type t777.

66 Characterization of the SCC elements was performed by searching for site-specific  
67 insertion sequences (ISS) characteristic of SCC elements [11] and associated direct  
68 and inverted repeats. Open reading frame (ORF) detection and annotation was  
69 performed using the RAST service [12] and all proteins were blasted [13] against the  
70 NCBI *nr* nucleotide database to search for the closest protein hits. Genomic  
71 comparison between SCC elements was conducted using a combination of Mauve  
72 Progressive [14] and *blastn* results [13].

73 Screening for the new SCC*mec* element in 40 MRSA isolated from blood cultures,  
74 during 2015 in the teaching hospital of Limoges (CHU Limoges), was performed using  
75 Kondo's PCR [15] primers targeting the concomitant presence of the recombinases  
76 complexes *ccrC* and *ccrAB* type 4.

### 77 **3. Results and Discussion**

78 We identified the presence of 4 ISS comprising direct repeat (DR) sequences typical  
79 of SCC-like cassettes. Thus, LIM88 carries a SCC composite island of 39.6 kb with 3  
80 SCC elements in tandem: a  $\Psi$ SCC<sub>*cop/ars*</sub> element (without recombinase genes), a SCC  
81 element with a *ccrC* recombinase (called SCC<sub>*Lim88A*</sub>) and a SCC*mec* element with a  
82 type 4 *ccrAB* complex (Figure 1). The nucleotide sequence of this novel SCC  
83 composite island was deposited in the NCBI database under the accession number  
84 GenBank KX646745.

85 Comparison of the 16.6 kb SCC*mec* (ORF25-40, Table S1) element including 16 ORFs  
86 found in strain LIM88 with the 23kb type VI SCC*mec* element of the New Paediatric  
87 ST5, t777 MRSA clone (strain HDE288) [9] reveals a high nucleotide similarity (>89%)  
88 of the "non-essential" region J3, the type B1 *mec* complex (IS431-*mecA*- $\delta$ *mecR*-  
89 IS1272), the "non-essential" region J2 and the *ccrAB* (type 4) complex found in both  
90 SCC*mec* elements (Figure 2A). Only the J1 regions are distinct (Figure 2A).  
91 Interestingly, the J1 region of LIM88 SCC*mec* type VI element shows an overwhelming  
92 similarity (more than 90% nucleotide Identity) with a region of a SCC element found in  
93 *S. epidermidis* strain ATCC12228 (Figure 2B), which encompasses the *ccrA4B4*  
94 complex and a *copA/cadA* resistance gene. Based on these data, the SCC*mec*  
95 element found in strain LIM88 can be classified as a novel subtype of SCC*mec* type  
96 VI element, named SCC*mec*VIb after consulting and with the agreement of the

97 International Working Group on the Classification of Staphylococcal Cassette  
98 Chromosome Elements (IWG-SCC).

99 Immediately downstream from the SCC<sub>mec</sub> element, a 11.6 kb SCC element (ORF13-  
100 24, Table S1) carrying 12 ORFs, among which a *ccrC* recombinase (allele 7) and no  
101 known specific virulence or resistance markers, was identified. This element was  
102 named SCC<sub>Lim88A</sub>. Genomic comparison reveals that this region is highly similar to the  
103 *rlmH* proximal J3 region of SCC<sub>mecZ<sub>H47</sub></sub>, a SCC<sub>mec</sub> element previously described in a  
104 CC5 strain isolated from drug-users in Switzerland [16] but, also, to the J3 region found  
105 in a composite island of SCC elements (SCC-CI) of the *S. haemolyticus* NW19A  
106 (GenBank KM369884) [177], a strain isolated from bovine milk (Figure 2C). This  
107 mosaic structure is even more surprising when we look at the SCC<sub>mec</sub> element  
108 inserted immediately downstream SCC<sub>Lim88A</sub>. The J3 and *mecA* complex itself of the  
109 SCC<sub>mec</sub> element are highly similar (90 % nucleotide identity) to the *mecA* complex  
110 and its proximal J3 region as found in 3 different SCC<sub>mec</sub> elements: i) the SCC<sub>mecZ<sub>H47</sub></sub>  
111 (SCC<sub>mec</sub> new subtype IV) but without the aminoglycoside resistance transposon  
112 Tn4001 inserted in the *mecR* gene (Figure 2C); ii) the SCC-CI of *S. haemolyticus*  
113 NW19A (Figure 2C) and the SCC<sub>mec</sub> type VIa element of strain HDE288 of the ST5-  
114 MRSA New Paediatrics clone, as presented in Figure 2A.

115 Finally, the third SCC element is, in fact, a pseudo-SCC, called  $\Psi$ SCC<sub>cop/ars</sub>, as it does  
116 not carry any recombinase. This 11.1 kb region, located immediately downstream from  
117 the *rlmH* gene, harbors 12 ORFS (ORF 1-12, Table S1). Almost all of them encode for  
118 heavy metal detoxification functions: two copper related resistance genes (ORF1 and  
119 ORF2) and a complete arsenic resistance operon (*ars* operon, ORF4-8, ORF10). As  
120 presented in Figures 2B and 2C, this detoxification cluster is present in SCC elements

121 found in other staphylococci species, such as the SCC composite island (SCC-CI)  
122 found in the SCC<sub>mec</sub> element of a *S. epidermidis* strain M13/0453 (GenBank  
123 MF062491.1) [18] or the SCC-CI of *S. haemolyticus* strain NW19A (GenBank  
124 KM369884). The comparison with other simple or composite SCC elements does not  
125 help to clarify the origin of this heavy metal resistance cluster as this element is part of  
126 canonical SCC elements (carrying within them a cassette chromosomal recombinase)  
127 (Figure 2B) but also is part of longer pseudo-SCC elements (SCC elements without  
128 the site specific recombinases) (Figure 2C). Nonetheless, the closeness of both  
129 functional and truncated IS nearby this heavy metal cluster in almost all SCC elements  
130 suggest that they may play a role in the transfer and insertion of this resistance cluster.  
131 No intermediate SCC elements were found in public databases including NCBI or  
132 EMBL. The shared similarity with different SCC elements from different staphylococcal  
133 species suggests an array of recombination events before the final structure of the  
134 SCC-CI, as found in strain LIM88, with no certainty as to the ancestral donor-SCC  
135 elements. The presence of this atypical composite island  $\Psi$ SCC<sub>cop/ars</sub>-SCC<sub>Lim88A</sub>-  
136 SCC<sub>mecVIb</sub> composed by 3 distinct SCC elements, with a non-SCC<sub>mec</sub> cassette  
137 inserted at the end of the *rlmH* gene, is likely the reason for the absence of amplification  
138 of the *orfX*-SCC<sub>mec</sub> junction when using the Xpert<sup>®</sup> MRSA/SA Blood Culture kit.  
139 Phylogenetic analysis of LIM88 and other CC5 MRSA strains, based on 2288 core  
140 SNP, suggests the emergence of a novel clonal ST5 MRSA population harboring this  
141 novel composite SCC-CI (Figure S1).

142 A preliminary screening of 40 MRSA isolated from blood culture during 2015,  
143 suggests that the new ST5-MRSA lineage, carrying the novel SCC-CI  $\Psi$ SCC<sub>cop/ars</sub>-  
144 SCC<sub>Lim88A</sub>-SCC<sub>mecVIb</sub> element, represents 15% (n=6 isolates) of blood culture

145 MRSA strains isolated in the CHU Limoges. LIM88 and the other 6 MRSA strains were  
146 coresistant to fluoroquinolones but susceptible to all other antibiotic classes, notably to  
147 kanamycin. One out of the other 6 strains was also resistant to fosfomycin.

148

#### 149 **4. Conclusion:**

150 We report an original mosaic structure of the staphylococcal chromosome cassette  
151 composite island  $\Psi$ SCC<sub>cop/ars</sub>-SCC<sub>Lim88A</sub>-SCC<sub>mecVIb</sub> element carried by a ST5 MRSA  
152 (strain LIM88) isolated in Limoges, France. Investigations are now ongoing to  
153 accurately characterize this novel lineage and to determine the prevalence and the  
154 regional *versus* national distribution of this emerging ST5 lineage in France.

155

#### 156 **Acknowledgments**

157 This work was presented at the 2016 ASM Microbe congress in June 2016 (Boston,  
158 USA), Poster Saturday-417. We thank the Limoges University BISCEm platform for  
159 technical assistance in WGS and the French “Groupe de Microbiologie Clinique”  
160 (GMC).

161

#### 162 **Declarations**

163 **Funding** : No funding

164 **Competing Interests** : No conflict of Interest for all authors

165 **Ethical Approval** : Not required

166 **References:**

- 167 [1] Utsui Y, Yokota T. Role of an altered penicillin-binding protein in methicillin- and  
168 cephem-resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother*  
169 1985;28:397–403.
- 170 [2] Katayama Y, Ito T, Hiramatsu K. Genetic Organization of the Chromosome  
171 Region Surrounding *mecA* in Clinical Staphylococcal Strains: Role of IS431-Mediated  
172 *mecI* Deletion in Expression of Resistance in *mecA*-Carrying, Low-Level Methicillin-  
173 Resistant *Staphylococcus haemolyticus*. *Antimicrob Agents Chemother*  
174 2001;45:1955–63. doi:10.1128/AAC.45.7.1955-1963.2001.
- 175 [3] Hiramatsu K. Vancomycin-resistant *Staphylococcus aureus*: a new model of  
176 antibiotic resistance. *Lancet Infect Dis* 2001;1:147–55.
- 177 [4] Nübel U, Roumagnac P, Feldkamp M, Song J-H, Ko KS, Huang Y-C, et al.  
178 Frequent emergence and limited geographic dispersal of methicillin-resistant  
179 *Staphylococcus aureus*. *P Natl Acad Sci* 2008;105:14130–5.  
180 doi:10.1073/pnas.0804178105.
- 181 [5] Chambers HF, Deleo FR. Waves of resistance: *Staphylococcus aureus* in the  
182 antibiotic era. *Nat Rev Microbiol* 2009;7:629–41. doi:10.1038/nrmicro2200.
- 183 [6] Monecke S, Müller E, Schwarz S, Hotzel H, Ehricht R. Rapid Microarray-Based  
184 Identification of Different *mecA* Alleles in Staphylococci. *Antimicrob Agents Chemother*  
185 2012;56:5547–54. doi:10.1128/AAC.00574-12.
- 186 [7] Ito T, Katayama Y, Hiramatsu K. Cloning and nucleotide sequence determination  
187 of the entire *mec* DNA of pre-methicillin-resistant *Staphylococcus aureus* N315.  
188 *Antimicrob Agents Chemother* 1999;43:1449–58.

- 189 [8] Sá-Leão R, Santos Sanches I, Dias D, Peres I, Barros RM, de Lencastre H.  
190 Detection of an archaic clone of *Staphylococcus aureus* with low-level resistance to  
191 methicillin in a pediatric hospital in Portugal and in international samples: relics of a  
192 formerly widely disseminated strain? *J Clin Microbiol* 1999;37:1913–20.
- 193 [9] Oliveira DC, Tomasz A, de Lencastre H. The evolution of pandemic clones of  
194 methicillin-resistant *Staphylococcus aureus*: identification of two ancestral genetic  
195 backgrounds and the associated *mec* elements. *Microb Drug Resist* Larchmt N  
196 2001;7:349–61. doi:10.1089/10766290152773365.
- 197 [10] Inouye M, Dashnow H, Raven L-A, Schultz MB, Pope BJ, Tomita T, et al.  
198 SRST2: Rapid genomic surveillance for public health and hospital microbiology labs.  
199 *Genome Med* 2014;6:90. doi:10.1186/s13073-014-0090-6.
- 200 [11] Ito T, Ma XX, Takeuchi F, Okuma K YH, HiramatsuK. Novel Type V  
201 Staphylococcal Cassette Chromosome *mec* Driven by a Novel Cassette Chromosome  
202 Recombinase, *ccrC*. *Antimicrob Agents Chemother* 2004;48:2637–51.
- 203 [12] Aziz RK, Bartels D, Best AA, DeJongh M, Disz T, Edwards RA, et al. The RAST  
204 Server: rapid annotations using subsystems technology. *BMC Genomics* 2008;9:75.  
205 doi:10.1186/1471-2164-9-75.
- 206 [13] Altschul S. Gapped BLAST and PSI-BLAST: a new generation of protein  
207 database search programs. *Nucleic Acids Res* 1997;25:3389–402.  
208 doi:10.1093/nar/25.17.3389.
- 209 [14] Darling AE, Mau B, Perna NT. progressiveMauve: Multiple Genome Alignment  
210 with Gene Gain, Loss and Rearrangement. *PLoS ONE* 2010;5:e11147.  
211 doi:10.1371/journal.pone.0011147.

- 212 [15] Kondo Y, Ito T, Ma XX, Watanabe S, Kreiswirth BN, Etienne J, et al. Combination  
 213 of multiplex PCRs for staphylococcal cassette chromosome mec type assignment:  
 214 rapid identification system for mec, ccr, and major differences in junkyard regions.  
 215 *Antimicrob Agents Chemother* 2007;51:264–74.
- 216 [16] Heusser R, Ender M, Berger-Bächli B, McCallum N. Mosaic Staphylococcal  
 217 Cassette Chromosome mec Containing Two Recombinase Loci and a New mec  
 218 Complex, B2. *Antimicrob Agents Chemother* 2007;51:390–3.
- 219 [17] Xue H, Wu Z, Li L, Li F, Wang Y, Zhao X. Coexistence of Heavy Metal and  
 220 Antibiotic Resistance within a Novel Composite Staphylococcal Cassette Chromosome  
 221 in a *Staphylococcus haemolyticus* Isolate from Bovine Mastitis Milk. *Antimicrob Agents*  
 222 *Chemother* 2015;59:5788–92. doi:10.1128/AAC.04831-14.
- 223 [18] Lazaris A, Coleman DC, Kearns AM, Pichon B, Kinnevey PM, Earls MR, et al.  
 224 Novel multiresistance cfr plasmids in linezolid-resistant methicillin-resistant  
 225 *Staphylococcus epidermidis* and vancomycin-resistant *Enterococcus faecium* (VRE)  
 226 from a hospital outbreak: co-location of cfr and optrA in VRE. *J Antimicrob Chemother*  
 227 2017;72:3252–7. doi:10.1093/jac/dkx292.
- 228 doi:10.1128/AAC.00165-06.

229 **Figure 1. Schematic representation of the SCC composite island  $\Psi$ SCC<sub>*cop/ars*</sub>-**  
 230 **SCC<sub>Lim88A</sub>-SCC<sub>mec</sub> Vlb element in ST5 MRSA LIM88.**

231 The sequence of the  $\Psi$ SCC<sub>*cop/ars*</sub>-SCC<sub>Lim88A</sub>-SCC<sub>mec</sub> composite island of strain  
 232 LIM88 is represented with open reading frames (ORFs) shown as gray arrows  
 233 indicating the transcription direction. Colored arrows highlight specific genes according  
 234 to the following criteria: orange = copper resistance related genes (*copA* and *mco*,

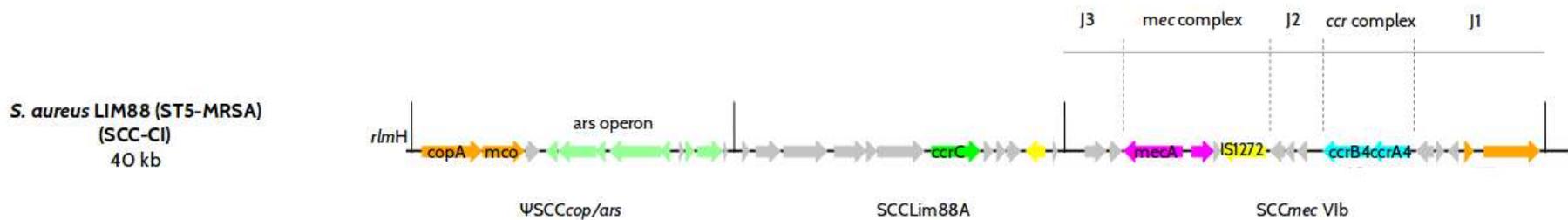
235 *copA/cadA*); light green = arsenic resistance related genes (*ars* operon); green =  
236 staphylococcal cassette recombinase type C gene (*ccrC*); cyan = staphylococcal  
237 cassette recombinase type AB genes (*ccrA4* and *ccrB4*); yellow = transposases (type  
238 IS431 and IS1272); magenta = *mecA* complex genes (*mecA* and truncated *mecR1*).  
239 The SSC*mec* element architecture with the “non-essential” J1, J2, J3 regions, *mec*  
240 complex and *ccr* complex are indicated above the SCC*mec* VIb element of strain  
241 LIM88.

242

243

244 **Figure 2. Comparison of the SCC composite island  $\Psi$ SCC<sub>*cop/ars*</sub>-SCC<sub>LIM88A</sub>-**  
245 **SCC*mec* in ST5 MRSA LIM88 with other SCC elements or SCC composite islands**  
246 **(SCC-CI) found in staphylococci.**

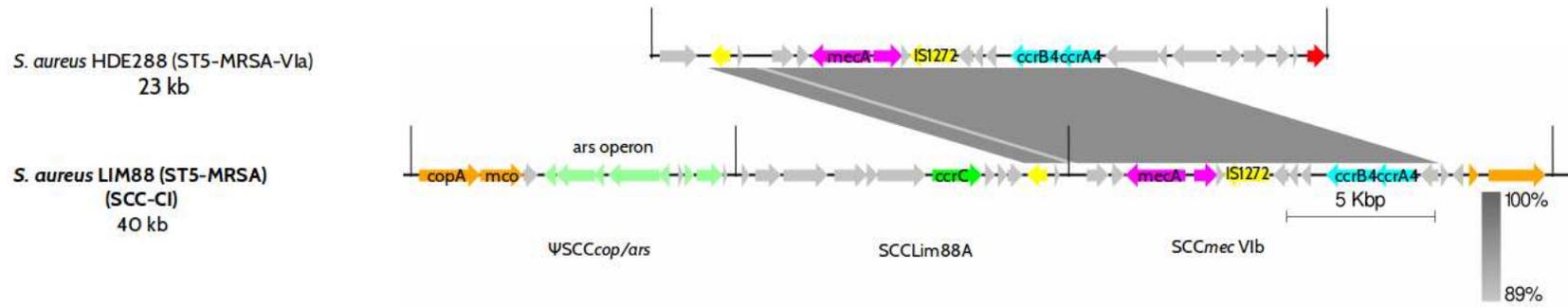
247 The SCC composite islands or SCC elements are represented with open reading  
248 frames (ORFs) shown as gray arrows indicating the transcription direction. Colored  
249 arrows highlight specific genes according to the following criteria: orange = copper  
250 resistance related genes; light green = arsenic resistance related genes; green =  
251 staphylococcal cassette recombinase type C gene (*ccrC*); cyan = staphylococcal  
252 cassette recombinase AB (*ccrA4B4*) genes; light blue = staphylococcal cassette  
253 recombinase AB (*ccrA2B2*) genes; dark blue = staphylococcal cassette recombinase  
254 AB (*ccrA3B3*) genes; yellow = transposases (type IS431 and IS1272); magenta =  
255 *mecA* complex genes and red = fusidic acid resistance gene (*fus*) in panel 2A or  
256 aminoglycoside resistance transposon Tn4001 in panel 2B. Homologous gene clusters  
257 between SCC elements are indicated by gray diamond areas. The percentage of  
258 homology is coded by a gray gradient as indicated in the figure.



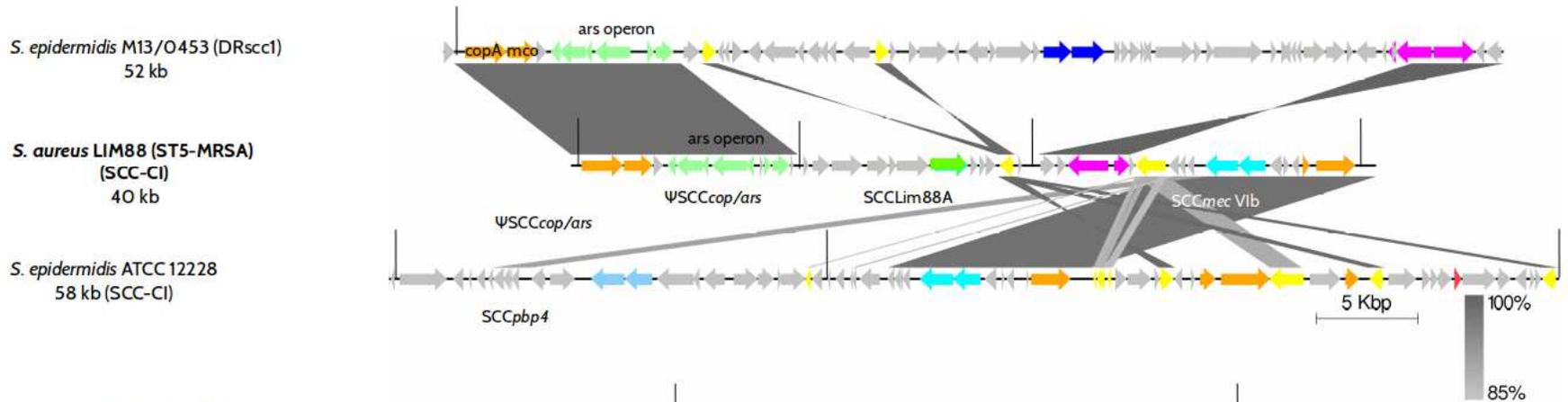
**Figure 1. Schematic representation of the SCC composite island  $\Psi$ SCC<sub>cop/ars</sub>-SCCLim88A-SCCmec VIb element in ST5 MRSA LIM88.**

The sequence of the  $\Psi$ SCC<sub>cop/ars</sub>-SCCLim88A-SCCmec composite island of strain LIM88 is represented with open reading frames (ORFs) shown as gray arrows indicating the transcription direction. Colored arrows highlight specific genes according to the following criteria: orange = copper resistance related genes (*copA* and *mco*, *copA/cadA*); light green = arsenic resistance related genes (*ars* operon); green = staphylococcal cassette recombinase type C gene (*ccrC*); cyan = staphylococcal cassette recombinase type AB genes (*ccrA4* and *ccrB4*); yellow = transposases (type *IS431* and *IS1272*); magenta = *mecA* complex genes (*mecA* and truncated *mecR1*). The SCCmec element architecture with the “non-essential” J1, J2, J3 regions, *mec* complex and *ccr* complex are indicated above the SCCmec VIb element of strain LIM88.

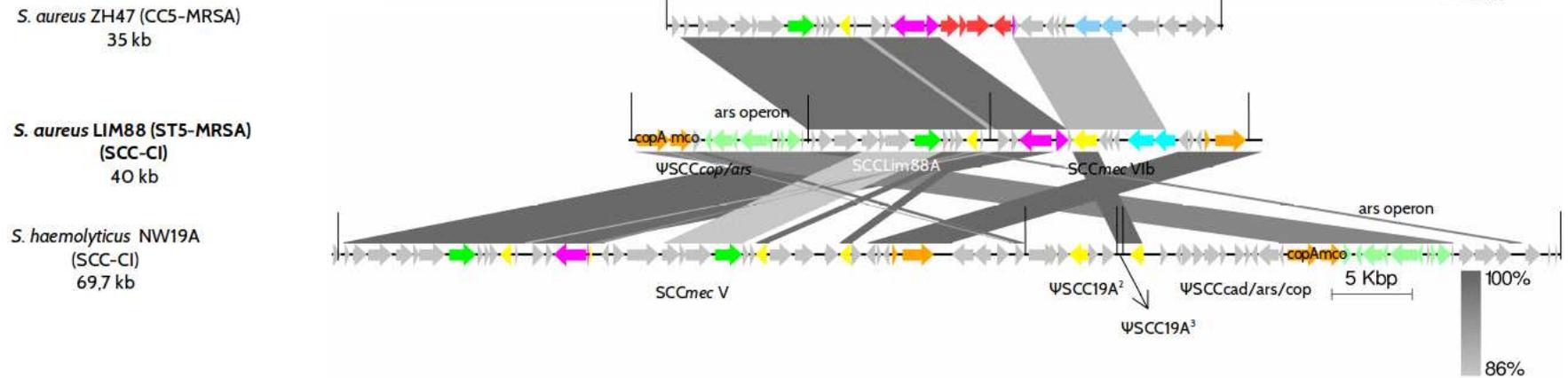
(A)



(B)



(C)



**Figure 2. Comparison of the SCC composite island  $\Psi$ SCC<sub>cop/ars</sub>-SCC<sub>Lim88A</sub>-SCC<sub>mec</sub> in ST5 MRSA LIM88 with other SCC elements or SCC composite islands (SCC-CI) found in staphylococci.**

The SCC composite islands or SCC elements are represented with open reading frames (ORFs) shown as gray arrows indicating the transcription direction. Colored arrows highlight specific genes according to the following criteria: orange = copper resistance related genes; light green = arsenic resistance related genes; green = staphylococcal cassette recombinase type C gene (*ccrC*); cyan = staphylococcal cassette recombinase AB (*ccrA4B4*) genes; light blue = staphylococcal cassette recombinase AB (*ccrA2B2*) genes; dark blue = staphylococcal cassette recombinase AB (*ccrA3B3*) genes; yellow = transposases (type IS431 and IS1272); magenta = *mecA* complex genes and red = fusidic acid resistance gene (*fus*) in panel 2A or aminoglycoside resistance transposon Tn4001 in panel 2B. Homologous gene clusters between SCC elements are indicated by gray diamond areas. The percentage of homology is coded by a gray gradient as indicated in the figure.