

COMMENTARY

Classification of Staphylococcal Cassette Chromosome *mec* (SCC*mec*): Guidelines for Reporting Novel SCC*mec* Elements^{∇†}

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

Staphylococci, which frequently colonize the skin and mucous membranes of humans and animals, have the capacity to acquire antimicrobial resistance determinants rapidly, particularly after the introduction of new antimicrobial agents into clinical practice. Because *Staphylococcus aureus* shows the highest pathogenic potential among the many species of staphylococci, the acquisition of resistance determinants by *S. aureus* has presented the greatest challenge to the treatment and control of staphylococcal infections. Methicillin-resistant *S. aureus* (MRSA) strains are particularly important because they are a leading cause of health care-associated infections worldwide, and have also emerged as a major cause of community-associated infections.

The defining feature of MRSA is the staphylococcal cassette chromosome *mec* (SCC*mec*). A detailed explanation for the term “SCC*mec*” is available at the website <http://www.staphylococcus.net>. This is a mobile genetic element that carries the central determinant for broad-spectrum beta-lactam resistance encoded by the *mecA* gene. The emergence of methicillin-resistant staphylococcal lineages is due to the acquisition and insertion of the SCC*mec* element into the chromosome of susceptible strains.

SCC*mec* elements are highly diverse in their structural organization and genetic content and have been classified into types and subtypes. It is now common practice to define MRSA clones by the combination of SCC*mec* type and the chromosomal background (i.e., sequence type [ST], as defined by multilocus sequence typing) in which SCC*mec* resides (e.g., ST22-SCC*mec* IV, abbreviated as ST22-IV) (5). Many types, subtypes, and variants of SCC*mec* elements and SCC elements lacking *mecA* have been reported without following any standardized, internationally agreed rules of nomenclature. Consequently, there are ambiguities and inconsistencies in the classification of SCC elements in the published literature to date. To address these issues, the International Working Group on the Classification of Staphylococcal Cassette Chromosome Elements (IWG-SCC) was organized to (i) form an intellectual network to contribute to the study of SCC elements, (ii) establish a consensus on

a uniform nomenclature system for SCC elements, (iii) define minimum requirements for the description of new SCC elements, and (iv) establish guidelines for the identification of SCC elements for epidemiological study (i.e., SCC*mec* typing). Herein, we propose guidelines for the classification of SCC*mec* and other SCC elements.

CHARACTERISTICS OF SCC*mec* ELEMENTS

Beta-lactams, which were among the first antimicrobial agents to be introduced into clinical practice, are still one of the most effective classes of antimicrobials used in human medicine. Methicillin, which was introduced in 1960, is a semisynthetic penicillin specifically designed for the treatment of infections caused by beta-lactamase-producing staphylococci. However, within 1 year following the introduction of methicillin into clinical practice, the first MRSA strains were reported from clinical infections. MRSA strains produce an additional penicillin-binding protein, known as either PBP2a or PBP2', which has a low affinity for most of the semisynthetic penicillins, e.g., methicillin, nafcillin, and oxacillin, as well as most cephem agents. PBP2a or PBP2' is encoded by an acquired gene, *mecA*, which has been cloned and sequenced along with the genes that control its expression, *mecRI* (encoding the signal transducer protein MecR1) and *mecI* (encoding the repressor protein MecI). When it became apparent that *mecA* was widely disseminated among multiple staphylococcal species, it was hypothesized that it could be carried on a mobile genetic element that could be easily transferred among staphylococcal species.

A genetic element that encoded methicillin resistance and carried unique site-specific recombinases designated as cassette chromosome recombinases (*ccr*) was subsequently identified and designated as SCC*mec* (8, 11). Soon after the initial description of SCC*mec*, several structurally different SCC*mec* elements were described. These elements shared several characteristics, as follows: (i) carriage of *mecA* in a *mec* gene complex, (ii) carriage of a *ccr* gene(s) (*ccrAB* and/or *ccrC*) in a *ccr* gene complex, (iii) integration at a specific site in the staphylococcal chromosome, referred to as the integration site sequence (ISS) for SCC, which serves as a target for *ccr*-mediated recombination, and (iv) the presence of flanking direct repeat (DR) sequences containing the ISS.

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TABLE 1. SCCmec types identified in *S. aureus*

SCCmec type	<i>ccr</i> gene complex ^a	<i>mec</i> gene complex
I	1 (A1B1)	B
II	2 (A2B2)	A
III	3 (A3B3)	A
IV	2 (A2B2)	B
V	5 (C)	C2
VI	4 (A4B4)	B
VII	5 (C)	C1
VIII	4 (A4B4) ^b	A

^a *ccr* genes in the gene complex are indicated in parentheses.

^b *ccrA4B4* genes found in type VIII SCCmec were nearly identical to those in the *S. epidermidis* SCC-CI element and showed nucleotide identities of 89.6% and 94.5% to those found in type VI SCCmec.

BASIC CONCEPTS FOR THE CLASSIFICATION OF SCCmec ELEMENTS

SCCmec elements are classified by a hierarchical system into types and subtypes. Types are defined by the combination of (i) the type of *ccr* gene complex, which is represented by the *ccr* gene allotype, and (ii) the class of the *mec* gene complex. These are the key elements of the cassette responsible for integration and excision of SCCmec and the beta-lactam resistance phenotype, respectively (Table 1 and Fig. 1).

***ccr* gene complex.** The *ccr* gene complex is composed of the *ccr* gene(s) and surrounding open reading frames (ORFs), several of which have unknown functions. Currently, three phylogenetically distinct *ccr* genes, *ccrA*, *ccrB*, and *ccrC*, have been identified in *S. aureus* with DNA sequence similarities below 50% (Fig. 2 and 3). The *ccrA* and *ccrB* genes that have been identified to date have been classified into four allotypes. In general, *ccr* genes with nucleotide identities more than 85% are assigned to the same allotype, whereas *ccr* genes that belong to different allotypes show nucleotide identities between 60% and 82%. All *ccrC* variants identified to date have shown $\geq 87\%$ similarity; thus, there is only one *ccrC* allotype. We suggest describing their differences as alleles by using previously used numbers, e.g., *ccrC1* allele 2 or *ccrC1* allele 8.

The classification of *ccr* genes is summarized in Fig. 2. In the proposed nomenclature, novel *ccr* genes should be defined based on DNA sequence similarities of $< 50\%$, and novel allotypes of *ccr* genes should be designated if their DNA sequence similarity identities are between 50% and 85%. This convention should be followed for naming novel *ccr* genes. In the future, it may be necessary to define additional allotypes, including those of *ccrC*.

The phylogenetic relationships and DNA sequence similarities of representative *ccr* genes, including those identified in staphylococci other than *S. aureus*, are illustrated (Fig. 3 and see Table S1 in the supplemental material, respectively). Although sequences derived from staphylococci other than *S. aureus* frequently diverge from those identified

in *S. aureus* isolates, all of them have been classified as *ccrA*, *ccrB*, or *ccrC*. In staphylococci other than *S. aureus*, a few extra *ccr* allotypes have been identified, as follows: *ccrA5* is the *ccrA* gene of *Staphylococcus pseudintermedius* KM241, *ccrB6* is the *ccrB* gene of *Staphylococcus saprophyticus* ATCC 15305, and *ccrB7* is the *ccrB* gene of *S. saprophyticus* TSU33.

The *ccr* gene complexes should be numbered according to the timing of their description. To date, two distinct groups have been reported, one carrying two adjacent *ccr* genes, *ccrA* and *ccrB*, and the other carrying *ccrC*. Based on allelic variations in *ccr*, a series of allotypes has been defined. The *ccr* gene complex identified in *S. aureus* includes type 1 (carrying *ccrA1B1*), type 2 (carrying *ccrA2B2*), type 3 (carrying *ccrA3B3*), type 4 (carrying *ccrA4B4*), and type 5 (carrying *ccrC*), which can be detected by conventional PCR analysis with pairs of specific primers.

***mec* gene complex.** The *mec* gene complex is composed of *mecA*, its regulatory genes, and associated insertion sequences. The class A *mec* gene complex (class A *mec*) is the prototype complex, which contains *mecA*, the complete *mecR1* and *mecI* regulatory genes upstream of *mecA*, and the hypervariable region (HVR) and insertion sequence IS431 downstream of *mecA*. The class B *mec* gene complex is composed of *mecA*, a truncated *mecR1* resulting from the insertion of IS1272 upstream of *mecA*, and HVR and IS431 downstream of *mecA*. The class C *mec* gene complex contains *mecA* and truncated *mecR1* by the insertion of IS431 upstream of *mecA* and HVR and IS431 downstream of *mecA*. There are two distinct class C *mec* gene complexes; in the class C1 *mec* gene complex, the IS431 upstream of *mecA* has the same orientation as the IS431 downstream of *mecA* (next to HVR), while in the class C2 *mec* gene complex, the orientation of IS431 upstream of *mecA* is reversed. C1 and C2 are regarded as different *mec* gene complexes since they have likely evolved independently. The class D *mec* gene complex is composed of *mecA* and Δ *mecR1* but does not carry an insertion sequence downstream of Δ *mecR1* (as determined by PCR analysis) (12).

Several variants within the major classes of the *mec* gene complex have been described, including insertions of IS431 or IS1182 upstream of *mecA* in the class A *mec* gene complex or insertion of Tn4001 upstream of *mecA* in the class B *mec* complex. These variants are indicated by a numerical string following the class (e.g., class B₂, indicated in Fig. 1).

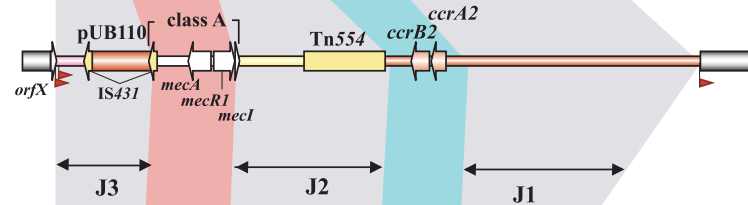
J regions: regions other than *mec* and *ccr* gene complexes. Besides the *mec* and *ccr* gene complexes, the SCCmec element also contains three so-called J regions, which constitute non-essential components of the cassette. These regions may carry additional antimicrobial resistance determinants. They were first designated as the L-C, C-M, and I-R regions but were later changed to J regions. We propose that the term J region refers to “joining region,” rather than the previously used “junkyard region.”

FIG. 1. Basic structures of representative SCCmec elements. The structures of SCCmec elements of representative strains are illustrated based on the following nucleotide sequences deposited in databases: NCTC10442 (AB033763), N315 (D86934), 85/2082 (AB037671), CA05 (AB063172), ZH47 (AM292304), WIS (AB121219), TSGH17 (AB512767), PM1 (AB462393), HDE288 (AF411935), JCSC6082 (AB373032), and C10684 (FJ390057). Red arrowheads indicate the ISS of SCC that comprise DR sequences.

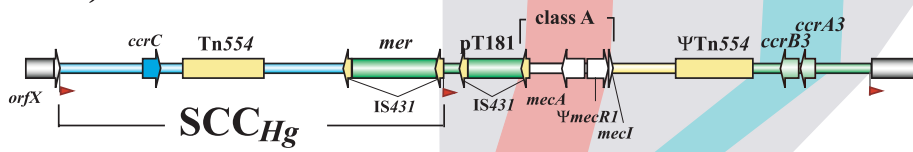
Type I(1B)
(NCTC10442)



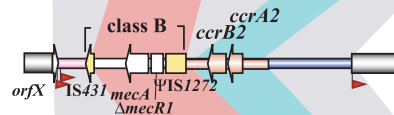
Type II(2A)
(N315)



Type III(3A)
(85/2082)



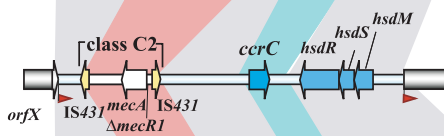
Type IV(2B)
(CA05)



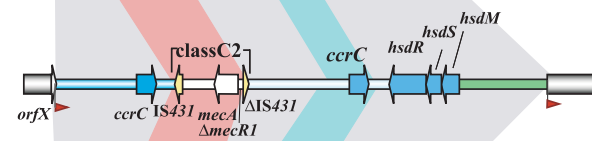
Type IV(2B&5)
(ZH47)



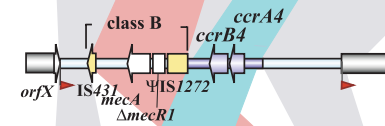
Type V(5C2)
(WIS)



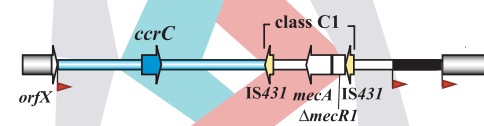
Type V(5C2&5)
(TSGH17, PM1)



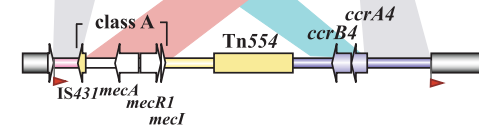
Type VI(4B)
(HDE288)



Type VII(5C1)
(JCSC6082)



Type VIII(4A)
(C10682)



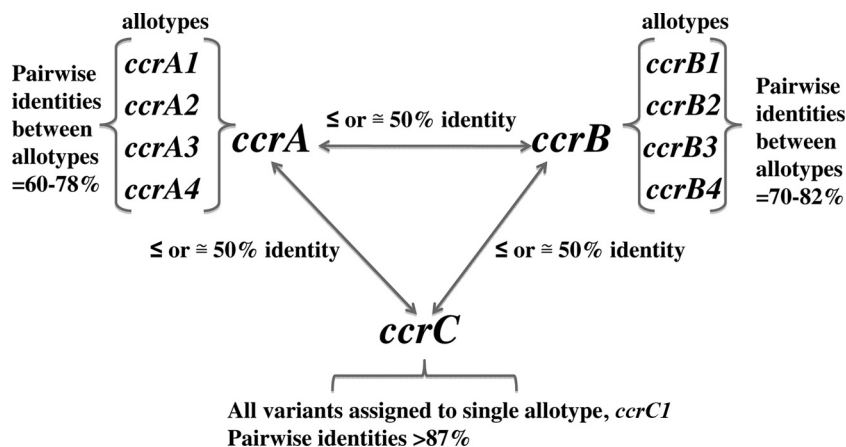


FIG. 2. Representation of the naming conventions for *ccr* genes in *S. aureus*.

J1 (formerly L-C) is the region between the right chromosomal junction and the *ccr* complex, J2 (C-M) is between the *ccr* gene complex and the *mec* gene complex, and J3 (I-R) is between the *mec* complex and the left chromosomal junction. Variations in the J regions within the same *mec-ccr* complex are used for defining SCC*mec* subtypes.

EIGHT CURRENTLY ESTABLISHED SCC*mec* TYPES

To date, eight SCC*mec* types have been described for *S. aureus* using the criteria described above (Table 1 and Fig. 1). The first three SCC*mec* elements were designated as types I, II, and III (8, 9). These were followed by reports of SCC*mec* types IV to VIII (1, 10, 15, 19, 23). This nomenclature should be retained, but an additional (more informative) system for naming the novel SCC*mec* elements, based on the type of *ccr* and class of *mec* present, is proposed. For example, type I (1B) SCC*mec* indicates an SCC*mec* harboring a type 1 *ccr* and a class B *mec* gene complex. The other known SCC*mec* types would be designated type II (2A), type III (3A), type IV (2B), type V (5C2), type VI (4B), type VII (5C1), and type VIII (4A). Thus, SCC*mec* types should be designated by roman numerals in the order in which they are reported, followed by the *ccr* gene complex and the *mec* gene complex together in parentheses.

Type III and VI SCC*mec* elements have been revised based on additional sequence information. The type III SCC*mec* element was reported to be 67 kb in length and was considered to be the longest SCC*mec* element (9). However, in 2006, it was reported that this 67-kb element was a composite of two smaller SCC elements; SCC*mercury* and type III (3A) SCC*mec* (carrying type 3 *ccr* and class A *mec*) integrated in tandem (4). To avoid confusing SCC*mercury* with SCC*mec*, the name of the former is changed to SCCHg. The SCC*mec* element carried by *S. aureus* strain HDE288 was first reported as type IV SCC*mec* (18) but was redefined as type VI SCC*mec* (4B) (19).

CLASSIFICATION OF SCC*mec* TYPES INTO SUBTYPES

Many different structures, including insertion sequences and transposons, have been identified among the major SCC*mec* types in regions other than the *mec* gene complex and *ccr* gene

complex, i.e., in the J regions. Each SCC*mec* type has therefore been further classified into subtypes based on the polymorphisms or variations in J regions within the same *ccr* gene complex and *mec* gene complex combination. Table 2 lists the SCC*mec* types/subtypes reported from *S. aureus* with major differences in the J regions for which either the entire or partial nucleotide sequences have been reported.

To avoid potential misclassification of new SCC*mec* elements into types or subtypes, reporting of novel SCC*mec* elements should be based on the entire nucleotide sequence of the element and not simply on PCR-based product sizes, which may be misleading.

Thus, novel SCC*mec* subtypes should be defined by the presence of specific DNA sequences located in J regions, including (i) characteristic genes, pseudogenes, or noncoding regions in J regions other than mobile genetic elements; and (ii) mobile genetic elements, e.g., insertion sequences, and plasmids or transposons, most of which encode antimicrobial resistance or other determinants.

To date, the following three methods have been used to describe subtypes of SCC*mec* elements: (i) expressing the J1 region differences as small letters, e.g., IVa, IVb, and IVc; (ii) expressing the differences due to the presence or absence of mobile genetic elements as capital letters, e.g., IA, IIA, and IVA; and (iii) expressing the differences in each J1, J2, and J3 region in Arabic numbers, which are given in the order of discovery, e.g., II.1.1.1, II.1.1.2, and II.2.1.1.

Since the first and second nomenclature systems have been used as markers for particular epidemic clonal lineages, the designations have been retained as generic names.

However, to cope with the increasing diversity of J regions of SCC*mec* elements being reported, the number of alphabetic letters will be limited. Therefore, we are developing a computer system to identify or specify the differences in J regions based on a binary system (i.e., the presence or absence of specific DNA regions) that has been developed by Stephens et al. (21). The system, which will be provided on a dedicated website (<http://www.SCCmec.org> [under construction]), will be helpful in delineating the differences in J regions among elements more clearly and will identify the sets of genetic markers needed to differentiate the elements efficiently. Once the com-

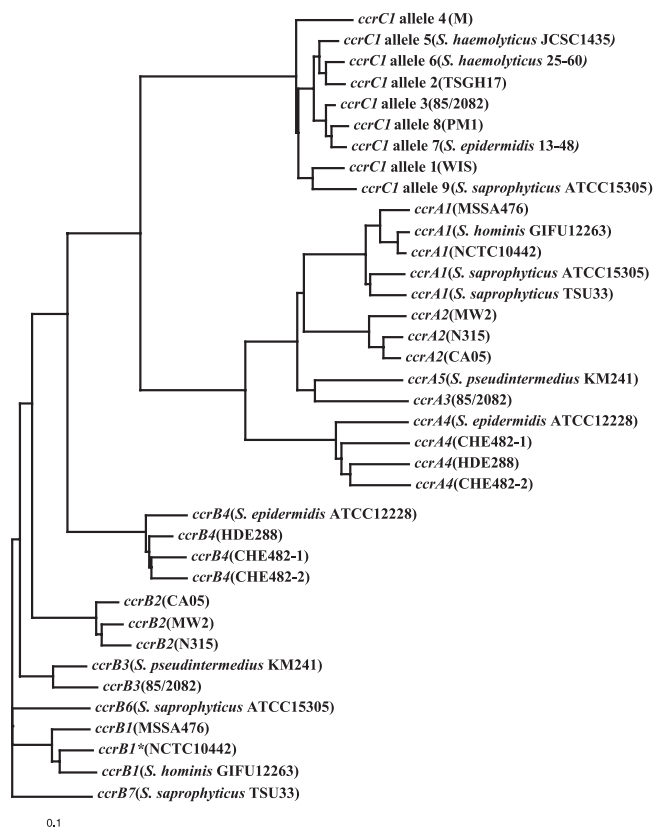


FIG. 3. Phylogenetic relationships among *ccrA* genes, *ccrB* genes, and *ccrC* genes. The nucleotide sequences of 37 *ccr* genes (14 *ccrA* genes, 14 *ccrB* genes, and 9 *ccrC* genes) (see Table S1 in the supplemental material) were aligned by using the ClustalX program. In parentheses, names of *S. aureus* strains carrying *ccr* genes are indicated. In the case of non-*S. aureus* strains, names of species as well as strains are indicated in parentheses. A phylogenetic tree was generated by the neighbor-joining method by creating 2,000 bootstrap replicates. The tree was visualized with TreeView software, which was obtained from the TreeView website (<http://taxonomy.zoology.gla.ac.uk/rd/treeview.html>).

puterized system is developed, new SCCmec subtype numbers will be assigned in an informative and definitive way.

COMPOSITES OF TWO OR MORE SCC ELEMENTS

Recently, SCCmec elements carrying two *ccr* gene complexes have been identified (Fig. 1). For example, the SCCmec carried by *S. aureus* strain ZH47 is composed of an SCC with *ccrC* and an SCCmec with a class B2 *mec* gene complex (a subclass of class B *mec* gene complex into which a transposon Tn4001 was integrated), a type 2 *ccr* gene complex, and a J1 region with homology to type IVc SCCmec (6). Although the two SCC elements are arranged in tandem, no characteristic DR sequence corresponding to ISS was identified at the junction regions, but two DR sequences were identified at the extremities of the composite element, suggesting that it is a single SCCmec containing two *ccr* gene complexes. Other examples include the SCCmec elements carried by Taiwanese *S. aureus* strains TSGH17 and PM1 (3, 22). These SCCmec elements are composed of an SCC with *ccrC1* allele 8 and an

SCCmec with a class C2 *mec* gene complex, a type 5 *ccr* gene complex carrying *ccrC1* allele 2, and J1 regions specific to the SCCmec and demarcated by two DR sequences at both extremities. When a composite SCC element carrying two *ccr* genes is identified, the association of *ccr* genes, *mec* gene complexes, and J regions in the composite should be compared to those described previously in order to identify if it harbors any extant type of SCCmec. Following this, the association of the SCCmec element with the other *ccr* gene should be determined in order to establish whether the presence of the two *ccr* genes is a result of two separately integrated SCC elements and/or the composite was generated by the fusion of the two elements following deletion of the original junction region containing the DR in ISS.

Ultimately, the element in *S. aureus* ZH47 was classified as a type IV SCCmec element (2B&5), and the elements in *S. aureus* strains TSGH17 and PM1 were classified as type V SCCmec elements (5C2&5), although that of PM1 had been tentatively reported as type VII SCCmec (22). In line with the proposed criteria, the SCCmec carried by *S. aureus* strain HU25, which was reported as type IIIA SCCmec, should be regarded as a composite of two SCC elements, SCCHg and type III SCCmec, because the region carrying characteristic nucleotide sequences at the junction of the two elements was deleted and only two DR sequences, one downstream of *orfX* and the other at the right end of type III SCCmec, could be detected (18).

It is likely that many such composite elements will be discovered since these deletions of the original junction region seem to occur frequently. It is difficult to discriminate the presence of composite elements from the presence of structures carrying two elements in tandem using the current PCR strategies for SCCmec typing. Thus, novel elements carrying two *ccr* genes should not be given a roman numeral as a novel “type,” but rather should be categorized as an SCCmec type variant based on the known type of SCCmec present in the composite element.

CLASSIFICATION OF SCC ELEMENTS THAT DO NOT CARRY *mecA*

Interestingly, SCC elements that do not carry *mecA* but contain other characteristic genes (e.g., capsule gene cluster, fusidic acid resistance, or the mercury resistance operon) have also been identified in staphylococci. These elements share the following characteristics with SCCmec: carriage of a *ccr* gene(s) (*ccrAB* and/or *ccrC*) in a *ccr* gene complex, integration at ISS in the staphylococcal chromosome, and the presence of flanking DR sequences containing the ISS.

We recommend that SCC elements be described by adding the suffix describing the genes’ names or their functions after SCC. For example, SCCcap1 carries the type 1 capsule gene cluster, SCCfur carries fusidic acid resistance, and SCCHg carries the mercury resistance operon. If no genes with inferable functions are found in the SCC, we recommend describing the SCC elements by adding the name of the strain, e.g., SCC₄₇₆.

In addition, staphylococci can also harbor SCC-like regions similar to SCC that are integrated at ISS and bracketed by ISS but differ from SCC in that they do not harbor a *ccr* gene(s). They are diverse in size, from the shortest (0.1 kb) to the longest (34 kb), and have been described in different ways, e.g., SCC-like elements, an arginine catabolic mobile element, a

TABLE 2. SCCmec elements identified in MRSA^a

SCCmec type ^b	Reported name ^c	Major characteristics of J regions ^d	Representative strain(s)	Reference(s) and/or accession no. ^e
I (1B)	I	J1, subtype 1-specific ORFs (<i>pls</i>); J3, <i>dcs</i>	NCTC10442, COL	9, 18
	I.2	J1, subtype 2-specific ORFs; J3, <i>dcs</i> and pUB110	PL72	18
II (2A)	II	J1, subtype 1-specific ORFs (<i>kdp</i>); J2, subtype 1-specific ORFs and Tn554; J3, <i>dcs</i> and pUB110	N315	18
	IIb	J1, subtype 2-specific ORFs; J2, subtype 1-specific ORFs and Tn554; J3, <i>dcs</i>	JCSC3063	7
	IIb	J1, subtype 3-specific ORFs; J2, subtype 1-specific ORFs; J3, <i>dcs</i> and pUB110	AR05/0.1345	20
	IIe	J1, subtype 3-specific ORFs; J2, short J2 region the same as subtype 1 and Tn554; J3, <i>dcs</i> and pUB110	AR13.1/3330.2	20
	II.4.1.1	J1, subtype 4-specific ORFs; J2, subtype 1-specific ORFs and Tn554; J3, <i>dcs</i> and pUB110	RN7170	13
III (3A)	III	J1, subtype 1-specific ORFs; J2, subtype 1-specific ORFs and Ψ Tn554; J3, subtype 1-specific ORFs and pT181	85/2082, ANS46	9, 18
	IIIA	J1, subtype 1-specific ORFs; J2, subtype 1-specific ORFs and Ψ Tn554; J3, subtype 1-specific ORFs, pT181, and SCC _{Hg} carrying <i>ccrC</i>	HU25	18
IV (2B)	IVa	J1, subtype 1-specific ORFs; J3, <i>dcs</i>	CA05, MW2	15
	IVb	J1, subtype 2-specific ORFs; J3, <i>dcs</i>	8/6-3P	15
	IVc	J1, subtype 3-specific ORFs; J3, <i>dcs</i> and Tn4001	81/108	16
	IVc	J1, subtype 3-specific ORFs; J3, <i>dcs</i>	2314	AY271717
	IVA	J1, subtype 3-specific ORFs; J3, <i>dcs</i> and pUB110	cm11	EU437549
	IVE	J1, subtype 3-specific ORFs; J3, subtype 2-specific ORFs	AR43/3330.1	20
	IVd	J1, subtype 4-specific ORFs; J3, <i>dcs</i>	JCSC4469	16
	IVg	J1, subtype 5-specific ORFs; J3, <i>dcs</i>	M03-68	14
	IVh	J1, subtype 6-specific ORFs; J3, <i>dcs</i>	EMRSA-15	17
	IVi	J1, subtype 7-specific ORFs; J3, <i>dcs</i>	JCSC6668	2
	IVj	J1, subtype 8-specific ORFs; J3, <i>dcs</i>	JCSC6670	2
IV (2B&5)	IV variant	J1, subtype 3-specific ORFs; J3, SCC carrying <i>ccrC</i>	ZH47	6
V (5C2)	V	J1, subtype 1-specific ORFs; J2, subtype 1-specific ORFs; J3, subtype 1-specific ORFs	WIS(WBG8318)	10
V (5C2&5)	VT, VII	J1, subtype 2-specific ORFs; J2, subtype 2-specific ORFs; J3, SCC carrying <i>ccrC</i>	TSGH17, PM1	3, 22
VI (4B)	VI	J1, subtype 1-specific ORFs; J3, <i>dcs</i>	HDE288	19
VII (5C1)	5C1	J1, subtype 1-specific ORFs; J2, subtype 1-specific ORFs; J3, subtype 1-specific ORFs	JCSC6082	1
VIII (4A)	VIII	J1, subtype 1-specific ORFs; J2, subtype 1-specific ORFs; J3, subtype 1-specific ORFs	C10682, BK20781	23; FJ670542

^a SCCmec elements that satisfy the following criteria are listed as follows: entire regions of SCCmec elements have been sequenced, or the essential parts of the *mec* gene complex and the *ccr* gene complex have been fully sequenced.

^b The first categories for classifying SCCmec elements. The combinations of the *ccr* gene complex and the *mec* gene complex carried by the elements are indicated in parentheses.

^c The names reported in original literature are listed. Assigned numbers or names that specify these elements would be given by IWG-SCC and would be seen at the website (<http://www.SCCmec.org> [under construction]).

^d Key loci are indicated in parentheses. *pls*, plasmin-sensitive surface protein; *dcs*, downstream constant segment; *kdp*, potassium-dependent ATPase operon.

^e GenBank/EMBL/DBJ accession numbers are indicated in cases of direct submission.

cassette chromosome, or an SCCmec insertion site genomic sequence. We suggest describing these elements as pseudo-SCC elements (ψ SCC). We recommend that these ψ SCC elements be designated by adding the suffix describing the genes' names or their functions or by adding the name of the strain, similar to the case of SCC. In some cases, these ψ SCCs are integrated in tandem with the SCCmec element as a region of a large cluster of foreign DNA in genome-sequenced staphylococcal strains.

RECOMMENDATIONS AND CONCLUSIONS

Researchers are encouraged to determine the entire nucleotide sequence of any putative novel SCCmec elements. It is also strongly recommended that all researchers about to submit a paper reporting a novel type of SCC element consult one of the members of the IWG-SCC in order to determine the most appropriate name for the new type. The working group will provide a Web page dedicated to the SCCmec element

with updated information on SCCmec elements, a detailed classification system based on the differences in J regions, and currently available typing methods at <http://www.staphylococcus.net> and/or <http://www.SCCmec.org/> (under construction). We hope that all researchers refer to this website to obtain relevant information on the epidemiological characterization of the SCCmec element.

Evaluation of the appropriate PCR-based strategies to be used in the epidemiological identification of SCCmec elements and the classification of SCC elements carried by staphylococcal strains other than those of *S. aureus* is under discussion and will be addressed in the future.

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REFERENCES

- Berglund, C., T. Ito, M. Ikeda, X. X. Ma, B. Söderquist, and K. Hiramatsu. 2008. Novel type of staphylococcal cassette chromosome *mec* in a methicillin-resistant *Staphylococcus aureus* strain isolated in Sweden. *Antimicrob. Agents Chemother.* **52**:3512–3516.
- Berglund, C., T. Ito, X. X. Ma, M. Ikeda, S. Watanabe, B. Soderquist, and K. Hiramatsu. 2009. Genetic diversity of methicillin-resistant *Staphylococcus aureus* carrying type IV SCCmec in Orebro County and the western region of Sweden. *J. Antimicrob. Chemother.* **63**:32–41.
- Boyle-Vavra, S., B. Ereshefsky, C. C. Wang, and R. S. Daum. 2005. Successful multiresistant community-associated methicillin-resistant *Staphylococcus aureus* lineage from Taipei, Taiwan, that carries either the novel staphylococcal chromosome cassette *mec* (SCCmec) type VT or SCCmec type IV. *J. Clin. Microbiol.* **43**:4719–4730.
- Chongtrakool, P., T. Ito, X. X. Ma, Y. Kondo, S. Trakulsomboon, C. Tienasitorn, M. Jamklang, T. Chavalit, J. H. Song, and K. Hiramatsu. 2006. Staphylococcal cassette chromosome *mec* (SCCmec) typing of methicillin-resistant *Staphylococcus aureus* strains isolated in 11 Asian countries: a proposal for a new nomenclature for SCCmec elements. *Antimicrob. Agents Chemother.* **50**:1001–1012.
- Enright, M. C., D. A. Robinson, G. Randle, E. J. Feil, H. Grundmann, and B. G. Spratt. 2002. The evolutionary history of methicillin-resistant *Staphylococcus aureus* (MRSA). *Proc. Natl. Acad. Sci. USA* **99**:7687–7692.
- Heusser, R., M. Ender, B. Berger-Bachi, and N. McCallum. 2007. Mosaic staphylococcal cassette chromosome *mec* containing two recombinase loci and a new *mec* complex, B2. *Antimicrob. Agents Chemother.* **51**:390–393.
- Hisata, K., K. Kuwahara-Arai, M. Yamamoto, T. Ito, Y. Nakatomi, L. Cui, T. Baba, M. Terasawa, C. Sotozono, S. Kinoshita, Y. Yamashiro, and K. Hiramatsu. 2005. Dissemination of methicillin-resistant staphylococci among healthy Japanese children. *J. Clin. Microbiol.* **43**:3364–3372.
- Ito, T., Y. Katayama, and K. Hiramatsu. 1999. Cloning and nucleotide sequence determination of the entire *mec* DNA of pre-methicillin-resistant *Staphylococcus aureus* N315. *Antimicrob. Agents Chemother.* **43**:1449–1458.
- Ito, T., Y. Katayama, K. Asada, N. Mori, K. Tsutsumimoto, C. Tienasitorn, and K. Hiramatsu. 2001. Structural comparison of three types of staphylococcal cassette chromosome *mec* integrated in the chromosome in methicillin-resistant *Staphylococcus aureus*. *Antimicrob. Agents Chemother.* **45**:1323–1336.
- Ito, T., X. X. Ma, F. Takeuchi, K. Okuma, H. Yuzawa, and K. Hiramatsu. 2004. Novel type V staphylococcal cassette chromosome *mec* driven by a novel cassette chromosome recombinase, *ccrC*. *Antimicrob. Agents Chemother.* **48**:2637–2651.
- Katayama, Y., T. Ito, and K. Hiramatsu. 2000. A new class of genetic element, staphylococcal cassette chromosome *mec*, encodes methicillin resistance in *Staphylococcus aureus*. *Antimicrob. Agents Chemother.* **44**:1549–1555.
- Katayama, Y., T. Ito, and K. Hiramatsu. 2001. Genetic organization of the chromosome region surrounding *mecA* in clinical staphylococcal strains: role of IS431-mediated *mecI* deletion in expression of resistance in *mecA*-carrying, low-level methicillin-resistant *Staphylococcus haemolyticus*. *Antimicrob. Agents Chemother.* **45**:1955–1963.
- Kondo, Y., T. Ito, X. X. Ma, S. Watanabe, B. N. Kreiswirth, J. Etienne, and K. Hiramatsu. 2007. Combination of multiplex PCRs for staphylococcal cassette chromosome *mec* type assignment: rapid identification system for *mec*, *ccr*, and major differences in junkyard regions. *Antimicrob. Agents Chemother.* **51**:264–274.
- Kwon, N. H., K. T. Park, J. S. Moon, W. K. Jung, S. H. Kim, J. M. Kim, S. K. Hong, H. C. Koo, Y. S. Joo, and Y. H. Park. 2005. Staphylococcal cassette chromosome *mec* (SCCmec) characterization and molecular analysis for methicillin-resistant *Staphylococcus aureus* and novel SCCmec subtype IVg isolated from bovine milk in Korea. *J. Antimicrob. Chemother.* **56**:624–632.
- Ma, X. X., T. Ito, C. Tienasitorn, M. Jamklang, P. Chongtrakool, S. Boyle-Vavra, R. S. Daum, and K. Hiramatsu. 2002. Novel type of staphylococcal cassette chromosome *mec* identified in community-acquired methicillin-resistant *Staphylococcus aureus* strains. *Antimicrob. Agents Chemother.* **46**:1147–1152.
- Ma, X. X., T. Ito, P. Chongtrakool, and K. Hiramatsu. 2006. Predominance of clones carrying Pantone-Valentine leukocidin genes among methicillin-resistant *Staphylococcus aureus* strains isolated in Japanese hospitals from 1979 to 1985. *J. Clin. Microbiol.* **44**:4515–4527.
- Milheiro, C., D. C. Oliveira, and H. de Lencastre. 2007. Multiplex PCR strategy for subtyping the staphylococcal cassette chromosome *mec* type IV in methicillin-resistant *Staphylococcus aureus*: 'SCCmec IV multiplex'. *J. Antimicrob. Chemother.* **60**:42–48.
- Oliveira, D. C., A. Tomasz, and H. Lencastre. 2001. The evolution of pandemic clones of methicillin-resistant *Staphylococcus aureus*: identification of two ancestral genetic backgrounds and the associated *mec* elements. *Microb. Drug Resist.* **7**:349–361.
- Oliveira, D. C., C. Milheiro, and H. de Lencastre. 2006. Redefining a structural variant of staphylococcal cassette chromosome *mec*, SCCmec type VI. *Antimicrob. Agents Chemother.* **50**:3457–3459.
- Shore, A., A. S. Rossney, C. T. Keane, M. C. Enright, and D. C. Coleman. 2005. Seven novel variants of the staphylococcal chromosomal cassette *mec* in methicillin-resistant *Staphylococcus aureus* isolates from Ireland. *Antimicrob. Agents Chemother.* **49**:2070–2083.
- Stephens, A. J., F. Huygens, and P. M. Giffard. 2007. Systematic derivation of marker sets for staphylococcal cassette chromosome *mec* typing. *Antimicrob. Agents Chemother.* **51**:2954–2964.
- Takano, T., W. Higuchi, T. Otsuka, T. Baranovich, S. Enany, K. Saito, H. Isobe, S. Dohmae, K. Ozaki, M. Takano, Y. Iwao, M. Shibuya, T. Okubo, S. Yabe, D. Shi, I. Reva, L. J. Teng, and T. Yamamoto. 2008. Novel characteristics of community-acquired methicillin-resistant *Staphylococcus aureus* strains belonging to multilocus sequence type 59 in Taiwan. *Antimicrob. Agents Chemother.* **52**:837–845.
- Zhang, K., J. A. McClure, S. Elsayed, and J. M. Conly. 2009. Novel staphylococcal cassette chromosome *mec* type, tentatively designated type VIII, harboring class A *mec* and type 4 *ccr* gene complexes in a Canadian epidemic strain of methicillin-resistant *Staphylococcus aureus*. *Antimicrob. Agents Chemother.* **53**:531–540.

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