Novel Organization of the Staphylococcal Cassette Chromosome mec Composite Island in Clinical *Staphylococcus haemolyticus* and *Staphylococcus hominis* Subspecies *hominis* Isolates from Dogs

Nathita Phumthanakorn, Thidathip Wongsurawat, Piroon Jenjaroenpun, Alongkorn Kurilung, Nuvee Prapasarakul

*Department of Pre-Clinic and Applied Animal Science, Faculty of Veterinary Science, Mahidol University, Nakhon Pathom, Thailand*

*Division of Bioinformatics and Data Management for Research, Research Group and Research Network Division, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

*Siriraj Metabolomics and Phenomics Center, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

*Department of Veterinary Microbiology, Faculty of Veterinary Science, Chulalongkorn University, Bangkok, Thailand*

*Center of Excellence in Diagnostic and Monitoring of Animal Pathogens, Chulalongkorn University, Bangkok, Thailand*

**ABSTRACT** *Staphylococcus haemolyticus* and *Staphylococcus hominis* subsp. *hominis* are common coagulase-negative *staphylococcus* opportunistic pathogens. In Thailand, the clinical strains *S. haemolyticus* 1864 and 48 and *S. hominis* subsp. *hominis* 384 and 371 have been recovered from sick dogs. These strains were methicillin resistant with the nontypeable staphylococcal cassette chromosome mec (NT-SCCmec). The SCCmec element distribution in the clinical isolates from dogs was analyzed using whole-genome sequencing, which revealed the presence of different SCCmec composite islands (CIs) and gene structure. The SCCmec-CIs of ψSCCmec1864 (13 kb) and ψSCCmec371 (11 kb) with a class C1 mec complex but no ccr gene were discovered in *S. haemolyticus* 1864. The CIs of ψSCCmec384 with a C1 mec complex (28 kb), SCCmec with ccr4A4B4 (23 kb), and ψSCCmec48 (2.6 kb) were discovered in *S. haemolyticus* 48. In SCCmec, insertion sequence IS256 contained an aminoglycoside-resistant gene (aph(2′)-la). Two copies of IS431 containing the tetracycline-resistant gene tet(K) were found downstream of ψSCCmec. In *S. hominis* subsp. *hominis*, the SCCmec-Cl in strain 384 had two separate sections: ψSCCmec384 (20 kb) and SCCmec (23 kb). ψSCCmec1864 lacked the ccr gene complex but carried the class A mec complex. Trimethoprim-resistant dihydrofolate reductase (dfrC) was discovered on ψSCCmec384 between two copies of IS257. In strain 371, SCCmec VIII (4A) (37 kb) lacking a direct repeat at the chromosomal end was identified. This study found SCCmec elements in clinical isolates from dogs that were structurally complex and varied in their genetic content, with novel organization.

**IMPORTANCE** In Thailand, the staphylococcal cassette chromosome mec (SCCmec) element, which causes methicillin resistance through acquisition of the mec gene, has been studied in clinical coagulase-negative *Staphylococcus* isolates from various companion animals, and *Staphylococcus haemolyticus* and *Staphylococcus hominis* subsp. *hominis* were found to have the most nontypeable (NT)-SCCmec elements. These species are more prone to causing illness and more resistant to a variety of antimicrobials than other coagulase-negative staphylococci. However, full characterization of NT-SCCmec in clinical *S. haemolyticus* and *S. hominis* subsp. *hominis* isolates from such animals has been limited. Our findings support the use of full nucleotide sequencing rather than PCR designed for *Staphylococcus aureus* in further research of novel SCCmec elements. Moreover, several antimicrobial resistance and heavy metal resistance genes were identified on the SCCmec elements; these are important as they could limit the therapeutic options available in veterinary medicine.
**KEYWORDS** Staphylococcus haemolyticus, Staphylococcus hominis subsp. hominis, SCCmec, composite island, dog

Antimicrobial resistance—specifically, methicillin-resistant staphylococci (MRS)—is a major problem in humans and animals. The acquisition of the mec gene on the staphylococcal cassette chromosome mec (SCCmec) element confers methicillin resistance, which has been linked to multiple antimicrobial resistance events (1). SCCmec elements are unique mobile genetic elements that encode resistance to methicillin and almost all β-lactam antibiotics; they integrate into the staphylococcal chromosomal attachment site (attB) within the orfX gene (2, 3). The mec gene complex, cassette chromosome recombinase (cr) gene complex, and adjoining region are the core structural and critical genetic components shared by SCCmec elements (3). SCCmec structures are highly complex, and a wide range of sizes are found in different Staphylococcus species (1). Horizontal mec and SCC gene transfer is known to be possible between coagulase-negative staphylococci (CoNS) and Staphylococcus aureus, implying that CoNS could be a source and reservoir for SCCmec (4–6). The transfer of genetic materials within SCCmec between human and animal strains, including as antimicrobial resistance genes and CRISPR/Cas system genes, was also detected (7, 8). Furthermore, SCCmec components are more common and diverse in CoNS from animals than those in S. aureus, although the overall structure has yet to be described (3, 9, 10). To increase our understanding of SCCmec evolution and expand the nomenclature of SCCmec types in CoNS, it will be necessary to fully characterize a unique and/or sub-type of SCCmec structure in CoNS isolates from animals (3).

In Thailand, the SCCmec element was previously studied in clinical CoNS isolates from dogs and cats (11). The most nontypeable (NT) SCCmec elements were found in Staphylococcus haemolyticus and S. hominis subsp. hominis, which were negative detection of the mec and/or ccr gene complex using multiplex PCR (11). Furthermore, they are more prone to causing illness and more resistant to various antimicrobials than are other CoNS (12). To date, full characterization of NT-SCCmec in clinical S. haemolyticus and S. hominis subsp. hominis, which could not be identified using multiplex PCR. Specifically, the structural and genetic content of novel SCCmec composite islands (CIs) was analyzed with the aim of elucidating the mechanisms by which SCCmec is acquired in the genome.

**RESULTS**

SCCmec containing the mec complex but lacking ccr in S. haemolyticus 1864. In S. haemolyticus 1864, the CIs of ψSCCmec1864 (13 kb) and ψSCCmec1864 (11 kb) were discovered. The ψSCCmec1864 element was located immediately downstream of orfX and was flanked by direct repeats (DRs) and their inverted repeat (IR) sequences (DR1-IR1 and DR2-IR2) (Fig. 1A). At this position, the class C1 mec complex of insertion sequence IS431-mecA-ΔmecR1-IS431, with two copies of IS431 orientated in the same direction, was discovered. The ccr gene was not discovered. The genes cadC, arsC, arsB, and copA, which encode cadmium, arsenic, and copper resistance, respectively, were found in ψSCCmec1864 (Fig. 1A; see also Table S1 in the supplemental material). The second region of ψSCCmec1864 was found immediately downstream from ψSCCmec1864 and flanked by DR2-IR2 and IR3. DR3 was not found at the chromosomal end of this element. The ISSep1, cadC, arsC, and arsB genes were found on ψSCCmec1864.

The SCCmec-CIs in S. haemolyticus 1864 were nearly identical (99.7% nucleotide similarity) to those of the SCCmec in S. haemolyticus Sh29/312/L2 (GenBank accession number CP011116), isolated from a human patient (13) (Fig. 1A). Detailed information on SCCmec in S. haemolyticus Sh29/312/L2 has not yet been determined. In contrast, the additional IS256 and I55ha1 insertion sequences were located at the chromosomal region in S. haemolyticus 1864 but not in S. haemolyticus Sh29/312/L2. ψSCCmec1864 showed high sequence similarity (>96%) to the previously described ψSCCmec
FIG 1 Comparative analysis of the structural elements in the staphylococcal cassette chromosome mec composite islands (SCCmec-CI) in (A) S. haemolyticus 1864 (GenBank accession number JAKUUX000000000), S. haemolyticus Sh29/312/L2 (CP011116), S. haemolyticus WCH1 (JQ764731), and (Continued on next page)
element in *S. haemolyticus* WCH1 (JQ764731.1), obtained from the blood of a patient in China (14), and to *ψSCCmecc* (HE984157.2) in an *S. pseudintermedius* clinical isolate from a dog (15) (Fig. 1A). Similar to WCH1, identical 8-bp sequences (-CTTTT/GC-) were discovered adjacent to two copies of IS431 in *ψSCCmecc* (16). The genetic characteristics and highest gene homology of SCCmec in 1864 are listed in Table S1.

**SCCmec-Cl of *ψSCCmecc*, SCC, and *ψSCCmecc* in *S. haemolyticus* 48.** The SCCmec-Cl element in *S. haemolyticus* 48 comprised 53.6 kb and was flanked by DR1-IR1 and DR4-IR4. Two additional DRs and IRs (DR2-IR2 and DR3-IR3) were found within the element, which was divided into three parts: *ψSCCmecc* (28 kb), SCC (23 kb), and *ψSCCmecc* (2.6 kb) (Fig. 1B). The first *ψSCCmecc* region contained a class C1 mec complex of IS431-meca-ΔmecR1-IS431 and two copies of IS431 organized in the same orientation. The genes *cad*, *ars*, and *cop* were discovered upstream and downstream of the *mec* gene complex. The second SCC region contained two copies of ccrA4 (477 and 882 bp) and one of ccrB4 (1,626 bp). The two copies of ccrA exhibited 99.79% (477 bp) and 99.32% (882 bp) nucleotide similarity, respectively, to the ccrA gene of *S. aureus* M06/0171 (GenBank accession number HE980450.1), whereas ccrB had 100% similarity to ccrB of *S. haemolyticus* 06 (KX524951.1) (Fig. 1B and Table S2). In addition, *aph(2')-la*, an aminoglycoside resistance gene, was discovered on the plasmid-like region of IS526-aph(2')-la-IS526. The *aph(2')-la* sequence was 100% identical to that in *S. aureus* UMC5758 (CP077738.1), Enterococcus faecalis E533 (CP086726.1), and Staphylococcus lugdunensis CGMH-SL118 (CP048008.1). The third chromosomal end of the *ψSCCmecc* region harbored lactococcin G-processing and transport ATP-binding protein (*lagD*) and 2 hypothetical protein genes. A plasmid-like region of IS431 harboring the tetracycline-resistant gene *tet(K)* was discovered adjacent to *ψSCCmecc* (Fig. 1B). The *tet(K)* gene had the highest nucleotide similarity to the gene sequences of *S. saprophyticus* UTI-056 plasmid pUTI-056-3 (100% similarity) and *S. haemolyticus* NW19A (99.85% similarity).

The gene homology and organization of *ψSCCmecc* were highly identical (99.9%) to those of the SCCmec element in *S. haemolyticus* SH32 (GenBank accession number KF006347.1), a clinical isolate from a human (5) (Fig. 1B). There were differences in the types of ccr gene complexes, with *S. haemolyticus* 48 having ccrA4B4 and *S. haemolyticus* SH32 having ccrA5B3. Furthermore, regions containing *aph(2')-la* and *tet(K)* were not found in the SCC element of *S. haemolyticus* SH32. The plasmid-like region of IS431 carrying *tet(K)* existed in SCCmec V (SC2&5c) of *S. haemolyticus* isolate NW19A from bovine milk (KM369884) (16) (Fig. 1B). The presence of an SCCmec element carrying class C1 mec complex and ccrA4B4 in *S. haemolyticus* 48 was similar to SCCmec in clinical human isolate *S. haemolyticus* 83131A (CP024809) (17) but organized in the opposite position in the SCCmec element (Fig. 1B).

**SCCmec-Cl of *ψSCCmecc* in *S. hominis* subsp. *hominis* 384.** The SCCmec-Cl of *S. hominis* subsp. *hominis* 384 (43 kb) consisted of *ψSCCmecc* (20 kb) and *ψSCCmecc* (23 kb) (Fig. 2A). *ψSCCmecc* was flanked by DR1-IR1 and DR2-IR2, carried a class A mec complex of IS431-meca-ΔmecR1-mecB1 but lacked a ccr gene complex (Table S3). Integration of the genes encoding trimethoprim-resistant dihydrofolate reductase (*dfrC*) and thymidylate synthase (*thyA*) was mediated by two copies of IS257 in this region. The *dfrC* gene showed 100% nucleotide similarity to the same gene in *S. saprophyticus* UTI-058 (GenBank accession number CP054441.1), *S. epidermidis* E73 (CP0355643.1), and *S. aureus* ER04164.3 (CP030542.1). In the *ψSCCmecc* region, the gene for spermidine N1-acetyltransferase (*speE*) and the arsenical resistance operon were identified. The small subregion between IR3 and DR3-IR4 carrying *copA*, *mco*, and *ydhK* was located downstream of *ψSCCmecc* (Table S3).

A comparative analysis was conducted of SCCmec in strain 384 versus the SCCmec element recently identified in *S. hominis* C34847 (GenBank accession number KU936053) (18).

**FIG 1 Legend (Continued)**

*S. pseudintermedius* 57395 (HE984157.2) and (B) *S. haemolyticus* 48 (JAKUV000000000), *S. haemolyticus* SH32 (KF006347), *S. hominis* 384 (CP024809), and *S. haemolyticus* NW19A (KM369884). The percentages represent the nucleotide sequence identities. The direct repeats (DRs) and inverted repeats (IRs) are indicated by black lines. The insertion sequences (ISs) associated with antimicrobial resistance genes are indicated by the red rectangles. The following color scheme is used: *orfX* in orange, IS431 and mec gene complex in pink, *ccr* genes in red, heavy metal resistance genes in yellow, ISs in purple, virulence genes in blue, restriction modification system in green, and antimicrobial resistant genes in turquoise.
FIG 2 Comparative analysis of the structural elements in the staphylococcal cassette chromosome mec (SCCmec) regions in (A) *S. hominis* subsp. *hominis* 384 (GenBank accession number JAKUUV000000000), *S. hominis* C34847 (KU936053), *S. hominis* S34-1 (CP040732), and *S. hominis* subsp. *hominis* TFGsh5-1 (AB930128) and (B) *S. hominis* subsp. *hominis* 371 (JAKUUU000000000), *S. hominis* 19A (NZ_CP031277), *S. hominis* C5 (CP093539), and *S. aureus* C10682 (FJ390057). The percentages represent the nucleotide sequence identities. The direct repeats (DRs) and inverted repeats (IRs) are indicated by black lines. The insertion sequences (ISs) associated with antimicrobial resistance genes are indicated by the red rectangles. The following color scheme is used: orfX in orange, IS431 and mec gene complex in pink, ccr genes in red, heavy metal resistance genes in yellow, ISs in purple, virulence genes in blue, restriction modification system in green, antimicrobial resistant genes in turquoise, speG in dark orange, transposases in brown, and metabolic genes in gray.
The gene content and arrangement of the $\psi$SCCmec$_{384}$ region in strain 384 differed from those of C34847, although the $\psi$SCC$_{ars}$ and SCC$_{384}$ regions were highly conserved (99.4%). C34847 had a class A mec complex like that of 384, but it was in an atypical order (Fig. 2A). The $\psi$SCC$_{ars}$ region also shared high sequence homology (>98%) and gene arrangement with $\psi$SCC-CI in the human commensal S. hominis S34-1 (CP040732) (19) and an SCC remnant in the human commensal isolate S. hominis subsp. hominis TFGsh5-1 (AB930128) (20) (Fig. 2A).

SCCmec VIII (4A) in S. hominis subsp. hominis 371. SCCmec (37 kb) harboring a class A mec complex and ccrA4B4 was found in strain 371. This element was assigned to SCCmec VIII (4A) according to the standard guidelines (21). The genes ccrA4 (1,629 bp) and ccrB4 (1,362 bp) shared 100% and 99.63% nucleotide similarity to ccrA4B4 in S. aureus AR466 (GenBank accession number CP029080.1), respectively. Only DR1 and an imperfect IR1 were found, and this SCCmec element lacked a DR at the chromosomal junction (Fig. 2B and Table S4). The ars operons and copA genes were identified near the chromosomal end of this SCCmec element (Fig. 2B).

According to a comparative sequence analysis, the structure of SCCmec VIII was highly similar to that of SCCmec-CI in S. hominis 19A isolates from buffalo milk, which had ccrA4B4 but lacked the mec gene complex (22) (Fig. 2B). The chromosomal end and flanking region of SCCmec VIII in S. hominis subsp. hominis 371 showed high sequence homology (>88%) and gene arrangement with S. hominis 19A and S. hominis C3 (GenBank accession number CP093539) (23). S. hominis C5 was a human commensal isolate that possessed the new SCCmec type of class A mec complex and ccrA1B1 (Fig. 2B). The mec and ccr gene complex in S. hominis subsp. hominis 371 was found in the opposite location from the prototype of SCCmec VIII in methicillin-resistant S. aureus (MRSA) strain C10682 (FJ390057) (24) due to gene shuffle (Fig. 2B).

**DISCUSSION**

The structures of four different SCCmec elements in S. haemolyticus 1864 and 48 and S. hominis subsp. hominis 384 and 371, isolated from sick dogs, were fully characterized in this study. Analysis of the SCCmec-CI complex highlighted the highly mosaic nature, diverse evolutionary mechanisms, and independence of gene acquisition events in clinical S. haemolyticus and S. hominis subsp. hominis. The mosaic structure of their SCCmec elements, which were composed of genes with high similarity from various backgrounds, could imply the occurrence of gene transfer mechanisms operating within and between species, as well as in different hosts (8, 25). Mobile genetic elements on plasmids, such as antimicrobial resistance genes, allow access to a larger reservoir of niche-adaptive functions (25). One health concept considers *Staphylococcus* spp. from pets, particularly dogs, as a potential source of resistant clones and the transfer of genetic material to the human microbiome (8, 26). Infection of humans and animals by bacterial species that share a host can result from the transmission of resistant strains (26). Using PCR for SCCmec typing, it is difficult to detect the interchange of such elements between staphylococci of various origins. These findings support the use of full nucleotide sequencing rather than PCR designed for *S. aureus* in further research of SCCmec and SCCmec typing (3, 27).

In previous research, isolates of *S. haemolyticus* with mecA but lacking a ccr gene complex were described; it was proposed that this SCCmec element might be the most common type in *S. haemolyticus* (6, 14). In WCH1, the mecA-carrying IS431-formed composite transposon has been designated Tn6191. Five copies of IS431 were found in WCH1, which served as a joining point and may have caused ccr gene deletion through homologous recombination (14). In contrast, two copies of IS431 were identified in $\psi$SCCmec$_{1864}$ and $\psi$SCCmec of *S. haemolyticus* Sh29/312/L2; therefore, the mechanism of ccr gene deletion in 1864 might differ from that in WCH1. The previous study found that methicillin-resistant *S. pseudintermedius* (MRSP) carrying $\psi$SCCmec$_{57395}$ was predominant in Thailand (15). The presence of mec but lack of ccr in *S. haemolyticus* and *S. pseudintermedius* suggested that the ccr gene complex existed autonomously in these
species (15). In addition, they may have shared an ancestral SCCmec structure but evolved through different mechanisms.

The entire structure of SCC-Cl (C1 + ccrAB4) was first characterized in S. haemolyticus 48. The unique combination of the C1 mec complex and ccrAB4 was previously reported in S. haemolyticus isolates from a patient in Bangladesh following multiplex PCR analysis (7). However, this SCCmec does not have a standard nomenclature. Nevertheless, five copies of IS431 were identified, similar to those in WCH1, although ccr was not deleted in 48, implying that it had a different mechanism of evolution. The structure of ISSCCmec48 was strikingly comparable to that of SCCmec in S. haemolyticus SH32 isolates from Chinese patients (5); the differences were the types of ccr gene complex and the insertion of IS256 and IS431 in 48. IS256 is a part of the composite transposon Tn4001, which mediates gentamicin resistance and is more common in human clinical S. epidermidis strains than in commensal isolates (28). In this respect, clinical S. haemolyticus, which has received more exposure to antimicrobial drugs than commensal S. haemolyticus in animals, may be similar to human clinical S. epidermidis. The plasmid-like region harboring tet(K) on SCCmec was previously observed in SCCmec type V (SC2&5c) in S. haemolyticus NW19A (16) and the CI of SCCmec type V (Vd) + SCCcad/ars/cop (29). In SCCmec, the genome plasticity and potential to acquire antimicrobial resistance genes mediated by IS integration are highlighted by the structural and genetic diversity of the element.

An SCCmec-carrying class A mec complex lacking ccr was observed in S. hominis subsp. hominis 384. Elements with a class A mec complex but lacking ccr were found at 6% and 29% in clinical S. hominis isolates in Tunisia and Mexico, respectively (12, 27), although the complete sequences were not examined in these cases. IS256-mediated plasmid and transposon Tn4003 recombination has been previously found in S. aureus and many CoNS, and this has been linked to trimethoprim resistance genes (dfr) (30). Due to the high degree of sequence similarity among S. saprophyticus, S. epidermidis, and S. aureus, it was assumed that dfrC in 384 was acquired from a non-S. hominis species.

SCCmec type VIII (4A) was identified in S. hominis subsp. hominis 371. In S. hominis, the prevalence of SCCmec type VIII (4A) has been previously reported as 10% (31), 15% (12), and 19% (32). However, there was less information on the gene arrangement and content in SCCmec VIII in S. hominis. The SCCmec element in strain 371 lacking DR at the chromosomal part could have been caused by homologous recombination (5). Other regions that were well conserved in strains 371, 19A, and C5 indicated the loss of the mec gene complex in 19A (5). It was suggested that SCCmec type VIII in MRSA C10682 derived from the homologous recombination between S. aureus and CoNS (24). The finding of loss and shared SCC structure between staphylococci supported the ability of SCC elements to be transferred and possibly evolve to a new type.

Multiple ISs may be involved in the variation of SCCmec-CIs in S. haemolyticus and S. hominis subsp. hominis, which is linked to genomic rearrangement, phenotypic diversification, and the acquisition of antimicrobial resistance (33, 34). Antimicrobial resistance genes, including aminoglycoside, tetracycline, and trimethoprim-sulfamethoxazole resistance genes coexisting on the SCCmec element, are important because they may limit the therapeutic options available in veterinary medicine. Related medications are commonly used to treat small animals in Thailand; therefore, coselection with SCCmec might have occurred in 48 and 384 (22). The presence of heavy metal resistance genes on SCCmec, including zinc, copper, arsenic, and cadmium resistance genes, suggests that they may have originated in CoNS (16). These pathogens could serve as a reservoir for a wide range of SCCmec elements and antimicrobial and heavy metal resistance genes, which could spread through clinical CoNS isolates from animals. This study described the distinct gene organization of SCCmec elements in clinical S. haemolyticus and S. hominis subsp. hominis isolates from dogs, which should help with further typing and provide better knowledge of evolution mechanisms. Due to their clinical importance, S. haemolyticus and S. hominis subsp. hominis from dogs may become a concern, and they may serve as a reservoir of genetic material and resistant strains for more pathogenic bacteria in close contact humans. Nonetheless, this study only looked at a small number of isolates. Continued investigation and
identification of novel SCCmec elements in clinical Staphylococcus haemolyticus and Staphylococcus hominis subsp. hominis using whole-genome sequencing will ensure that they are properly detected and monitored.

MATERIALS AND METHODS

Bacterial isolates, This investigation contained two clinical Staphylococcus haemolyticus and two clinical Staphylococcus hominis subsp. hominis strains. Staphylococcus haemolyticus 1864 was isolated from the urine of a sick dog, whereas Staphylococcus hominis 48 was obtained from a skin wound of a dog in 2018. Staphylococcus hominis subsp. hominis 384 was recovered from a skin wound of a dog, and Staphylococcus hominis subsp. hominis 371 was isolated from the abdominal cavity of a dog in 2017. All isolates were collected by veterinarians at a veterinary hospital and analyzed at the Veterinary Diagnostic Laboratory, Faculty of Veterinary Science, Chulalongkorn University, Thailand, using standard microbiological methods. Genetic analysis and classification as NT-SCCmec were performed as described in a previous study (11).

Whole-genome sequencing and analysis. Genomic DNA was extracted from the four strains using DNeasy blood and tissue kits (Qiagen, Hilden, Germany), following the manufacturer’s instructions. The genomes were first sequenced using Illumina NovaSeq 6000 instrument, which yielded 150-bp paired-end reads, and sequencing libraries were produced using NEB Next Ultra II DNA library prep kit (Illumina, San Diego, USA). In addition, the genomes of the four strains were sent for long-read sequencing to obtain the entire sequences. Genomic DNA was extracted using a ZymoBIOMICS DNA miniprep kit (Zymo Research, USA) according to the manufacturer’s instructions for Gram-positive bacteria. The MiNiON platform (Oxford Nanopore Technologies [ONT], UK) was used to sequence the genomes. The libraries were prepared using a rapid barcoding kit 004 (SQK-RBK004) and loaded onto a MiNiON R9.4.1 flow cell (ONT), after which they were sequenced using a MiNiON Mk1C device (ONT).

The Illumina raw reads were processed using fastp 0.20.1 (35), and de novo assembly was performed using SPAdes 3.15.2 (36). Where the contig size was >200 bp, contigs were used for gene annotation in Prokka (37). The long-read sequences were trimmed using Porechop (38). The NanoPlot tool (http://nanoplot.bioinf.be) was used to assess the quality. Read assembly and read mapping were performed using Unicycler (39), and gene annotation was conducted using DFAST (40) and Prokka (37). The structural and genetic content of SCCmec was manually examined. Figures showing the structural elements and comparative analyses of SCCmec-Cs were generated using Easyfig 2.2.2.

Data availability. This whole-genome shotgun project has been deposited at DDBJ/ENA/GenBank under the accession numbers JAKUUUX0000000000 (1864), JAKUUV0000000000 (48), JAKUUV00000000000 (384), and JAKUU1000000000 (371). The versions described in this paper are the first versions. The raw data are available under BioProject accession number PRJNA808897.

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

SUPPLEMENTAL FILE 1, PDF file, 0.3 MB.

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