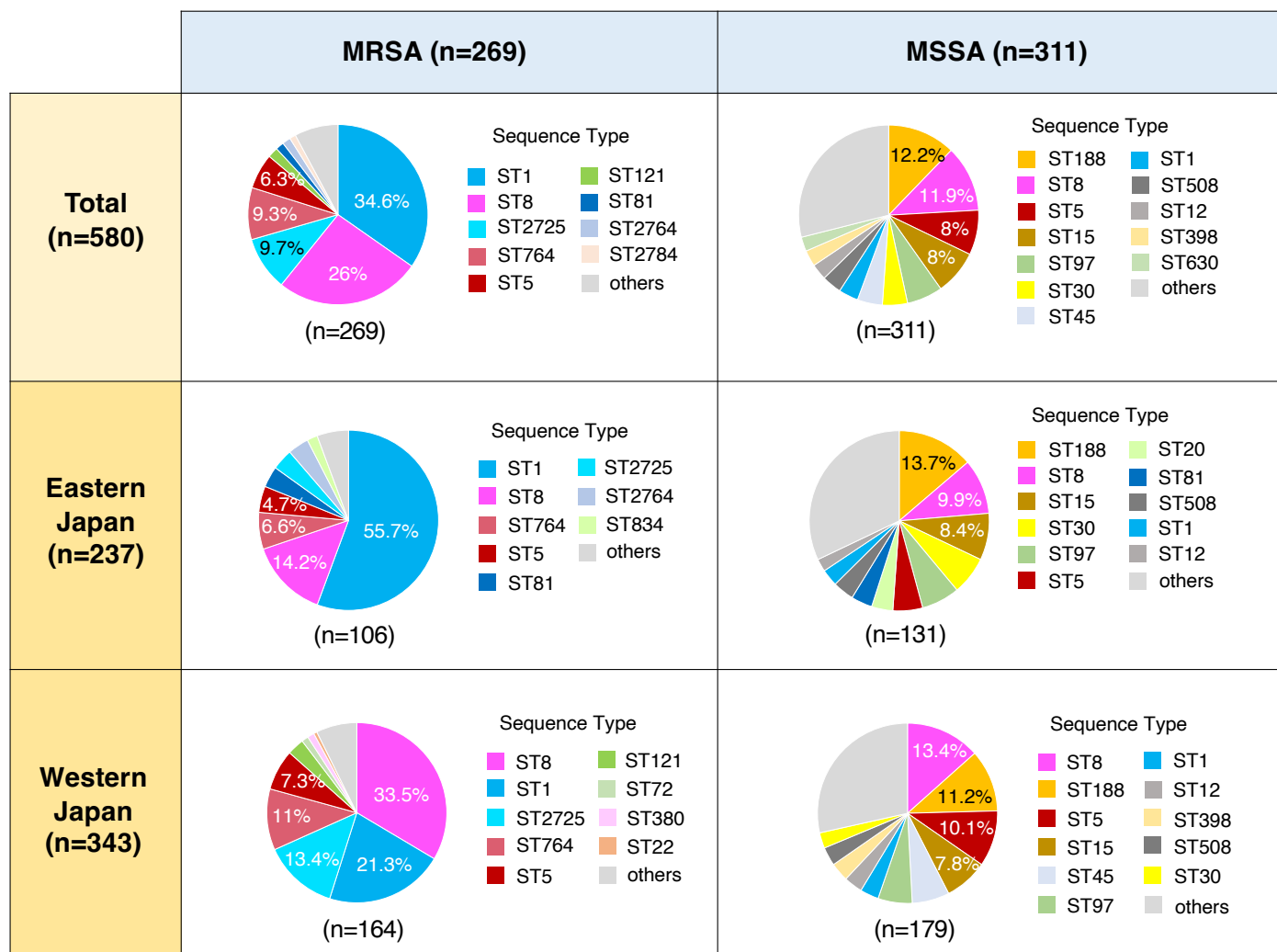
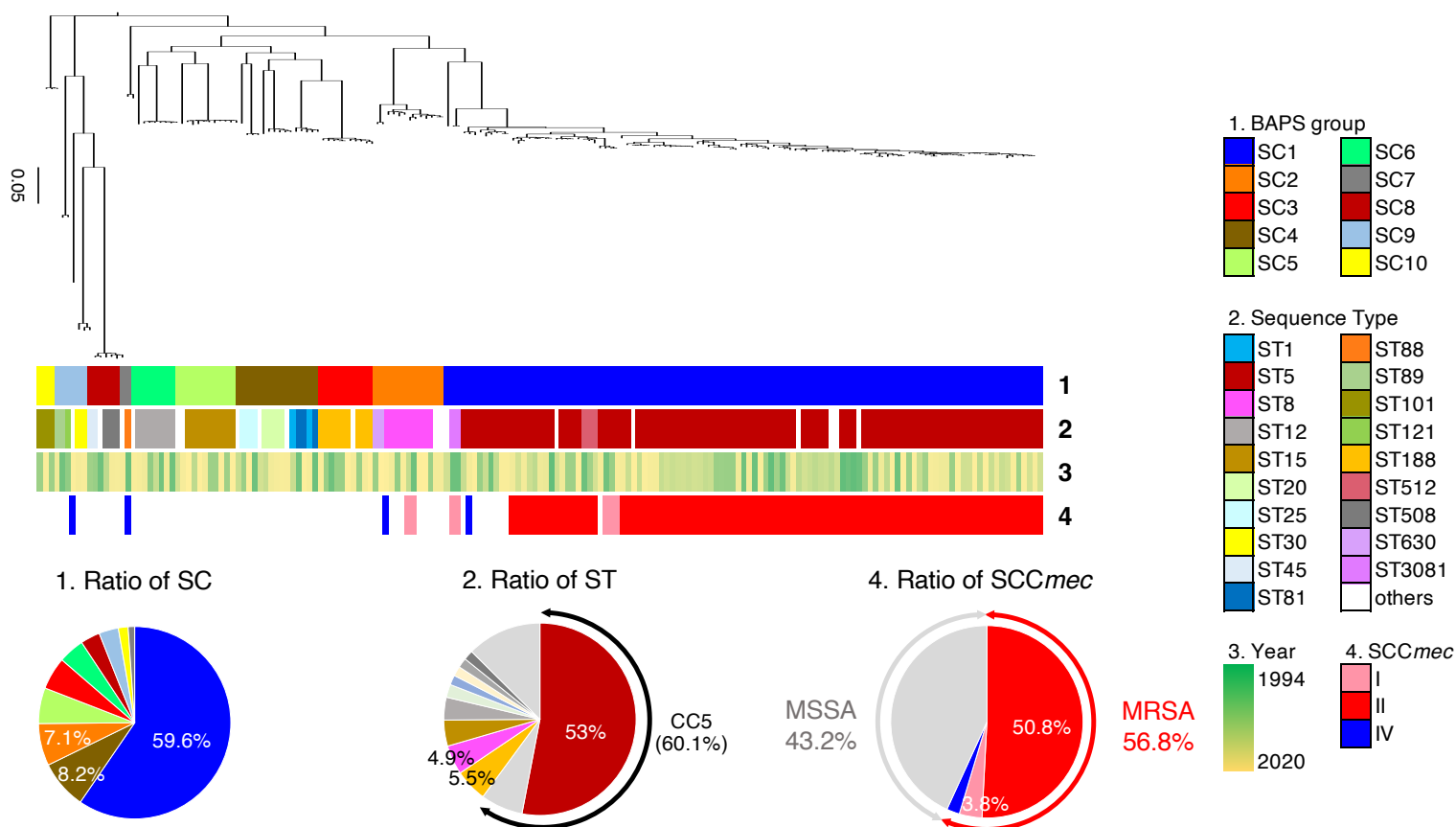


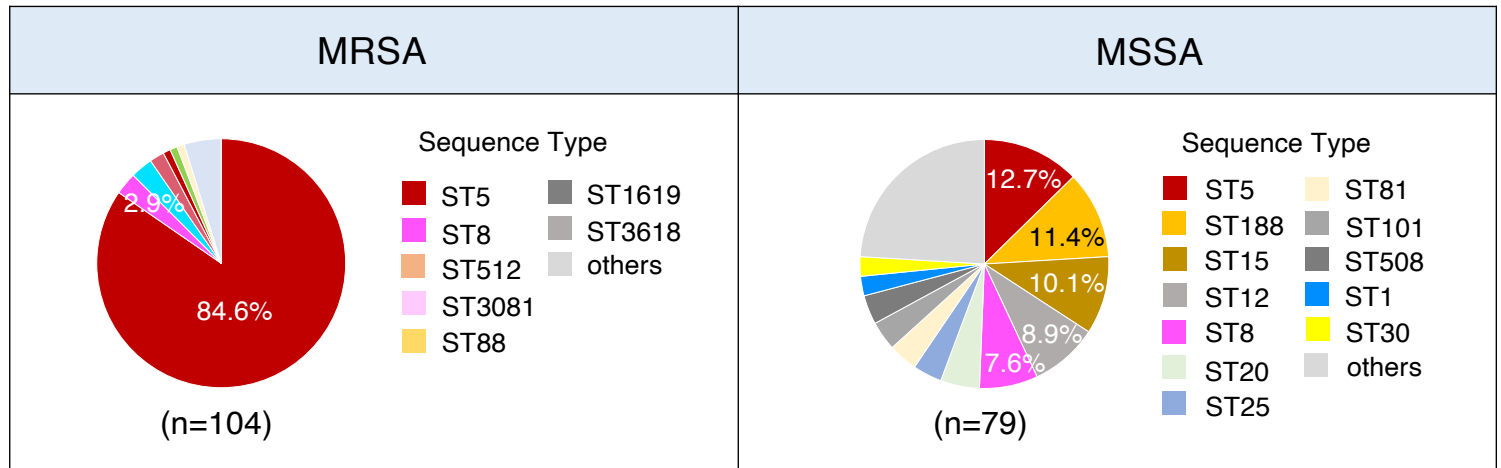


Supplementary Fig. 1 | Comparison of geographic proportions of STs are shown in MRSA (n=269) or MSSA (n=311). ST with less than 3 isolates are included in “other.” The color tone shown is the same pattern used in Fig. 1.

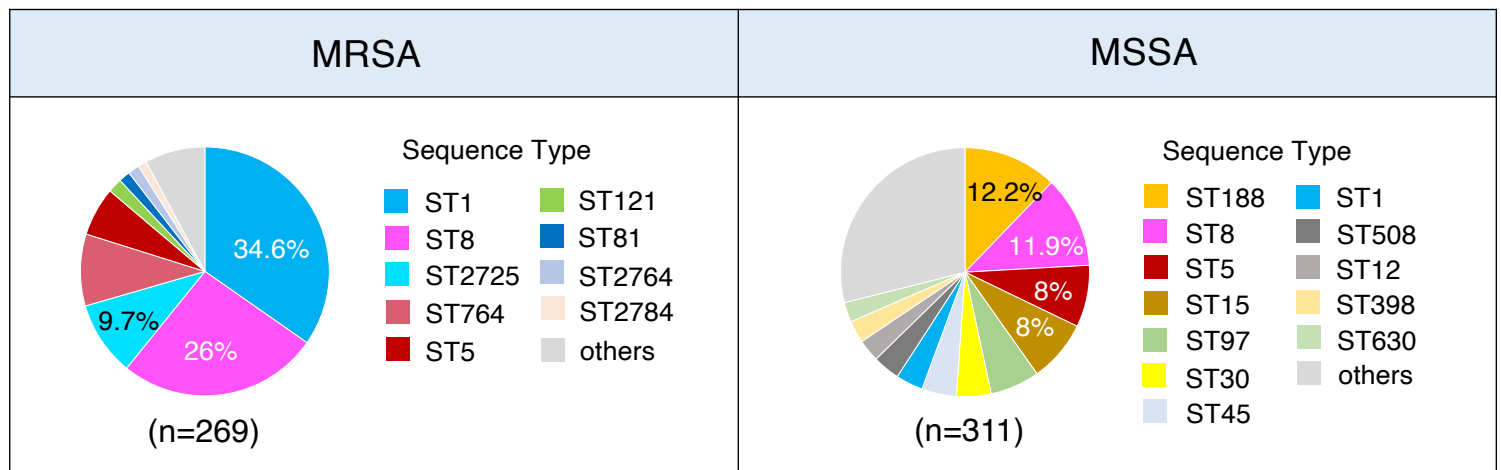


Supplementary Fig. 2 | Population structure of BSI-derived *S. aureus* in 1994–2000. Midpoint-rooted ML tree showing the phylogenetic structure of 183 *S. aureus* isolates in 1994–2000. Scale bar represents the number of nucleotide substitutions per site. Matrix of metadata 1, 2, and 4 show the same as those of Fig. 1. Metadata 3 indicates *S. aureus* isolation year. The color tone is shown in the same pattern as Fig. 1. Metadata information of 183 *S. aureus* isolates in 1994–2000 is summarized in Supplementary Table 2.

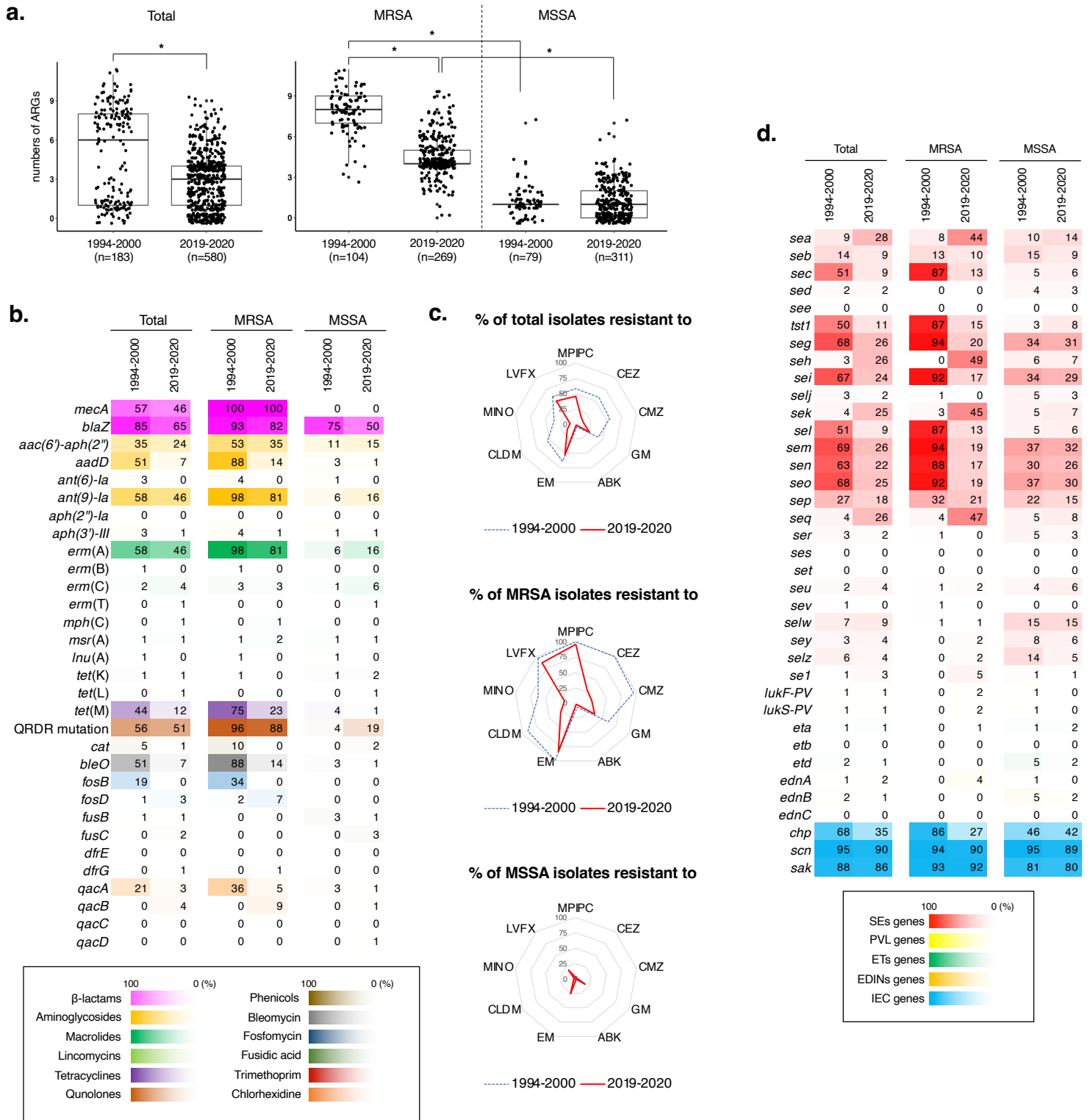
1994-2000 (n=183)



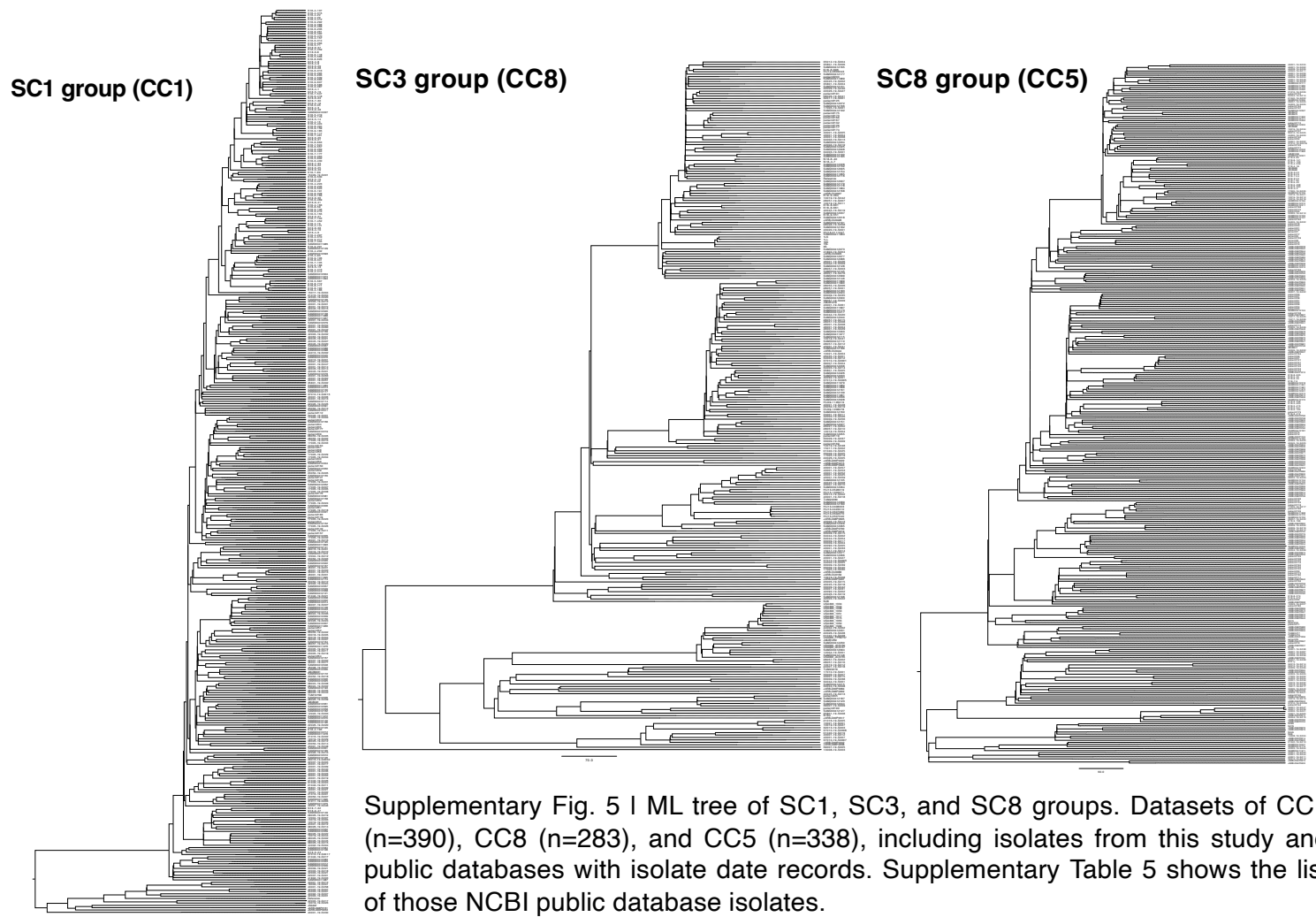
2019-2020 (n=580)



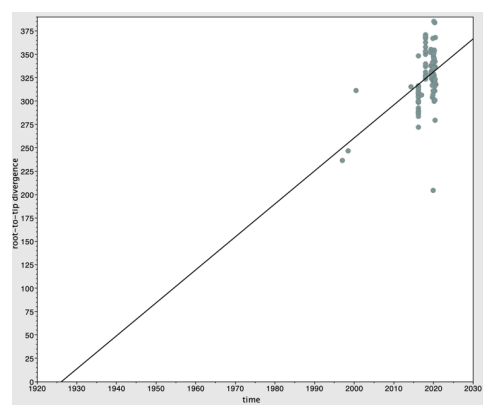
Supplementary Fig. 3 | Shift of ST proportion in 1994–2000 and 2019–2020. STs with less than 3 isolates are included in “other.” The color tone is shown in the same pattern as Fig 1.



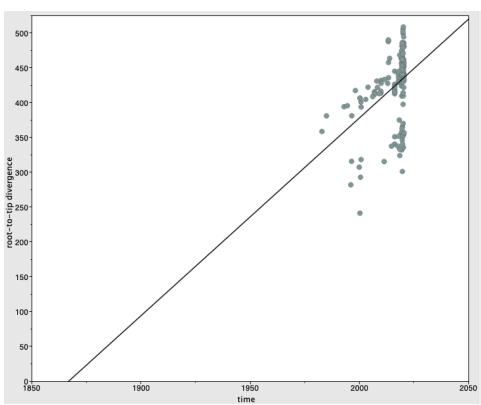
Supplementary Fig. 4 | Comparison of ARG distribution and antimicrobial resistance levels in 1994–2000 and 2019–2020. In 1994–2000: total (n=183), MRSA (n=104), and MSSA (n=79). In 2019–2020: total (n=580), MRSA (n=269), MSSA (n=311). **a.** Number of ARGs per strain. Black dots indicate isolates in 1994–2000 or 2019–2020. * $p < 0.01$. **b.** Prevalence heatmap of major ARGs and QRDR mutations identified. **c.** Antimicrobial susceptibility profile of blood-derived *S. aureus*. The radar chart shows the resistance rates of isolates in 1994–2000 and 2019–2020. Blue dotted and red lines indicate isolates of 1994–2000 and 2019–2020, respectively. **d.** Heatmap of VFG distribution in 1994–2000 and 2019–2020. In 1994–2000: total (n=183), MRSA (n=104), and MSSA (n=79). In 2019–2020: total (n=580), MRSA (n=269), and MSSA (n=311). Prevalence heatmap of major VFGs identified.



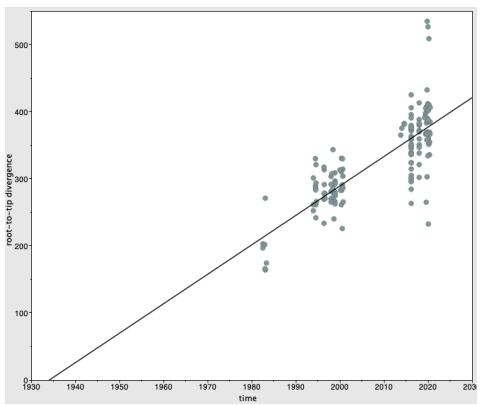
a. CC1



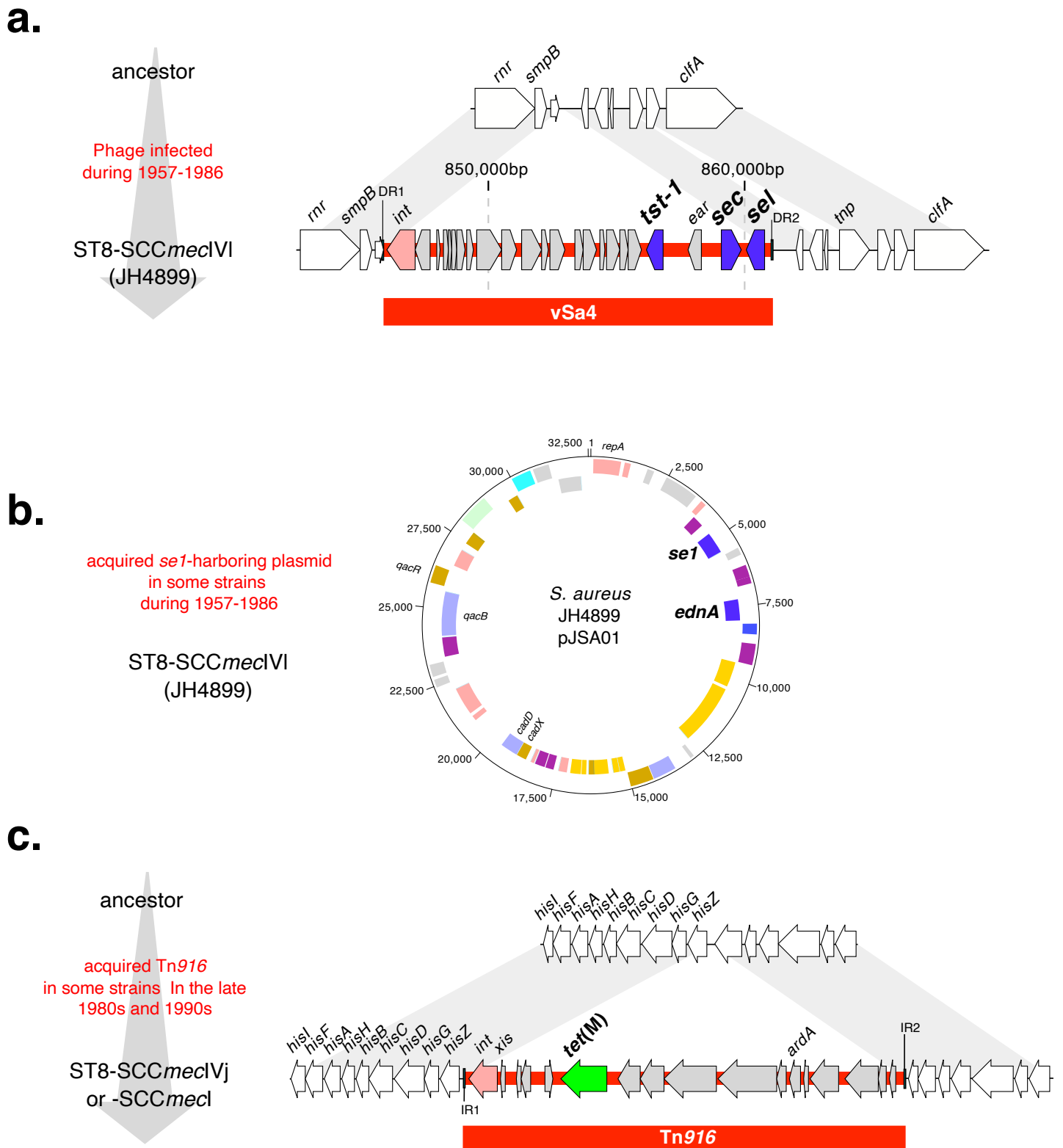
b. CC8



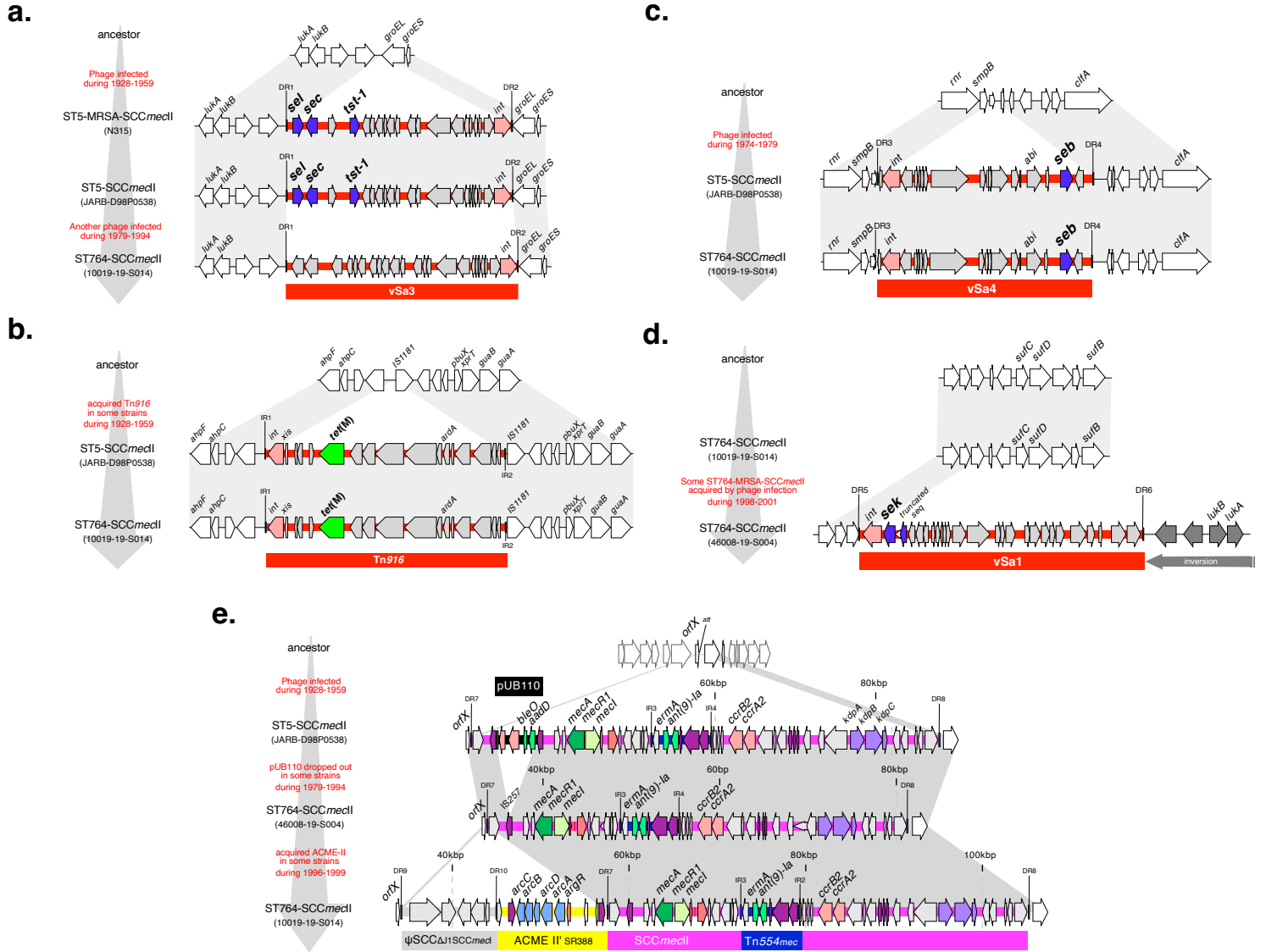
c. CC5



Supplementary Fig. 6 | Regressions of sampling time vs. root-to-tip genetic distance in a. CC1, b. CC8, and c. CC5 lineages.

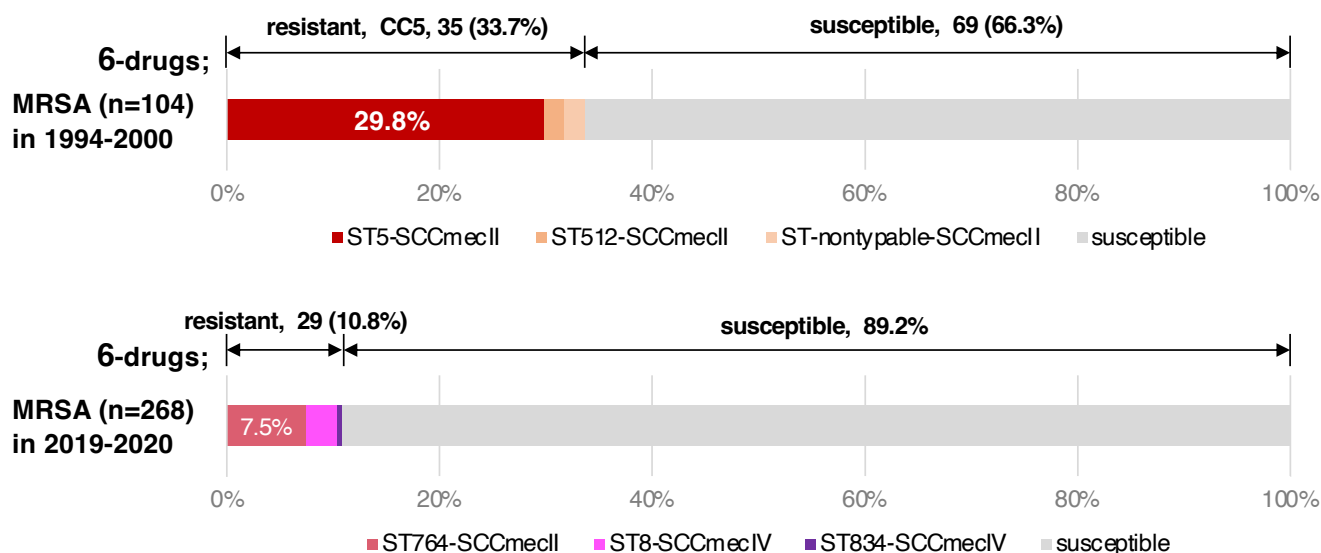


Supplementary Fig. 7 | Acquisition of genomic islands or *se1*-carrying plasmid during the replacement of ST8 ancestor by ST8-SCC*meclVI* (MRSA/J). **a.** The ancestor of ST8-SCC*meclVI* (MRSA/J) acquired the genomic island vSa4 (carrying *sec*, *tst-1*, and *se1*) somewhere between 1957–1986 (see parallel with Fig. 4b). Vertical lines indicate the position of the direct repeat (DR): DR1, AATCCCGCCGTCTCCAT; DR2, AACTCCCGCCGTCTCCAT. **b.** Plasmid map of pJSA01-harboring *S. aureus* JH4899 (accession #, AP014922), as MRSA/J. **c.** The ancestor of ST8-SCC*meclIVj* or -SCC*mecl* acquired the *tet(M)*-harboring Tn916-like transposable unit somewhere in the late 1980s and 1990s (see parallel with Fig. 4b). Vertical lines indicate the position of the inverted repeat (IR): IR1, TTTGCATATTT; IR2, TTTGAATATTT.

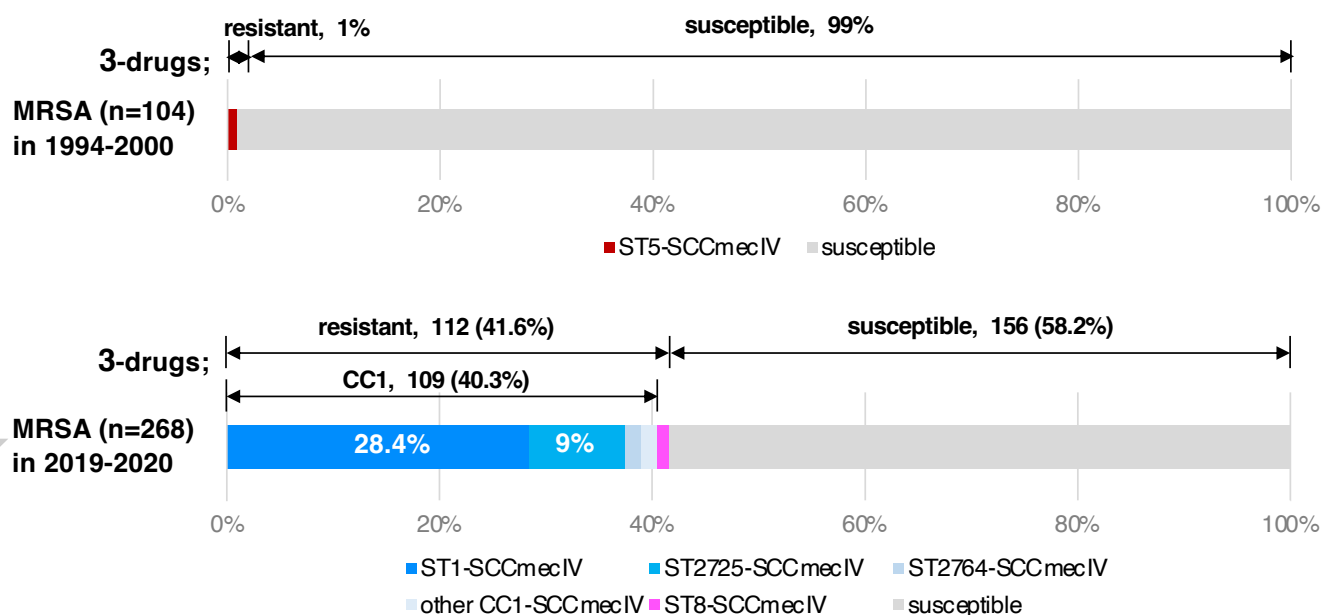


Supplementary Fig. 8 | Stepwise acquisition of genomic islands or *SCCmec* composition island during the replacement of ST5-MSSA ancestor by ST764-*SCCmecII* (see parallel with Fig. 4c). **a.** Genetic structure around genomic island vSa3. Vertical lines indicate the position of the direct repeat (DR): DR1, GTTTTACATCATCCCGGCAT; DR2, GTTTTACATCATCCCGGCAT. **b.** Genetic structure around *tet(M)*-harboring Tn916-like transposable unit. Vertical lines indicate the position of the inverted repeat (IR): IR1, GCTTTTTTTA; IR2, GCTTTTTTGA. **c.** Genetic structure around genomic island vSa4. Vertical lines indicate the position of the direct repeat (DR): DR3, AAATCCCGCCGTCTCCAT; DR4, AACTCCCGCCGTCTCCAT. **d.** Genetic structure around genomic island vSa1. Vertical lines indicate the position of the direct repeat (DR): DR5, AAGATGATAAGAAAATCA; DR6, AAGATGCTGAGAGAATCA. **e.** Genetic structure around *SCCmec* region. Vertical lines indicate the position of the direct repeat (DR): DR7, GGAGAAGCATATCATAA; DR8, GCAGAGGCGTATCATAA; IR1, TAAGACATCAC; IR3, GAGATGTATTA; DR9, AGAAGCGTACCACAA; DR10, GAAGCGTATCATAAGTGA.

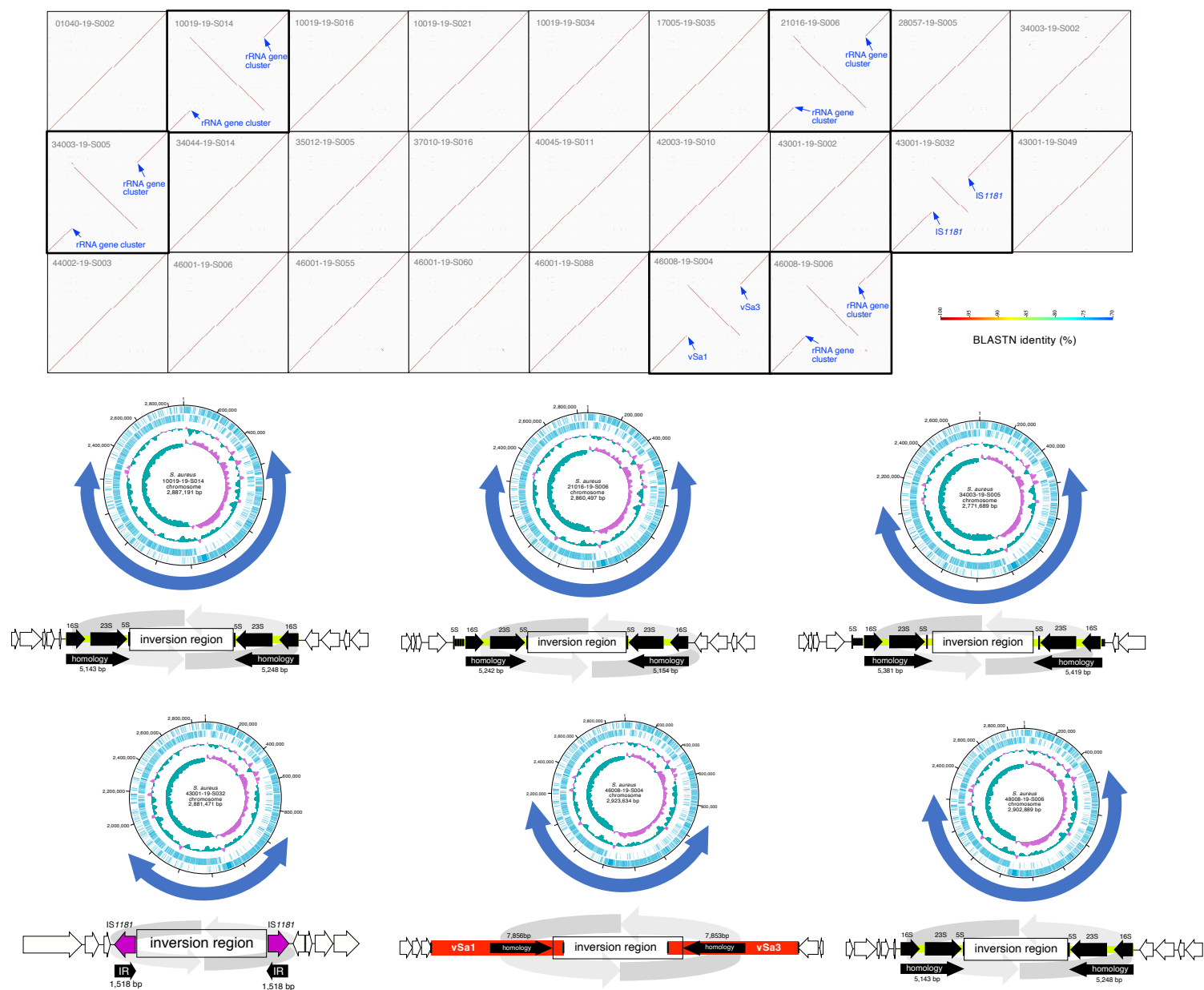
a.



b.



Supplementary Fig. 9 | Phylogenetic transition of BSI-derived MRSA isolates resistant to six or three drugs between the two periods. Each bar graph shows the proportion of BSI-derived MRSA lineages resistant to **a** six drugs (MIPIC, GEN, EM, CLDM, MINO, and LVFX) or **b** three drugs (MIPIC, EM, and LVFX).



Supplementary Fig. 10. Synteny analysis of the chromosome sequence of completely sequenced ST764-SCC*meclI* isolates in this study. The chromosome sequence of N315 (accession #, BA000018) was used as reference sequence. In the chromosomes of ST764-SCC*meclI* six strains (10019-19-S014, 21016-19-S006, 34003-19-S005, 43001-19-S032, 46008-19-S004, and 48008-19-S006), blue indicates the sequence regions where the inversion originates.