

**Supplementary methods table 1. Strains used on this study**

Strain	Relevant genotype	Description	Source or reference
<i>S. epidermidis</i> RP62a	<i>crispr</i> <sup>+</sup> , neomycin <sup>R</sup> , erythromycin <sup>R</sup>	Used as the wild type <i>S. epidermidis</i> strain with a functional native type III-A CRISPR-Cas system	1
<i>S. epidermidis</i> LAM104	$\Delta$ <i>crispr</i> , neomycin <sup>R</sup> , erythromycin <sup>R</sup>	Isogenic strain of <i>S. epidermidis</i> RP62a with a deletion of the CRISPR spacer array.	2
<i>S. aureus</i> TB4 pWJ245 (gp14)	<i>crispr</i> <sup>+</sup>	<i>S. aureus</i> TB4 transformed with a plasmid carrying the type III-A CRISPR-Cas system of <i>S. epidermidis</i> RP62a with a targeting spacer towards the gp14 gene of $\phi$ NM1 $\gamma$ 6	This study
<i>S. aureus</i> TB4 pGG-Bsal	$\Delta$ spacer	<i>S. aureus</i> TB4 transformed with a plasmid carrying the type III-A CRISPR-Cas system of <i>S. epidermidis</i> RP62a with non-targeting spacer	This study
<i>S. aureus</i> TB4 pWJ248 (gp14, dCsm3/dCsm6)	<i>crispr</i> <sup>+</sup> , <i>csm3</i> (D32A), <i>csm6</i> (R364A,H369A)	<i>S. aureus</i> TB4 pWJ245, but with catalytically inactive Csm3 and Csm6	This study
<i>S. aureus</i> TB4 pJTR122 (gp14, dHD/dCsm3)	<i>crispr</i> <sup>+</sup> , <i>cas10</i> (H14A, D15A), <i>csm3</i> (D32A)	<i>S. aureus</i> TB4 pWJ245, but with catalytically inactive HD domain of Cas10	This study
<i>S. aureus</i> JAV6 pWJ245 (gp14, <i>lexA</i> K168A)	<i>crispr</i> <sup>+</sup> , <i>lexA</i> K168A	SOS-deficient strain of <i>S. aureus</i> TB4 strain with pWJ245	This study
<i>S. aureus</i> TB4 pWJ191 (gp43)	<i>crispr</i> <sup>+</sup>	<i>S. aureus</i> TB4 transformed with a plasmid carrying the type III-A CRISPR-Cas system of <i>S. epidermidis</i> RP62a with a targeting spacer towards the gp43 gene of $\phi$ NM1 $\gamma$ 6	This study
<i>S. aureus</i> TB4 pJTR109 (gp43, dHD)	<i>crispr</i> <sup>+</sup> , <i>cas10</i> (H14A, D15A)	<i>S. aureus</i> TB4 pWJ191, but with catalytically inactive HD domain of Cas10	This study
<i>S. aureus</i> RN4220 pWJ242 (gp43, dCsm3/dCsm6), pJTR162	<i>crispr</i> <sup>+</sup> , <i>csm3</i> (D32A), <i>csm6</i> (R364A,H369A), P <sub>tet</sub> <sup>-</sup> Target	<i>S. aureus</i> RN4220 co-transformed with a dCsm3/dCsm6 type III-A CRISPR-Cas system and an inducible target plasmid	This study
<i>S. aureus</i> RN4220 pWJ242 (gp43, dCsm3/dCsm6), pWJ153	<i>crispr</i> <sup>+</sup> , <i>csm3</i> (D32A), <i>csm6</i> (R364A,H369A), P <sub>tet</sub> <sup>-</sup> NonTarget	<i>S. aureus</i> RN4220 co-transformed with a dCsm3/dCsm6 type III-A CRISPR-Cas system and an inducible plasmid lacking the target sequence	This study
<i>S. aureus</i> RN4220 pJTR127 (gp43, dHD/dCsm3/dCsm6), pJTR162	<i>crispr</i> <sup>+</sup> , <i>cas10</i> (H14A, D15A), <i>csm3</i> (D32A), <i>csm6</i> (R364A,H369A), P <sub>tet</sub> <sup>-</sup> Target	<i>S. aureus</i> RN4220 co-transformed with a dHD/dCsm3/dCsm6 type III-A CRISPR-Cas system and an inducible target plasmid	This study
<i>S. aureus</i> RN4220 pJTR127 (gp43, dHD/dCsm3/dCsm6), pWJ153	<i>crispr</i> <sup>+</sup> , <i>cas10</i> (H14A, D15A), <i>csm3</i> (D32A), <i>csm6</i> (R364A,H369A), P <sub>tet</sub> <sup>-</sup> NonTarget	<i>S. aureus</i> RN4220 co-transformed with a dHD/dCsm3/dCsm6 type III-A CRISPR-Cas system and an inducible plasmid lacking the target sequence	This study
<i>S. aureus</i> TB4 pDVB51 (pSauCas9)	<i>crispr</i> <sup>+</sup>	<i>S. aureus</i> TB4 transformed with a plasmid carrying the type II-A CRISPR-Cas system	This study

		from <i>S. aureus</i> , with a spacer targeting $\phi$ NM1 $\gamma$ 6	
<i>S. aureus</i> TB4 pWJ245, pAV22 (gp14)	<i>crispr</i> <sup>+</sup>	<i>S. aureus</i> TB4 transformed pWJ245 and the SOS reporter plasmid	This study
<i>S. aureus</i> JAV6 pWJ245, pAV22 (gp14, <i>lexA</i> K168A)	<i>crispr</i> <sup>+</sup> , <i>lexA</i> K168A	SOS-deficient strain of <i>S. aureus</i> TB4 strain with pWJ245 and the SOS reporter plasmid	This study

## References

- 1 Gill, S. R. *et al.* Insights on evolution of virulence and resistance from the complete genome analysis of an early methicillin-resistant *Staphylococcus aureus* strain and a biofilm-producing methicillin-resistant *Staphylococcus epidermidis* strain. *J. Bacteriol.* **187**, 2426-2438.
- 2 Marraffini, L. A. & Sontheimer, E. J. CRISPR interference limits horizontal gene transfer in staphylococci by targeting DNA. *Science* **322**, 1843-1845.

**Supplementary methods table 2. Oligos used in this study**

Plasmid	Description	Sequence
CYM-Pm128	Forward primer to amplify the <i>rpoB</i> locus from the <i>S. aureus</i> genome	CTTGTCCTCCGGTAACTAGTAATTAATATGCTTATGGTATTTAGCTAAAAGC
CYM-Pm129	Reverse primer to amplify the <i>rpoB</i> locus from the <i>S. aureus</i> genome	TGCGAGCTAGCATCTGCAGTTTAAATCAGTAACCTCTTTTGTGTTTCAGGAGCATC
CYM-Pm733	Forward primer to amplify the spacer array of the type III-A CRISPR-Cas locus of <i>S. epidermidis</i>	ATCATATAATCTTGTACTAGTGATTGTC
CYM-Pm734	Reverse primer to amplify spacer array of the type III-A CRISPR-Cas locus of <i>S. epidermidis</i>	TTTTTCCATCCCCTAGAAATTAATCAATGCG
CYM-MWS51	Sequencing adapter oligo from Kennedy et al. <i>Nature Protocols</i> . 2014	AATGATACGGCGACCACCGAGATCTACACTCTTCCCTACACGACGCTCTTCCGATCT
CYM-MWS55	Sequencing adapter oligo with randomized barcodes from Kennedy et al. <i>Nature Protocols</i> . 2014	TCTTCTACAGTCANNNNNNNNNNNNAGATCGGAAGAGCACACGTCTGAACTCCAGTCAC
CYM-MWS13	Forward primer to amplify adaptor-ligated genomic fragments, from Kennedy et al. <i>Nature Protocols</i> . 2014	AATGATACGGCGACCACCGAG
CYM-MWS21-1	Reverse primer to amplify adaptor-ligated genomic fragment, with TruSeq index sequence 1	CAAGCAGAAGACGGCATAACGAGATATCACGGTGACTGGAGTTCAGACGTGTGC
CYM-MWS21-2	Reverse primer to amplify adaptor-ligated genomic fragment, with TruSeq index sequence 2	CAAGCAGAAGACGGCATAACGAGATCGATGTGTGACTGGAGTTCAGACGTGTGC
CYM-MWS21-3	Reverse primer to amplify adaptor-ligated genomic fragment, with TruSeq index sequence 3	CAAGCAGAAGACGGCATAACGAGATTTAGGCGTGACTGGAGTTCAGACGTGTGC
CYM-MWS21-4	Reverse primer to amplify adaptor-ligated genomic fragment, with TruSeq index sequence 4	CAAGCAGAAGACGGCATAACGAGATTGACCAGTGACTGGAGTTCAGACGTGTGC
GG424	For cloning pJTR127 (amplifies <i>cas</i> genes from pJTR126, R)	CATATTGCCTGATGAAGTGAATAG
GG425	For cloning pJTR127 (amplifies gp43 spacer from pWJ191, R)	CTATTCACTTCATCAGGCAATATG
W614	For cloning pJTR127 (amplifies <i>cas</i> genes from pJTR126, F)	GGTTATACTAAAAGTCGTTTGTGG
W852	For cloning pJTR127 (amplifies gp43 spacer from pWJ191, F)	CCAACAAACGACTTTTAGTATAACC
W915	Forward primer for qPCR amplification of <i>S. aureus rho</i> gene	GTCAATGACCATAACGCAGAAG
W916	Reverse primer for qPCR amplification of <i>S. aureus rho</i> gene	CAATCGGTGTTACTAAATCCATG
W1051	For cloning gp14 spacer into pJTR116 backbone	GAACCTACGTCCGTAATGCTAGGATTTGCAAATTTCTTA
W1052	For cloning gp14 spacer into pJTR116 backbone	GATCTAAGAAATTTGCAAATCCTAGCATTACGGACGTAG
NP112	Primer to amplify the GFP coding sequence from pCN54	TCCAGATCTTCTTCAGGTTATGACCATGTCACTTTGCTTGATATATGAG
NP114	Primer to amplify pLZ12spec	TGGTCATAACCTGAAGGAAGATCTG
AV119	Primer to amplify pLZ12spec	CAGGAAACAGCTATGACCATGATTAC
AV129	Primer to amplify the promoter from the SOS-responsive gene 4-oxalocrotonate tautomerase	ATGGTCATAGCTGTTTCTGTCAATTATTAATTTGAGTATATCATGTAATAC
AV130	Primer to amplify the promoter from the SOS-responsive gene 4-oxalocrotonate tautomerase	AGTTCTTCTCCTTACTCATTGTATTTCTCCCTTACTTGAATC
AV131	Primer to amplify the GFP coding sequence from pCN54	ATGAGTAAAGGAGAAGAAGACTTTTC
oDVB146	BsaI Cloning in pDVB47 Sau type II-A CRISPR, spacer targeting phiNM1 gp12	AGACGCGAAATCATACGCAAAAATATTCATGTTAG
oDVB147	BsaI Cloning in pDVB47 Sau type II-A CRISPR, spacer targeting phiNM1 gp12	AAAACATACATGAATATTTTTCGATGATTTTCGC

JTR1008	Forward primer for qPCR of <i>S. aureus umuC</i> gene	CGAGTGTTTCTTGTATTGAAAAGGGC
JTR1009	Reverse primer for qPCR of <i>S. aureus umuC</i> gene	GTGGTATTTCAAACAATCGCGACCC
B585	Amplification of pDB114 backbone for construction of pDB236	GGAGAGGCGTATCATCAAACGAAAATTGGATAAAGTGGG
B586	Amplification of pDB114 backbone for construction of pDB236	TATTTTATTATGCATCGTTTGTGAACTAATGGGTGC
B587	Amplification of type II-A CRISPR-cas locus of <i>S. aureus</i> M06/0171 into pDB236	TTAGTTCAACAACGATGCATAATAAAATACAGGTCC
B588	Amplification of type II-A CRISPR-cas locus of <i>S. aureus</i> M06/0171 into pDB236	TCCAATTTTCGTTTGATGATACGCCCTCTCCCTATCAGTG
oDVB96	Amplification of pDB236 fragment to replace the CRISPR array for a Bsal cloning site	AGCATTTTCAGGTATAGGTGTTTTGGGAAACAATTTCCCGAACCATTTATATTCTCTAC
oDVB97	Amplification of pDB236 fragment to replace the CRISPR array for a Bsal cloning site	TTTCCCAAACACCTATACCTGAAAATGCTTTTCTCTTTCTATTATCCATGACTTCA
oDVB126	Amplification of pDB236 fragment to replace the CRISPR array for a Bsal cloning site	TGAAAAAATTAAGCTGCACGATATGCAAGAAGGGAAATGTTTATACTCGTTAG AAGCAAT
oDVB127	Amplification of pDB236 fragment to replace the CRISPR array for a Bsal cloning site	GAGACTTTGAGCTTCCGAGACTGGTCTCAGTCTACCTCATACTAAAATTAC AGAGTACTAAAACCTCTAGCATCATTATAAATCCTCA
oDVB128	Amplification of pDB236 fragment to replace the CRISPR array for a Bsal cloning site	TGAGACCAGTCTCGGAAGCTCAAAGGTCTCGTTTTAGTACTCTGTAATTTTAG GTATGAGGTAGACAGCAAATCACTGATAGGGAGAGG
oDVB129	Amplification of pDB236 fragment to replace the CRISPR array for a Bsal cloning site	TCTTGCATATCGTGCAGCTTAATTTTTTCAATTAATATTTAGCATTTTCTTT ACCTGTC

### Supplementary methods table 3. Plasmids used in this study

Plasmid	Description	Source or reference
pGG-BsaI ( $\Delta$ spc)	type III-A CRISPR-Cas with a BsaI cloning site inserted between the first and second repeats, used as a non-targeting spacer control	1
pWJ245 (gp14)	type III-A CRISPR-Cas with a spacer targeting the <i>gp14</i> gene of $\phi$ NM1 $\gamma$ 6	2
pWJ248 (gp14, dCsm3/dCsm6)	type III-A CRISPR-Cas with a spacer targeting the <i>gp14</i> gene of $\phi$ NM1 $\gamma$ 6 and <i>csm3</i> (D32A), <i>csm6</i> (R364A,H369A) mutations	2
pJTR122 (gp14, dHD/dCsm3)	type III-A CRISPR-Cas with a spacer targeting the <i>gp14</i> gene of $\phi$ NM1 $\gamma$ 6 and <i>cas10</i> (H14A, D15A) and <i>csm3</i> (D32A) mutations	This study
pWJ191 (gp43)	type III-A CRISPR-Cas with a spacer targeting the <i>gp43</i> gene of $\phi$ NM1 $\gamma$ 6	2
pJTR109 (gp43, dHD)	type III-A CRISPR-Cas with a spacer targeting the <i>gp43</i> gene of $\phi$ NM1 $\gamma$ 6 and <i>cas10</i> (H14A, D15A) mutations	3
pWJ242 (gp43, dCsm3/dCsm6)	type III-A CRISPR-Cas with a spacer targeting the <i>gp43</i> gene of $\phi$ NM1 $\gamma$ 6 and <i>csm3</i> (D32A), <i>csm6</i> (R364A,H369A) mutations	2
pJTR127 (gp43, dHD/dCsm3/dCsm6)	type III-A CRISPR-Cas with a spacer targeting the <i>gp43</i> gene of $\phi$ NM1 $\gamma$ 6 and <i>cas10</i> (H14A, D15A), <i>csm3</i> (D32A), <i>csm6</i> (R364A,H369A) mutations	This study
pWJ153	pE194-based plasmid vector with an inducible P <sub>tet</sub> promoter, used as a non-targeting spacer control	1
pJTR162	pE194-based plasmid with a target sequence matching the <i>gp43</i> spacer under the control of the P <sub>tet</sub> promoter	3
pDVB51 (pSauCas9)	Type II-A CRISPR-Cas system of <i>S. aureus</i> with a spacer targeting <i>gp12</i> in $\phi$ NM1 $\gamma$ 6.	This study
pAV22	SOS reporter plasmid with Green Fluorescent Protein (GFP) under the control of the 4-oxalocrotonate tautomerase promoter of <i>S. aureus</i> .	This study

### References

- 1 Goldberg, G. W., Jiang, W., Bikard, D. & Marraffini, L. A. Conditional tolerance of temperate phages via transcription-dependent CRISPR-Cas targeting. *Nature* **514**, 633-637.
- 2 Jiang, W., Samai, P. & Marraffini, L. A. Degradation of phage transcripts by CRISPR-associated RNases enables type III CRISPR-Cas immunity. *Cell* **164**, 710-721.
- 3 Rostol, J. T. & Marraffini, L. A. Non-specific degradation of transcripts promotes plasmid clearance during type III-A CRISPR-Cas immunity. *Nat Microbiol* **4**, 656-662.