nature portfolio

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Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☐	☒	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No custom software and code was used.
Data analysis	Trimmomatic v. 0.33 (Bolger et al., 2014) http://www.usadellab.org/cms/?page=trimmomatic SPAdes v3.11.1 (Bankevich et al., 2012) https://cab.spbu.ru/files/release3.11.1/manual.html Prokka v.1.14 (Seemann, 2014) https://github.com/tseemann/prokka SAMtools v.0.1.19-44428cd (Li et al., 2009) https://www.htslib.org/ IGV (Integrative Genomics Viewer) v.2.10.0 (Thorvaldsdottir et al., 2013) https://igv.org/ SnpEff v.4.11 (Cingolani et al., 2012) https://pcingola.github.io/SnpEff/ RAxML v. 8.2.10 (Letunic and Bork, 2007) https://github.com/stamatak/standard-RAxML. PHYLOViZ (Ribeiro-Goncalves et al., 2016) https://www.phyloviz.net/ Guppy 4.2.3 (Wick et al., 2019) https://community.nanoporetech.com/docs/prepare/library_prep_protocols/Guppy-protocol/v/gpb_2003_v1_revax_14dec2018/guppy-software-overview Porechop 0.2.4 https://github.com/rrwick/Porechop Nanofilt 2.7.1 (De Coster et al., 2018) https://bioconda.github.io/recipes/nanofilt/README.html SeqKit 0.8.1 (Shen et al., 2016) https://github.com/annalam/seqkit Canu 2.1.1 (Koren et al., 2017) https://github.com/marbl/canu/releases Pilon 1.22 (Walker et al., 2014) https://github.com/broadinstitute/pilon/releases/ bwa 0.7.17 (Li and Durbin, 2009) https://github.com/lh3/bwa Circlator 1.5.5 (Hunt et al., 2015) https://github.com/sanger-pathogens/circlator Gepard 1.40 (Krumsiek et al., 2007) https://github.com/univieCUBE/gepard BLAST Ring Image Generator 0.95-dev.0004 (Alikhan et al., 2011) https://sourceforge.net/projects/brig/

ResFinder https://cge.cbs.dtu.dk/services/ResFinder/
SMRT Link 11.1.0.166339 https://www.pacb.com/wp-content/uploads/SMRT_Link_Installation_v11.1.pdf
pbmm2 1.9.0 https://github.com/PacificBiosciences/pbmm2
pb-CpG-tools 2.3.1 https://github.com/PacificBiosciences/pb-CpG-tools
DESeq2 (Love et al., 2014) https://bioconductor.org/packages/3.14/bioc/html/DESeq2.html
Salmon (Patro et al., 2017) https://combine-lab.github.io/salmon/
GraphPad Prism 9 GraphPad Software Prism 9 for macOS
Trim Galore v.0.6.4 https://github.com/FelixKrueger/TrimGalore
Bismark v.0.23.1 https://www.bioinformatics.babraham.ac.uk/projects/bismark/
bsseq https://bioconductor.org/packages/release/bioc/html/bsseq.html

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

All DNA sequencing and RNA sequencing data are available at DNA Data Bank of Japan, BioProject ID: PRJDB5246[https://ddbj.nig.ac.jp/search/entry/bioproject/PRJDB5246]

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	NICU: Our analysis was conducted retrospectively using clinical bacteria isolates from a NICU setting. The isolates were linked to limited patient data that did not include specific details on sex, gender, or race. Therefore, we were unable to incorporate these factors in our analysis. COVID-19 patients: Ten bacterial strains isolated from 10 patients with COVID-19 pneumonia were used in this study. The patients ranged in age from their 30s to 80s and included three females and seven males. This information is provided in Supplementary Table 5.
Reporting on race, ethnicity, or other socially relevant groupings	n/a, Our analysis was conducted retrospectively using clinical bacteria isolates and we were unable to incorporate these factors in our analysis.
Population characteristics	n/a, Our analysis was conducted retrospectively using clinical bacteria isolates and we were unable to incorporate these factors in our analysis.
Recruitment	n/a, No patients recruitment was performed in this study.
Ethics oversight	The Biomedical Research Ethics Committee of the Graduate School of Medicine, Chiba University approved the study protocol (ID: 3250 and M10368). Our study is a retrospective clinical investigation where we utilized de-identified data to ensure participant privacy and confidentiality. In this context, we implemented an opt-out consent process. Although we did not have a specific guardian consent form, the University Hospital posted study information on its website. This allowed guardians the opportunity to decline participation in the study on behalf of their wards.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	We did not predetermine the sample size for clinically isolated S. aureus because of the retrospective study and there is no exclusion criteria for this clinical study. We calculated the sample size required for our animal study using statistical power calculations with consideration of the expected death of

	animals. These calculations were based on preliminary data that indicated the magnitude of the effect we anticipated, along with standard deviations observed in previous similar studies. Sample sizes for in vitro experiments were determined based on standard practices in the field and our prior experience with similar assays. No formal sample size calculation was performed, as these experiments are typically exploratory in nature and focus on detecting biologically relevant trends rather than statistical significance. We chose sample sizes that were feasible within the constraints of time and resources, while ensuring the reproducibility of observed trends across independent experiments.
Data exclusions	All samples from the initial period of outbreak were analyzed in clinical study. No data exclusion was performed in in vitro and in vivo experiments.
Replication	For each in vitro and in vivo experimental setup, a minimum of three independent repetitions were conducted to guarantee the reliability of our findings.
Randomization	Animals, cells and bacteria were randomly divided into experimental groups.During handling, all samples were numbered and processed in random order to avoid introduction of bias into the samples.
Blinding	In both our in vitro and in vivo experimental systems, the small size of our research group limited our ability to separate roles for sample handling and data analysis without introducing additional logistical challenges. However, for bioinformatics analyses such as genomic analysis, the researchers responsible for the analysis were blinded to group assignments until the analyses were completed, ensuring blinding in these aspects of the study.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	anti-protein A antibody (Abcam ab60206) and (Nakamura et al., 2013) for western blotting. The antibodies were used at a 1:1000 (anti-protein A) and 1:250 (anti-δ-toxin) dilution.
Validation	anti-protein A antibody (Abcam ab60206) https://www.abcam.co.jp/products/primary-antibodies/protein-a-antibody-ab60206.html anti-δ-toxin antibody (Nakamura et al., 2013) https://www.nature.com/articles/nature12655

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	Mouse: C57BL/6J, The Jackson Laboratory (CLEA Japan) JAX: 000664
Wild animals	n/a
Reporting on sex	Mice systemic infection model was only conducted in female mice.
Field-collected samples	n/a
Ethics oversight	All mice used in this study had a C57BL/6 background and were kept under specific pathogen-free conditions in an animal facility at the Osaka University (Osaka, Japan). During the infection experiments, mice were kept in BSL2 animal facility. All mice were housed in an environment with a 12-hour light/dark cycle, maintaining an ambient temperature between 21°C and 25°C, and humidity levels controlled at 40-60%. All experiments were approved by the Animal Care and Use Committee of Osaka University (ID: 01-027-016) . All mice used in this study were euthanized under anesthesia.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*