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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees 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

Genome sequencing, spacer library sequencing, and transcript 5' end mapping data were collected using Illumina MiSeq Control Software v2.6.2.1
Conventional RNA-seq data was collected using Illumina NextSeq 500 Control Software v4.0
qPCR data in Figure 3a was collected using Applied Biosystems QuantStudio 12k flex
Growth curve data in Figs 3b, Extended Data 4b and 5b were collected with Tecan i-control v2.0
Resorufin fluorescence data in Extended Data 5d were collected with Tecan i-control v2.0

Data analysis

For genome sequencing:
Reads were quality-trimmed using Sickle (https://github.com/najoshi/sickle)
Reads were assembled into contigs using Abyss (https://github.com/bcgsc/abyss)
Contigs were mapped to reference L. seeligeri and L. ivanovii genomes using Medusa (http://combo.dbe.unifi.it/medusa)

Spacer library analysis:
Spacer reads were mapped to the phage genome using bowtie2 (http://bowtie-bio.sourceforge.net/bowtie2/index.shtml)
Custom Perl scripts were used to normalize spacer read counts, filter spacers containing fewer than 10 reads (pre-infection), and calculate enrichment ratios. These scripts are available upon request, as mentioned in the Code Availability statement below (and in the Methods section).

RNA-seq analysis:
RNA-seq reads (both conventional and 5' end mapping) were mapped to the host and phage genomes using bowtie2 (http://bowtiebio.sourceforge.net/bowtie2/index.shtml)
Custom Perl scripts were used to designate transcriptional start sites, count transcript 5' ends within and downstream of the transcriptional start sites, filter trancripts containing fewer than 20 reads, and calculate corresponding cleavage ratios for each transcript. These scripts are available upon request, as mentioned in the Code Availability statement below (and in the Methods section).

Code Availability statement: Custom scripts used in analysis of spacer library data as well as RNA 5' end mapping data are available upon request.

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

The L. seeligeri RR4 and L. ivanovii RR3 genome sequences, along with raw reads from the spacer library deep sequencing, paired end RNA-seq, and 5' end mapping have been deposited in the Sequence Read Archive under BioProject accession number PRJNA512236. Lists of strains, plasmids, and oligonucleotides used in this study are available in Supplementary Information 5.

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	No sample size calculation was performed. All experiments were performed with sample sizes based on standard protocols in the field.
Data exclusions	In spacer library analysis, spacers with fewer than 10 reads (pre-infection) were discarded to reduce noise and report accurate enrichment values. For transcript 5' end analysis, the transcriptional start sites could not be accurately determined for transcripts with fewer than 20 reads, therefore these data were excluded from analysis.
Replication	All measurements of phage infection efficiency, phage DNA content, and cell survival were performed in at least biological triplicate. NGS experiments were performed in biological duplicates.
Randomization	n/a. Animal or human research subjects were not involved in this study. None of the experiments were randomized.
Blinding	n/a. Animal or human research subjects were not involved in this study. None of the investigators were blinded.

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
☒	☐ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data

Methods

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