

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☐	☒ 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
☒	☐ 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 <i>d</i> , Pearson's <i>r</i>), 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	The custom code used to select appropriate start codons and calculate their relative frequency per gene is available at https://github.com/lukasmalfi/startcodons .
Data analysis	All data analysis softwares used in this study are described in the Materials and Methods. For mouse experiments, non-parametric statistical testing was performed using GraphPad Prism 8 for Windows. BLAST (blastn) was used to create databases from selected metabolic regulator genes in E. coli, and to search all genomes for them. The metabolic regulator sequences in Enterobacteriaceae families were selected using PIRATE v1.0.5. Prodigal v 2.6.3 was then used to call putative ORFs, and results were plotted with ggplot2 v3.3.5 in R 3.6.3. For statistical comparison of start codon usage between carbohydrate related and unrelated regulators, non-parametric statistical testing was performed in R 3.6.3. Phylogenetic trees were calculated with gtdbtk v 2.1.0 and visualized in iTOL v6.9.1 (https://itol.embl.de/version_history.cgi). The custom code used to select appropriate start codons and calculate their relative frequency per gene is available at https://github.com/lukasmalfi/startcodons . The whole genome assembly and annotation was performed with Flye 2.9.2, CLC workbench 23.0.1 (for polishing) and prokka 1.14.5. CLC workbench was also used for mutation analysis.

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 data needed to evaluate the conclusions in the article are presented in the paper and the supplementary information. The sequenced genomes of the E. coli 8178 WT, ATGlacI and GTGlacI strains have been deposited in NCBI (Bioproject ID: PRJNA1096466) under the accession number SAMN40757031, SAMN40757032, SAMN40757033 respectively. Source data are available for Figures 2-5 and Extended Data Figs 1-5. The accession numbers of all downloaded genomes used for bioinformatic analysis are specified in Supplementary Table 6. The 10,643 Escherichia coli genomes as well as the genomes used for other families were downloaded from the Progenomes3 database (<https://progenomes.embl.de/>). Sequences of E. coli K-12 MG1665 metabolic regulator genes were obtained from Biocyc (<https://biocyc.org/>).

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

N/A

Reporting on race, ethnicity, or other socially relevant groupings

N/A

Population characteristics

N/A

Recruitment

N/A

Ethics oversight

N/A

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](https://www.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

At least 5 mice were used in each group. Sample size was chosen according to institutional directives and in accordance with the 3Rs rules (Replacement, Reduction and Refinement) guiding principles underpinning the humane use of animals in research, but no statistical analyses were performed to predetermine the sample sizes

Data exclusions

No data were excluded from the analysis.

Replication

All the experiments were performed at least twice, with all attempts at data replication being successful

Randomization

Mice were randomly allocated to different treatments

Blinding

Blinding does not apply to this study because the investigators needed to identify the cages of mice for subsequent treatments/infections with respective bacterial strains.

Behavioural & social sciences study design

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

Study description

N/A

Research sample	N/A
Sampling strategy	N/A
Data collection	N/A
Timing	N/A
Data exclusions	N/A
Non-participation	N/A
Randomization	N/A

Ecological, evolutionary & environmental sciences study design

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

Study description	N/A
Research sample	N/A
Sampling strategy	N/A
Data collection	N/A
Timing and spatial scale	N/A
Data exclusions	N/A
Reproducibility	N/A
Randomization	N/A
Blinding	N/A

Did the study involve field work? ☐ Yes ☒ No

Field work, collection and transport

Field conditions	N/A
Location	N/A
Access & import/export	N/A
Disturbance	N/A

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-LacI Antibody (Sigma-Aldrich; 05-503-I); RNA polymerase beta Antibody (ThermoFischer Scientific, MA125425); Goat Anti-Mouse IgG Antibody Alkaline Phosphatase conjugate (Sigma-Aldrich, AP124A).

Validation

The LacI antibody was validated by western blot by the manufacturer in E. coli BL21 (<https://www.sigmaaldrich.com/CH/de/product/mm/05503i>). The RNA polymerase beta antibody was used and validated in the following studies : Zhou et al., Structure of the human cGAS-DNA complex reveals enhanced control of immune surveillance, Cell 2018; Lennings et al., Polar localization of the ATPase ClpV-5 occurs independent of type VI secretion system apparatus proteins in Burkholderia thailandensis, BMC Research Notes, 2019).

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)

N/A

Authentication

N/A

Mycoplasma contamination

N/A

Commonly misidentified lines
(See [ICLAC](#) register)

N/A

Palaeontology and Archaeology

Specimen provenance

N/A

Specimen deposition

N/A

Dating methods

N/A

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight

N/A

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

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

8 - to 12-week old C57BL/6 and 129S6/SvEvTac mice (The Jackson Laboratory) mice were held under specific pathogen-free (SPF) conditions at the EPIC facility at ETH Zürich (light/dark cycle 12:12 h, room temperature 21±1 °C, humidity 50±10%). Germ-free mice were bred in flexible film isolators under strict exclusion of microbial contamination at the isolator facility (EPIC).

Wild animals

No wild animals were used

Reporting on sex

8-12 weeks old mice of both sexes were randomly assigned to experimental groups

Field-collected samples

This work does not involve samples collection from fields

Ethics oversight

All animal experiments were reviewed and approved by Kantonales Veterinäramt Zürich under license ZH158/2019, ZH108/2022; ZH109/2022, complying with the cantonal and Swiss legislation

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

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration	N/A
Study protocol	N/A
Data collection	N/A
Outcomes	N/A

Dual use research of concern

Policy information about [dual use research of concern](#)

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes
☒	☐ Public health
☒	☐ National security
☒	☐ Crops and/or livestock
☒	☐ Ecosystems
☒	☐ Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes
☒	☐ Demonstrate how to render a vaccine ineffective
☒	☐ Confer resistance to therapeutically useful antibiotics or antiviral agents
☒	☐ Enhance the virulence of a pathogen or render a nonpathogen virulent
☒	☐ Increase transmissibility of a pathogen
☒	☐ Alter the host range of a pathogen
☒	☐ Enable evasion of diagnostic/detection modalities
☒	☐ Enable the weaponization of a biological agent or toxin
☒	☐ Any other potentially harmful combination of experiments and agents

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A

ChIP-seq

Data deposition

- ☐ Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- ☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links
May remain private before publication.

N/A

Files in database submission

N/A

Genome browser session
(e.g. [UCSC](#))

N/A

Methodology

Replicates

N/A

Sequencing depth

N/A

Antibodies

N/A

Peak calling parameters

N/A

Data quality

N/A

Software

N/A

Flow Cytometry

Plots

Confirm that:

- ☐ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- ☐ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- ☐ All plots are contour plots with outliers or pseudocolor plots.
- ☐ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation

N/A

Instrument

N/A

Software

N/A

Cell population abundance

N/A

Gating strategy

N/A

- ☐ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.

Magnetic resonance imaging

Experimental design

Design type

N/A

Design specifications

N/A

Behavioral performance measures

N/A

Acquisition

Imaging type(s)	N/A	
Field strength	N/A	
Sequence & imaging parameters	N/A	
Area of acquisition	N/A	
Diffusion MRI	☐ Used	☐ Not used

Preprocessing

Preprocessing software	N/A
Normalization	N/A
Normalization template	N/A
Noise and artifact removal	N/A
Volume censoring	N/A

Statistical modeling & inference

Model type and settings	N/A
Effect(s) tested	N/A
Specify type of analysis:	☐ Whole brain ☐ ROI-based ☐ Both
Statistic type for inference	N/A
(See Eklund et al. 2016)	
Correction	N/A

Models & analysis

n/a	Involvement in the study
☒	☐ Functional and/or effective connectivity
☒	☐ Graph analysis
☒	☐ Multivariate modeling or predictive analysis
Functional and/or effective connectivity	N/A
Graph analysis	N/A
Multivariate modeling and predictive analysis	N/A