

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	Microbial compositional data and host transcriptional data were deposited at NCBI GEO GSE293364 (superseries containing RNA sequencing of colons from mice with the different antibiotics and 16s amplicon sequences from fecal samples of these mice) and GSE293029 (RNA sequencing data from SPF and GF mice treated with vancomycin IP and sampled every 6 hours over 24 hours). The paired antibiotics with stool metagenomics and 16S amplicon sequencing is deposited in NBCI Bioproject PRJNA1442090 with metadata in SI Table S9. The RNA sequencing of the PC12 cells in NCBI GEO GSE324684.
Data analysis	Code was deposited at https://github.com/AmirErez/CompoRes . The scripts used to analyze the data were deposited at https://github.com/AmirErez/Manuscript-Analysis-of-Host-and-Microbiome-Responses-to-Antibiotics .

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](#)

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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

Reporting on race, ethnicity, or other socially relevant groupings

Population characteristics

Recruitment

Ethics oversight

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

Data exclusions

Replication

Randomization

Blinding

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	For immunofluorescence, tissues were incubated in a blocking buffer (10% FBS, 0.1% Triton X-100) and then treated overnight at 4°C with a mouse anti-β3-tubulin primary antibody (Abcam, 1:200). Following primary incubation, a secondary anti-mouse Alexa Fluor 594 antibody (1:300) was applied for one hour at room temperature.
Validation	N/A

Eukaryotic cell lines

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

Cell line source(s)	Mode-K cells were acquired from Kaiserlian, D and described in Vidal, K., Grosjean, I., evillard, J.P., Gespach, C., and Kaiserlian, D. (1993). Immortalization of mouse intestinal epithelial cells by the SV40-large T gene. Phenotypic and immune characterization of the MODE-K cell line. J Immunol Methods 166, 63–73. https://doi.org/10.1016/0022-1759(93)90329-6 .
Authentication	Not authenticated.
Mycoplasma contamination	Not tested.
Commonly misidentified lines (See ICLAC register)	N/A

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	C57BL6/J and Swiss Webster mice were bred and maintained under a 12-hour light/dark cycle at 25°C and fed standard chow in either SPF or germ-free conditions at the Azrieli Faculty of Medicine of the Bar-Ilan University. Male SPF C57BL6/J mice were used for experiments with multiple antibiotics (Fig. 1-3), and female SPF and germ-free Swiss Webster were used to study diurnal function (Fig. 4 and 5). Wild type C57BL6/J were purchased from Envigo RMS Israel Ltd, Nmu ^{-/-} mice ⁷¹ (Nmu ^{<tm1Mko>} (RBRC04549), RIKEN Japan) were generated from frozen sperm by the Bar-Ilan University transgenic core. 8- to 12-week-old mice were used for all experiments.
Wild animals	N/A
Reporting on sex	The sex of the mice is described in the relevant methods section. Female mice were mostly used for ease of co-caging.
Field-collected samples	N/A
Ethics oversight	All experiments using mice were conducted in compliance with the EU directive regarding the protection of animals used for experimental and other scientific purposes. Experiments were approved by the institutional animal care and use committee (IACUC) of the Bar-Ilan University (study ID #25-04-2019).

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

Plants

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