

## 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  |
|-------------------------------------|--|
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The exact sample size ( $n$ ) for each experimental group/condition, given as a discrete number and unit of measurement  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided<br><i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>   |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A description of all covariates tested   |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> 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) |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. $F$ , $t$ , $r$ ) with confidence intervals, effect sizes, degrees of freedom and $P$ value noted<br><i>Give <math>P</math> values as exact values whenever suitable.</i>                            |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings  |
| <input type="checkbox"/>            | <input checked="" type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes   |
| <input checked="" type="checkbox"/> | <input type="checkbox"/> 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	None
Data analysis	<p>ANCHOR v.1 Gonzalez et al. 201935 <a href="https://github.com/gonzalezem/ANCHOR">https://github.com/gonzalezem/ANCHOR</a></p> <p>Mothur v.1.44.1 Schloss et al.152 <a href="https://mothur.org/">https://mothur.org/</a></p> <p>USEARCH v.9 Edgar 153 <a href="https://drive5.com/usearch/">https://drive5.com/usearch/</a></p> <p>BLAST Altschul et al.154 <a href="https://blast.ncbi.nlm.nih.gov/doc/blast-help/references.html#blast-programs">https://blast.ncbi.nlm.nih.gov/doc/blast-help/references.html#blast-programs</a></p> <p>DESeq2 Love et al.155 <a href="https://bioconductor.org/packages/release/bioc/html/DESeq2.html">https://bioconductor.org/packages/release/bioc/html/DESeq2.html</a></p> <p>Phyloseq v.1.27 McMurdie and Holmes156 <a href="https://joey711.github.io/phyloseq/index.html">https://joey711.github.io/phyloseq/index.html</a></p> <p>R v.4.0.2 R Core Team157</p>

<https://www.r-project.org>

Trim Galore! v0.6.6 Felix Krueger, Babraham Institute <https://github.com/FelixKrueger/TrimGalore>

Cutadapt v2.10 Martin 2011158  
<https://cutadapt.readthedocs.io>

Fastqc v0.11.5 Andrews 2010159  
<https://www.bioinformatics.babraham.ac.uk/projects/fastqc/>

BBMAP v37.78 Bushnell 2014160  
<https://www.osti.gov/biblio/1241166>

ORNA v.0.4 Durai et al. 2018161  
<https://github.com/SchulzLab/ORNA>

MEGAHIT v1.2.9 Li et al. 2016162  
<https://github.com/voutcn/megahit>

Prodigal v2.6.3 Hyatt et al. 2010163  
<https://github.com/hyattpd/Prodigal>

GhostKOALA Kanehisa et al. 2016164  
<https://www.kegg.jp/ghostkoala/>

MetaBAT2, v2.12.1 Kang et al. 2019165  
<https://bitbucket.org/berkeleylab/metabat>

CheckM v1.1.6 Parks et al. 2015166  
<https://ecogenomics.github.io/CheckM/>

CAT v5.2.3 von Meijenfeldt et al. 2019167  
<https://github.com/dutilh/CAT>

MultiQC v1.13 Ewels et al. 2016168  
<https://multiqc.info/>

STAR v2.7.10 Dobin et al. 2013169  
<https://github.com/alexdobin/STAR>

RSEM v1.3.3 Li et al. 2011170  
<https://github.com/deweylab/RSEM>

Webgestalt web server Liao et al. 201984  
<https://www.webgestalt.org/>

PathView v3.18 Luo et al. 2013171  
<https://pathview.uncc.edu/>

Cluster Profiler v4.7.1.003 Wu et al. 2021172  
<https://guangchuangyu.github.io/software/clusterProfiler/>

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 datasets generated and/or analyzed during the study are available in supplementary materials or have been deposited in publicly accessible repositories in line with NASA Open Science principles.

## 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/r

Reporting on race, ethnicity, or other socially relevant groupings

n/r

Population characteristics

n/r

Recruitment

n/r

Ethics oversight

n/r

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://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

Sample sizes were determined by the SpaceX payload and ISS rodent habitat constraints.

Data exclusions

No data was excluded.

Replication

n varied from 7 to 10 mice per group.

Randomization

Mice were randomly assigned to groups from an initial cohort. No inter-cage controls were used (presented in the study limitations).

Blinding

Blinding was not relevant.

## 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

## 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

Mus musculus, C57BL/6N

Wild animals

The study did not involve wild animals

Reporting on sex

Female mice only were used. Recent Rodent Research missions are diversifying sex but space mission research is extremely n limited. This is discussed in review.

Field-collected samples

In addition to methodology details. Mission reports are linked in the manuscript which provide extensive sampling and background, and are a permanent destination.

Ethics oversight

The study uses data made publicly available by NASA and the co-authors did not directly conduct the animal experiments in space or on Earth. The ethics for the rodent research 6 mission was approved by NASA.

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

## Plants

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Seed stocks

N/R

Novel plant genotypes

N/R

Authentication

N/R