

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 <i>P</i> 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	Untargeted LC–MS/MS data were acquired using Thermo Scientific Xcalibur v[version] on a Vanquish UHPLC system coupled to a Q Exactive HF-X mass spectrometer. Targeted amino acid LC–ESI–MS/MS data were acquired using Analyst v1.6.3 on an ExionLC AD UPLC system coupled to a QTRAP 6500+ mass spectrometer.
Data analysis	Metagenomic data were processed using fastp v0.23.4, KneadData v0.12.0, Kraken2 v2.1.2 and Bracken v2.8, with species annotations filtered against the Human Oral Microbiome Database. PCoA and LEfSe analyses were performed using the OECloud platform (https://cloud.oebiotech.com/#/home), and Spearman correlation analysis was performed using R v4.4.1. Untargeted LC–MS/MS data were converted to mzML format using ProteoWizard v3.0.2 and processed using XCMS v4.8.0. Missing values were processed using K-nearest-neighbour or minimum-value-based imputation, and peak areas were corrected using support vector regression. Metabolites were annotated using in-house and public databases together with metDNA v1.23. Metabolomic PCoA and other visualizations were generated using the Metware Cloud platform, and OPLS-DA was performed using MetaboAnalystR v1.0.1. For targeted amino acid metabolomics, LC–MS/MS data were processed using Analyst v1.6.3, and chromatographic peaks were integrated and corrected using MultiQuant v3.0.3. Metabolites were identified against the MetWare Database using authentic standards and quantified using external standard curves. Differential metabolites were identified based on fold-change thresholds, and heatmaps were generated using the Metware Cloud platform. Statistical analyses were performed using GraphPad Prism 9.

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](#)

The subgingival plaque metagenomic sequencing data used in this study are publicly available from the Sequence Read Archive (SRA) under BioProject accessions: PRJNA230363 (<https://www.ncbi.nlm.nih.gov/bioproject/PRJNA230363>), PRJNA932553 (<https://www.ncbi.nlm.nih.gov/bioproject/PRJNA932553>), PRJNA255922 (<https://www.ncbi.nlm.nih.gov/bioproject/255922>), PRJNA508385 (<https://www.ncbi.nlm.nih.gov/bioproject/PRJNA508385>), PRJDB11203 (<https://www.ncbi.nlm.nih.gov/bioproject/?term=PRJDB11203>). The raw metabolomics data generated in this study have been deposited in the MetaboLights repository under accession codes: MTBLS14827 (<https://www.ebi.ac.uk/metabolights/MTBLS14827>), MTBLS14833 (<https://www.ebi.ac.uk/metabolights/MTBLS14833>), MTBLS14834 (<https://www.ebi.ac.uk/metabolights/MTBLS14834>). Source data are provided with this paper.

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

No new human participants were recruited for this study. Human data were obtained from publicly available, de-identified metagenomic datasets. Sex was not included as an analytical variable because sex metadata were not consistently available across the included datasets, and gender information was not available.

Reporting on race, ethnicity, or other socially relevant groupings

This study used publicly available, de-identified human metagenomic datasets from multiple international cohorts. Information on race, ethnicity, and other socially relevant groupings was not consistently available across the included datasets and was not analyzed in this study.

Population characteristics

This study used five publicly available, de-identified human subgingival plaque metagenomic datasets from China, the United States, and Japan. The integrated cohort included 102 samples, comprising 44 periodontally healthy controls and 58 patients with periodontitis. Detailed sample information is provided in Supplementary Table 5. Age, sex, and other participant-level characteristics were not consistently available across all included datasets.

Recruitment

No new human participants were recruited for this study. This work analyzed publicly available, de-identified subgingival plaque metagenomic datasets from China, the United States, and Japan. Recruitment was performed by the original studies, and the present study represents a secondary analysis of these public datasets.

Ethics oversight

No new human participants were recruited and no new human biological materials were collected for this study. The human data analyzed were obtained from publicly available, de-identified subgingival plaque shotgun metagenomic datasets (PRJNA230363, PRJNA932553, PRJNA255922, PRJNA508385, and PRJDB11203). Ethics oversight, participant recruitment, and informed consent were the responsibility of the original studies. The present work represents a secondary analysis of publicly available de-identified data.

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

Sample sizes were determined empirically and according to extensive literature on the Porphyromonas gingivalis infection models and periodontitis model, and appropriate statistical analyses were performed. Each in vitro experiment was repeated with at least 3 individual biological replicates. The in vivo study was employed once, with n=5/10 mice per group, and each mouse was considered an independent biological replicate. The animal experiment was not repeated in a separate cohort to avoid unnecessary animal use in accordance with the 3Rs principle, as biological replication was incorporated within each experimental group. Exact sample sizes are provided in the corresponding figure legends.

Data exclusions	No data was excluded from analysis.
Replication	The animal experiment was performed only once, whereas the reproducibility of all other experimental data was confirmed by two or three independent experiments. The animal experiment was not repeated in a separate cohort to avoid unnecessary animal use in accordance with the 3Rs principle, as biological replication was incorporated within each experimental group.
Randomization	Mice were received from vendors and randomly assigned to experimental groups.
Blinding	Blinding was not performed.

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	Six-week-old male C57BL/6 mice
Wild animals	The study did not involve wild animals.
Reporting on sex	Only male mice were used in the study.
Field-collected samples	No field-collected samples were used in the study.
Ethics oversight	The animal experiments conducted in this research were approved by the Ethics Committee of West China Hospital of Stomatology, Sichuan University (Protocol Number: WCHSIRB-D-2019-185).

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