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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 (*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	Not applicable
Data analysis	Not applicable

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 authors confirm that the date supporting the findings of this study are available within the article.

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	Not applicable
Reporting on race, ethnicity, or other socially relevant groupings	Not applicable
Population characteristics	Not applicable
Recruitment	Not applicable
Ethics oversight	Not applicable

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

Life sciences study design

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

Sample size	The sample size□5-10 size mice per group for each experiment) was set as in the previous study. (Hiyoshi, T. et al. Neutrophil elastase aggravates periodontitis by disrupting gingival epithelial barrier via cleaving cell adhesion molecules. Sci Rep 12, 8159, doi:10.1038/s41598-022-12358-3 (2022).Tamura, H. et al. Effects of Erythromycin on Osteoclasts and Bone Resorption via DEL-1 Induction in Mice. Antibiotics (Basel) 10, doi:10.3390/antibiotics10030312 (2021).)
Data exclusions	A criterion was set that mice with unraveled ligature will be excluded. No mice were excluded from the study.
Replication	The same experiment was performed two or three times with independent groups in both in vivo and in vitro, and the same trend was observed.
Randomization	Ligation and injection were performed on one mouse from each group in turn to minimize potential confounders. Briefly, mice randomly were tied around the maxillary second molar to induce periodontitis and injected each reagents into the palatal gingiva of the molar.
Blinding	All animal experiments were conducted by a researcher who analyzed the results and was blinded to the actual experiment.

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	SLPI antibody (Novus Bio, Centennial, USA, Catalog Number: NBP1-76803, Lot: 4249-1904), Alexa Fluor 488 conjugated anti-rabbit secondary antibody (Invitrogen, Carlsbad, CA, Catalog Number: A11034, Lot: 2018207),
Validation	SLPI antibody (https://www.novusbio.com/products/slpi-antibody_nbp1-76803#PublicationSection)

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	The murine osteoblastic progenitor cell line , MC3T3-E1, obtained from the RILEN Bioresource Center(RCB1126).
Authentication	MC3T3-E1 cells were subjected to periodic microscopic morphological checks and cell growth curve analysis to authenticate the cell line.
Mycoplasma contamination	All cell lines tested negative for mycoplasma contamination OR.
Commonly misidentified lines (See ICLAC register)	MC3T3-NM4 (Accession: CVCL_B6H0)

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	Male 7-8 week-old BALB/cA mice
Wild animals	The BALB/cA mice was purchased from CLEA Japan, Inc. (Tokyo, Japan), maintained under standard conditions in individual cages, and provided with sterile food and water ad libitum. All animal experiments were approved by the Institutional Animal Care and Use Committee of Niigata University (approval no. SA00181). After the study, All mice were anesthetized with a mixture of medetomidine hydrochloride, midazolam, and butorphanol and sacrificed.
Reporting on sex	It has been suggested that estrogen, a female hormone, suppresses gingival inflammation and the production of inflammatory cytokines, and influences susceptibility to periodontitis. (Shiau HJ, Reynolds MA. Sex differences in destructive periodontal disease: exploring the biologic basis. J Periodontol. 2010 Nov;81(11):1505-17. doi: 10.1902/jop.2010.100045. Epub 2010 Jul 1. PMID: 20594052.) Therefore, we have studied the pathogenesis of periodontitis in male mice. (Hiyoshi, T. et al. Neutrophil elastase aggravates periodontitis by disrupting gingival epithelial barrier via cleaving cell adhesion molecules. Sci Rep 12, 8159, doi:10.1038/s41598-022-12358-3 (2022).)In this study, we used male mice to analyze the pathogenesis of periodontitis, in reference to previous studies.
Field-collected samples	The study did not involve collected from the field.
Ethics oversight	All animal experiments were approved by the Institutional Animal Care and Use Committee of Niigata University (approval no. SA00181).

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

Plants

Seed stocks	Not applicable
Novel plant genotypes	Not applicable
Authentication	Not applicable