

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	No custom software was used for data collection. Commercial instruments and manufacturer-provided software were used for data acquisition, including microscopy imaging systems and sequencing platforms as described in the Methods section.
Data analysis	Data analysis was performed using R software (version 4.2.1), RStudio (version 2022.12.0-353), and GraphPad Prism (version 8.0). Transcriptomic differential expression analysis was conducted using the R package limma. Gene Ontology (GO) and KEGG pathway enrichment analyses were performed using the R package clusterProfiler. Heatmaps and volcano plots were generated using pheatmap and ggplot2. No custom code or unpublished algorithms were used in this study.

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 sequencing data has been deposited in the NCBI database with the following details: - Submission: SUB15316822 - BioProject: PRJNA1262076

The SRA IDs are listed below: Control group: - SRR33537231 - SRR33537230 - SRR33537229

LL37 group: - SRR33537228 - SRR33537227 - SRR33537226

GBP group: - SRR33537225 - SRR33537224 - SRR33537223.

Uncropped and unedited blot/gel images (Supplementary Figure 5) are provided in the Supplementary Information.

Numerical source data underlying the graphs and charts presented in the main figures can be found in Supplementary Data file

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	Sex was recorded for all participants based on self-report. Both male and female patients with rosacea were included in this study. Sex and gender were not considered as variables in the study design or statistical analyses, as the study was not powered to detect sex- or gender-specific effects and no sex- or gender-based differences were hypothesized.
Reporting on race, ethnicity, or other socially relevant groupings	Information on race or ethnicity was not collected in this study. All participants were recruited from a single clinical center in China, and race or ethnicity was not considered as a variable in the study design or analyses.
Population characteristics	The study included 60 newly diagnosed and untreated patients with rosacea. Participants were adults diagnosed according to the 2017 National Rosacea Society Expert Committee diagnostic criteria. Patients with systemic diseases, other skin disorders, pregnancy or lactation, recent use of systemic immunomodulators or antibiotics, or metabolic comorbidities were excluded. Baseline demographic and clinical characteristics were recorded prior to treatment and are summarized in Table 2.
Recruitment	Participants were consecutively recruited from the Department of Dermatology at the First Affiliated Hospital of Chongqing Medical University between January and December 2023. Eligible patients were screened according to predefined inclusion and exclusion criteria and were randomly assigned to the gabapentin treatment group or the minocycline plus hydroxychloroquine combination treatment group. As patients were recruited from a single tertiary medical center, some degree of selection bias may be present.
Ethics oversight	The study protocol was approved by the Clinical Ethics Committee of Chongqing Medical University (Approval No. 2024-111-01). All participants provided written informed consent prior to enrollment. The study was conducted in accordance with the Declaration of Helsinki and all relevant ethical regulations.

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	Sample sizes were determined based on prior literature and similar experimental designs in the field. No formal statistical methods were used to predetermine sample size. For animal experiments, five mice per group were used, consistent with previous studies employing LL37-induced rosacea-like models. For clinical studies, a total of 60 patients (30 per group) were enrolled to allow comparison between treatment groups. These sample sizes were considered sufficient to detect biologically meaningful differences.
Data exclusions	No data were excluded from the analyses. All collected samples and measurements that met the predefined inclusion criteria were included in the final analyses.
Replication	All experiments were repeated independently with similar results. For animal experiments, each mouse was treated as an independent biological replicate. For in vitro experiments, assays were performed with multiple independent biological replicates. The main findings

reported in this study were reproducible.

Randomization

For clinical studies, patients were randomly assigned to the gabapentin treatment group or the minocycline plus hydroxychloroquine combination treatment group. For animal experiments, mice were randomly allocated to experimental groups prior to treatment. No other stratification factors were applied.

Blinding

Investigators were not blinded to group allocation during treatment administration. However, outcome assessments and data analyses were performed using predefined criteria, and quantitative analyses were conducted in an objective manner. Blinding was not applied due to the nature of the experimental design.

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

The following primary antibodies were used in this study: anti-PGP9.5 (MA1-83428, Invitrogen), anti-NF-κB p65 (ab32536, Abcam), anti-ICAM-1 (#4915, Cell Signaling Technology), anti-VCAM-1 (#32653, Cell Signaling Technology), anti-IκB-α (ab32518, Abcam), anti-IKKα (ab32041, Abcam), anti-TNF-α (ab183218, Abcam), anti-β-actin (ab8226, Abcam), and anti-Histone H1 (PA5-30055, Invitrogen). Secondary antibodies included HRP-conjugated anti-rabbit IgG (7074, Cell Signaling Technology) and HRP-conjugated anti-mouse IgG (ab205719, Abcam). Antibody dilutions are provided in the Methods section.

Validation

All antibodies used in this study were commercially available and validated by the manufacturers for the reported species and applications. Antibody validation information is available on the manufacturers' websites. In addition, antibody specificity was confirmed by observing bands at the expected molecular weights in Western blot analyses and by appropriate staining patterns in immunohistochemistry and immunofluorescence experiments.

Eukaryotic cell lines

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

Cell line source(s)

The murine microglial cell line BV2 was obtained from BFB Bioscience (catalog number BFN608006363). BV2 cells are derived from mouse microglia. The sex of the original donor animal was not reported by the supplier.

Authentication

The BV2 cell line was not independently authenticated by the authors.

Mycoplasma contamination

The BV2 cell line was not tested for mycoplasma contamination.

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

The BV2 cell line is not listed as a commonly misidentified cell line by the ICLAC register.

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

Female BALB/c mice aged 6–8 weeks and weighing 23 ± 2 g were used in this study. Mice were obtained from Beijing VitalHD Animal Experimental Technology Co., Ltd. and housed under specific pathogen-free (SPF) conditions with controlled temperature (22–25 °C), humidity (60–65%), and a 12 h light/12 h dark cycle, with ad libitum access to food and water.

Wild animals

This study did not involve wild animals.

Reporting on sex

Female mice were used for all animal experiments. Sex-based analyses were not performed, as the study was not designed or powered to assess sex-specific effects.

Field-collected samples	This study did not involve samples collected directly from the field.
Ethics oversight	All animal experiments were approved by the Animal Ethics Committee of Chongqing Medical University (No. IACUC-CQMU-2024-0832). This study was approved by the Clinical Ethics Committee of Chongqing Medical University (No. 2024-111-01) and adhered to the principles of the Helsinki Declaration, all patients signed informed consent forms. All ethical regulations relevant to human research participants were followed.

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	This study was not registered in a public clinical trial registry. The study was designed as an investigator-initiated, single-center clinical study and was approved by the institutional ethics committee prior to participant enrollment.
Study protocol	The full study protocol, including eligibility criteria, treatment regimens, and outcome assessments, is described in the Methods section of the manuscript.
Data collection	Clinical data were collected at the Department of Dermatology, the First Affiliated Hospital of Chongqing Medical University. Participants were recruited between January and December 2023. Clinical assessments and blood sample collection were performed at baseline and after four weeks of treatment. Serum samples were collected following overnight fasting and stored at -80°C until analysis.
Outcomes	The primary outcomes were changes in clinical disease severity, assessed using the Investigator's Global Assessment (IGA) and Clinical Erythema Assessment (CEA) scores after four weeks of treatment. Secondary outcomes included changes in serum inflammatory and neuropeptide-related biomarkers, measured by ELISA. Outcomes were assessed using predefined scoring criteria and standardized laboratory methods.

Plants

Seed stocks	This study did not involve plants.
Novel plant genotypes	This study did not involve plants.
Authentication	This study did not involve plants.

Magnetic resonance imaging

Experimental design

Design type	This study did not involve magnetic resonance imaging.
Design specifications	This study did not involve magnetic resonance imaging.
Behavioral performance measures	This study did not involve magnetic resonance imaging.

Acquisition

Imaging type(s)	Not applicable.
Field strength	Not applicable.
Sequence & imaging parameters	Not applicable.
Area of acquisition	Not applicable.
Diffusion MRI	☐ Used ☒ Not used

Preprocessing

Preprocessing software	Not applicable
Normalization	Not applicable
Normalization template	Not applicable
Noise and artifact removal	Not applicable
Volume censoring	Not applicable

Statistical modeling & inference

Model type and settings	Not applicable
Effect(s) tested	Not applicable
Specify type of analysis:	☐ Whole brain ☐ ROI-based ☐ Both
Statistic type for inference	Not applicable
(See Eklund et al. 2016)	
Correction	Not applicable

Models & analysis

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