

Reporting Summary

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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

In some experiments, the WinROOF software (Mitani Corporation, Tokyo, Japan) or the ImageJ software was used for quantification and raw data collection. The Olympus BX50 microscope with an OlympusDP70 digital camera was used for data collection. Data collection during the single-cell study was Single-cell RNA sequencing was conducted by Takara Bio Inc. (Shiga, Japan) (<https://www.takarabio.com/>). Custom algorithms were not used to collect data.

Data analysis

The GraphPad Prism version 10.4.1 (GraphPad Software, Inc., San Diego, CA) was used to perform the statistical analysis. The public domain NIH ImageJ program was used for image analysis. Analysis of the single-cell data was performed at Takara Bio Inc.

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 data supporting the findings of this study are available within the manuscript, its supplementary materials, and the open-access repository Figshare (<https://doi.org/10.6084/m9.figshare.31668937>). The complete genome sequences of bacterial DNA isolated from the BALF of patients and healthy subjects are available at the NCBI BioProject database (https://www.ncbi.nlm.nih.gov/sra?linkname=bioproject_sra_all&from_uid=1218794). Source data are provided with this paper.

Code availability. No custom code was developed for this study. All relevant analysis procedures are described in the Methods section.

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

The term "sex" is used throughout the manuscript to refer to biological attributes. The study evaluated the presence of corisin sequences and corisin activity in bronchoalveolar lavage fluid from patients with idiopathic pulmonary fibrosis and healthy subjects, including both male and female individuals. A sex-stratified analysis was performed and showed no significant influence of biological sex on the detection of corisin sequences or corisin activity. Therefore, comparisons between patients and healthy subjects were conducted using individuals of both sexes. In the experimental studies using corisin transgenic mice, only male mice were used in the bleomycin-induced pulmonary fibrosis model to investigate the role of corisin in fibrotic lung injury. This approach was based on previous observations demonstrating that male and female mice develop comparable degrees of pulmonary fibrosis following bleomycin administration. In experiments evaluating spontaneous fibrosis in corisin transgenic mice, both male and female animals were used.

Reporting on race, ethnicity, or other socially relevant groupings

The study on idiopathic pulmonary fibrosis patients was conducted exclusively among Japanese subjects. Inclusion of individuals from other racial groups was not feasible due to the homogeneity of the Japanese population and the study being conducted solely within Japan.

Population characteristics

This study included 14 Japanese patients with idiopathic pulmonary fibrosis (IPF) (mean age 69.0 ± 7.2 years; 13 males and 1 female) and three healthy Japanese male volunteers. BALF samples were obtained from the patients during the stable phase of disease and again during acute exacerbation. Patient characteristics are summarized in Supplementary Table 1. The study population consisted exclusively of Japanese participants, reflecting the demographic composition of the local patient cohort and the clinical setting in which the study was conducted.

Recruitment

This study enrolled 14 Japanese patients with idiopathic pulmonary fibrosis and three healthy controls. The diagnosis of IPF was established according to internationally accepted criteria. Bronchoscopic procedures were performed in accordance with the American Thoracic Society guidelines, and bronchoalveolar lavage fluid samples were obtained from all 14 patients with IPF and from the three healthy controls.

Ethics oversight

The study protocol was approved by the Ethical Committee for Clinical Investigation of Mie University (approval No. H2019064, date: 25/04/2019).

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 for the experiments was determined using power calculations performed with GraphPad Prism software (version 10.4.1; GraphPad Software, Inc., San Diego, CA).

Data exclusions

The inclusion criteria for the clinical study were a diagnosis of idiopathic pulmonary fibrosis with or without acute exacerbation. Patients receiving anticancer therapy, those with incomplete clinical data or inadequate sample quality, and those who did not provide informed consent were excluded. In contrast, no data exclusions were applied in the in vitro or in vivo experiments using experimental animal models.

Replication

Repeated experiments were conducted to ensure the reproducibility of the findings. All measurements were consistent, and every replication

attempt was successful.

Randomization

In the clinical study, subjects were categorized according to the diagnosis of idiopathic pulmonary fibrosis with or without acute exacerbation. In the in vivo experimental studies using animal models of the disease, animals were randomly assigned to control, disease, treated, and untreated groups.

Blinding

The research adhered to the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines for animal studies, and all variables were measured in a blinded manner with respect to the treatment groups.

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 monoclonal antibody mAb21 (clone IgG2bk), raised in rats against the corisin peptide, was developed and characterized in our laboratory and used in the experiments.

A mouse monoclonal antibody against p21 (Waf1/Cip1) (clone F-5; IgG2bk; catalog no. sc-6246; dilution 1:50; Santa Cruz Biotechnology, Dallas, TX, USA) was used for Western blotting. According to the manufacturer's datasheet, this antibody is reactive with both human and mouse antigens and has been validated for immunoblotting applications.

The following additional antibodies were used in this study: anti- β -actin (catalog no. 4970T, Cell Signaling Technology), anti-E-cadherin (catalog no. ab1416, Abcam), anti-collagen I (catalog no. 600-401-103-0, Rockland Immunochemicals), and anti- α -tubulin (catalog no. sc-5286, Santa Cruz Biotechnology). Antibody specificity and performance were validated by the manufacturers for applications including Western blotting and/or immunostaining, with detection of proteins at the expected molecular weights as indicated in the respective product datasheets.

Validation

The specific binding of the anticorin monoclonal antibody mAb21 to the corisin peptide, including the identification of its binding site (epitope) on the peptide, was established in a previous study (Nat Commun. 2022 Mar 23;13(1):1558). The inhibitory effect of the corisin monoclonal antibody on the peptide's biological activity was validated through both in vitro assays and experimental in vivo models, as reported in prior studies (Nat Commun. 2022 Mar 23;13:1558; J Thromb Haemost. 2024 Jul;22:1919-1935). Antibody specificity and performance of the remaining antibodies were validated by the manufacturers for applications including Western blotting and/or immunostaining, with detection of proteins at the expected molecular weights as indicated in the respective product datasheets.

Eukaryotic cell lines

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

Cell line source(s)

The human lung epithelial cell line A549 was obtained from the American Type Culture Collection (ATCC, Manassas, VA, USA). Primary human pulmonary alveolar epithelial cells (PAEpi) and the corresponding culture medium (AEpiCM; Cat. No. 3201) were purchased from ScienCell Research Laboratories (Carlsbad, CA, USA).

Authentication

The A549 cell line was originally obtained from ATCC and has been widely used in our previous studies. Authentication of the cell line was previously performed according to ATCC standards. Primary human pulmonary alveolar epithelial cells were obtained directly from the commercial supplier and used according to the manufacturer's specifications. Cells were used at low passage numbers. Mycoplasma contamination was routinely tested and not detected.

Mycoplasma contamination

None of the cells were contaminated with Mycoplasma

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

Commonly misidentified cell lines were not used in the study

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 wild-type C57BL/6J mice were purchased from Nihon SLC (Hamamatsu, Japan). Corisin transgenic (TG) mice on a C57BL/6J genetic background were generated in our laboratory and maintained as a breeding colony under specific pathogen-free conditions. Mice used in the experiments were 8–9 weeks old and weighed 20–26 g at the start of the study.
Wild animals	The present study did not involve wild animals.
Reporting on sex	In the experimental studies using corisin transgenic mice, only male mice were used in the bleomycin-induced pulmonary fibrosis model to investigate the role of corisin in fibrotic lung injury. This approach was based on previous observations demonstrating that male and female mice develop comparable degrees of pulmonary fibrosis following bleomycin administration. In experiments evaluating spontaneous fibrosis in corisin transgenic mice, both male and female animals were used.
Field-collected samples	All experimental animals were bred and kept in a specific pathogen-free environment within the experimental animal facility at Mie University. The facility maintained a consistent temperature of 21°C and operated on a 12-hour light/dark cycle. Each mouse cage was furnished with wood-wool nesting material, and the animals were provided with unrestricted access to food and water.
Ethics oversight	The Recombinant DNA Experiment Safety Committee (approval No: I-744 (henko1); date: 11 June 2025); approval No: I-745, date: 11 October 2024) and the Committee for Animal Investigation (approval No: 2024-41, date: 21 January 2025; approval No: 2024-40-hen1, date: 22 July 2025; approval No: 2023-17-hen1, date: 2 March 2025) of Mie University approved the experimental protocols and all procedures were performed following internationally approved principles of laboratory animal care published by the National Institute of Health (https://olaw.nih.gov/).

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 is not a clinical trial
Study protocol	This study is not a clinical trial. All subjects participating in the clinical investigation provided written informed consent, and the study protocol was approved by the Ethical Committee for Clinical Investigation of Mie University, Matsusaka Municipal Hospital and conducted following the Principles of the Declaration of Helsinki.
Data collection	Data was collected from bronchoalveolar lavage fluid samples of the patients. The patients with IPF were consecutively enrolled, and BALF samples were obtained from the same patients during both stable and acute exacerbation phases. Three healthy Japanese volunteers were included as controls. During acute exacerbation, BALF was performed only in patients who met predefined institutional safety criteria, including a PaO ₂ /FiO ₂ ratio >150. Therefore, a potential selection bias toward patients with less severe acute exacerbations cannot be excluded. In addition, the small sample size, male predominance, and differences in age and sex distribution between patients and healthy controls may limit the generalizability of the findings. These limitations should be considered when interpreting the results.
Outcomes	To evaluate the sequences of corisin in the bronchoalveolar lavage fluid samples of the patients

Plants

Seed stocks	Plants were not used in the study
Novel plant genotypes	Plants were not used in the study
Authentication	Plants were not used in the study

Flow Cytometry

Plots

Confirm that:

- ☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- ☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- ☒ All plots are contour plots with outliers or pseudocolor plots.
- ☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation

Cells were maintained in RPMI 1640 medium supplemented with 10% fetal calf serum, 0.03% (w/v) L-glutamine, 100 IU/mL penicillin, and 100 µg/mL streptomycin at 37 °C in a humidified atmosphere containing 5% CO₂. For apoptosis assays, cells (4×10^5 per well) were seeded in 12-well plates and allowed to grow to subconfluence. Cells were then serum-starved for 12 h before stimulation for 48 h. Apoptosis was assessed by flow cytometry (FACScan, BD Biosciences, Oxford, UK) using fluorescein-labelled annexin V and propidium iodide (FITC Annexin V Apoptosis Detection Kit with PI; BioLegend, San Diego, CA, USA).

Instrument

We used a flow cytometer (FACScan) from BD Biosciences

Software

Cellquest software from BD Biosciences was used for data analysis

Cell population abundance

We utilized cell lines with a well-defined and adequate number of cells, obviating the need for flow cytometry-based cell sorting.

Gating strategy

Gates were placed around cell populations with common characteristics after determining forward scatter, side scatter and marker expression.

- ☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.