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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees 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	Data collection was performed using Microsoft Excel (Version 14-16) and GraphPad Prism (Version 5-7).
Data analysis	Data analysis was performed in GraphPad Software Prism 7 and the open source software R (Version 2.1). The human and mouse plasma datasets were pre-processed with standard code as follows: factors with more than 85% missing values due to concentrations below the detection threshold were excluded. For the remaining factors missing values were imputed with the lowest measurable concentration. The plasma data was standardized by log2 transformation and z-scoring. Outliers defined as subjects with more than one factor that is more than 3 standard deviations away from the mean were excluded from the dataset. In order to get maximal matching of age and gender distribution 10 male and 10 female subjects were randomly selected per age group from the human dataset. In the mouse cohort 5 males and 5 females were included per age group. The open source software Gene Cluster (Version 3) was used for unsupervised clustering of mean values from each age group. Data was visualized using the open source software Java TreeView (Version 3). R software was used to calculate Spearman's rank correlations between measured factors and age. Adobe Photoshop and Illustrator (CS4-6) were used for preparation of the figures.

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/reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

There are no restrictions on data availability. Raw data can be provided upon request.

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	No power calculations were performed. Sample size was determined based on previous experiments and expected significance levels.
Data exclusions	Unlike otherwise stated, no data were excluded. Aged mice with obvious tumors were removed from the datasets. For plasma measurements, factors with more than 85% missing values due to concentrations below the detection threshold were excluded.
Replication	Individual experiments were repeated at least twice with similar results. Data is shown as representation of one experiment or as a combination of multiple independent experiments, as indicated in the text.
Randomization	Age- and sex-matched animals were randomly assigned to groups at the beginning of each experiment.
Blinding	The investigators were blinded for data aquisition and analysis.

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
☐	☒ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used

Antibody name, clone and provider are indicated in the materials and methods section. Antibodies were u
sed as indicated by the provider.

Murine cells were stained with combinations of the following antibodies: anti-mouse CD45.2 (104, BioLegend), CCR3 (J073E5, BioLegend), F4/80 (BM8, BioLegend), Siglec-F (E50-2440, BD Pharmingen, BD Bioscience), CD3e (145-2C11 and 17A2, BioLegend), CD19 (6D5, BioLegend), CD11b (M1/70, BioLegend), NK1.1 (PK136, BioLegend), VCAM (429[MVCAM.A]), integrin 7 (6A11,MBL), CD16/32 (93, BioLegend)), c-kit (2B8, BioLegend), sca-1 (D7, BioLegend), CD127 (A7R34, BioLegend), CD34 (RAM34; BioLegend), CD51 (RMV-7, BioLegend), CD31 (390, BioLegend), CD45 (30-F11, BioLegend), Ter-119 (Ter-119, BioLegend), GR-1 (RB6-8C5, BioLegend), IgD (11-26, eBioscience), B220 (RA3-6B2, BDBioscience), IgM (II-41, BDBioscience), PNA-biotin, Streptavidin-PacificBlue (Molecular Probes). CountBrightTM beads (Life Technologies) were added to each sample to determine absolute cell numbers. Eosinophils were gated as live, singlet, CD45+, Lin- (CD3, CD19, NK1.1) cells co-expressing CD11b and Siglec-F. Macrophages were gated as live, singlet, CD45+, Lin- (CD3, CD19, NK1.1) cells co-expressing CD11b and F4/80.

Human omental adipose tissue stromal vascular fraction was stained with live/dead stain (Life Technologies) followed by a combination of anti-human CD16 (3G8, Biolegend), Biotinylated MBP (BMK-13, BioRAD), CD11b (ICRF44, Biolegend), Siglec-8 (7C9, Biolegend), CD193 (5E8, Biolegend), CD3 (OKT3, Biolegend), CD19 (HIB19, Biolegend), CD56 (HCD56, Biolegend), Streptavidin-PE (eBioscience). Human adipose tissue eosinophils were gated as live, singlet, CD45+, Lin- (CD3, CD19, CD56), CD11bInter and cells co-expressing CD193, MBP and Siglec-8.

IL-1b, IL-6, TNFa and MCP-1 cytokine levels were determined in cell lysates and plasma samples by enzyme-linked immunosorbent assay (IL-6, TNFa and MCP-1 all from Biolegend and IL-1 from Invitrogen and Biolegend) using manufacturer`s instructions.

The InVivoMAb anti-mouse IL-6 (MP5-20F3, BioXcell) was administered through intraperitoneal (i.p.) injections twice a week.

Vehicle (InVivoMAb rat IgG1 Isotype control (HRPN, BioXcell)) injections were performed in the same way.

Western blots Blots were incubated with primary antibodies used were HSP-90a/b, CCL2 and CCL11 (R&D Systems) and secondary anti-mouse (Bio Rad), anti-rabbit (Bio Rad), anti-rat or anti-goat (both Santa Cruz) antibodies conjugated to horseradish peroxidase (HRP).

Validation

All antibodies used in this study were validated for flow cytometry, Western Blot, ELISA or ELISpot by the provider or manufacturer.

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	Wild-type (WT) C57BL/6 young (2-3 months) and aged mice (18-22months) were purchased either from Janvier Labs or Envigo and housed in specific pathogen-free (SPF) conditions at the central animal facility of the Medical School of the University of Bern. IL-5 transgenic mice C57BL/6-Tg(Il5)1638Jlee (kindly provided by Prof. James J. Lee and Prof. Hans-Uwe Simon), C57BL/6-Il4tm1Nnt and C57BL/6-Tg(UBC-GFP) 30Scha/J mice (The Jackson Laboratory) were bred at the University of Bern and Stanford University.
Wild animals	does not apply
Field-collected samples	does not apply
Ethics oversight	Procedures involving animal subjects have been approved by the Institutional Animal Care and Use Committee (IACUC) at Stanford University and the Swiss ethical guidelines approved by the local Animal Experimentation Committee of the Canton of Bern.

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

Human research participants

Policy information about studies involving human research participants

Population characteristics	Plasma and omental adipose tissue samples of different age groups have been collected.
Recruitment	Healthy human blood donors were selected by specialized academic centers based on standardized inclusion and exclusion criteria. Anonymized plasma samples were received together with age and gender information. Human omental adipose tissue was received from routinely intestinal resection surgery from the clinic of visceral surgery together with age, bmi and gender information.
Ethics oversight	All procedures were performed in accordance with local Institutional Review Board guidelines and have been approved by the cantonal ethics commissions (KEK/Swissethics).

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

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	Tissue dissection and cell preparation: Mice were euthanized with CO2 followed by transcardial perfusion with PBS prior tissue collection. Muscle, liver, spleen, brain, lung, kidney, thymus, skin, mesenteric lymph nodes, colon, epididymal- and subcutaneous fat were dissected, lysed, immediately snap frozen, formalin fixed or embedded in OCT for further applications. Omental adipose tissue from human donors was obtained from the University Hospital of Berne and has been approved by the local ethic Committee of the Canton of Bern. All donors provided informed consent. Tissue sections were immediately fixed in 4% PFA overnight and embedded in paraffin for histological approaches. To separate adipocytes from the stromal vascular cell (SVC) fraction, visceral adipose tissue was digested in 1 mg/ml Collagenase type IV (Sigma) in RPMI medium (Gibco, supplemented with 2 nM L-glutamine, 10% FBS and 1% PenStrep) per gram tissue for 30 minutes at 37°C on an orbital shaker prior to filtration through a 70 µm cell strainer (Huber Lab). Adipocytes were separated from SVCs by centrifugation at 600g for 5 min. Both fractions were recovered and immediately snap frozen on dry ice or used for subsequent flow cytometric analyses after red blood cell lysis with ACK (Ammonium-Chloride-Potassium) lysing buffer. Isolation of primary human eosinophils. Human eosinophils were isolated from healthy volunteers who provided informed

consent in accordance with the Declaration of Helsinki. The study has been approved by the local ethic Committee under license 108/14. Donors were defined by age (young ≥ 29 and old ≤ 64). In brief: Peripheral human blood granulocytes were purified from venous EDTA-blood by dextran sedimentation of red blood cells followed by Percoll density gradient centrifugation (1.0791 and 1.0695 and 1.901 g/mL, GE Healthcare) and further purified by negative selection (anti-CD16 Microbeads and Glycophorine A beads (Miltenyi Biotec). Absolute cell number and purity was measured by FACSCalibur flow cytometer (Becton Dickinson) using BD Truecount Tubes (BD Biosciences). Eosinophil purity of higher 90% was assessed by flow cytometry as CD16-, CD193+ and Siglec-8+ cells.

Sort-purification and adoptive transfers. Terminal bleeding of wildtype, IL-5 transgenic, IL-5-UBI-GFP+ mice or IL-5 transgenic mice on an IL4 knockout background (2-3 months) was performed and red blood cells were lysed with ACK buffer. Primary eosinophils and in vitro generated wild-type BMDE were sort purified according the following gating strategy: Live, CD45+, CD3–, CD19–, NK1.1–, GR1Int, CD11b+ Siglec-F+ eosinophils were sort-purified using a BD FACSAria™ III cell sorter (BD Bioscience) to 98% purity and 1.5x106 eosinophils were immediately transferred by intraperitoneal (i.p.) injection to indicated aged recipients. Given the eosinophil half-life of a few days in vivo, transfers were performed twice a week for 4 consecutive weeks. In some studies, mice were treated with eosinophils for once, 2 times a week or for 5 weeks, twice a week. As a control group, live, CD45 +, CD3–, CD19-, NK1.1–, Ly6G+, CD11b+ neutrophils were isolated from the bone marrow of WT C57BL/6 mice (2-3 months) and 1.5x10^6 cells were injected i.p. into aged mice twice a week for 4 consecutive weeks. When indicated, eosinophils were pre-treated in vitro with 100 ng/ml pertussis toxin (Sigma-Aldrich) for 2 h at 37°C in complete RPMI 1640 Medium and/or sort-purified eosinophils were labelled with CSFE (Molecular probes) using standard protocols to distinguish endogenous from transferred eosinophils.

Muscle stem cells (satellite cells) were isolated as described (Rando et al.). Satellite cells were sort-purified as CD45-, CD31-, Sca-1-, Vcam+ and Integrin-a7+ cells.

Instrument

- BD LSRII flow cytometer (BD Biosciences)
- BD FACSAriaTM III cell sorter (BD Bioscience)
- FACSCalibur flow cytometer (Becton Dickinson,Heidelberg, Germany)

Software

- BD FACSDIVA™ Software
- FlowJo software version 10.1 (FlowJo LCC).

Cell population abundance

- Eosinophil sorts from IL-5Tg mice: 15-20% of total live, singlet cells.
- Eosinophils in adipose tissue: 15-35% of live, singlet, CD45+ CD11b+ cells depending on age.

Gating strategy

Gating strategies see Materials and Methods sections: ''Flow cytometry''&''sort-purification''

- Mouse ATE: live, singlet, CD45+, Lin- (CD3, CD19, NK1.1) cells co-expressing CD11b and Siglec-F.
- Mouse ATM: live, singlet, CD45+, Lin- (CD3, CD19, NK1.1) cells co-expressing CD11b and F4/80.
- Eosinophils from IL-5Tg mice for sorts: Live, singlet, CD45+, CD3–, CD19–, NK1.1–, GR1int, CD11b+ Siglec-F+.
- Mouse Neutrophils: live, singlet, CD45+, CD3–, CD19-, NK1.1–, Ly6G+, CD11b+ .
- Mouse muscle stem cells: live, singlets, CD45-, CD31-, Sca-1-, VCAM+, integrin-a7+.
- Mouse GCBs: live, singlets, B220+, IgD/IgM-, CD38-, PNA+
- Mouse HSC-AD: singlets, Lin-, CD34-, CD135-
- Mouse HSC-SLAM: singlets, Lin-, CD48-, CD150+
- Human ATE: live, singlet, Lin-(CD3, CD19, CD56), CD16low, CD11+, cells co-expressing Siglec-8 and MBP.

The purity of sorted cells was determined by re-sorting a fraction of the recovered cells (>98%).

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