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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.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	No software was used.
Data analysis	Data analysis was performed using Sigmastat, Systat Software v11. Flowcytometry data analysis was performed using FlowJo v. 10.4.2

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 upon request. 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

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-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 from the power of the statistical test performed.
Data exclusions	No data were excluded from the analyses.
Replication	The experiments were performed in replicates and all attempts at replication were successfully reproduced.
Randomization	Group allocation was randomized.
Blinding	Investigators were blinded to group allocation during data collection and analysis.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☐	☒ Unique biological materials
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

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

Unique biological materials

Policy information about availability of materials

Obtaining unique materials	All unique materials are available from the authors.

Antibodies

Antibodies used	Rabbit anti-Keratin14 (K14) (Covance # PRB155P) or Rabbit anti-Pgp9.5 (Dako # Z5116) antibodies (1:200 dilution). Secondary anti-Rabbit Alexa488 antibody was diluted 1:1000. 0.5 µg /1x10^6 cells PE anti-mouse CD207 (Langerin) (Biolegend # 144204) or 0.25 µg /1x10^6 cells Alexa Fluor 488 anti-mouse IA/IE (MHCII) (Biolegend # 107616) antibodies. anti STAT3 (Cell Signaling #9139), anti phospho STAT3 (Tyr705) (Cell Signaling #9131), anti MAPK (Cell Signaling #4695), anti phospho MAPK (Thr202/Tyr204) (Cell Signaling #9106), anti AKT (Cell Signaling #4691), anti phospho AKT (Ser473) (Cell Signaling #9271), anti-Actin (Cell signaling #4970).
Validation	Rabbit anti-Keratin14 (K14) (Covance # PRB155P) recommended for immunohistochemistry by the provider; Rabbit anti-Pgp9.5 (Dako # Z5116) recommended for immunohistochemistry by the provider; PE anti-mouse CD207 (Langerin) (Biolegend # 144204) validated for flow cytometry; Alexa Fluor 488 anti-mouse IA/IE (MHCII) (Biolegend # 107616) quality tested for flow cytometry by the provider; anti STAT3 (Cell Signaling #9139) validated for western blot by the provider; anti phospho STAT3 (Tyr705) (Cell Signaling #9131) validated for western blot by the provider; anti MAPK (Cell Signaling #4695) approved for western blot by the provider; anti phospho MAPK (Thr202/Tyr204) (Cell Signaling #9106) approved for western blot by the provider; anti AKT (Cell Signaling #4691) approved for western blot by the provider; anti phospho AKT (Ser473) (Cell Signaling #9271) approved for western blot by the provider; anti-Actin (Cell signaling #4970) approved for western blot by the provider.

Animals and other organisms

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

Laboratory animals	C57BL/6J male mice were used in the study. All mice were bred and maintained in accordance with Italian legislation (Art. 9, 27. Jan 1992, no 116). Experiments were performed under license from the Italian Ministry of Health, and in compliance with the ARRIVE guidelines.
Wild animals	The study did not involve wide animals.
Field-collected samples	The study did not involve samples collected from the field.

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	Briefly, the back skin was cut in 1-cm pieces and digested overnight at 4 °C in 1 mg/ml Dispase II (Roche # 4492078001). The next day, the skin pieces were further digested in an enzymatic solution of 1 mg/ml Collagenase IV (Worthington # CLS4 LS004188) and 0.5 mg/ml DNase (Sigma # DN25) at 37 °C for 2 hours. Finally, the cell suspension was filtered with a 100 µm cell strainer, washed with PBS + 0.5 M EDTA + 2% FBS, and centrifuged at 1,700 rpm for 5 minutes at 8 °C. Cells were re-suspended in HBSS + 5 mM MgCl2 + 100 µg/ml DNase + 1% BSA, and labelled.
Instrument	BD FACSAria, SN:P650036A8001
Software	Collection: BD FACSDiva v8.0.2 Analysis: FlowJo v10.4.2
Cell population abundance	Analysis only.
Gating strategy	After spectral spillover compensation was preformed for each time point, the SSC/FSC was used to gate light-scatter-based homogeneous populations followed by doublet discrimination with FSCA/FSCW, FSCW/FSCH, SSCA/SSC or SSCW/SSCH gating. Live cells were selected by using the PI FMO control to identify the PI negative population. The double positive +MHCII +Langerin-gated population was determined with AF488 MHCII and PE Langerin FMOs. This process was repeated by using FMO controls for each time point.

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