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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	FPLC: UNICORN 7 (GE Healthcare Life Sciences). Flow cytometry: BD FACS Diva 8.0.1
Data analysis	RNA Seq:Reads were trimmed by a Trimmomatic program after quality control checks on raw sequence data by FastQC. The alignment of reads to the human genome was performed by the TopHat program followed by Cuffdiff execution to find significant changes in transcript expression between treated and untreated samples. The results of the RNAseq data analysis pipeline were uploaded to IPA software to identify signaling pathways. Graphs and statistical analysis: Graph Prism Flow cytometry: BD FACS Diva 8.0.1, FlowJo v.10

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 materials, data, and any associated protocols that support the findings of this study are available from the corresponding authors upon 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	No sample size calculation was performed. The exact n values used to calculate the statistics are provided and a reasonable sample size was chosen to ensure adequate reproducibility of results.
Data exclusions	No data were excluded from the analysis. For RNAseq data, only genes with the expression values in FPKM>200 were shown. We did not show genes with the lower FPLM values due to their low levels of expression, but all data will be available and are not excluded.
Replication	Experiments were replicated several times (3-5) with reproducible results, as indicated in each figure legend.
Randomization	Figure 1: Random anonymous donors (n=5) Figure 2: Not applicable, we tested the defined chemical compounds Figure 3: Not applicable, we tested the defined biochemical fractions Figure 4: Not applicable, we tested the defined chemical compounds Figure 5: Not applicable. Figure 6: Age- and sex-matched mice were separated as WT and S100a11 KO. Mice were co-housed to minimize the microbiota effects.
Blinding	Figures 1-5: not blinded Figure 6: The investigator was blinded (the genotypes were not revealed prior T. gondii infection).

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

Antibodies

Antibodies used	S100A11 Abs: generated against highly purified recombinant S100A11 protein. hCCL2 (Cat #14-7099-68, lot E05354_1635) and IL-12p40 (cat #14-7125-68, lot E05380-1635) ELISA kit antibodies were purchased from eBiosciences. anti-RAGE antibody (Cat #AF1179, lot GWZ0416081) and rh-RAGE/Fc reagent (Cat #1145-RG, lot #FAU0714061) were purchased from R&D Systems.

	CD11b antibodies (clone M1/70, cat # 557872, lot 5009911) were purchased from BD Bioscience. CD45 antibodies (clone 30-F11, cat # 565967, lot 8037968) were purchased from BD Bioscience; Ly6C antibodies (clone HK1.4, cat# 45-5932-82, lot E10161-1634) were purchased from eBioscience Ly6G antibodies (clone 1A8, cat # 17-9668-82, lot 4286053) were purchased from eBioscience (ThermoFisher).
Validation	S100A11 Abs validated for specificity against the following control proteins: A100A1, A12, A13, A4, A7, A8, A9 proteins (no reactivity). CCL2 and IL-12p40 Abs (eBiosciences) were validated by the vendor and extensively characterized in the past by our lab. RAGE Abs: these Abs blocked RAGE-induced activation caused by a previously described unrelated RAGE-ligand (HMGB1) All the flow cytometry antibodies used are from commercial sources and have been validated by the vendors. Validation data are available on the manufacturer's website.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	THP-1 cells (TIB-202) and Hs27 fibroblasts (RL-1634) were purchased from ATCC.
Authentication	THP-1 and Hs27 cells were authenticated by morphology
Mycoplasma contamination	THP-1 cells (TIB-202) and Hs27 fibroblasts (RL-1634) were routinely tested for mycoplasma (every 4 weeks). All results were negative
Commonly misidentified lines (See ICLAC register)	No misidentified cells were involved in the experiments.

Palaeontology

Specimen provenance	*Provide provenance information for specimens and describe permits that were obtained for the work (including the name of the issuing authority, the date of issue, and any identifying information).*
Specimen deposition	*Indicate where the specimens have been deposited to permit free access by other researchers.*
Dating methods	*If new dates are provided, describe how they were obtained (e.g. collection, storage, sample pretreatment and measurement), where they were obtained (i.e. lab name), the calibration program and the protocol for quality assurance OR state that no new dates are provided.*

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Animals and other organisms

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

Laboratory animals	All mice used for experiments were on a C57BL/6J genetic background and 6-12 weeks-old. To generate S100a11-/- mice, exons 2 and 3 of the S100a11 gene were targeted by two sgRNAs using CRISPR–Cas9 technology (Supplementary Fig. 7) at the Mouse Genome Editing (MGE) Resource at the University of Rochester Medical Center. Genotyping of S100a11-/- mice was performed using primers S100a11 wtF (5'- gaggcactgcgctcctctggcacact -3') and S100a11 wtR (5'-ctcctgctaccagcttccatgtcac -3') that result in PCR products of 2.7 kb for WT mice and 557 bp for the S100a11 KO allele, as a result of deletion of exons 2 and 3. C57BL/6 mice were initially purchased from the Jackson Labs and were bred at the University of Rochester.
Wild animals	The study did not involve wild 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	Isolation of lamina propria cells was performed as follows. The small intestine was removed on day 7 post infection and carefully cleaned of the mesentery and Peyer patches. The intestine was then opened longitudinally, washed of fecal contents, cut into smaller sections and subjected to 2 sequential incubations in PBS with 5 mM EDTA and 1mM DTT at 37°C with agitation to remove epithelial cells. The solution was discarded between incubation steps and replaced. The remaining tissue was agitated in PBS and then filtered through a 100-µm strainer. The tissue was then incubated for 30 min with gentle agitation in 0.4 mg/ml of Collagenase D and 50 mg/ml of DNase I at 37 °C. The samples were then washed through a strainer (100 µm). Peritoneal exudate cells were collected on day 5 post infection
Instrument	BD LSRII
Software	BD FACS Diva 8.0.1 software was used for data collection and FlowJo v.10 was used for data analysis.
Cell population abundance	Post-sort cells were analyzed on BD LSRII and the purity of CD14+ cells was at least 98.5%
Gating strategy	Among live, single, CD45+ cells, Neutrophils were gated as: CD11b+Ly6G+Ly6C- Monocytes were gated as CD11b+Ly6C+Ly6G-

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