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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 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 (*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	FlowJo 9.3.2
Data analysis	Statistical analyses comprising calculation of degrees of freedom were done using Sigma Plot 12.5 or GraphPadPrism 6.04

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 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 data that support the findings of this study are available from the corresponding author 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	The sample size (n) was chosen differently for different experimentst, considering the following relation: n≥2sigma(Zalpha/D)2 where sigma is substituted by an extimate of variance (s2); alpha is at 0.05 (and Zalpha=-2) and D is the difference among treatments.
Data exclusions	We did not exclude data from the study.
Replication	All attemps to replicate the results were successful.
Randomization	For the experiments animals were randomly chosen among different colonies before the treatments with the differents compounds.
Blinding	The investigators performing experiment analyses where blinded to group allocation; they always received the samples from a third laboratory member, not directly involved in data 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 and archaeology
☐	☒ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

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

Antibodies

Antibodies used	Pacific Blue-conjugated CD4 antibody (clone RPA-T4) (BD Biosciences Cat# 558116, RRID:AB_397037); ID1 antibody (clone B-8) (Santa Cruz Biotechnology Cat# sc-133104, RRID:AB_2122863); GAPDH antibody (Millipore Cat# MAB374, RRID:AB_2107445); Anti-mouse IgG peroxidase conjugated secondary antibody (Vector Laboratories Cat# PI-2000, RRID:AB_2336177); iNOS Antibody (Cell signaling Technology, cat.# 13120S, RRID: AB_2798613); Arginase-1 Antibody (Cell signaling Technology, cat.# 93668S, RRID: AB_2800207); α/β-Tubulin Antibody (Cell signaling Technology, cat.# 2148S, RRID: AB_2288042); CD45.2 antibody (ThermoFisher 47-0454-82 RRID:AB_1272211); NK1.1 antibody (ThermoFisher 17-5941-82 RRID:AB_469479); CD3 antibody (ThermoFisher 45-0031-82 RRID:AB_529513); NKG2D antibody (ThermoFisher 12-5882-82 RRID:AB_465996).
Validation	The antibodies were validated according to the manufacturer.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	L929 Cell Line from mouse (Mouse C3H/An connective tissue, ECACC Cat# 85011425, RRID:CVCL_0462)
Authentication	The cell lines used in the research are regularly checked to ensure they are authentic and are not infected with mycoplasma.

Mycoplasma contamination	The cell lines used in the research are regularly checked to ensure they are authentic and are not infected with mycoplasma. Mycoplasma test: The cell lines are checked regularly using MycoAlert Mycoplasma detection kit from Lonza or Universal Mycoplasma detection kit from ATCC. Cell lines that were mycoplasma contaminated will be discarded or cured if necessary using Plasmocin from InVivoGen or BM-Cyclin from Sigma-Aldrich.
Commonly misidentified lines (See ICLAC register)	*Name any commonly misidentified cell lines used in the study and provide a rationale for their use.*

Animals and other organisms

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

Laboratory animals	C57BL/6J male mice 8-week-old and female between 2 to 4 month-old (for bone marrow source); Wistar rat pups P0-P1 used to obtain microglia cultures
Wild animals	The study did not involve wild animals.
Field-collected samples	No field-collected samples were used.
Ethics oversight	Experiments described in the present work were 1) approved by the Italian Ministry of Health (authorization n. 78/2017-PR) in accordance with the guidelines on the ethical use of animals from the European Community Council Directive of September 22, 2010 (2010/63/EU), and from the Italian D.Leg 26/2014; 2) housed in the animal facility of the Institute for Advanced Biosciences (France) according to institutional guidelines (agreeement reference 2015062612254918); mice were maintained in fully controlled environment (temperature, humidity and light cycles), with food and drink free access. Mice were euthanized by carbone dioxide exposure following the rules of the local Ethic comity.

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	*Describe the covariate-relevant population characteristics of the human research participants (e.g. age, gender, genotypic information, past and current diagnosis and treatment categories). If you filled out the behavioural & social sciences study design questions and have nothing to add here, write "See above."*
Recruitment	Human samples were recruited from the healthy voluntary donors at Umberto I Hospital in Rome. Informed consent was obtained from all the subjects.
Ethics oversight	For patients in Rome, from the Ethic committee of Umberto I Hospital in Rome.

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	Immune cells from mice were enriched by centrifugation on percoll 40%, washed in PBS and immunostained with fluorochrome-conjugated anti-CD3, anti-NK1.1, and anti-CD45.2 to identify NK cells (NK1.1 +CD3-).
Instrument	FACSCanto II (BD Biosciences) and BD-LSRII (BD Biosciences)
Software	FlowJo Version 9.3.2 software (TreeStar); FACSDiva 6.3.1 software (BD Biosciences); FCS Express V3 and V6 software (De Novo Software).
Cell population abundance	Purity of the sorted cell fractions was confirmed by flow cytometry resulting in a purity of the sorted cells of >98%., as determined by reanalysing by FACS a fraction of sorted cells.
Gating strategy	For gating , immune cells were gated using forward scatter height (FSC-H) versus side scatter height (SSC-H).

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