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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	N.A.
Data analysis	Flow Cytometry data analysis was performed using FlowJo software (Tree Star, version 10) For qualified cluster analysis we used String (www.String-db.org) Clustering of differentially expressed genes was visualized using Cytoscape 3.5.0 software Statistical analysis between groups was performed with GraphPad Prism 5 and 7 Differential expression analysis was done using EdgeR 3.14.2 and Limma 3.28.1 In data analysis MS Excel was also used

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 data that support the findings of this study are available from the corresponding author upon request. The accession codes are: SRX4548789, SRX4548788, SRX4548787, SRX4548786, SRX4548785, SRX4548784, SRX4548783, SRX4548782, SRX4548781

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 size was determined by power analysis based on pilot experiments and previous findings (Zafirova et. al.,Immunity 2009.)
Data exclusions	No data was excluded
Replication	All data was successfully replicated at least two times. How many times each experiment was performed and which statistical analysis was used is indicated in the figure legends.
Randomization	Mice were age and sex matched. Mice were allocated to groups by an independent animal caretaker.
Blinding	In our experiments we used mostly genetically modified mice which were genotyped before start of each experiment to determine appropriate number of animals per group to ensure statistical power of results for each experiment. However, individual mice and from them derived samples were numbered regardless of genotype, which finally allowed blind analysis of samples though. The samples were matched with their genotype only after the 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

Antibodies

Antibodies used

Flow Cytometry:
Name / Clone name / Catalog no. / (most used) Lot no. / dilution factor / manufacturer
CD3e/145-2C11/ 45003182/4304569/1:300/eBioscience
NK1.1/PK136/45594182/l4331619/1:400/eBioscience
CD49b/DX5/13597183/E03102-1631/1:100/eBioscience
FNγ/XMG1.2/17731182/4332526/1:200/eBioscience
TNFα /MP6-XT22/11732181/1927449/1:100/eBioscience
IL-6/8C9 /21670064/LO144/1:100/Immuno tools
GM-CSF/MP1-22E9/12-7331-41/E031118/1:100/eBioscience

NKG2D (CD314)/CX5/25-5882-82/4275095/1:50/eBioscience
CD247 (CD3ζ)/6B10.2/12-2479-80/4291757/1:50/eBioscience
ZAP-70/1E7.2/11-6695-82/4308883/1:400/eBioscience
CD122 /TM-b1/17-1222-80/E004801633/1:100/eBioscience
CD11b/M1/70/ 25011281/4289817/1:400/eBioscience
c-kit (CD117)/ACK2/11-1171-82/E004741631/1:100/eBioscience
FcεR1γ /1D6/M191-3/ 1:100/MBL
CD247 (CD3ζ)/H146-968/ ab91493/6R3198401-1/1:100/ Abcam.
Ly49H (3D10) and Ly49D (4e4) were kind gift from W. Yokoyama (Washington University in St. Louis, USA)/1:100
CD34 /RAM34/14-0341-81/E02497-1631/1:100/eBioscience
Flt3L /A2F10.1/17-1351-80/E02731-1633/1:100/eBioscience
CD127 /A7R34/14-1271-82/E014711633/1:100/eBioscience
CD16/32 /93/14-0161-81/E06356-1631/1:100/eBioscience
Sca1/D7/17598181/E073531635/1:100/eBioscience
pSyk(Y348)/moch1ct/12901442/4325047
pPLCγ(Y786M9S/14008/1:400/Cell Signaling
Sla/rabbit polyclonal/PA5-22356/TA2506553/1:50/Invitrogen
Fusion proteins (NCR1-Fc, NKG2D-Fc and hPVR-Fc) were produced by our in-house facility and used 10µg/sample

Western blot:
Name / Clone name / Catalog no. / (most used) Lot no. / dilution factor / manufacturer
Syk/D3Z1E/3198/2/1:1000/Cell signaling
FcR1γ/rabbit polyclonal/06-727/2882662/1:500/ Merckmillipore
Zap70/99F2/2705/10/1:500/Cell signaling
CD3ζ /rabbit polyclonal/SAB4503580/210468/1:500/Sigma
Akt /11E7/4685/6/1:80000/Cell signaling
β-actin/C4/MAB/2665057/1:80000/Santa Cruz

Validation

Validation of purchased antibodies was done by the suppliers. Data on the validation of in-house generated reagents (fusion proteins), has been provided in the supplementary figures.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)

The B16-F10 cell line was purchased from ATCC (CRL-6475)

Authentication

Authentication was provided by ATCC

Mycoplasma contamination

The cell line was confirmed to be negative for mycoplasma contamination by PCR.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified cell lines were used.

Animals and other organisms

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

Laboratory animals

Mice used in experiments were 6-12 weeks old. Both male and female mice were used but they were strictly age- and sex-matched within experiments.
Klrk1-/- Zafirova et al., 2009.
Klrk1flox/flox Lenartić et al., 2017.
Klrk1Δ/Δ Zafirova et al., 2011.
NCR1gfp/gfp Gazit et al., 2006.
IFNγ-/- Jackson Laboratories(2287)
C57BL/6 Jackson Laboratories (B6; strain 664)
Hcst-/- Laboratory of M. Colonna
Tyrobp-/- Laboratory of M. Colonna
Rag1cre/+ Laboratory of M. Busslinger
Rosa26-foxed STOP YFP Laboratory of Ari Waisman
NCR1cre Laboratory of V. Sexl
CD4cre Laboratory of D. Littman
CD3ζ-/- CNRS, Orleans (B6-Cd3z tm1Mal)
Deleter-cre (B6.C-Tg(CMV-cre)1Cgn/J) Jackson Laboratories (6054)
Balb/c Jackson Laboratories (strain 00651)
Sla-/- Laboratory of Jane McGlade4)

Wild animals

Study did not involve wild animals

Field-collected samples

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	Samples were prepared as described in the methods section. Briefly, animals were sacrificed according to European guidelines and spleens and bone marrow were removed. Single cell suspensions were generated by mashing organs through a 70uM sieve (spleen) or by smashing bones with a mortar, after which suspensions were run through a sieve. Erythrocytes were lysed using a hypotonic solution. Before staining with specific antibodies, cells were pretreated with Fc block (clone 2.4G2, produced in-house). To-pro3 (life Technologies) or Fixable Viability Dye (eBioscience) was used to exclude dead cells.
Instrument	BD FACS ARIA and BD FACS VERSE
Software	FlowJo software (Tree Star, version 10)
Cell population abundance	After sorting we purity was determined to be 97-99%.
Gating strategy	pecific gating strategies are specified in the figure legends and/or methods section. Briefly, doublets were excluded using FSC-H vs. FSC-A gating, followed by SSC-H vs. SSC-A gating. Dead cells were excluded by viability dye. Based on FSC/SSC properties gating for lymphocytes was performed. Next, markers for specific cell populations were used to define populations. In most experiments, murine NK cells were investigated, which were defined as CD3-NK1.1+ or CD3-NKp46+, depending on the experiment and/or genotype of the mice under investigation. For cytokine production or for specific marker expression, positive gates were set based on isotype control, FMO, or on cells genetically deficient for the specified marker (e.g. NKG2D, NCR1, CD3zeta). For analysis of haematopoietic precursors in the bone marrow, a lineage channel was used, as well as specific markers to define precursor populations.

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