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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	LAS X (Leica); FACS Diva (BD Biosciences)
Data analysis	FlowJo V10 software (TreeStar) ; Graph Pad Prism V7 (GraphPad Software); Fji 2.0.0 (ImageJ); Cufflinks 2.2.1; R Studio 3.3.2, GSEA v2.2.3, GIMP 2.8

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

RNA-Seq data is available at the ArrayExpress (http://www.ebi.ac.uk/arrayexpress/) with the accession number E-MTAB-6723.

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	Three to twenty mice were used per experiment. The precise numbers are stated in the Figure legends and are visible as separate dots in the graph. In preliminary experiments the D value (Difference in means)/(Standard Deviation) was calculated. The exact sample size was determined under consideration of the D value, available resources (genotypes) and ethical aspects (implementing the three Rs). If an insufficient number of animals was available for a reliable significance prediction, biologically independent repetition experiments were performed and data pooled for analysis.
Data exclusions	Data points that fulfilled Peirce's criterion for outliers were considered carefully. If the investigators concluded that they were presented with an uncorrectable measurement error, it was not considered for further analysis. Exclusion of outliers, as they happen in biomedical research with living animals, was pre-established in the laboratory.
Replication	Experiments were repeated that the presented data is based on at least two to three biologically independent experiments with similar results (for most important conclusions up to ten times e.g. apoptosis induction). If group size was small (due to limited availability of specialized reagents and mouse strains), data from replicate experiments were pooled for graphical representation. All replicates are biological replicates obtained from biologically independent experiments.
Randomization	We did not use randomization to assign animals to experimental groups. As whenever possible littermate controls were used, age did not constitute a variable (and was matched for non-littermates) and sex ratios were distributed evenly among experimental groups. Furthermore, we did not observe sex-specific differences in our findings.
Blinding	Investigators were not blinded to group allocations during the experiment and data analysis. Since treatment and experimental analysis could not be separated, blinding of the investigators was not possible. Histological scoring was performed by two researchers according to pre-set criteria. For quantification pre-defined algorithms/analysis sequence was performed by image analysis software and specific criteria were documented.

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	1-MIM-OH, Detailed description for synthesis has been provided in PMID: 20846518. All other Materials are available at commercial vendors.

Antibodies

Antibodies used	Flow Cytometry Target Clone Vendor Cat number Most recent Lot# CD3e 145-2C11 eBioscience 13-0031-82 E02347-1633 CD5 53-7.3 eBioscience 13-0051-82 4319149

CD19 MB19-1 eBioscience 13-0191-85 E02440-1633
Gr-1 RB6-8C5 eBioscience 13-5931-82 4310389
F4/80 BM8 Biolegend 123106 B203671
CD64 X54-5/7.1 Biolegend 139318 B224829
CD45.2 104 eBioscience 47-0454-82 4302540
TCRb H57-597 eBioscience 45-5961-80 E08409-1633
TCRgd GL3 Biolegend 118123 B211410
CD4 RM4-5 eBioscience 48-0042-82 4313102
RORgt B2D eBioscience 17-6981-82 4291992
IL-22 1H8PWSR eBioscience 12-7221-80 4299218
IL-17a eBio17B7 eBioscience 11-7177-81 E08894-1632
EpCam G8.8 eBioscience 17-5791-82 4298465
CD24 30-F1 eBioscience 12-0241-81 B180222
CD45 30-F11 eBioscience 25-0451-82 4302540
Cleaved Caspase 3 C92-605 BD Biosciences 560626 7179554
FoxP3 MF-14 Biolegend 126409 B239211
IL-10 JES5-16E3 eBiosciences 53-7101-82 4325142
Atm 2C1 (1A1) Abcam #ab78 GR3192658-10
anti-mouse-Al555 Polyclonal Life Technologies A21425 1635618

Histology
Target Clone Vendor Cat number Most recent Lot#
DAPI Sigma-Aldrich 32670-5MG-F 075M4010V
EpCam G8.8 eBioscience 17-5791-82 4298465
cleaved Caspase-3 5A1E CST #9664 18
gH2AX 20E3 CST #9718 10
Il22ra1 496514 Thermo Fisher MA5-24205 GR272657-7
anti-rabbit-Al555 Polyclonal Life Technologies A31572 1806147
anti-rabbit-APC Polyclonal Life Technologies A10931 1351950
anti-rat-Al647 Polyclonal Life Technologies A21247 1939630

Western Blot
Target Clone Vendor Cat number Most recent Lot#
Puma polyclonal Abcam ab9643 GR255116-3
p21 F5 Santa Cruz Biotechnology sc-6246 F2612
Beta-Actin AC-15 Sigma-Aldrich A5441-100UL
Atm D2E2 CST 2873S 3
H2AX D17A3 CST 7631P 4
p-p53 D4S1H CST 12571S 3
p-SMC D7S8Y CST 58052S 1
SMC 8E6 CST 6892S 1
anti-rabbit-HRP Jackson ImmunoResearch 111-035-144 49411
anit-mouse-HRP Jackson ImmunoResearch 115-035-003 130129

ChIP
Target Clone Vendor Cat number
STAT3 C-20 Santa Cruz Biotechnology sc-482 X

Validation

All antibodies were validated by the commercial manufacturers (according to the vendor's websites).

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)

IEC6 were kindly provided by M. Hornef (Aachen, Germany)

Authentication

The cells were not authenticated, but were tested to be specifically responsive to IL-22.

Mycoplasma contamination

All cell lines in the laboratory are randomly tested for Mycoplasma contamination by PCR. IEC6 were Mycoplasma negative.

Commonly misidentified lines
(See ICLAC register)

No commonly misidentified cell lines were used in this study.

Animals and other organisms

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

Laboratory animals

C57BL/6N, Lgr5EGFP-IRES-CreERt2/+, Rosa26R-Confetti, Ahr fl/fl;Rorc(γt)-CreTg, Il22-/- , Stat3fl/fl;Vil1-Cre, Il22ra1fl/fl;Vil1-Cre, Ahr-/-. All mice had been crossed onto a C57BL/6N background for at least 10 generations.

	Mice were 8 to 10 weeks of age. Male and female mice were used in a ratio 1:1. Glucosinolate-chow experiments were performed with only female C57BL/6N.
Wild animals	No wild animals were used in this study.
Field-collected samples	No field-collected samples were used in this study.

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	This information is provided in detail in the M&M section.
Instrument	BD FACS CANTO II for Analysis, BD FACS ARIA III for Cell Sorting
Software	FACS DIVA (BD Biosciences) and FlowJo V10 (TreeStar)
Cell population abundance	Purity of sorted populations was assessed by post-sort analysis on the BD FACS ARIA III. Purity of over 98% was routinely achieved.
Gating strategy	An example for the Lgr5 sorting strategy is provided in Fig S4a. For lymphocyte analysis cells were gated the following way: SSC-A/FSC-A (Lymphocytes)-- SSC-A/SSC-W (Singlets)--CD45+(Lymphocyte marker)--seperated into Lin(CD3,CD5,CD19,Gr-1,CD64,F4/80)pos CD4+ (CD4+ Tcells), Lin neg RORgt+ (ILC3), Lin pos gdTCR+ (gd Tcells), Lin pos CD4+ FoxP3+ (FoxP3+ Tcells)

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