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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	BD LSRFortessaTM X20 and BD FACSAriaTM Fusion were used for flow cytometry data collection. Zeiss AxioCam 702 sCMOS Mono was used for acquisition of microscopy data.
Data analysis	Flow Cytometry data were analyzed by FlowJo V10 (Treestar); Statistical analysis all conducted using GraphPad Prism V9 and SAS v.9.4.

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

Data will be provided online when the manuscript are accepted.

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	A reasonable sample sizes were determined based on our and other investigators experience and similar research reported in the literature to ensure adequate reproducibility of results. The sample size and associated statistics are indicated in the figures and respective legends.
Data exclusions	No data were excluded from the analyses.
Replication	All experiments were reliably reproduced and results are represented as mean +/-SD as appropriate, which is indicated in figure legends. One-way ANOVA model was utilized to compare three or more conditions. Experiments were repeated with at least two to three biologically independent for all results presented in the manuscript. When needed, P values were adjusted for multiple comparisons using Holm's or the Bonferroni method procedure. A P value of 0.05 or less was considered statistically significant, which is described in the methods section of the main text.
Randomization	Peripheral blood cones used to isolate healthy ILC1s, peripheral blood from patients with AML used to isolate LSCs, or umbilical cord blood used to isolate CD34+ cells were de-identified and randomly picked up. Six- to eight-week-old mice were matched by age and sex and randomly assigned to specific treatment groups.
Blinding	Experimenters were blinded to observe survival of mice. Otherwise, blinding was not performed, such as during in vitro experiments, where experimenters were required to know the conditions of each well.

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

Anti-human CD3-FITC BD Biosciences Cat# 561802, RRID:AB_10893003
Anti-human CD4-FITC BD Biosciences Cat# 555346, RRID:AB_395751
Anti-human CD8-FITC BD Biosciences Cat# 555634, RRID:AB_395996
Anti-human CD14-FITC BD Biosciences Cat# 555397, RRID:AB_395798
Anti-human CD15-FITC BD Biosciences Cat# 555401, RRID:AB_395801
Anti-human CD16-FITC BD Biosciences Cat# 555406, RRID:AB_395806
Anti-human CD19-FITC BD Biosciences Cat# 555412, RRID:AB_395812
Anti-human CD20-FITC BD Biosciences Cat# 555622, RRID:AB_395988
Anti-human CD33-FITC BD Biosciences Cat# 555626, RRID:AB_395992
Anti-human CD34-FITC BD Biosciences Cat# 555821, RRID:AB_396150
Anti-human CD203C-FITC Thermo Fisher Scientific Cat# MA5-28586, RRID:AB_2745545
Anti-human FcepsilonRIalpha-FITC Biolegend Cat# 334608, RRID:AB_1227653
Anti-human CD56-FITC BD Biosciences Cat#562794, RRID:AB_2737799
Anti-human CD127-BV421BD Biosciences Cat# 562437, RRID:AB_11151911
Anti-human CD117-PE BD Biosciences Cat# 555714, RRID:AB_396058
Anti-human CRTH2-PE-Cy7 Biolegend Cat# 350118, RRID:AB_2562470
Anti-human CD38-PE-Cy7 BD Biosciences Cat# 560677, RRID:AB_1727473

Anti-human CD34-PE BD Biosciences Cat# 555822, RRID:AB_396151
Anti-human CD11b-AF647 BD Biosciences Cat# 557686, RRID:AB_396796
Anti-human CD206-PECy5 BD Biosciences Cat# 5551136,RRID:AB_394066
Anti-human CD235a-FITC BD Biosciences Cat# 349104, AB_10613463
Anti-human CD161-BV786 BD Biosciences Cat# 744096,RRID:AB_2741990
Anti-human T-BET-APC Biolegend Cat# 1644814,RRID:AB_10901173
Anti-human EOMES-BUV395 BD Biosciences Cat# 567171,RRID:AB_2916488
Anti-human IFN-g-BV786 BD Biosciences Cat# 5563731,RRID:AB_2738391
Anti-human IFN-g-BV421 BD Biosciences Cat# 564791,RRID:AB_2738952
Human Hematopoietic Lineage Antibody Cocktail, FITC Thermo Fisher Scientific Cat# 22-7778-72, RRID:AB_1311229
7-AAD Staining Solution 2mL antibody BD Biosciences Cat# 559925, RRID:AB_2744712
DAPI Solution BD Biosciences Cat# 564907, RRID:AB_2869624

Validation

All antibodies commercially available flow cytometry antibodies for staining mouse and human samples and validated by the manufacturer.
BD Biosciences (https://www.bdbiosciences.com/en-us/reagents/research-reagents/antibodies-and-buffers)
BioLegend (https://www.biolegend.com/nl-nl/reproducibility)
Thermofisher Scientific (https://www.thermofisher.com/us/en/home/life-science/antibodies/invitrogenantibody-validation.html)
These antibodies are further validated and routinely used in our lab.

Animals and other organisms

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

Laboratory animals	NSG-SGM3 mice were purchased from the Jackson laboratory. All mice were used at 6-8 weeks of age. Mouse care and experimental procedures were performed in accordance with federal guidelines and protocols approved by the Institutional Animal Care and Use Committee.
Wild animals	No wild animals were used in this study.
Field-collected samples	The study did not involve samples collected from the field.
Ethics oversight	All animal procedures used in this study were performed in accordance with protocols approved by the Institutional Animal Care and Use Committee of City of Hope National Medical Center (COHNMC) .

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	Human samples were obtained from donors at COHNMC. AML patient samples were obtained from COHNMC.
Recruitment	All patients were recruited through regular visits at COHNMC.
Ethics oversight	All patients who provided informed consent had samples collected under a protocol approved by COHNMC.

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	Cells were collected, washed with 1 % FBS + DPBS, stained with different fluorescence-conjugated antibodies at 4°C for 30 min, 1 % FBS + DPBS twice, and then analyzed using BD LSRFortessaTM X20 and BD FACSAriaTM Fusion.
Instrument	Cells were either analyzed on BD LSRFortessaTM X20 or sorted by BD FACSAriaTM Fusion.
Software	Flow Cytometry data were analyzed by FlowJo V10 (Treestar).

Cell population abundance	The purity of sorted cells was detected via D FACSAriaTM Fusion and samples with purity >90% were used.
Gating strategy	ILC1s from human peripheral blood were identified using surface staining with a live/dead cell viability cell staining kit and the following monoclonal antibodies: lineage (anti-CD3, anti-CD4, anti-CD8, anti-CD14, anti-CD15, anti-CD16, anti-CD19, anti-CD20, anti-CD33, anti-CD34, anti-CD203c, anti-FceRI), anti-CD56, anti-CD127, anti-CRTH2, and anti-c-Kit. Human LSCs were identified by lineage (anti-CD2, anti-CD3, anti-CD4, anti-CD8, anti-CD14, anti-CD19, anti-CD20, anti-CD11b, anti-CD56, and anti-CD235a), anti-CD45, anti-CD34, and anti-CD38. Human ILC1s were gated by Lin-CD56-CD127+CRTH2-c-Kit- or Lin-CD56-CD127+CD161+CRTH2-c-Kit-. Human LSCs were gated by CD45dimLin-CD34+CD38-.

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