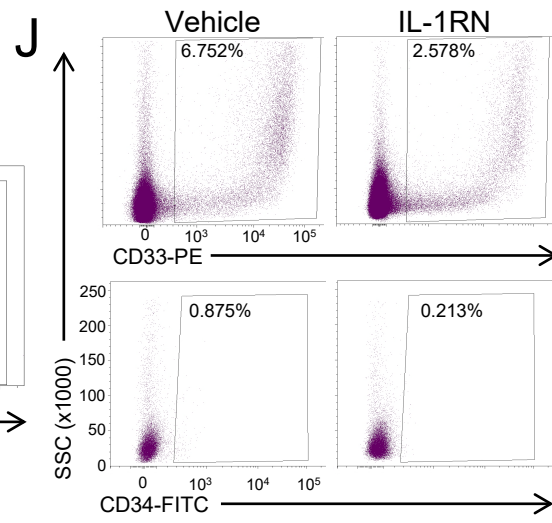
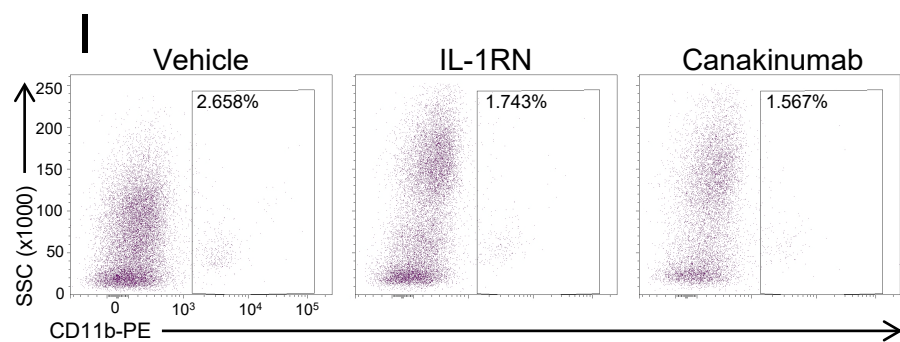
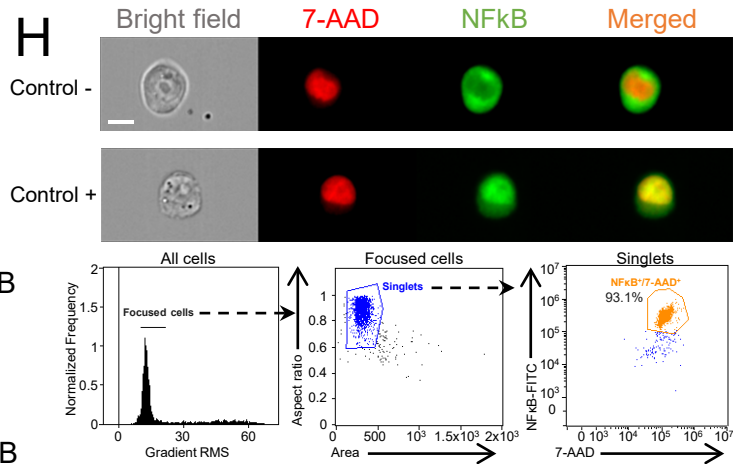
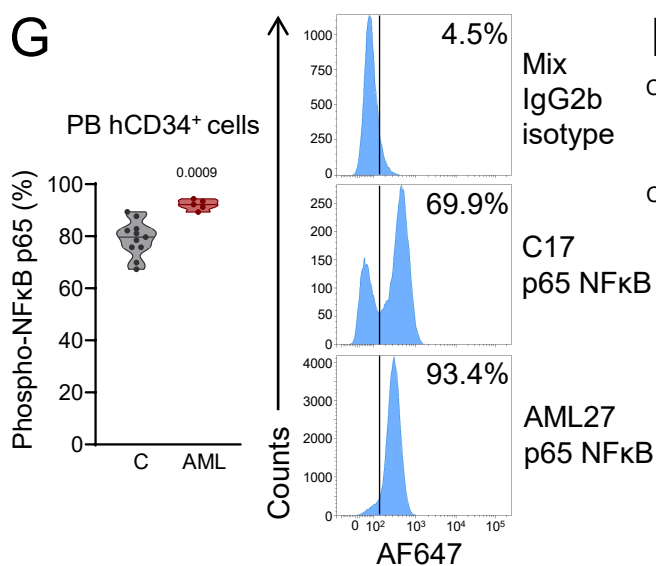
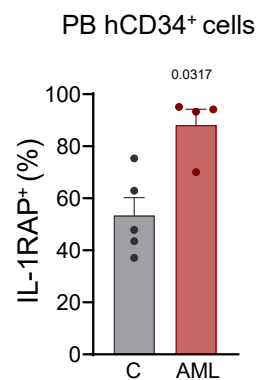
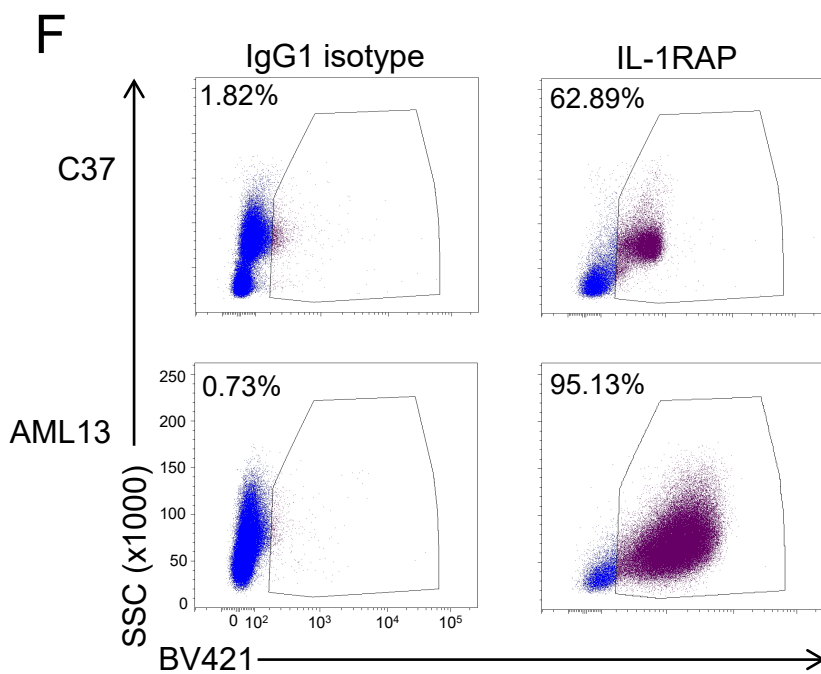
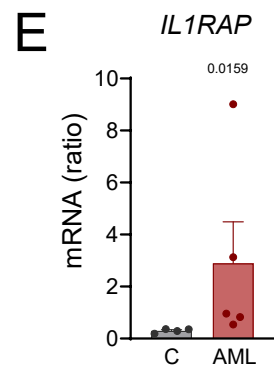
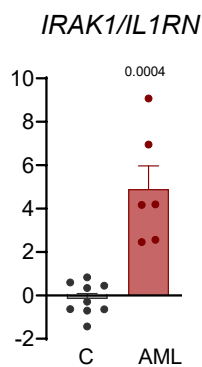
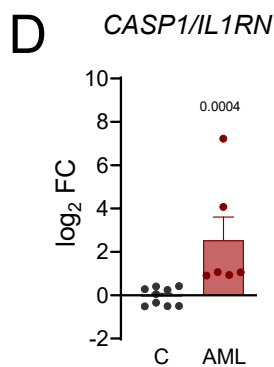
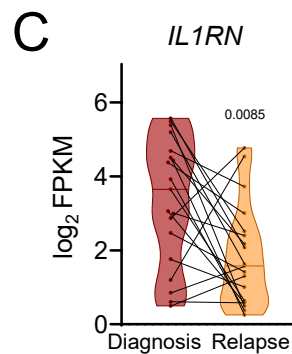
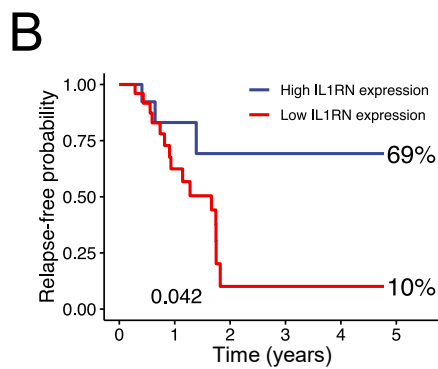
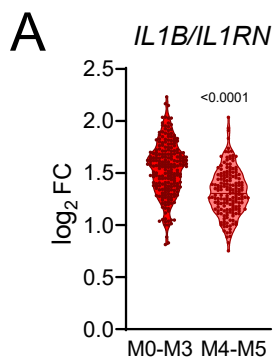
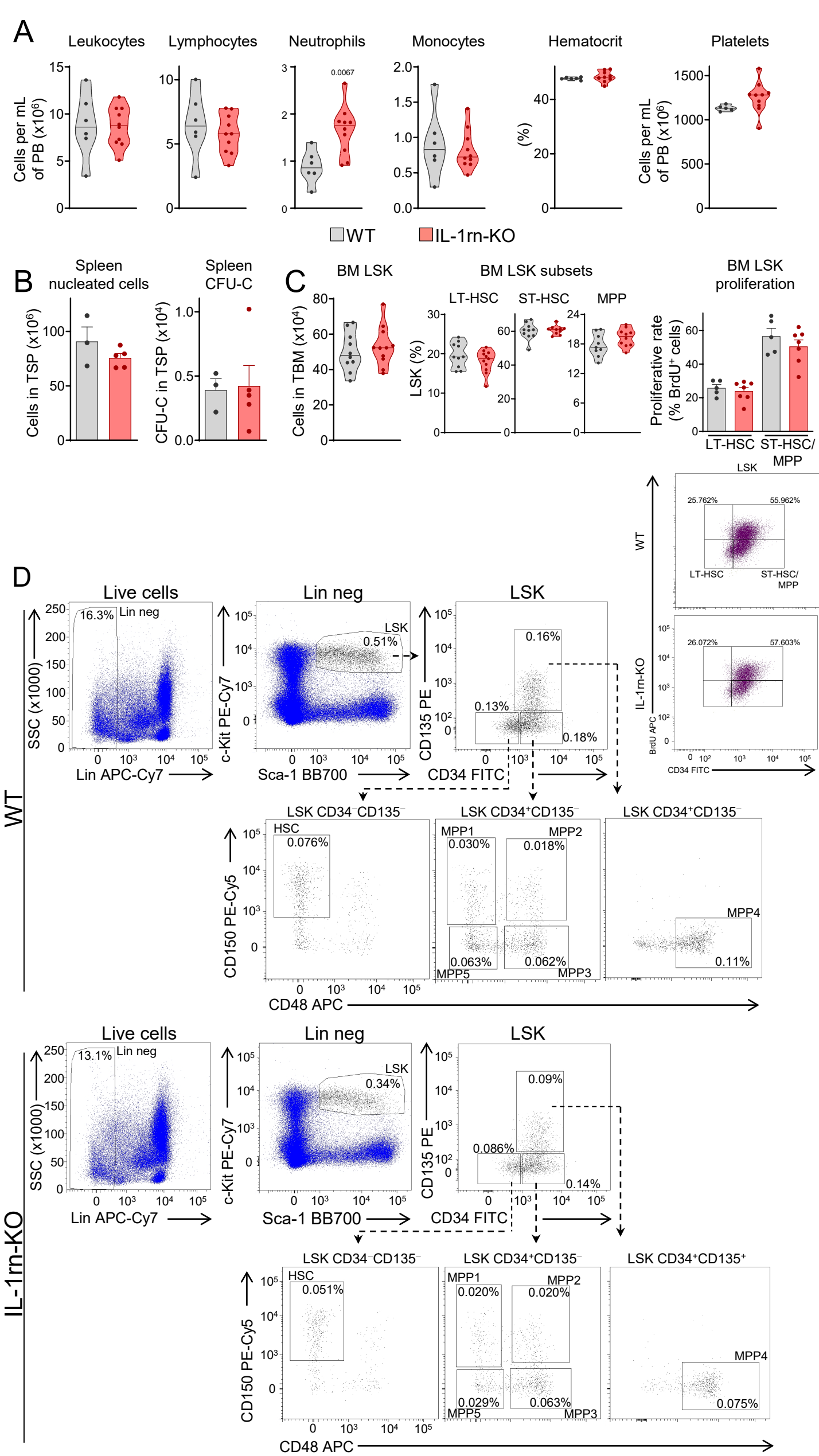
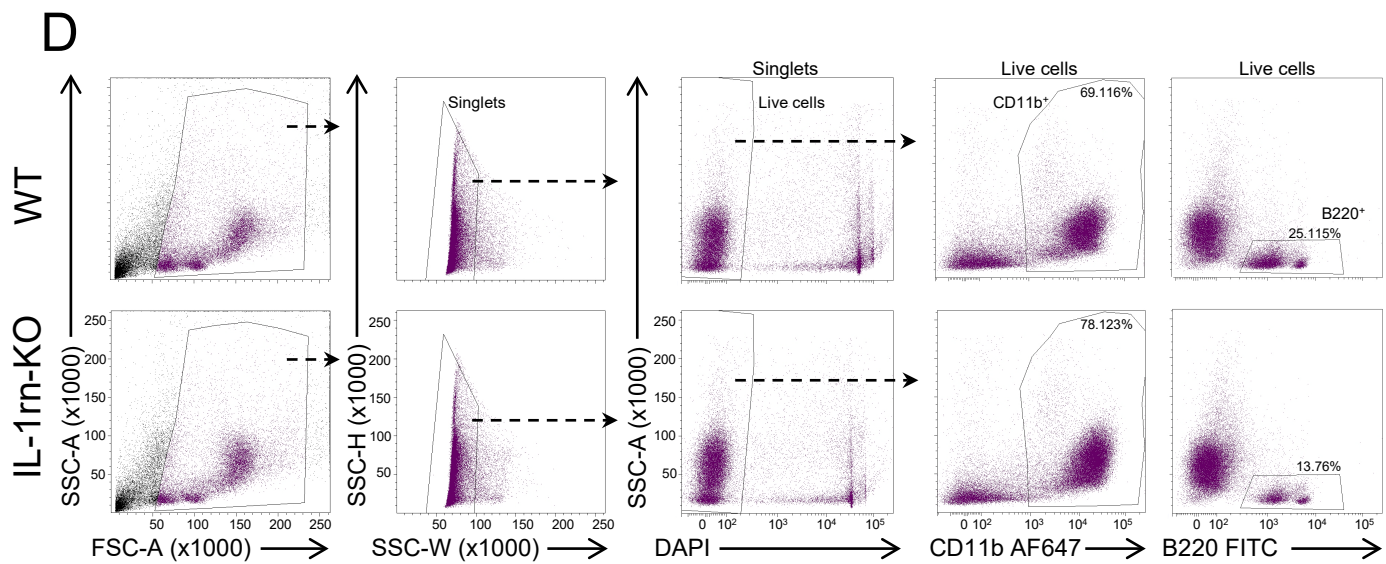
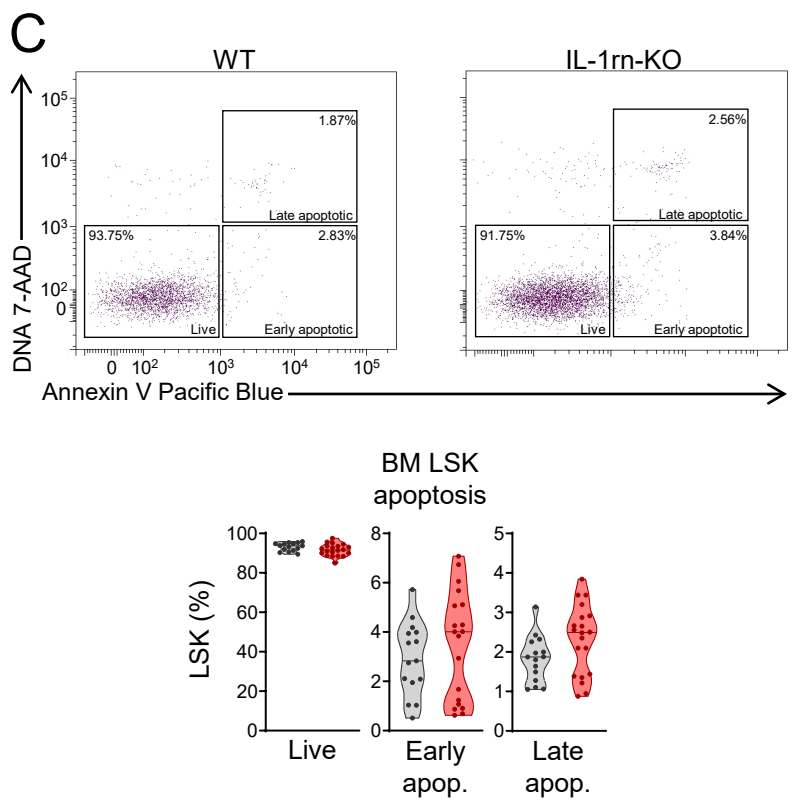
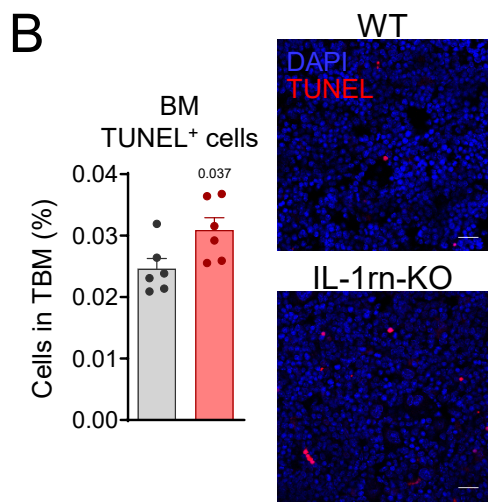
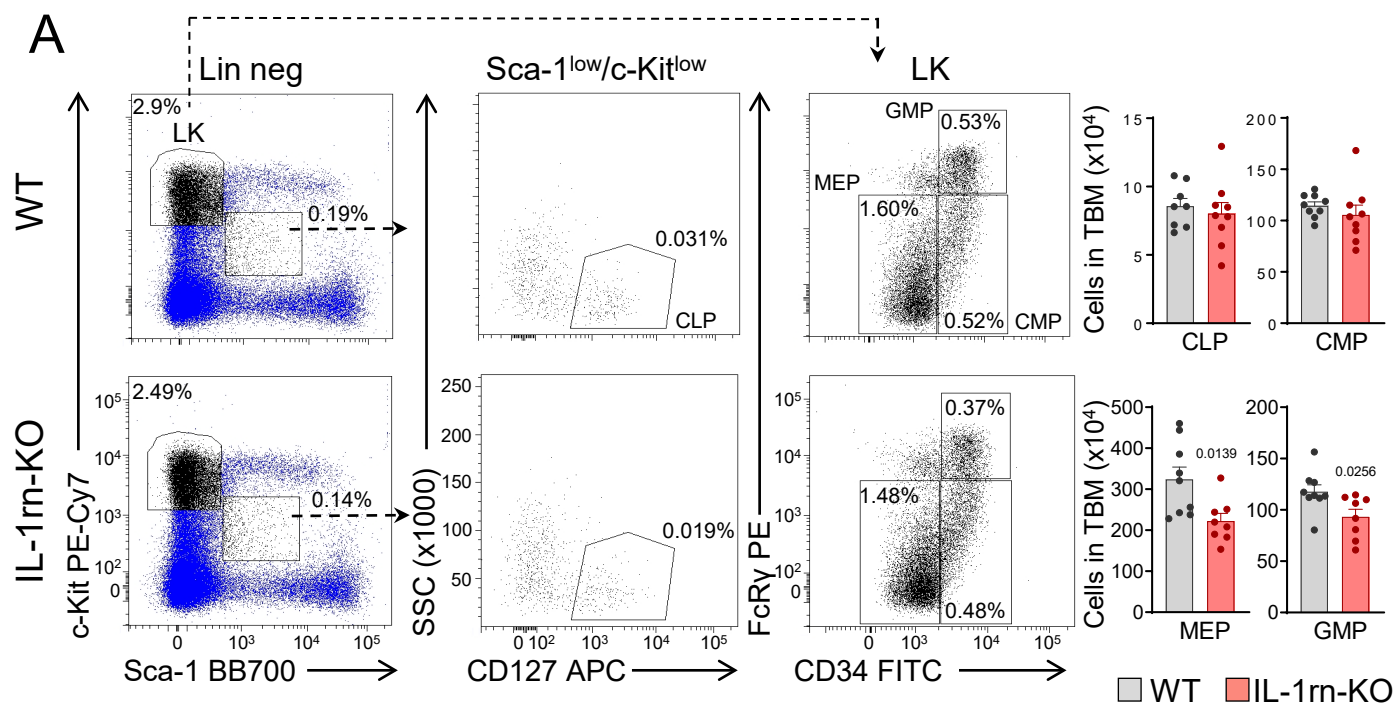


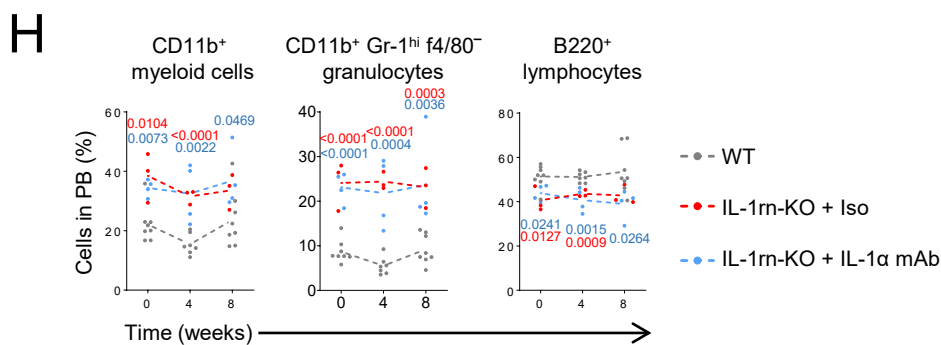
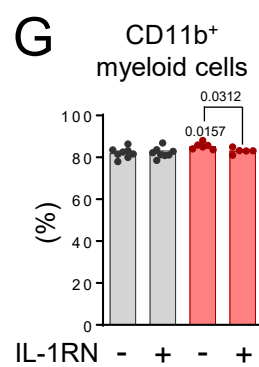
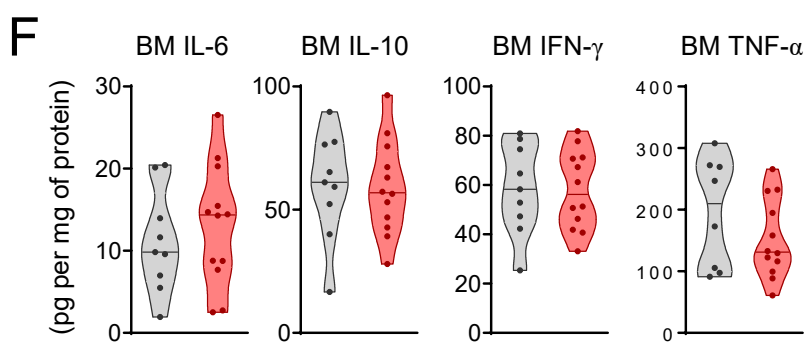
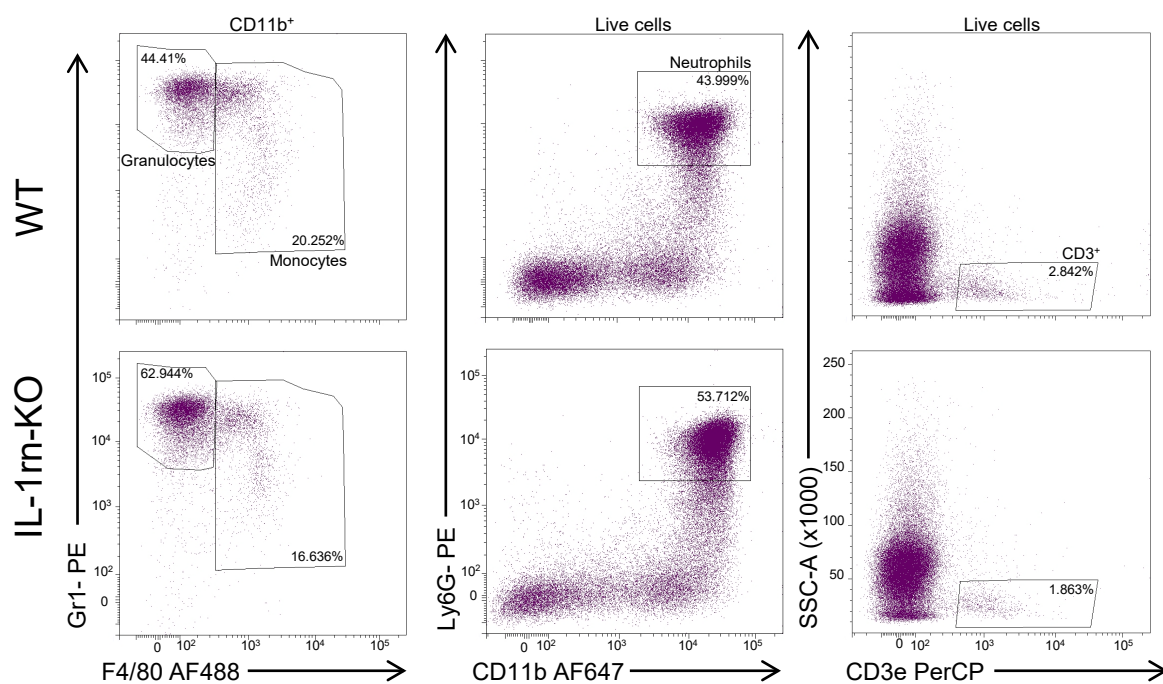
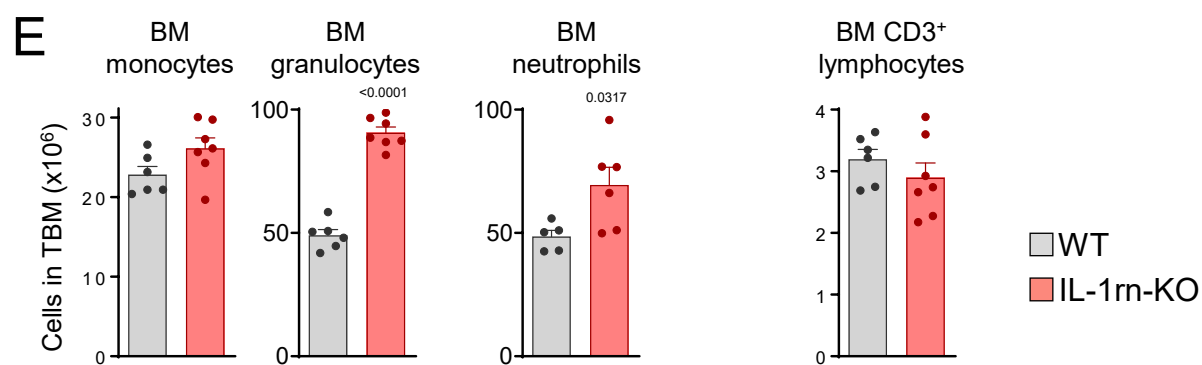


Supplementary Figure S1 (Related to Figure 1). Low IL-1RN predicts AML progression in patients. (A) Analyses of publicly available gene expression profiling of AML blasts from AML patients (GSE14468). mRNA expression of *IL1B* versus *IL1RN*, comparing AML subtypes M0-M3 (n=224) versus M4-M5 (n=171). FC, fold change. (B-C) Analyses of publicly available RNA sequencing of AML blasts obtained from 19 matched-pair AML patients (dbGaP accession phs001027). (B) AML patient relapse-free probability analyzed as a function of *IL1RN* expression. p value indicates log-rank test. (C) Expression of *IL1RN* in paired diagnosis-relapse AML samples. FPKM, fragments per kilobase per million mapped fragments. (D) qRT-PCR mRNA expression of *CASP1* and *IRAK1* versus *IL1RN* in CD34⁺ progenitors from volunteers (C, n=9) and AML patients (n=6). (E) qRT-PCR mRNA expression of *IL1RAP* in CD34⁺ progenitors from volunteers (C, n=4) and AML patients (n=5). (F) Representative fluorescence-activated cell sorting (FACS) analysis (cells in CD34⁺ cells, %) and frequencies of CD34⁺ progenitors expressing IL-1 receptor accessory protein (IL-1RAP) in volunteers (C, n=5) and AML patients (n=4). PB, peripheral blood; h, human. (G) Frequencies of CD34⁺ progenitors positive for phosphorylated NFκB in volunteers (C, n=11) and AML patients (n=5) and representative FACS histograms (cells in CD34⁺ cells, %). (F-G) Isotype staining was used as negative control. (H) Representative images of bright field, 7-AAD, NFκB, and 7-AAD/NFκB merged channels for THP-1 cells unstimulated (negative control) or stimulated (positive control) with lipopolysaccharide, over 3 independent experiments; scale bar, 10μm, and representative flow cytometry analysis of previous gating (unstimulated cells in culture, %). RMS, root mean square. (I-J) AML xenografts. (I) Representative FACS analysis of human CD11b⁺ cells in PB from mice treated with vehicle, IL-1RN or canakinumab, over 3 independent experiments (cells in PB, %). (J) Representative FACS analysis of human CD33⁺ and CD34⁺ cells in total bone marrow (TBM) of mice treated with vehicle or IL-1RN (cells in TBM, %). Data are biologically independent samples or animals, and means ± S.E.M. for bar plots or medians for violin plots. Statistical analyses were performed with two-tailed Student's *t*-test (A), Kaplan-Meier survival analysis (B), paired two-tailed Student's *t*-test (C) or two-tailed Mann-Whitney U test (D-G). p values ≤ 0.05 are reported. Source data are provided as a Source Data file.



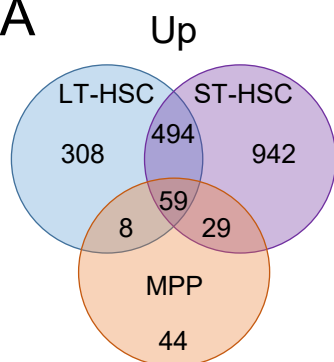
Supplementary Figure S2 (Related to Figure 2). Deletion of IL-1rn triggers IL-1 β -induced myelopoiesis in the absence of immunogenic stimulus. (A) Peripheral blood (PB) counts from C57BL/6J wild-type (WT, n=6; platelets n=5) and IL-1rn knockout (IL-1rn-KO, n=10; hematocrit n=9) mice. (B) Total number of spleen nucleated cells (TSP) and SP colony-forming unit cells (CFU-C) from WT (n=3) and IL-1rn-KO (n=5) mice. (C) Total bone marrow (TBM) number of Lin⁻c-Kit⁺Sca-1⁺ (LSK) cells (WT, n=10; IL-1rn-KO, n=11), frequencies of BM LSK subsets: LSK CD34⁻Flt3⁻, long-term hematopoietic stem cells (LT-HSC) (WT, n=10; IL-1rn-KO, n=11); LSK CD34⁺Flt3⁻, short-term HSC (ST-HSC) (WT, n=10; IL-1rn-KO, n=10); LSK CD34⁺Flt3⁺, multipotent progenitors (MPP) (WT, n=9; IL-1rn-KO, n=10), and (up) proliferative rate in BM LSK subsets CD34⁻ (LT-HSC) and CD34⁺ (ST-HSC/MPP) (WT, n=5; IL-1rn-KO, n=7) and (down) representative fluorescence-activated cell sorting (FACS) analysis (cells in LT-HSC or ST-HSC/ MPP, %). (D) Representative FACS analysis (cells in TBM, %) of BM hematopoietic stem and progenitor cell subsets corresponding to HSC (LSK CD34⁻Flt3⁻CD48⁻CD150⁺), MPP1 (LSK CD34⁺Flt3⁻CD48⁻CD150⁺), MPP2 (LSK CD34⁺Flt3⁻CD48⁺CD150⁺), MPP3 (LSK CD34⁺Flt3⁻CD48⁺CD150⁻), MPP4 (LSK CD34⁺Flt3⁺CD48⁺CD150⁻) and MPP5 (LSK CD34⁺Flt3⁻CD48⁻CD150⁻) from WT and IL-1rn-KO mice. Data are biologically independent animals, and means $\pm$ S.E.M for bar plots or medians for violin plots. Statistical analyses were performed with two-tailed Student's *t*-test. *p* values $\leq$ 0.05 are reported. Source data are provided as a Source Data file.



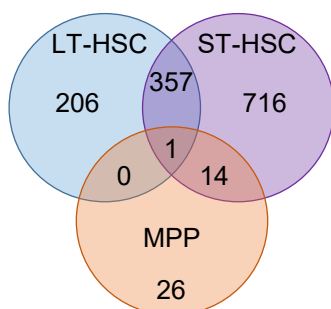


Supplementary Figure S3 (Related to Figure 2). Deletion of IL-1 α triggers IL-1 β -induced myelopoiesis in the absence of immunogenic stimulus. (A) Representative fluorescence-activated cell sorting (FACS) analysis (cells in total bone marrow; TBM, %) and total bone marrow (TBM) number of common lymphoid progenitors (CLP, Lin⁻c-Kit^{low}Sca-1^{low}CD127⁺), common myeloid progenitors (CMP, Lin⁻c-Kit⁺Sca-1⁻ (LK) CD34⁺FcR γ ⁻), megakaryocyte erythroid progenitors (MEP, LK CD34⁺FcR γ ⁻) and granulocyte-monocyte progenitors (GMP, LK CD34⁺FcR γ ⁺) from C57BL/6J wild-type (WT) and IL-1 α knockout (IL-1 α -KO) mice. (B) Apoptotic rate in TBM (n=6 per group), and representative TUNEL (terminal deoxynucleotidyl transferase dUTP nick end labeling staining, red) of BM sections; nuclei were counterstained with DAPI (blue). Scale bar, 20 μ m. (C) Representative FACS analysis to identify the fraction of live, early apoptotic and late apoptotic cells within the Lin⁻c-Kit⁺Sca-1⁺ (LSK) compartment in the BM from WT and IL-1 α -KO mice (cells in LSK cells, %), and apoptotic rate within the BM LSK compartment (Live: WT n=15, IL-1 α -KO n=20; Early apoptotic: WT n=15, IL-1 α -KO n=19; Late apoptotic: WT n=15, IL-1 α -KO n=20). (D) Representative FACS analysis of CD11b⁺ myeloid cells and B220⁺ lymphocytes in the BM of WT and IL-1 α -KO mice (cells in TBM, %). (E) TBM number of CD11b⁺Gr-1^{hi}f4/80⁻ monocytes, CD11b⁺Gr-1^{hi}f4/80⁻ granulocytes, CD11b⁺Ly6G⁺ neutrophils and CD3⁺ lymphocytes from WT (n=6; neutrophils n=5) and IL-1 α -KO (n=7, neutrophils n=6) mice, and representative FACS analysis (cells in TBM, %). (F) Cytokine levels in BM extracellular fluid from WT (n=9, TNF- α n=8) and IL-1 α -KO mice (n=12). (G) Frequency of CD11b⁺ myeloid cells differentiated *ex vivo* from lineage-negative progenitors from the BM of WT (n=8) and IL-1 α -KO (vehicle (-), n=6; IL-1 α (+), n=5) mice. (H) Frequency evolution of CD11b⁺ myeloid cells, CD11b⁺Gr-1^{hi}f4/80⁻ granulocytes and B220⁺ lymphocytes in peripheral blood (PB) of WT (n=8) and IL-1 α -KO mice treated with IgG isotype (Iso; n=3) or IL-1 α monoclonal antibody (IL-1 α mAb; n=4). Data are biologically independent animals, and means $\pm$ S.E.M for bar plots or medians for violin plots. Statistical analyses were performed with two-tailed Student's *t*-test. *p* values $\leq$ 0.05 are reported. Source data are provided as a Source Data file.

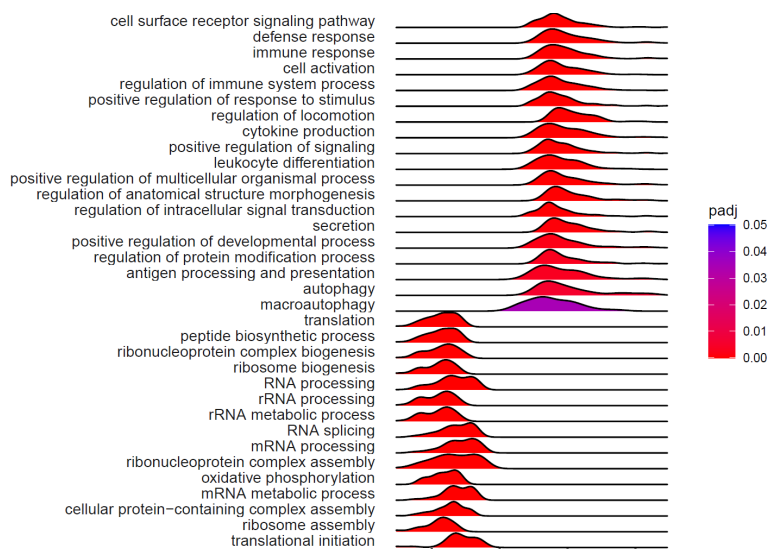
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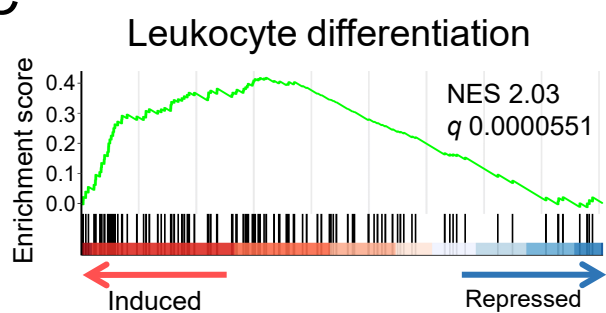
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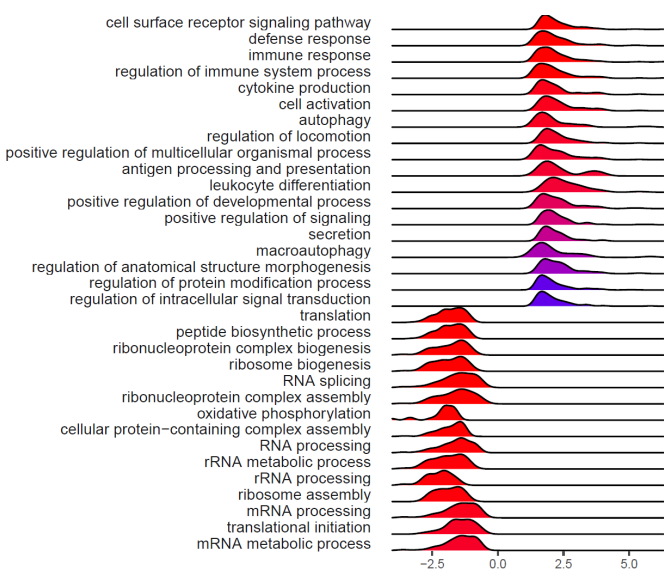
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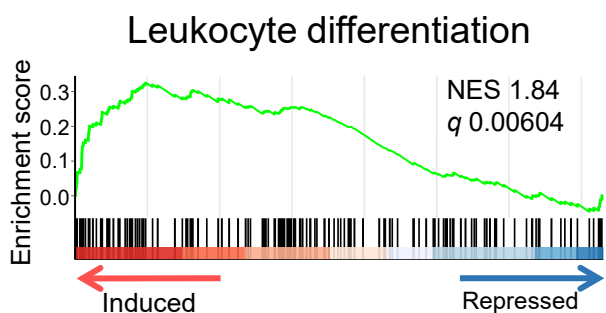
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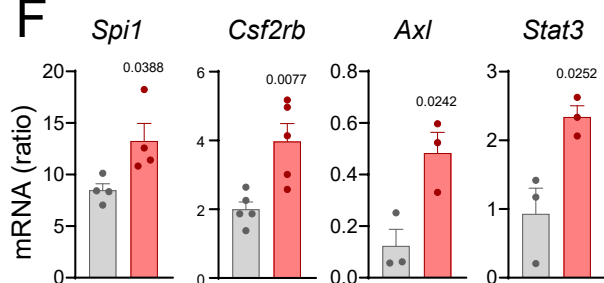
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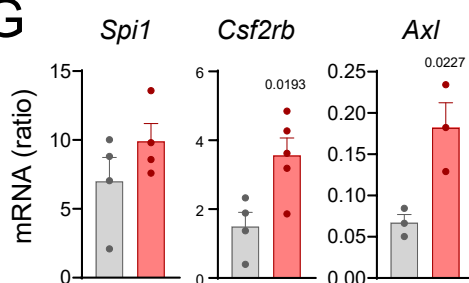
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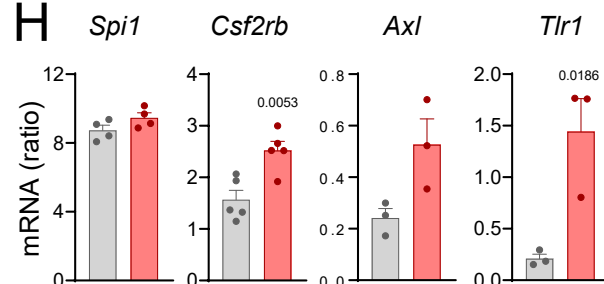
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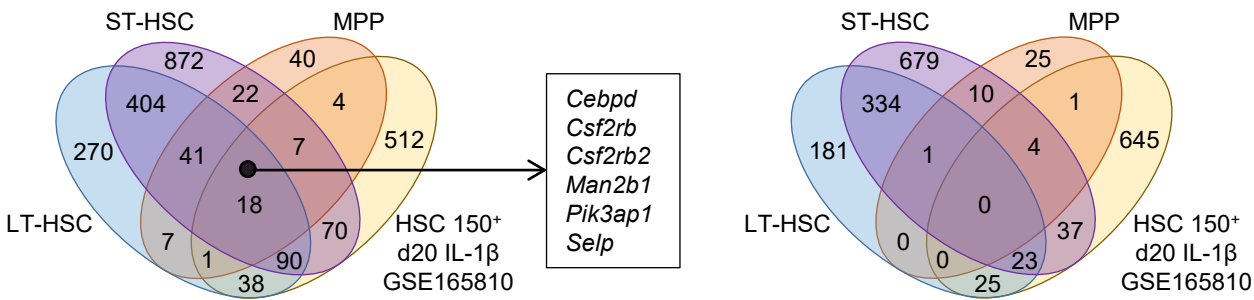


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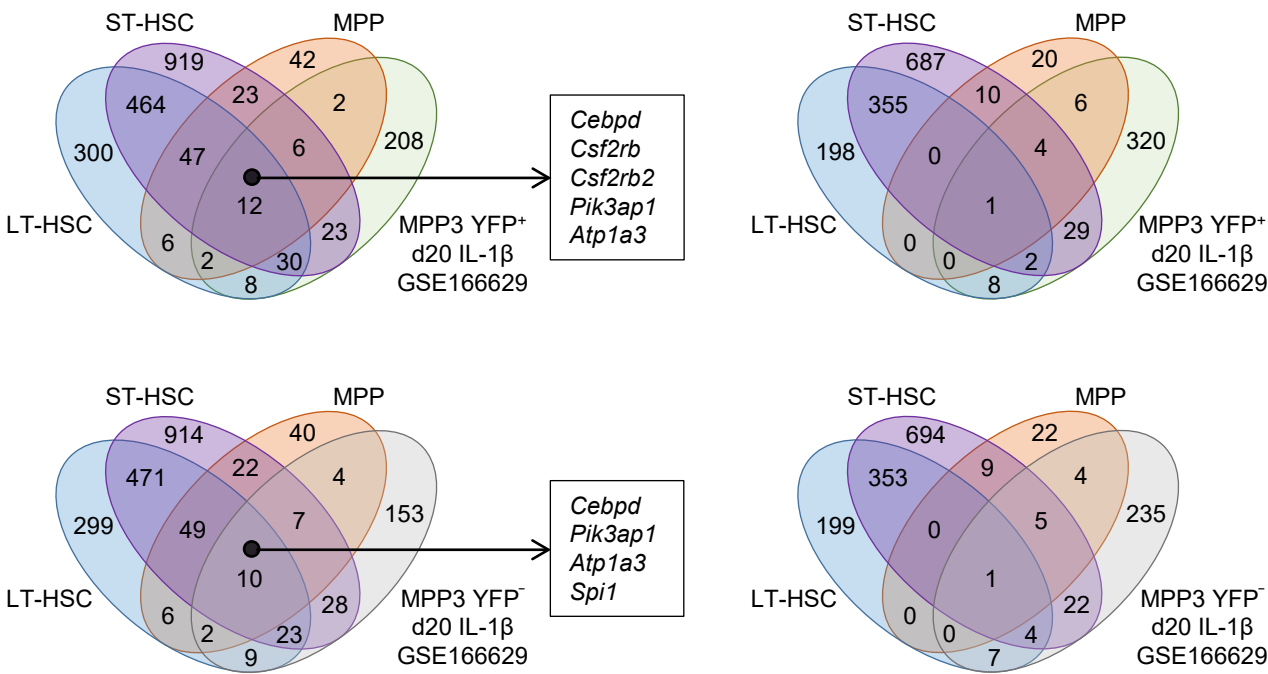
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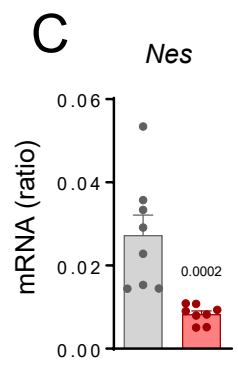
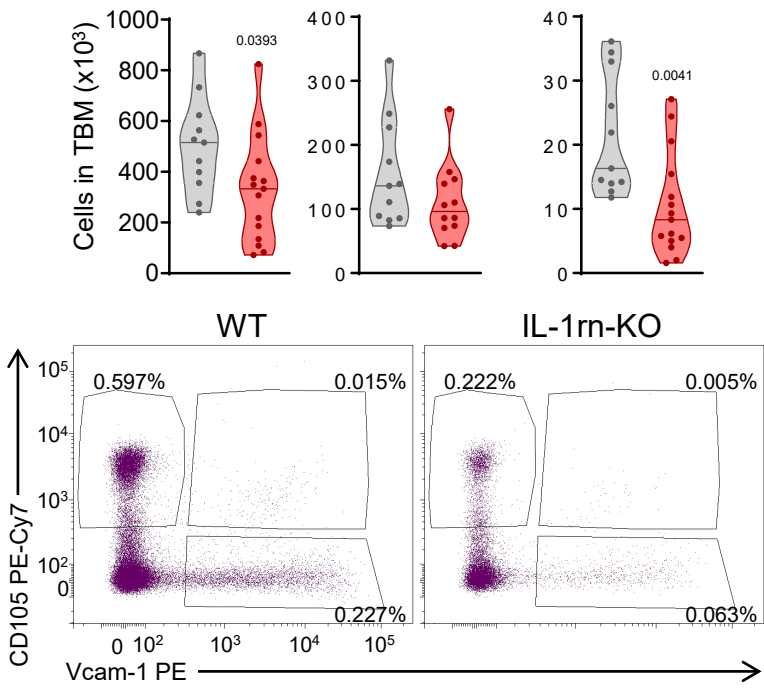
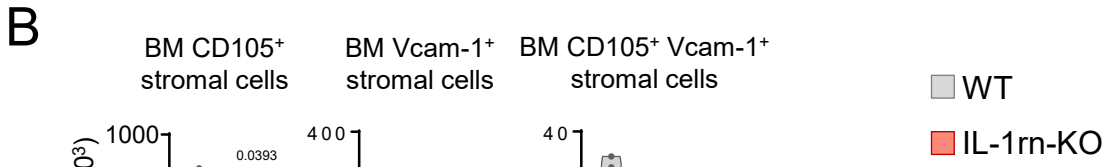
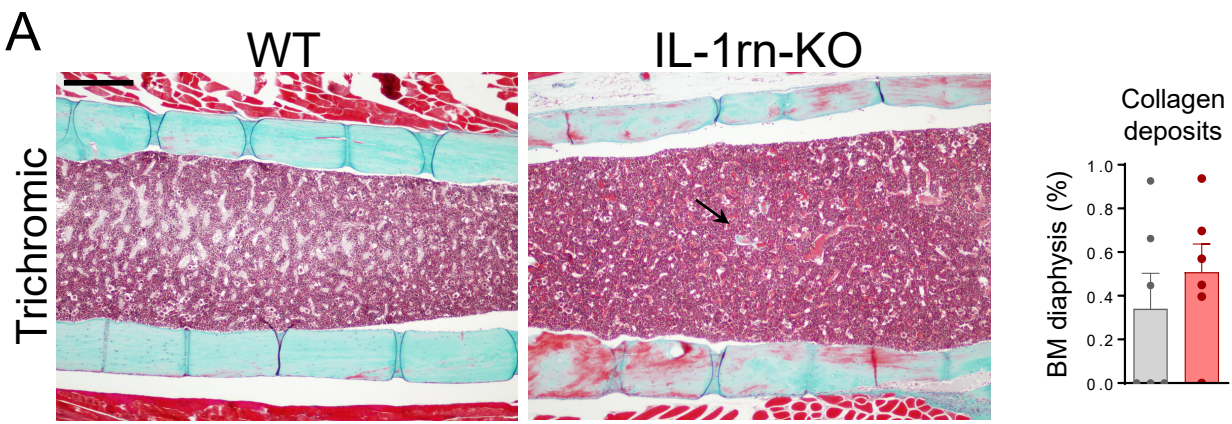
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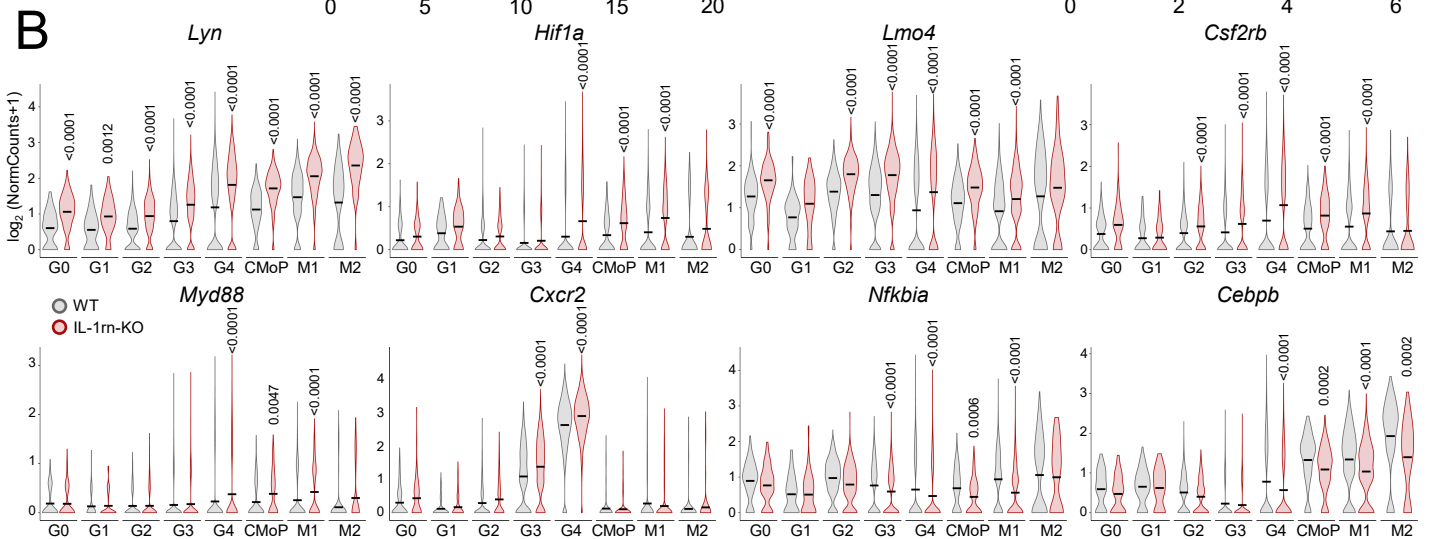
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Supplementary Figure S4 (Related to Figure 3). IL-1 β -induced myelopoiesis after IL-1rn deletion is mediated by NF κ B activation. (A-E) RNA sequencing (RNA-Seq) in bone marrow Lin⁻c-Kit⁺Sca-1⁺ (LSK) subsets; LSK CD34⁻Flt3⁻, long-term hematopoietic stem cells (LT-HSC); LSK CD34⁺Flt3⁻, short-term HSC (ST-HSC); LSK CD34⁺Flt3⁺, multipotent progenitors (MPP), from C57BL/6J wild type (WT) and IL-1rn knockout (IL-1rn-KO) mice (n=3 per group). (A) Venn diagrams show number of up- and down-regulated genes in LT-HSC, ST-HSC and MPP from IL-1rn-KO mice versus WT, and overlap of genes. (B-E) Gene Ontology biological processes and kernel density plots showing differences in core enriched gene sets in (B) LT-HSC and (D) ST-HSC, selected within gene set enrichment analysis (GSEA) enriched categories in common. Enrichment plot of coordinated changes of genes induced or repressed in leukocyte differentiation in (C) LT-HSC and (E) ST-HSC. NES, normalized enrichment score. (F-H) qRT-PCR validation of selected RNA-Seq hits in independent biological samples, in (F) LT-HSC, (G) ST-HSC and (H) MPP (*Spil*: n=4 per group; *Csf2rb*: WT, n=5; ST-HSC n=4; IL-1rn-KO, n=5; *Axl*, *Stat3*, *Tlr1*: n=3 per group). (I) Venn diagrams show number of up- and down-regulated genes in LT-HSC, ST-HSC and MPP from IL-1rn-KO mice versus C57BL/6J WT and in LSK Flt3⁻CD48⁻CD150⁺ cells from C57BL/6 WT mice exposed to chronic IL-1 β versus vehicle in GSE165810 (n=4 per group). Overlap of genes, and up-regulated genes shared by all LSK subsets identified as NF κ B targets from Synapse ID syn4956655, <https://bioinfo.lifl.fr/NF-KB> and <https://www.bu.edu/nf-kb/gene-resources/target-genes> (Supplementary Data 1). (J) Venn diagrams show number of up- and down-regulated genes in LT-HSC, ST-HSC and MPP from IL-1rn-KO mice versus C57BL/6 WT and in LSK Flt3⁻CD48⁺CD150⁻ (MPP3) from CD45.1 recipient mice transplanted with LSK (YFP⁺) and competitor whole bone marrow cells (YFP⁻) and exposed to chronic IL-1 β versus vehicle in GSE166629 (n=3 per group). Overlap of genes, and up-regulated genes shared by all LSK subsets identified as NF κ B targets. Data in (F-H) are biologically independent animals, and means $\pm$ S.E.M. in bar plots. Statistical analyses were performed with GSEA with Benjamini-Hochberg correction for multiple comparisons (B, D), or two-tailed Student's *t*-test (F-H). Adjusted *p* < 0.05 (B, D) or *p* values $\leq$ 0.05 (F-H) are reported. Source data are provided as a Source Data file.

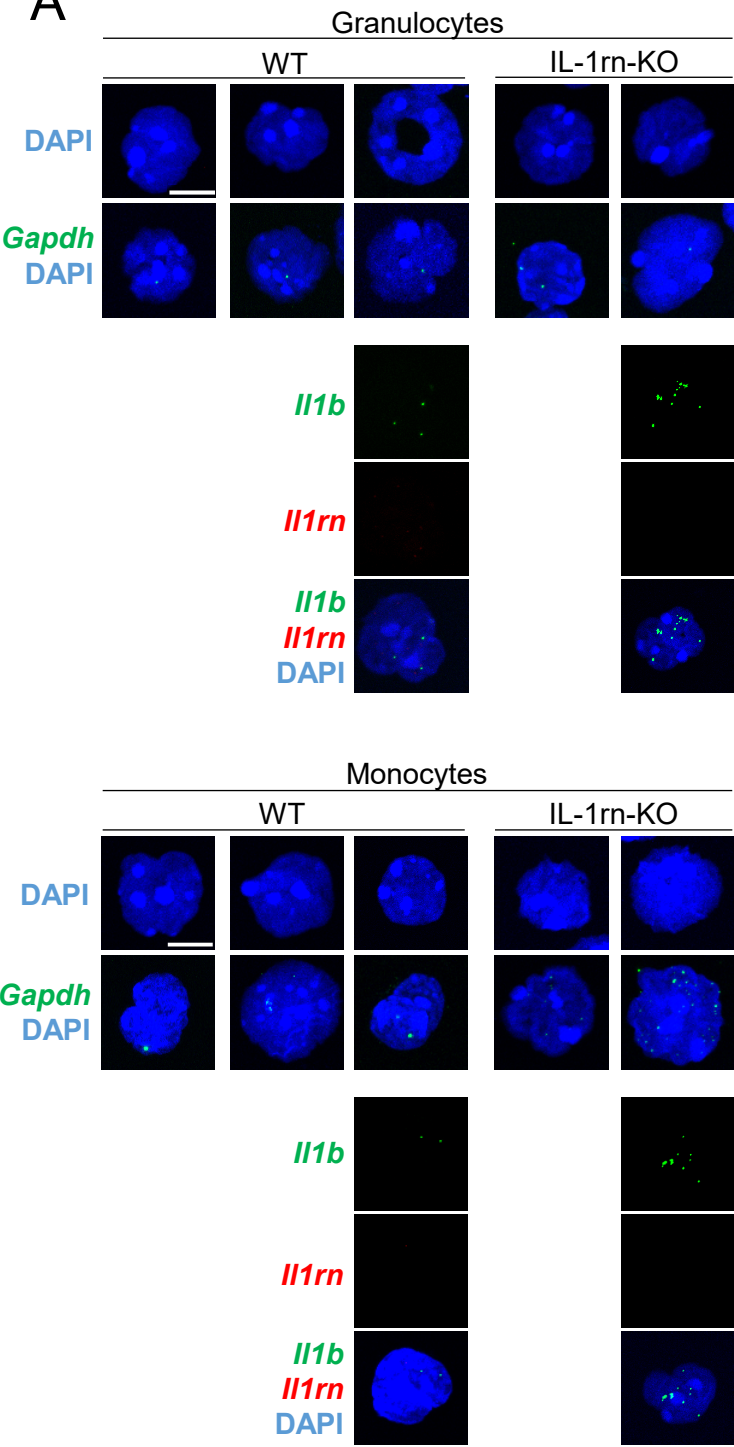


Supplementary Figure S5 (Related to Figure 4). Deletion of IL-1rn causes IL-1 β -induced damage to the bone marrow stroma in the absence of immunogenic stimulus. (A) Representative Masson's trichrome staining of femoral bone marrow (BM) sections; scale bar, 500 μ m, and quantification of collagen deposits (arrow) in BM diaphysis from C57BL/6J wild-type (WT) and IL-1rn knockout (IL-1rn-KO) mice (n=6 per group). (B) Total BM (TBM) number and representative fluorescence-activated cell sorting analysis (cells in TBM, %) of CD45⁻CD31⁻Ter119⁻CD105⁺ (WT, n=11; IL-1rn-KO, n=15), CD45⁻CD31⁻Ter119⁻Vcam-1⁺ (WT, n=11; IL-1rn-KO, n=12) and CD45⁻CD31⁻Ter119⁻CD105⁺Vcam-1⁺ (WT, n=11; IL-1rn-KO, n=15) stromal cells. (C) qRT-PCR mRNA expression of *Nes* in BM nucleated cells (n=8 per group). (D) t-SNE plots visualizing expression of selected genes from publicly available single-cell RNA sequencing analysis to characterize mouse BM mesenchymal stromal cells (GSE108892). Vascular cells (VE-Cad⁺, V1-2; perivascular LEPR⁺ cells (LEPR⁺, P1-4); osteoblasts (COL2.3⁺, O1-3). Color bar, log₁₀(TP10K). Data are biologically independent animals, and means $\pm$ S.E.M. for bar plots or medians for violin plots, except (D). Statistical analyses were performed with two-tailed Student's *t*-test (B) or two-tailed Mann-Whitney U test (C). p values $\leq$ 0.05 are reported. Source data are provided as a Source Data file.

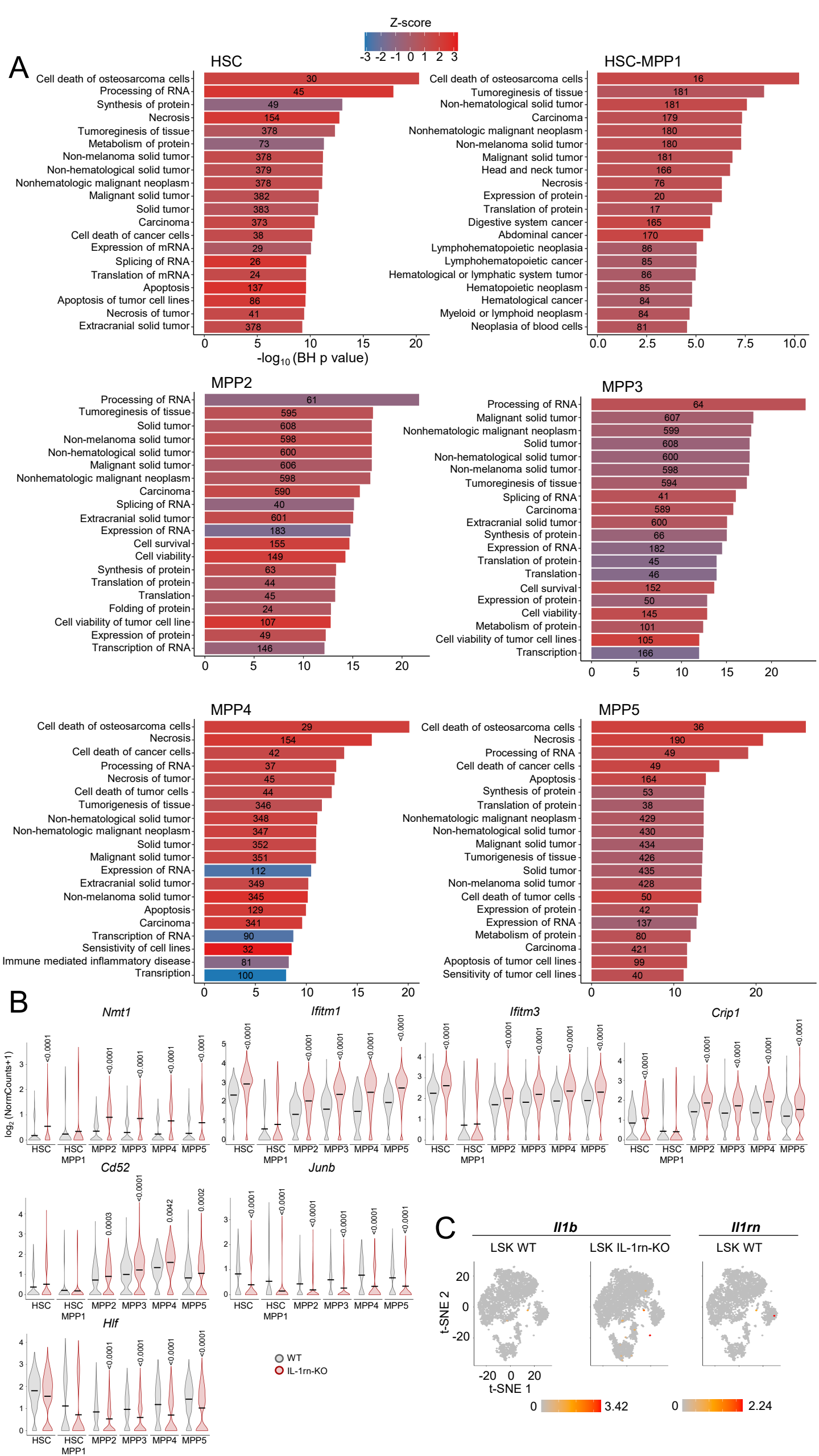


Supplementary Figure S6 (related to Figure 5). Single-cell RNA sequencing from CD11b⁺ myeloid cells in bone marrow of C57BL/6J wild-type and IL-1rn knock-out mice. Single-cell RNA sequencing from bone marrow CD11b⁺ myeloid cells from C57BL/6J wild-type (WT, n=1 sample from 2 biologically independent animals) and IL-1rn knockout (IL-1rn-KO, n=1 sample from 2 biologically independent animals) mice. (A) Ingenuity pathway analysis (IPA) of “Diseases and Functions” of gene sets enriched in the clusters G0 to G4 neutrophils, common monocyte progenitors (CMoP I), and type I and II monocytes from IL-1rn-KO versus WT mice. Selected significantly enriched functions are shown with their $-\log_{10}$ (Benjamini-Hochberg (BH) adjusted p value) in x axis, number of genes stated in the bar plots and Z-score as color scale. (B) Expression level ($\log_2$ (NormCounts + 1)) of selected genes for the same clusters. Data are means for violin plots. Statistical analyses were performed with right-tailed Fisher’s exact test (A) or two-tailed Wilcoxon Rank Sum test (B), with Benjamini-Hochberg correction for multiple comparisons. Adjusted p values < 0.05 are reported. Complete lists of detected genes are provided as Supplementary Data 2. Source data are provided as a Source Data file.

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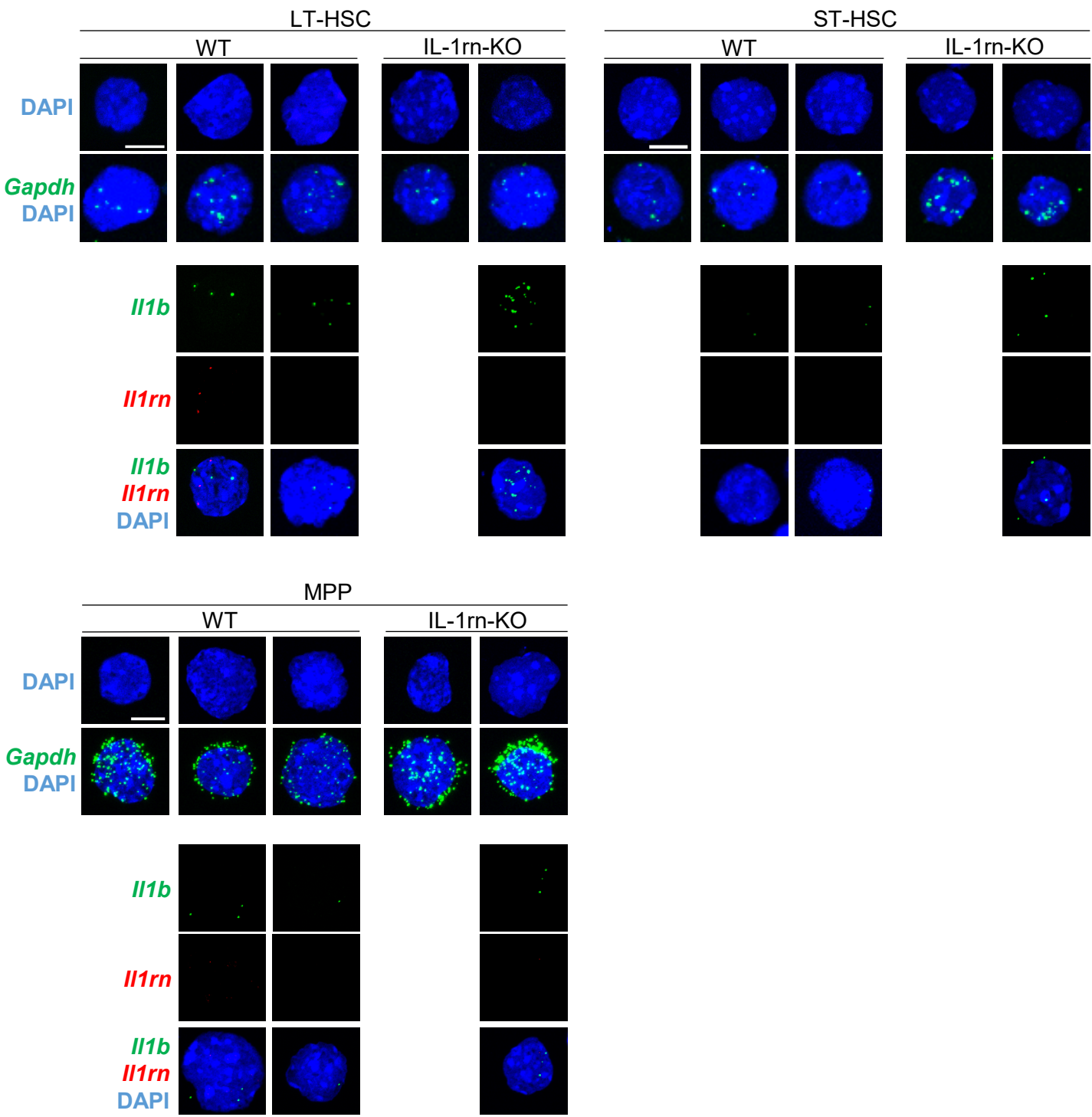


Supplementary Figure S7 (related to Figure 5). Identification of the sources of IL-1 β and IL-1rn in the bone marrow CD11b⁺ myeloid compartment at the single cell level by RNA-FISH. (A) RNA fluorescent in situ hybridization (RNA-FISH) in bone marrow CD11b⁺Gr-1^{hi}f4/80⁻ granulocytes and CD11b⁺Gr-1⁺f4/80⁺ monocytes from C57BL/6J wild-type (WT) and IL-1rn knockout (IL-1rn-KO) mice (n=4 biologically independent animals per group). Representative images of cells expressing *Il1b* (green) and/or *Il1rn* (red). Nuclei were counterstained with DAPI, no probes were used in negative controls and expression of *Gapdh* (green) was used as positive control. Scale bar, 10 μ m.

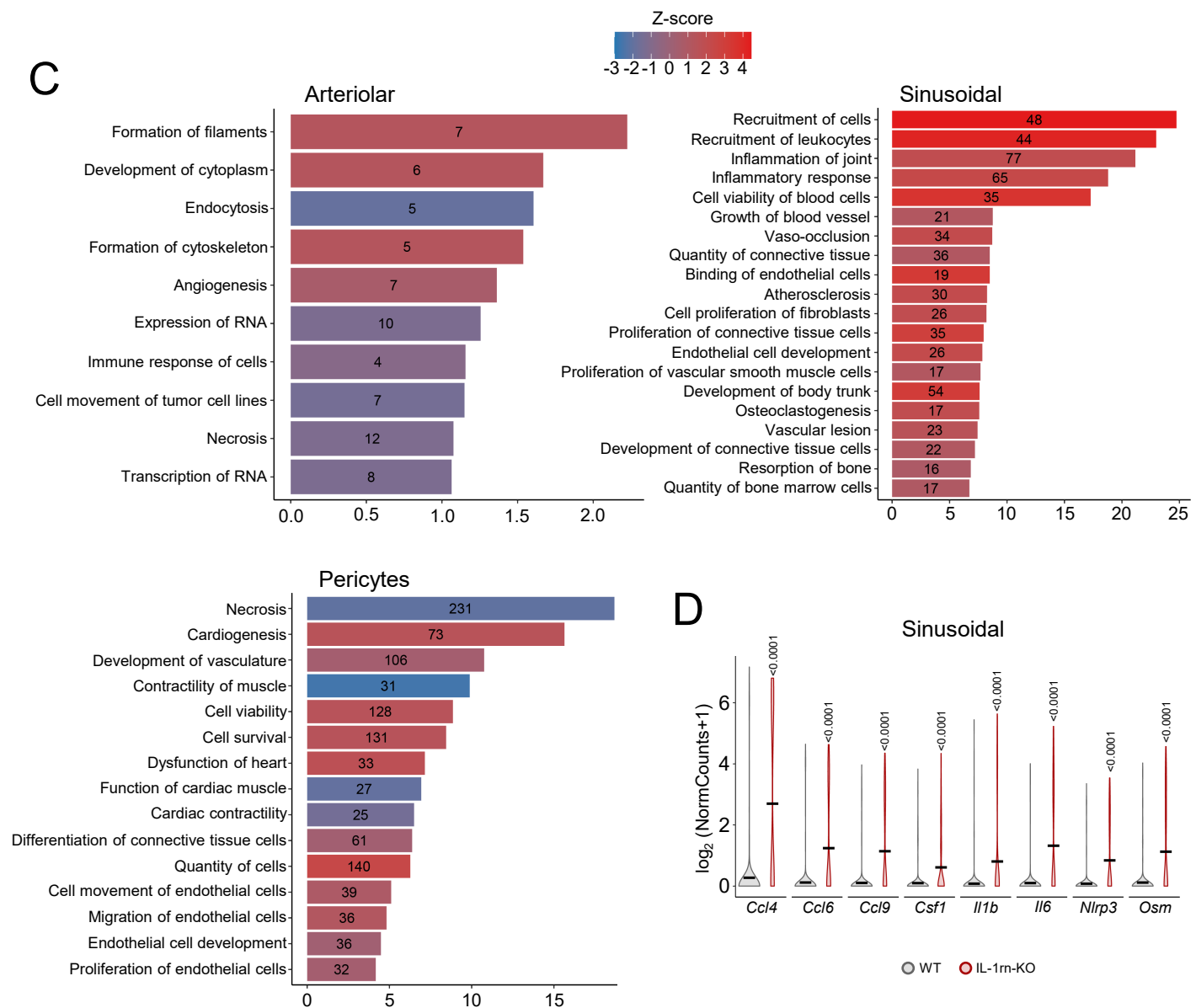
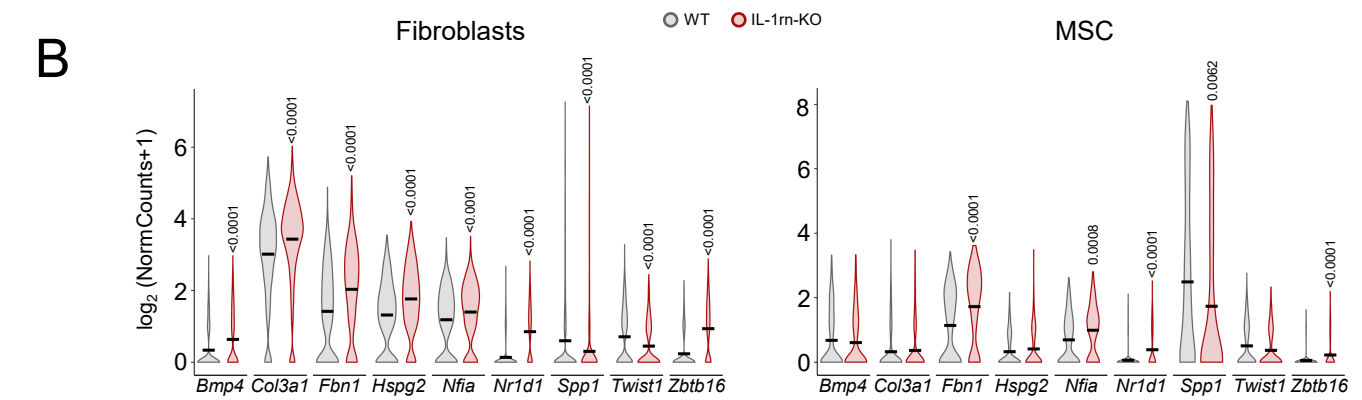
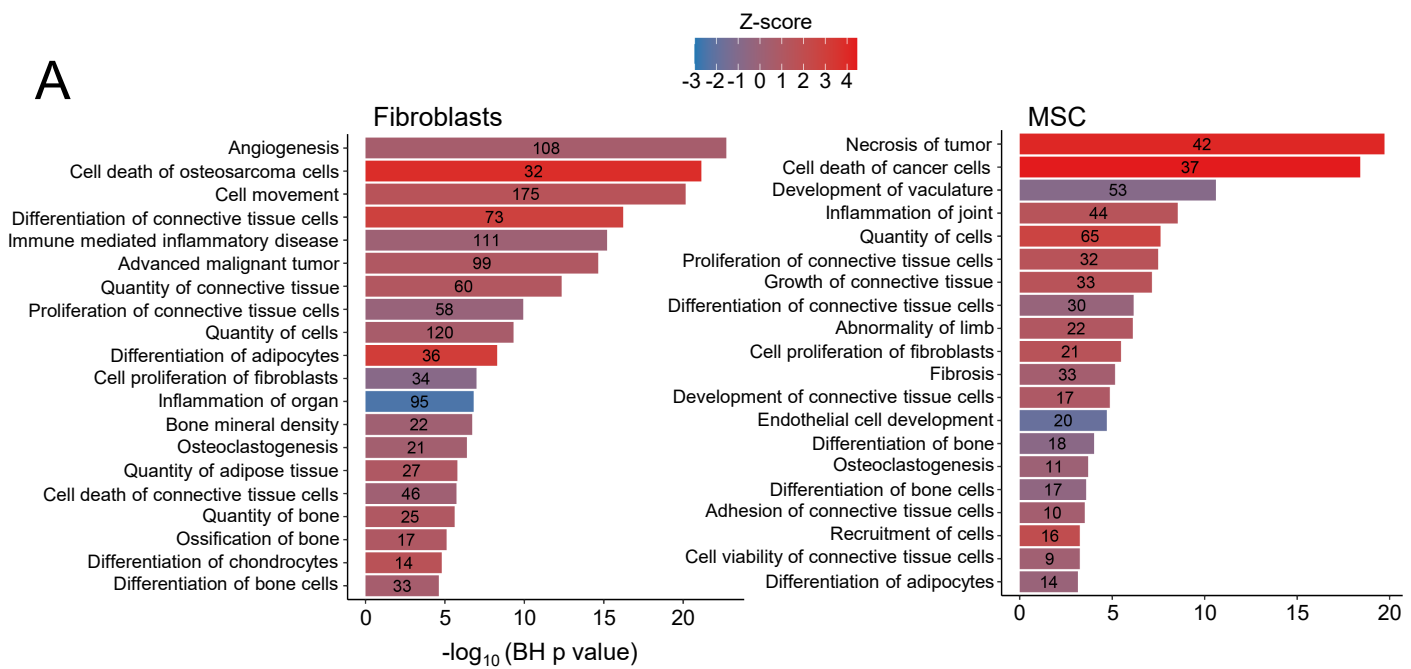


Supplementary Figure S8 (related to Figure 6). Single-cell RNA sequencing from hematopoietic stem and progenitor cells in bone marrow of C57BL/6J wild-type and IL-1rn knock-out mice. Single-cell RNA sequencing from bone marrow Lin⁻Sca-1⁺c-Kit⁺ (LSK) cells from C57BL/6J wild-type (WT, n=1 sample from 2 biologically independent animals) and IL-1rn knockout (IL-1rn-KO, n=1 sample from 2 biologically independent animals) mice. (A) IPA of “Diseases and Functions” of gene sets enriched in the clusters hematopoietic stem cells (HSC), multipotent progenitors (MPP) 1, MPP2, MPP3, MPP4, MPP5 from IL-1rn-KO versus WT mice. Selected significantly enriched functions are shown with their $-\log_{10}$ (BH adjusted p value) in x axis, number of genes stated in the bar plots and Z-score as color scale. (B) Expression level ($\log_2$ (NormCounts + 1)) of selected genes for each cluster of BM LSK from WT and IL-1rn-KO mice. (C) t-SNE plots visualizing expression levels of *Il1b* and *Il1rn*. Color bar, $\log_{10}$ (TP10K). Data are means for violin plots. Statistical analyses were performed with right-tailed Fisher’s exact test (A) or two-tailed Wilcoxon Rank Sum test (B), with Benjamini-Hochberg correction for multiple comparisons. Adjusted p values < 0.05 are reported. Complete lists of detected genes are provided as Supplementary Data 3. Source data are provided as a Source Data file.

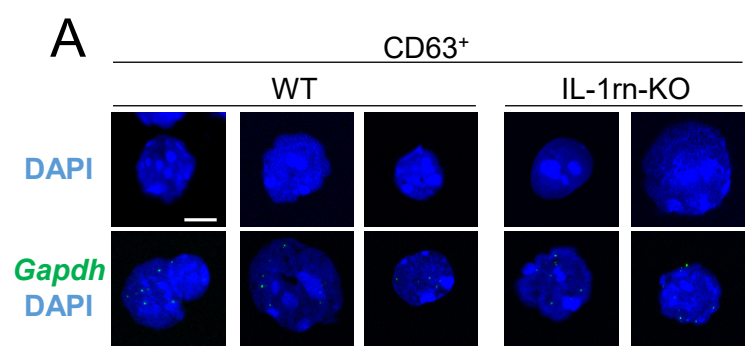
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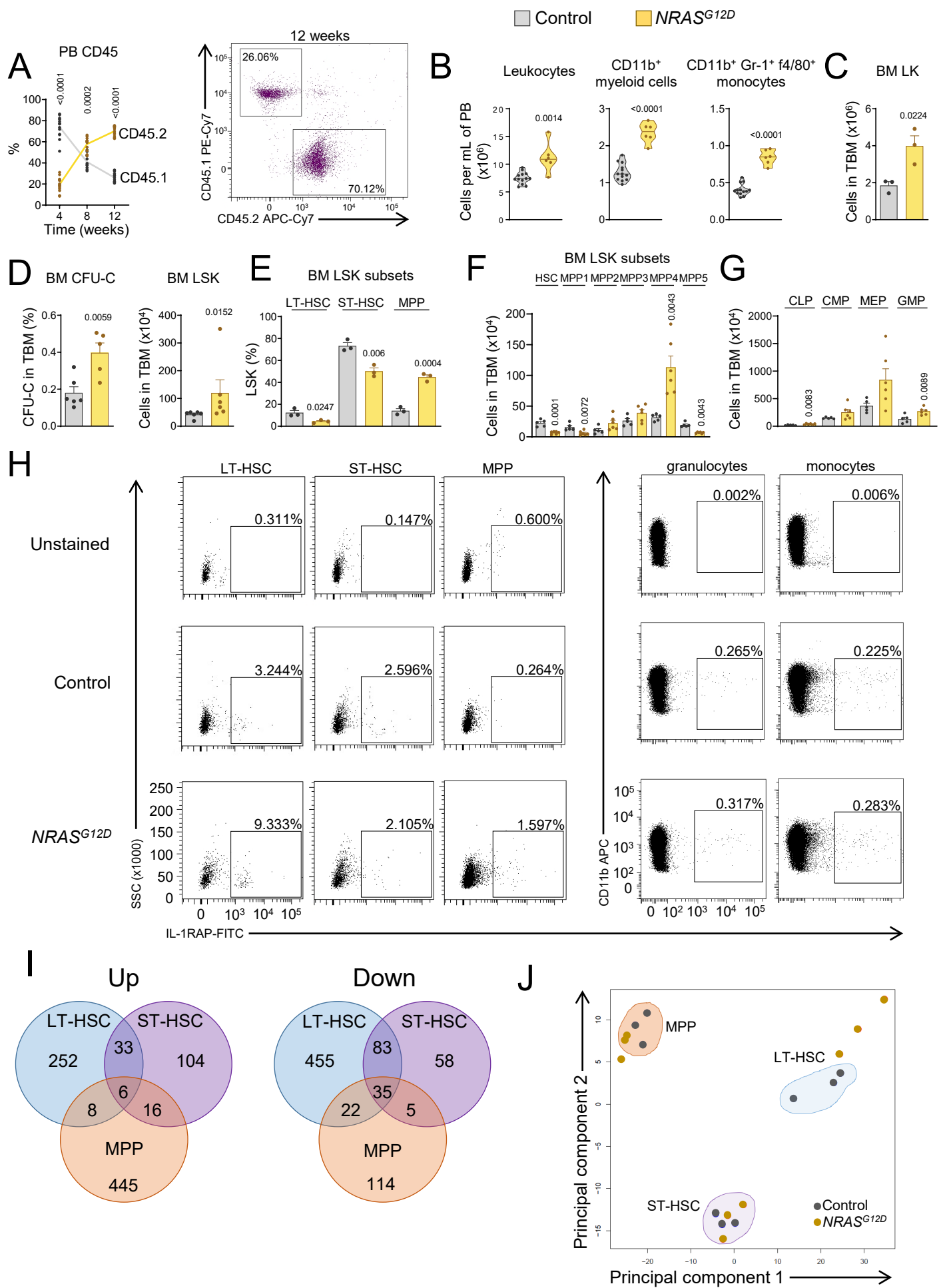
Supplementary Figure S9 (related to Figure 6). Identification of the sources of IL-1 β and IL-1rn in the bone marrow hematopoietic stem and progenitor cell compartment at the single cell level by RNA-FISH. (A) RNA fluorescent in situ hybridization (FISH) in bone marrow Lin⁻Sca-1⁺c-Kit⁺ (LSK) CD34⁻Flt3⁻, long-term HSC (LT-HSC); LSK CD34⁺Flt3⁻, short-term HSC (ST-HSC) and LSK CD34⁺Flt3⁺, multipotent progenitors (MPP), from C57BL/6J wild-type (WT) and IL-1rn knockout (IL-1rn-KO) mice (n=3 biologically independent animals per group). Representative images of cells expressing *Il1b* (green) and/or *Il1rn* (red). Nuclei were counterstained with DAPI, no probes were used in negative controls and expression of *Gapdh* (green) was used as positive control. Scale bar, 10 μ m.



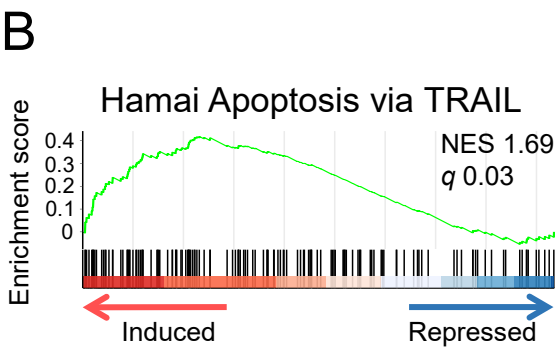
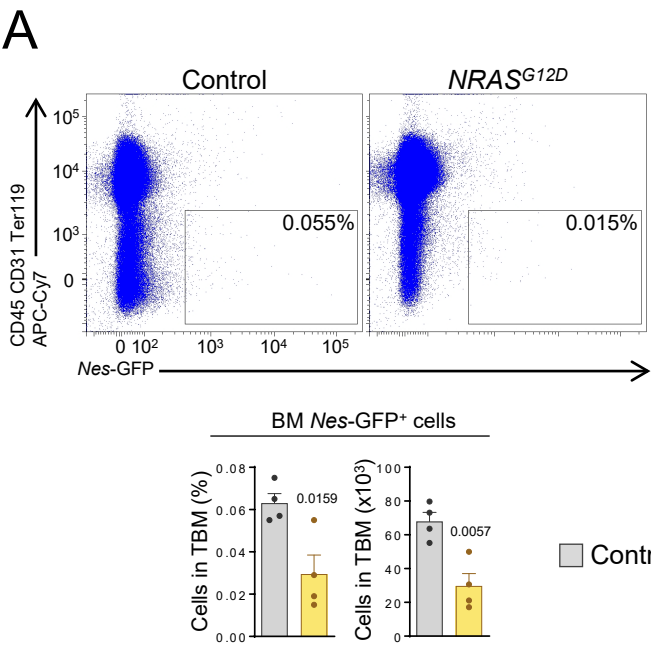
Supplementary Figure S10 (related to Figure 7). Single-cell RNA sequencing from CD63⁺ stromal cells in bone marrow of C57BL/6J wild-type and IL-1rn knock-out mice. Single-cell RNA sequencing from bone marrow CD45⁻CD31⁻Ter119⁻CD63⁺ stromal cells from C57BL/6J wild-type (WT, n=1 sample from 2 biologically independent animals) and IL-1rn knockout (IL-1rn-KO, n=1 sample from 2 biologically independent animals) mice. (A) IPA of “Diseases and Functions” of gene sets enriched in the clusters fibroblasts and mesenchymal stromal cells (MSC) from IL-1rn-KO versus WT mice. Selected significantly enriched functions are shown with their $-\log_{10}$ (BH adjusted p value) in x axis, number of genes stated in the bar plots and Z-score as color scale. (B) Expression level ($\log_2$ (NormCounts + 1)) of selected genes for fibroblast and MSC clusters within CD45⁻CD31⁻Ter119⁻CD63⁺ stromal cells from WT and IL-1rn-KO mice. (C) IPA of “Diseases and Functions” of gene sets enriched in the clusters arteriolar, sinusoidal and pericytes from IL-1rn-KO versus WT mice. Selected significantly enriched functions are shown with their $-\log_{10}$ (BH adjusted p value) in x axis, number of genes stated in the bar plots and Z-score as color scale. (D) Expression level ($\log_2$ (NormCounts + 1)) of selected genes for sinusoidal cluster within CD45⁻CD31⁻Ter119⁻CD63⁺ stromal cells from WT and IL-1rn-KO mice. Data are means for violin plots. Statistical analyses were performed with right-tailed Fisher’s exact test (A, C) or two-tailed Wilcoxon Rank Sum test (B, D), with Benjamini-Hochberg correction for multiple comparisons. Adjusted p values < 0.05 are reported. Complete lists of detected genes are provided as Supplementary Data 4. Source data are provided as a Source Data file.



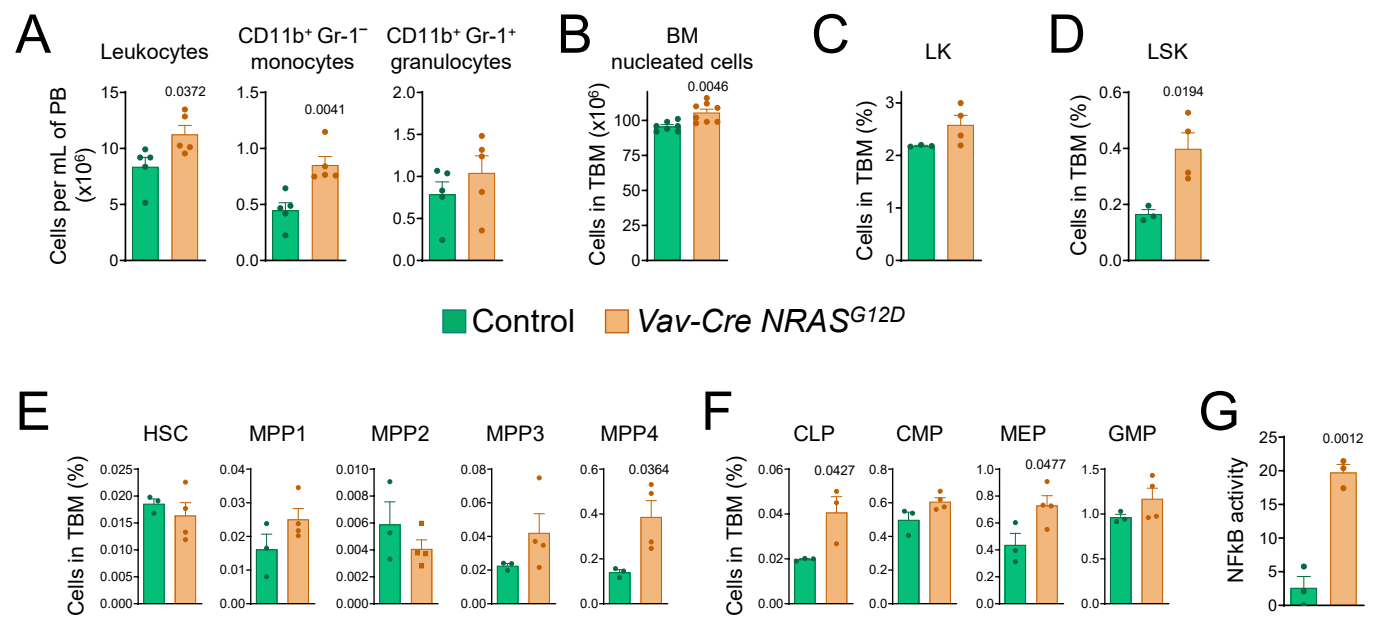
Supplementary Figure S11 (related to Figure 7). Identification of the sources of IL-1 β and IL-1rn in the bone marrow CD63⁺ stromal cell compartment at the single cell level by RNA-FISH. (A) RNA fluorescent in situ hybridization (FISH) in bone marrow CD45⁻CD31⁻Ter119⁻CD63⁺ stromal cells from C57BL/6J wild-type (WT) and IL-1rn knockout (IL-1rn-KO) mice (n=4 biologically independent animals per group). Nuclei were counterstained with DAPI, no probes were used in negative controls and expression of *Gapdh* (green) was used as positive control. Scale bar, 10 μ m.



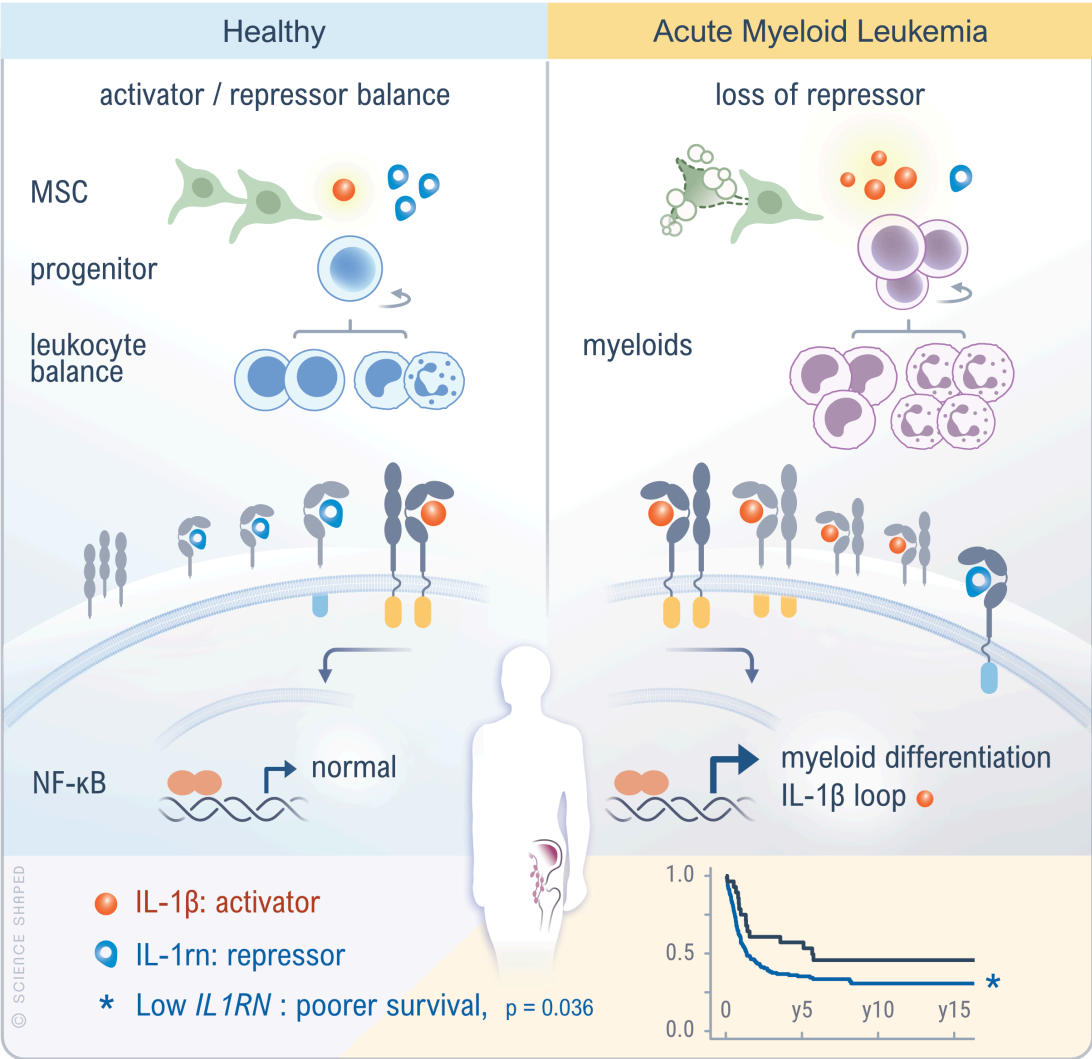
Supplementary Figure S12 (Related to Figure 8). Low IL-1rn is present in a mouse model of pre-leukemic myelopoiesis. (A) Competitive repopulation with CD45.2⁺ NRAS-G12D⁺ bone marrow (BM) cells and CD45.1⁺ B6.SJL healthy cells (1:1) in B6.SJL mice (n=14; 4 weeks n=13). Peripheral blood (PB) chimerism evolution and representative fluorescence-activated cell sorting (FACS) analysis (cells in PB, %). (B-G) Analysis of hematopoiesis in NRAS-G12D⁺ (*Mx1-Cre⁺ NRAS^{G12D}*) and control (*Mx1-Cre⁻ NRAS^{G12D}*) mice. (B) Number of leukocytes, CD11b⁺ myeloid cells and CD11b⁺Gr-1⁺f4/80⁺ monocytes in PB (control, n=13; NRAS-G12D⁺, n=6). (C) Total BM (TBM) number of Lin⁻c-Kit⁺Sca-1⁻ (LK) progenitors (n=3 per group). (D) BM frequency of colony-forming unit cells (CFU-C) (control, n=6; NRAS-G12D⁺, n=5) and total number of Lin⁻Sca-1⁺c-Kit⁺ (LSK) (n=6 per group). (E) Frequencies of LSK subsets within the BM; LSK CD34⁻Flt3⁻ long-term hematopoietic stem cells (LT-HSC), LSK CD34⁺Flt3⁻ short-term HSC (ST-HSC) and LSK CD34⁺Flt3⁺ multipotent progenitors (MPP) (n=3 per group). (F) TBM number of hematopoietic stem and progenitor cell subsets corresponding to HSC (LSK CD34⁻Flt3⁻CD48⁻CD150⁺), MPP1 (LSK CD34⁺Flt3⁻CD48⁻CD150⁺), MPP2 (LSK CD34⁺Flt3⁻CD48⁺CD150⁺), MPP3 (LSK CD34⁺Flt3⁻CD48⁺CD150⁻), MPP4 (LSK CD34⁺Flt3⁺CD48⁺CD150⁻) and MPP5 (LSK CD34⁺Flt3⁻CD48⁻CD150⁻) (control, n=5; NRAS-G12D⁺, n=6). (G) TBM number of common lymphoid progenitors (CLP, Lin⁻c-Kit^{low}Sca-1^{low}CD127⁺), common myeloid progenitors (CMP, LK CD34⁺FcRγ⁻), megakaryocyte erythroid progenitors (MEP, LK CD34⁻FcRγ⁻) and granulocyte-monocyte progenitors (GMP, LK CD34⁺FcRγ⁺) (control, n=5; NRAS-G12D⁺, n=6). (H) Representative FACS analysis of IL-1 receptor accessory protein (IL-1RAP) staining and unstained negative control in BM LT-HSC, ST-HSC, MPP, CD11b⁺Gr-1^{hi}f4/80⁻ granulocytes and CD11b⁺Gr-1⁺f4/80⁺ monocytes (cells in each cell subset, %). (I-J) RNA sequencing in BM LT-HSC, ST-HSC and MPP (n=3 per group) from NRAS-G12D⁺ versus control mice. (I) Venn diagrams show number of up- and down-regulated genes in BM LT-HSC, ST-HSC and MPP from NRAS-G12D⁺ versus control mice, and overlap of genes. (J) Principal component analysis. Data are biologically independent animals, and means ± S.E.M for bar plots or medians for violin plots, except (I). Statistical analyses were performed with paired two-tailed Student's *t*-test (A), two-tailed Student's *t*-test (B except leukocytes, C, D BM CFU-C, E, F HSC, MPP1, G), or two-tailed Mann-Whitney U test (B leukocytes, D BM LSK, F MPP4, MPP5). *p* values ≤ 0.05 are reported. Source data are provided as a Source Data file.



Supplementary Figure 13 (Related to Figure 9). Damage to the bone marrow stroma in a mouse model of pre-leukemic myelopoiesis. *Nes-gfp* mice were used as recipients of bone marrow (BM) nucleated cells from NRAS-G12D⁺ and control mice. (A) Representative fluorescence-activated cell sorting analysis (cells in total BM, TBM, %) and TBM number of *Nes*-GFP⁺ stromal cells (n=4 per group). (B) RNA sequencing in BM *Nes*-GFP⁺ stromal cells (n=2 per group). Enrichment plot of coordinated changes of genes previously reported to be induced or repressed in apoptosis (E-MEXP-247). TRAIL, tumor necrosis factor-related apoptosis inducing ligand. Data are biologically independent animals, and means $\pm$ S.E.M (A). Statistical analyses were performed with two-tailed Student's *t*-test (A). p values $\leq$ 0.05 are reported. Source data are provided as a Source Data file.



Supplementary Figure S14 (Related to Figure 8). Hematopoietic abnormalities and NFκB activation in an alternative model of pre-leukemic myelopoiesis. (A-F) Analysis of hematopoiesis in NRAS-G12D⁺ (*Vav-Cre*⁺ *NRAS*^{G12D}) and control (*Vav-Cre*⁺) mice. (A) Number of leukocytes, CD11b⁺ Gr-1⁻ monocytes and Cd11b⁺Gr-1⁺ granulocytes in peripheral blood (PB, n=5 per group). (B) Total number of bone marrow (TBM) nucleated cells (control, n=7; NRAS-G12D⁺, n=8). (C) BM frequency of Lin⁻c-Kit⁺Sca-1⁻ (LK) progenitors (control, n=3; NRAS-G12D⁺, n=4). (D) BM frequency of Lin⁻Sca-1⁺c-Kit⁺ (LSK) progenitors (control, n=3; NRAS-G12D⁺, n=4). (E) BM frequency of hematopoietic stem and progenitor cell subsets corresponding to hematopoietic stem cells (HSC, LSK CD34⁻Flt3⁻CD48⁻CD150⁺), multipotent progenitors 1 (MPP1, LSK CD34⁺Flt3⁻CD48⁻CD150⁺), MPP2 (LSK CD34⁺Flt3⁻CD48⁺CD150⁺), MPP3 (LSK CD34⁺Flt3⁻CD48⁺CD150⁻) and MPP4 (LSK CD34⁺Flt3⁺CD48⁺CD150⁻) (control, n=3; NRAS-G12D⁺, n=4). (F) BM frequency of common lymphoid progenitors (CLP, Lin⁻c-Kit^{low}Sca-1^{low}CD127⁺), common myeloid progenitors (CMP, LK CD34⁺FcRγ⁻), megakaryocyte erythroid progenitors (MEP, LK CD34⁻FcRγ⁻) and granulocyte-monocyte progenitors (GMP, LK CD34⁺FcRγ⁺) (control, n=3; NRAS-G12D⁺, n=4). (G) NFκB transcription factor activity in BM LK progenitors (n=3 per group) calculated based on NFκB target gene expression levels, identified from Synapse ID syn4956655 (Supplementary Data 1), in publicly available RNA sequencing (PRJNA774277). Data are biologically independent animals, and means ± S.E.M. Statistical analyses were performed with two-tailed Student's *t*-test. *p* values ≤ 0.05 are reported. Source data are provided as a Source Data file.



Supplementary Figure S15. IL-1 receptor antagonist restricts healthy and malignant myeloproliferation. Illustration of the proposed model. Under steady-state, hematopoietic stem and progenitor cell (progenitor) differentiation is controlled by balanced IL-1 β /IL-1rn, resulting in low NF κ B activation (left). Low IL-1rn contributes to biased IL-1 β -induced myelopoiesis dependent on NF κ B activation in healthy conditions and pre-leukemic disease, is a prognostic marker for AML patients, and provides a new rationale for IL-1 β blockade therapeutic potential (right). MSC, mesenchymal stromal cells.

Supplementary Table S1. Characteristics of human and mice used in this study.

Human cohorts. Figure 1 and associated Supplementary Figure S1.

Panel	Number, sex and age (years)		
1a	Global: 188 Low and 16 High, women, aged 43 (19-60), 158 Low and 19 High, men, aged 45 (19-61)	M4-M5: 80 Low and 14 High, women, aged 43 (22-59), 56 Low and 14 High, men, aged 46 (19-60)	
1b	M0-M3: 114, women, aged 43 (19-60) 108, men, aged 43 (19-60)	M4-M5: 94, women, aged 43 (19-60) 77, men, aged 43 (19-60)	
	Healthy donor	AML	MDS
1c-d	19, women, aged 45 (27-65) 13, men, aged 42 (23-79)	7, women, aged 68 (52-94) 14, men, aged 65 (52-74)	2, men, aged 52 and 68
1e	10, women, aged 42 (27-58) 9, men, aged 39 (23-79)	5, women, aged 72 (52-84) 7, men, aged 64 (52-72)	
1f	6, women, aged 40 (27-58) 4, men, aged 36 (27-43)	1, woman, aged 52 5, men, aged 63 (52-71)	
1g	3, women, aged 27 (22-30) 2, men, aged 52 and 79	2, women, aged 52 and 73 2, men, aged 54 and 79	

S1A	M0-M3: 114, women, aged 43 (19-60) 108, men, aged 43 (19-60)	M4-M5: 94, women, aged 43 (19-60) 77, men, aged 43 (19-60)
S1B-C	7, women, aged 47 (27-67) 12, men, aged 48 (18-67)	
	Healthy donor	AML
S1D	5, women, aged 42 (27-58) 4, men, aged 36 (27-43)	1, woman, aged 52 5, men, aged 64 (52-71)
S1E	2, women, aged 22 and 29 2, men, aged 52 and 79	3, women, aged 64 (52-72) 2, men, aged 54 and 79
S1F	3, women, aged 27 (22-30) 2, men, aged 52 and 79	2, women, aged 52 and 72 2, men, aged 54 and 79
S1G	5, women, aged 42 (30-48) 6, men, aged 40 (28-79)	4, women, aged 74 (52-94) 1, man, aged 71

Animal cohorts.

Figure 1 and associated Supplementary Figure S1.

Panel	Sex	Strain	Donor	Age at transplant (weeks)	Initiation of treatment (weeks after transplant)	Duration of treatment (weeks)
1h	Females	NSG-SGM3	AML9	10-11	4	4
			AML7		7	16
1i	Females		AML7	10-11	7	16
1j	Males		AML21	7-8	6	4
			AML22			
			AML23			
1k	Females		AML3	15-16	6	36

Panel	Sex	Strain	Donor	Age at transplant (weeks)	Initiation of treatment (weeks after transplant)	Duration of treatment (weeks)
S1I	Males	NSG-SGM3	AML21	7-8	6	4
			AML22			
			AML23			
S1J	Females		AML3	15-16	6	36

Figure 2 and associated Supplementary Figure S2 and S3.

			Age (weeks)	
Panel	Sex	Strain	WT	KO
2a	Females	Wild-type (WT, C57BL/6J) IL-1rn knockout (KO, C57BL/6J)	10-22	13-33
2b	Males		43-55	49-61
2c	Females		15-17	14-21
2d	Females		10-14	14-21
2e	Females		2, aged 11	4, aged 14-18
	Males		7, aged 31	8, aged 36-37
2f	Females		10-22	19-33
2k: <i>Il1b</i>	Females		14-25	13-35
2k: <i>Il1r1</i>			8-25	8-35
2k: <i>Il1rap</i>			8-12	8-12
2l: <i>Il1b, Il1r1</i>	Females		13-15	13-15
2l: <i>Il1rap</i>			8-12	8-12
2m	Females	14	13-15	

Panel	Sex	Strain	Age at initiation of treatment (weeks)	Duration of treatment (weeks)
2g	Females	IL-1rn knockout (KO, C57BL/6J)	9-16	4
2h	Females		9-16	10
2i	Males		9-21	16
2j	Males		9-21	18

Panel	Sex	Strain	Age (weeks)	
			WT	KO
S2A	Females	Wild-type (WT, C57BL/6J) IL-1rn knockout (KO, C57BL/6J)	15-17	14-21
S2B	Females		15	16-21
S2C	Females		11-14	15-21
S2D	Males		43-55	49-61

Panel	Sex	Strain	Age (weeks)	
			WT	KO
S3A	Males	Wild-type (WT, C57BL/6J) IL-1rn knockout (KO, C57BL/6J)	43-55	49-61
S3B	Females		20-34	19-28
S3C	Females		7-22	14-33
S3D-E	Females		10-14	14-21
S3F	Females		2, aged 11	4, aged 14-18
	Males		7, aged 31	8, aged 36-37
S3G	Males		38-48	38-48

Panel	Sex	Strain	Age at initiation of treatment (weeks)	Duration of treatment (weeks)
S3H	Females	Wild-type (WT, C57BL/6J) IL-1rn knockout (KO, C57BL/6J)	15-22	0, 4 and 8

Figure 3 and associated Supplementary Figure S4

Panel	Sex	Strain	Age (weeks)	
			WT	KO
3a-c	Females	Wild-type (WT, C57BL/6J) IL-1rn knockout (KO, C57BL/6J)	24	24-25

Panel	Sex	Strain	Age at initiation of treatment (weeks)	Duration of treatment (weeks)
3d	Females	IL-1rn knockout (KO, C57BL/6J)	18-34	12

Panel	Sex	Strain	Age (weeks)	
			WT	KO
S4A-E, I-J	Females	Wild-type (WT, C57BL/6J)	24	24-25
S4F-H	Males	IL-1rn knockout (KO, C57BL/6J)	44	44

Panel	Sex	Strain	Age (weeks)	
S4I: GSE165810	Females and males	Wild-type (C57BL/6)	6-12	20 days of treatment
S4J: GSE166629	Not disclosed	Boy/J mice (CD45.1) transplanted with sorted hematopoietic progenitor cells from <i>HSC-SCL-Cre-ER^T R26R-EYFP</i> <i>Cebpa</i> ^{+/+} (C57BL/6, CD45.2) and competitor bone marrow from wild-type (C57BL/6, CD45.2)	Not disclosed	20 days of treatment

Figure 4 and associated Supplementary Figure S5

			Age (weeks)	
Panel	Sex	Strain	WT	KO
4a	Females	Wild-type (WT, C57BL/6J) IL-1rn knockout (KO, C57BL/6J)	14-17	15-21
4b	Females		14-22	14-33
4c	Females		31-34	36-38
4f	Females		22	22
4g: <i>Lepr</i> , <i>Vcam1</i> , <i>Angpt1</i>	Males		36	40
4g: <i>Cxcl12</i> , <i>Adipoq</i> , <i>Il1rn</i>			16-20	14-16

Panel	Sex	Strain	Age at initiation of treatment (weeks)	Duration of treatment (weeks)
4d	Females	IL-1rn knockout	9-16	10
4e	Males	(KO, C57BL/6J)	9-21	18

Panel	Sex	Strain	Age (weeks)	
			WT	KO
S5A	Females	Wild-type (WT, C57BL/6J) IL-1rn knockout (KO, C57BL/6J)	14-17	15-21
S5B	Females		14-22	14-33
S5C	Females		11-13	15-21
S5D: GSE108892	Females and males	<i>VEcad-Cre R26R-tdTomato</i> (C57BL/6) <i>Lepr-Cre R26R-tdTomato</i> (C57BL/6) <i>Col2.3-Cre R26R-tdTomato</i> (C57BL/6)	4-12	

Figure 5-7 and associated Supplementary Figure S6-S11

			Age (weeks)	
Experiment	Sex	Strain	WT	KO
scRNA-Seq	Females	Wild-type (WT, C57BL/6J)	13-15	14
RNA-FISH	Males	IL-1rn knockout (KO, C57BL/6J)	33	34

Figure 8 and associated Supplementary Figure S12

Panel	Sex	Strain	Age (weeks)	Induction time (weeks)	
8a	Females	<i>Mx1-Cre⁻ NRAS^{G12D}</i> (Control, C57BL/6J) <i>Mx1-Cre NRAS^{G12D}</i> (<i>NRAS^{G12D}</i> , C57BL/6J)	24	20	
8b	Females		14-34	10-30	
8c	Females		38-45	28-32	
8d, <i>Il1b</i> and <i>Il1rn</i>	Males		32-44	12	
8d, <i>Il1rap</i>	Females		24-33	8	
8e, <i>Il1b</i> and <i>Il1rn</i>	Males		32-41	11-12	
8e, <i>Il1rap</i>	Females		24-30	8	
8f	Males		28-32	18	
8g	Males		34	6	
8h	Females		59-62	52	8 weeks of treatment

Panel	Sex	Strain	Donor cells	Age at transplant (weeks)	Analysis (weeks after transplant)
S12A	Females	Wild-type (B6.SJL, CD45.1)	<i>Mx1-Cre NRAS^{G12D}</i> (C57BL/6J, CD45.2) and wild-type (B6.SJL, CD45.1)	6-8	4, 8 and 12

Panel	Sex	Strain	Age (weeks)	Induction time (weeks)
S12B	Males	<i>Mx1-Cre⁻ NRAS^{G12D}</i> (Control, C57BL/6J) <i>Mx1-Cre NRAS^{G12D}</i> (<i>NRAS^{G12D}</i> , C57BL/6J)	20	6
S12C-E	Females		36	20
S12F-G	Males		56-58	44
S12H	Males		28-32	18
S12I-J	Males		34	6

Figure 9 and associated Supplementary Figure S13 and S14

Panel	Sex	Strain	Age (weeks)	Induction time (weeks)
9a	Females	<i>Mx1-Cre⁻ NRAS^{G12D}</i> (Control, C57BL/6J)	38-45	28-32
9b	Males		51-69	39-40
9c, <i>IIIb</i> and <i>IIIrn</i>	Females		32-44	10-30
9c, <i>IIIrap</i>			24-33	8

Panel	Sex	Strain	Donor cells	Age at transplant (weeks)	Analysis (weeks after transplant)
S13A-B	Males	<i>Nes-gfp</i> (C57BL/6J)	<i>Mx1-Cre⁻ NRAS^{G12D}</i> (Control, C57BL/6J) <i>Mx1-Cre NRAS^{G12D}</i> (<i>NRAS^{G12D}</i> , C57BL/6J)	28	4

Panel	Sex	Strain	Number and age (weeks)	
			Control	<i>NRAS^{G12D}</i>
S14A	Females	C57BL/6J <i>Vav-Cre</i> (Control, C57BL/6J) <i>Vav-Cre NRAS^{G12D}</i> (<i>NRAS^{G12D}</i> , C57BL/6J)	3, aged 6-7	2, aged 6-7
	Males		2, aged 6-7	4, aged 6-7
S14B	Females		4, aged 6-7	4, aged 6-7
	Males		3, aged 6-7	4, aged 6-7
S14C-F	Females		2, aged 6-7	2, aged 6-7
	Males		1, aged 6-7	2, aged 6-7
S14G: PRJNA774277	Females		1, aged 30-40	1, aged 30-40
	Males		2, aged 30-40	2, aged 30-40

Figure 10

Panel	Sex	Strain	Donors	Age at transplant (weeks)	Analysis (weeks after transplant)
10a-c	Females	Wild-type (WT, C57BL/6J)	Wild-type (WT, C57BL/6J) and IL-1rn knockout (KO, C57BL/6J) Wild-type (WT, C57BL/6J) and <i>Mx1-Cre NRAS^{G12D}</i> (<i>NRAS^{G12D}</i> , C57BL/6J) IL-1rn knockout (KO, C57BL/6J) and <i>Mx1-Cre NRAS^{G12D}</i> (<i>NRAS^{G12D}</i> , C57BL/6J)	16	32
10d-f	Females	Wild-type (WT, C57BL/6J) IL-1rn knockout (KO, C57BL/6J)	<i>Mx1-Cre⁻ NRAS^{G12D}</i> (Control, C57BL/6J) <i>Mx1-Cre NRAS^{G12D}</i> (<i>NRAS^{G12D}</i> , C57BL/6J)	9-20	4-8

Panel	Sex	Strain	Age at induction (weeks)	Initiation of treatment (weeks after induction)	Analysis (weeks after initiation of treatment)
10g-i	Males	<i>Mx1-Cre NRAS^{G12D}</i> (<i>NRAS^{G12D}</i> , C57BL/6J)	12-13	2	4

Supplementary Table 2: List of reagents used in this article

Antibodies			
Product	SOURCE	IDENTIFIER	
Flow cytometry			Dilution
Alexa Fluor 647 rat anti-mouse CD11b	BD Biosciences	Cat# 557686; RRID AB_396796; clone M1/70	1/100
PE rat anti-mouse Ly-6G/Ly-6C (Gr-1)	BD Biosciences	Cat# 553128; RRID AB_394644; clone RB6-8C5	1/100
FITC rat anti-mouse CD45R/B220	BD Biosciences	Cat# 553088; RRID AB_394618; clone RA3-6B2	1/100
PE-Cy5 hamster anti-mouse CD3e	BD Biosciences	Cat# 553065; RRID AB_394598; clone 145-2C11	1/100
PE rat anti-mouse Ly-6G	BD Biosciences	Cat# 551461; RRID AB_394208; clone 1A8	1/100
PE rat anti-mouse Ly6A/E (Sca-1)	BD Biosciences	Cat# 553336; RRID AB_394792; clone E13-161.7	1/100
FITC rat anti-mouse CD34	BD Biosciences	Cat# 553733; RRID AB_395017; clone RAM34	1/100 and 2/100
Alexa Fluor 647 rat anti-mouse CD34	BD Biosciences	Cat# 560230; RRID AB_1645199; clone RAM34	1/100
APC rat anti-mouse CD135 (Flt3)	BD Biosciences	Cat# 560718; RRID AB_1727425; clone A2F10.1	1/100
PE-Cy7 rat anti-mouse CD117 (c-Kit)	BD Biosciences	Cat# 558163; RRID AB_647250; clone 2B8	1/100
PE rat anti-mouse CD63	BD Biosciences	Cat# 564222; RRID AB_2738678; clone NVG-2	1/100
PE rat anti-mouse CD106 (VCAM)	BD Biosciences	Cat# 561613; RRID AB_10897990; clone 429(MVCAM.A)	1/100
Alexa Fluor 647 rat anti-mouse CD121a (IL-1r1)	BD Biosciences	Cat# 563629; RRID AB_2738332; clone 35F5	1/100
PE-Cy7 rat anti-mouse CD105 (Endoglin)	BioLegend	Cat# 120410; RRID AB_1027700; clone MJ7/18	1/100
Alexa Fluor 488 rat anti-mouse F4/80	eBioscience Thermo Fisher	Cat# 53-4801-82; RRID AB_469915; clone BM8	1/100
Biotin rat anti-mouse CD31	BD Biosciences	Cat# 553371; RRID AB_394817; clone MEC13.3	1/100
Biotin rat anti-mouse TER-119/Erythroid cells	BD Biosciences	Cat# 553672; RRID AB_394985; clone TER-119	1/100
Biotin mouse anti-mouse CD45.2	BD Biosciences	Cat# 553771; RRID AB_395040; clone 104	1/100
BB700 rat anti-mouse Ly6A/E (Sca-1)	BD Biosciences	Cat# 742089, RRID AB_2871369, clone D7	1/100
PE rat anti-mouse CD135 (Flt3)	BD Biosciences	Cat# 553842, RRID AB_395079, clone A2F10.1	1/100
PE rat anti-mouse CD16/32 (FcR γ)	BD Biosciences	Cat# 567020, RRID AB_2870010, clone Ab93	1/100

PE-Cy5 rat anti-mouse CD150 (SLAM)	BioLegend	Cat# 115912, RRID AB_493598, clone TC15-12F12.2	2/150
APC hamster anti-mouse CD48	BD Biosciences	Cat# 562746, RRID AB_2737765, clone HM48-1	1/100 and 2/100
APC rat anti-mouse CD127 (IL-7R)	BD Biosciences	Cat# 564175, RRID AB_2732843; clone SB/199	2/100
FITC rabbit anti-mouse IL-1rap	ProteoGenix	Clone R5P1-A1; Customized; Batch #15893-113021-A01	15/100
Biotin Mouse Lineage Depletion Cocktail	BD Biosciences	Cat# 51-9000794	5/100
Biotin rat anti-mouse CD45R (B220)	eBioscience Thermo Fisher	Cat# 13-0452-82; RRID AB_466449; clone RA3-6B2	0.25µg/150µl
Biotin rat anti-mouse CD19	eBioscience Thermo Fisher	Cat# 13-0193-82; RRID AB_657656; clone eBio1D3 (1D3)	0.25µg/150µl
Biotin rat anti-mouse CD4	eBioscience Thermo Fisher	Cat# 13-0041-82; RRID AB_466325; clone GK1.5	0.25µg/150µl
Biotin rat anti-mouse CD8a	eBioscience Thermo Fisher	Cat# 13-0081-82; RRID AB_466346; clone 53-6.7	0.25µg/150µl
Biotin armenian hamster anti-mouse CD3e	eBioscience Thermo Fisher	Cat# 13-0031-82; RRID AB_466319; clone 145-2C11	0.25µg/150µl
Biotin rat anti-mouse IgM	eBioscience Thermo Fisher	Cat# 13-5790-82; RRID AB_466675; clone II/41	0.25µg/150µl
Biotin rat anti-mouse Ly-6G/Ly-6C (Gr-1)	eBioscience Thermo Fisher	Cat# 13-5931-82; RRID AB_466800; clone RB6-8C5	0.25µg/150µl
Biotin rat anti-mouse TER-119	eBioscience Thermo Fisher	Cat# 13-5921-82, RRID AB_466797, clone TER-119	0.25µg/150µl
FITC rat anti-mouse CD11b	eBioscience Thermo Fisher	Cat# 11-0112-41; RRID AB_11042156; clone M1/70	0.25µg/150µl
PE rat anti-mouse Ly-6G/Ly-6C (Gr-1)	eBioscience Thermo Fisher	Cat# 12-5931-82; RRID AB_466045; clone RB6-8C5	0.25µg/150µl
APC rat anti-mouse CD127	eBioscience Thermo Fisher	Cat# 17-1271-82; RRID AB_469435; clone A7R34	0.25µg/150µl
PerCP-Cy5.5 rat anti-mouse Ly-6A/E (Sca-1)	eBioscience Thermo Fisher	Cat# 45-5981-82; RRID AB_914372; clone D7	0.25µg/150µl
FITC rat anti-mouse CD34	eBioscience Thermo Fisher	Cat# 11-0341-82; RRID AB_465021; clone RAM34	0.25µg/150µl
PE-Cy7 rat anti-mouse CD117 (c-Kit)	eBioscience Thermo Fisher	Cat# 25-1171-82; RRID AB_469644; clone 2B8	0.25µg/150µl
APC rat anti-mouse CD16/CD32 (FcγRII/III)	eBioscience Thermo Fisher	Cat# 17-0161-82; RRID AB_469356; clone 93	0.25µg/150µl
APC rat anti-mouse CD135 (Flt3)	eBioscience Thermo Fisher	Cat# 17-1351-82; RRID AB_10717261; clone A2F10	0.25µg/150µl
APC-eFluor 780 Armenian hamster anti-mouse CD48	eBioscience Thermo Fisher	Cat# 47-0481-82; RRID AB_2573962; clone HM48-1	0.25µg/150µl
PE Rat anti-mouse CD150 (SLAM)	BioLegend	Cat# 115904; RRID AB_313683; clone TC15-12F12.2	1/100

PE-Cy7 mouse anti-mouse CD45.1	BD Biosciences	Cat# 560578; RRID: AB_1727488; clone A20	1/100
FITC rat anti-mouse CD45	BD Biosciences	Cat# 553080; RRID: AB_394610; clone 30-F11	1/100
PE-Cy7 rat anti-mouse F4/80	BioLegend	Cat# 123113; RRID AB_893490; clone BM8	1/100
FITC rat anti-mouse Ly-6A/E (Sca-1)	eBioscience Thermo Fisher	Cat# 11-5981-82, RRID AB_465333; clone D7	1/100
V450 rat anti-mouse CD45	BD Biosciences	Cat# 560501, RRID AB_1645275; clone 30-F11	1/100
Pacific Blue rat anti-mouse TER-119	BioLegend	Cat# 116231, RRID AB_2149212; clone TER-119	1/100
FITC rat anti-mouse CD31 (PECAM-1)	Invitrogen Thermo Fisher	Cat# 11-0311-85, RRID AB_465013; clone 390	1/100
PE-Cy7 rat anti-mouse CD63	BioLegend	Cat# 143910, RRID AB_2565500; clone NVG-2	1/100
FITC mouse anti-human CD45	BD Biosciences	Cat# 345808; RRID AB_2732010; clone 2D1	15/150 and 20/150
PE mouse anti-human CD11b	BD Biosciences	Cat# 557321; RRID AB_396636; clone ICRF44	10/150
PE mouse anti-human CD33	BD Biosciences	Cat# 555450; RRID AB 395843; clone WM53	15/150
FITC mouse anti-human CD34	BD Biosciences	Cat# 560942; RRID AB 10562559; clone 581	15/150
Alexa Fluor 488 anti-human NFκB p50	Luminex Corporation	Cat# 4700-1674	5/100
BV421 mouse anti-human IL-1RAcP (IL-1R3)	BD Biosciences	Cat# 748107; RRID AB_2872568; clone 89412	10/100
BV421 mouse IgG1, κ Isotype Control	BD Biosciences	Cat# 562438; RRID AB_11207319; clone X40	10/100
Alexa Fluor 647 Mouse anti-human NFκB p65 (pS529)	BD Biosciences	Cat# 558422, RRID AB_647136, clone K10-895.12.50	20/100
Alexa Fluor 647 Mouse IgG2b, κ Isotype Control	BD Biosciences	Cat# 558713, RRID AB_1645618, clone 27-35	20/100
Pacific Blue conjugated Annexin V antibody	Invitrogen Thermo Fisher	Cat# A35122	5/100
APC mouse anti-BrdU	BD Biosciences	Cat# 552598; RRID AB_2861367; clone B44	2/100
Immunofluorescence			Dilution
Goat polyclonal anti-mouse IL-1r1	R&D system	Cat# AF771; RRID AB_355587	2/100
Donkey polyclonal anti-goat IgG H&L (Cy3)	Abcam	Cat# ab6949; RRID AB_955018	1/200

<i>In vivo treatments</i>		
PRODUCT	SOURCE	IDENTIFIER
Rat anti-mouse IL-1 β monoclonal	Novus Biologicals	Cat# NB600-1379; RRID AB 2124612; clone 1400.24.17
Mouse anti-mouse IL-1 β monoclonal antibody	Invitrogen Thermo Fisher	Cat# MM425B; RRID AB 223529; clone 1400.24.17
Mouse IgG1 kappa isotype control	Invitrogen Thermo Fisher	Cat# 14-4714-82; RRID AB 470111; clone P3.6.2.8.1
InVivoMab hamster anti-mouse IL-1 α	BioXCell	Cat# BE0243; RRID AB 2687724; clone ALF-161
InVivoMab armenian hamster IgG isotype control	BioXCell	Cat# BE0091; RRID AB 1107773
Anti-human IL-1 β therapeutic antibody (FDA-approved ILARIS® - Canakinumab)	Novartis	European Agency Number EMEA/H/C/001109
Anakinra (Kineret®)	Swedish Orphan Biovitrum (Sobi)	European Agency Number EMEA/H/C/000363
Bortezomib	Thermo Scientific Thermo Fisher	Cat# J60378.MB
Human IL-1 β	Peprotech	Cat# 200-01B

<i>Cytokine measurements</i>		
PRODUCT	SOURCE	IDENTIFIER
Bio-Plex Pro Human Cytokine IL-1 β Set	Bio-Rad	Cat# 171B5001M
Bio-Plex Pro Human Cytokine IL-1RA Set	Bio-Rad	Cat# 171B5002M
Bio-Plex Pro Mouse Cytokine IL-1 β Set	Bio-Rad	Cat# 171G5002M
Bio-Plex Pro Mouse Cytokine IL-6 Set	Bio-Rad	Cat #171G5007M
Bio-Plex Pro Mouse Cytokine IL-10 Set	Bio-Rad	Cat# 171G5009M
Bio-Plex Pro Mouse Cytokine IFN- γ Set	Bio-Rad	Cat# 171G5017M
Bio-Plex Pro Mouse Cytokine TNF- α Set	Bio-Rad	Cat# 171G5023M
Mouse IL-1RA AimPlex bead-based immunoassay	Aimplex Biosciences	Cat# PN: B211239

Fluorophores and Fluorophore-conjugated products		
PRODUCT	SOURCE	IDENTIFIER
Flow cytometry		
Amnis® NFκB Translocation Kit	Luminex Corporation	Cat# ACS10000
7-Amino-Actinomycin D (7-AAD)	Luminex Corporation	Cat# 4000-0290
APC-Cy7-conjugated streptavidin	BD Biosciences	Cat# 554063; RRID AB_10054651
PE-TR conjugated streptavidin	Invitrogen Thermo Fisher	Cat# SA1017
PE-conjugated streptavidin	eBioscience Thermo Fisher	Cat# 12-4317-87
Streptavidin Particles Plus - DM	BD Biosciences	Cat# 51-9000810
4',6-diamidino-2-phenylindole (DAPI)	Sigma-Aldrich Merck	Cat# D8417
Deep Red Anthraquinone 7 (DRAQ7)	BD Biosciences	Cat# 564904; RRID AB_2869621
7-Amino-Actinomycin D (7-AAD)	Invitrogen Thermo Fisher	Cat# A1310
Immunofluorescence		
Cy3-Streptavidin conjugate (ZyMAX™ grade)	Invitrogen Thermo Fisher	Cat# 438315

RNA fluorescent <i>in situ</i> hybridization (FISH)		
PRODUCT	SOURCE	IDENTIFIER
Mouse <i>Gapdh</i> probe type 4	Invitrogen Thermo Fisher	Cat# VB4-10414
Mouse <i>Il1b</i> probe type 4	Invitrogen Thermo Fisher	Cat# VB4-18866
Mouse <i>Il1rn</i> probe type 1	Invitrogen Thermo Fisher	Cat# VB1-3028457
Mouse <i>Il1rn</i> probe type 6	Invitrogen Thermo Fisher	Cat# VB6-3198573
ViewRNA™ ISH Cell Assay Kit	Invitrogen Thermo Fisher	Cat# QVC0001
Preamplifier Mix	Invitrogen Thermo Fisher	Cat# QVC0001 (18818)
Amplifier Mix	Invitrogen Thermo Fisher	Cat# QVC0001 (18819)
Label probe Mix	Invitrogen Thermo Fisher	Cat# QVC0001 (18820)
4', 6-Diamidino-2-Phenylindole (DAPI)	Invitrogen Thermo Fisher	Cat# QVC0001 (18821)
Detergent Solution QC	Invitrogen Thermo Fisher	Cat# QVC0509
Wash buffer components 1 and 2	Invitrogen Thermo Fisher	Cat# QG0507 (19885)

Primers		
GENE	FORWARD	REVERSE
Mouse qRT-PCR primers		
<i>Il1b</i>	GAAATGCCACCTTTTGACAGTG	TGGATGCTCTCATCAGGACAG
<i>Il1r1</i>	TTACCCGAGGTCCAGTGGTA	CCCCCGGAACGTATAGGACA
<i>Il1rap</i>	TCCTCAATGACACGGGCAAT	GGGAAATGCAACTTTGCTGC
<i>Il1rn</i>	GAGAAACAACCAGCTCATTGC	GGATGCCCAAGAACACACTATG
<i>Cxcl12</i>	TGCATCAGTGACGGTAAACCA	TTCTTCAGCCGTGCAACAATC
<i>Adipoq</i>	TGTTCTCTTAATCCTGCCCA	CCAACCTGCACAAGTTCCCTT
<i>Axl</i>	ATCACAGGTGCCAGAGGACT	CTGTCCATCTCGAAGCCACA
<i>Stat3</i>	CATTGACCTGCCGATGTCCC	TCAAACGTGAGCGACTCAAAC
<i>Tlr1</i>	CAGTTGGTGAAGAACTCAGGC	CCACATGGGTATAGGACGTTT
<i>Spi1</i>	CCCTCCATCGGATGACTTG	ACATGGTGTGCGGAGAAATC
<i>Csf2rb</i>	GGGCCAGTGTCTACACCCG	GTAAGCCATCTTCTGAGTTTCCCAAT GC
<i>Nes</i>	GTCAGATCGCTCAGATCCT	GTGTCTGCAAGCGAGAGTTC
<i>Vcam1</i>	TGGAGGTCTACTCATTCCCTGA	GACAGGTCTCCCATGCACAA
<i>Angpt1</i>	CTCGTCAGACATTCATCATCCAG	CACTTCTTTAGTGCAAAGGCT
<i>Lepr</i>	AGCTGCACTTAACCTGGCAT	AAAGCCGAGGCATTGTTTGG
<i>B2m</i>	ACCGTCTACTGGGATCGAGA	TGCTATTTCTTTCTGCGTGCAT
<i>Gapdh</i>	CTCCCACTCTTCCACCTTCG	GCCTCTCTTGCTCAGTGTCC
Human qRT-PCR primers		
<i>IL1B</i>	CTGTCCTGCGTGTTGAAAGA	TTGGGTAATTTTGGGATCTACA
<i>ILRN</i>	TGCAAGCCTTCAGAATCTGGG	TCCTTGCAAGTATCCAGCAACT
<i>CASP1</i>	ACCAACTACAGAAGAGTTTGAGGA	ACATTATCTGGTGTGGAAGAGC
<i>IRAK1</i>	TGTGCCGCTTCTACAAAGTGA	ACGATCAGGGCGGCGAAC
<i>IL1RAP</i>	TAGAAGCCTCACTCTTGCCCC	TGGATTTGCCTCATGGTGTCTA
<i>B2M</i>	AGTATGCCTGCCGTGTGAAC	TTCAAACCTCCATGATGCTGCT

Histology		
PRODUCT	SOURCE	IDENTIFIER
Parafinne	VWR	Cat# 1116099025
Hematoxylin	Sigma-Aldrich Merck	Cat# H3136
Eosin	Sigma-Aldrich Merck	Cat# HT110316
Harris solution	Sigma-Aldrich Merck	Cat# HHS80
DPX MOUNTANT	Casa Alvarez	Cat# 10-8500
Bouin's solution	Sigma-Aldrich Merck	Cat# HT 10132-L
Ponceau BS (Biebrich Scarlet)	Sigma-Aldrich Merck	Cat# B6008
Phosphomolybdic acid hydrate 80%	Acros Organic	Cat# 206380250
Phosphotungstic acid hydrate	Sigma-Aldrich Merck	Cat# P4006
Ammonium solution	Sigma-Aldrich Merck	Cat# 105432
Fast Green FCF	Sigma-Aldrich Merck	Cat# F7252
Acetic acid	Riedel-de Haen	Cat# 27221
Xylene	VWR	Cat# 28973363
Potassium permanganate	Sigma-Aldrich Merck	Cat# 399124
Oxalic acid	Sigma-Aldrich Merck	Cat# 194131
Iron alum	Sigma-Aldrich Merck	Cat# 221260
Gold chloride	Sigma-Aldrich Merck	Cat# HT 1004
Sodium Thiosulfate	Sigma-Aldrich Merck	Cat# 72049
Iron (III) chloride	Sigma-Aldrich Merck	Cat# 157740
Silver nitrate	Sigma-Aldrich Merck	Cat# S6506
Sodium hydroxide pellets (NaOH)	Sigma-Aldrich Merck	Cat# 1064821000
Formaldehyde solution 4% buffered (Titripack)	VWR	Cat# 11699408
Ethanol absolute	VWR	Cat# 3001918

IL-1RAP antibody generation

PRODUCT	SOURCE	IDENTIFIER
Tween 20	Sigma-Aldrich Merck	Cat# P2287
Tris hydrochloride	Sigma-Aldrich Merck	Cat# RES3098T-B7
Glycine	Sigma-Aldrich Merck	Cat# G7126
PEG	Sigma-Aldrich Merck	Cat# 181986
PBS	Gibco Thermo Fisher	Cat# 10010023
Pierce™ Protein-Free (PBS) Blocking Buffer	Thermo Scientific Thermo Fischer	Cat# 37572
Rabbit LiAb-SFRab™ phage library	ProteoGenix	Cat# LiAb-SFRab™
E Coli TG1	Lucigen	Cat# 60502-1
M13KO7 Helper phage	NEB	Cat# N0315S
Anti-M13 HRP-conjugated mouse monoclonal antibody	ProteoGenix	Cat# ATX-PDAB-HRP
Coomassie blue staining	Sigma-Aldrich Merck	Cat# 6104-58-1
tetramethyl benzidine substrate	ProteoGenix	Cat# PTX-TMB
pXten1 Expression Vector	ProteoGenix	Cat# PX-XTE-002
XtenCHO™ Expression Medium	ProteoGenix	Cat# PX-XTE-003
Antibody Expression Positive Control Vector	ProteoGenix	Cat# PX-XTE-004
XtenFect Reagent, Stock solution	ProteoGenix	Cat# PX-XTE-005
XtenFect Reagent, Working solution	ProteoGenix	Cat# PX-XTE-006
XtenCHO™ Enhancer	ProteoGenix	Cat# PX-XTE-007
FITC conjugation kit	Sigma-Aldrich Merck	Cat# FITC1-1KT
Protein A purification kit	Thermo Scientific Thermo Fisher	Cat# 44667
Extracellular portion of mouse IL-1RAP protein	Sinobiological	Cat# 52657-M08H

Eukaryotic cell lines

PRODUCT	SOURCE	IDENTIFIER
THP-1 cells	DSMZ	Cat# ACC 16
XtenCHO™ cells	ProteoGenix	Cat# PX-XTE-001

Other reagents		
PRODUCT	SOURCE	IDENTIFIER
Lympholyte®-H Cell Separation Media	Cedarlane	Cat# CL5015
EasySep™ Human CD34 Positive Selection Kit II	Stem Cell Technologies	Cat# 15086
StemSpan Serum-free Expansion Medium (SFEM)	Stem Cell Technologies	Cat# 9650
MethoCult™ GF M3434	Stem Cell Technologies	Cat# 03434
Ammonium Chloride Solution	Stem Cell Technologies	Cat# 07850
Ammonium chloride (NH ₄ Cl)	Sigma-Aldrich Merck	Cat# A9434
Collagenase Type I	Stem Cell Technologies	Cat#7902
RPMI 1640 Medium	Gibco Thermo Fisher	Cat# 11835030
Murine thrombopoietin	Peprotech	Cat# 315-14
Recombinant murine stem cell factor	Peprotech	Cat# 250-03
Murine Flt3-Ligand	Peprotech	Cat# 250-31L
Penicilin-Streptomycin-Glutamine	Gibco Thermo Fisher	Cat# 10378016
Pierce™ 16% Formaldehyde (w/v), Methanol-free	Thermo Scientific Thermo Fisher	Cat# 28908
Methanol	VWR International	Cat# 20847.318
Tri Reagent®	Sigma-Aldrich Merck	Cat# T9424
Dynabeads™ mRNA DIRECT™ Purification Kit	Invitrogen Thermo Fisher	Cat# 61012
PicoPure™ RNA Isolation Kit	Applied Biosystems Thermo Fischer	Cat# KIT0204
Sucrose	Sigma-Aldrich Merck	Cat# 84097
Tissue-Tek® OCT™	Sakura Finetek	Cat# 4583
High capacity reverse transcription kit	Applied Biosystems Thermo Fisher	Cat# 4368814
qPCR Human Reference Total RNA	Clontech TaKaRa Bio	Cat# 636690
Mouse Universal Reference Total RNA	Clontech TaKaRa Bio	Cat# 636657
SYBR green PCR master mix	Applied Biosystems ThermoFisher	Cat# 4309155
RNA-ase DNA-ase free water	Cytiva Life Sciences	Cat# SH30538.02
Heat Inactivated Fetal Bovine Serum (FBS)	Gibco Thermo Fisher	Cat# 10082147
PBS Tablets	Gibco Thermo Fisher	Cat# 18912-014
Bovine serum albumin (BSA)	Sigma-Aldrich Merck	Cat# A7906
poly-inosine:poly-cytosine (polyI:polyC)	Sigma-Aldrich Merck	Cat# P9582
Lypopolysaccharides from E.Coli	Sigma-Aldrich Merck	Cat# L4391
Busulfan (Busilvex®)	Pierre Fabre Pharmaceuticals	EMA/H/C/000472; EU/1/03/254/002
Dimethyl sulfoxide (DMSO)	Sigma-Aldrich Merck	Cat# 472301
5-Bromo-2Deoxyuridina (BrdU)	BD Biosciences	Cat# 423361
Ethylenediaminetetraacetic acid (EDTA)	Sigma-Aldrich Merck	Cat# E6758

Lipopolysaccharide (LPS)	Sigma-Aldrich Merck	Cat# L4391
Triton X-100	Sigma-Aldrich Merck	Cat# T8787
TdT buffer	Invitrogen Thermo Fischer	Cat# 16314015
Biotin-16-dUTP	Sigma-Aldrich Merck	Cat# 11093070910
TUNEL Enzyme	Sigma-Aldrich Merck	Cat# 11767305001
DNase I	ZYMO research	Cat# E1011-A
Vectashield	Vector Laboratories	Cat# H-1000
Potassium chloride (KH ₄ Cl)	Sigma-Aldrich Merck	Cat# P9541
SMART-Seq® v4 Ultra® Low Input RNA Kit for Sequencing	Clontech TaKaRa Bio	Cat# 634892
Low Input Library Prep Kit v2	Clontech TaKaRa Bio	Cat# 634899
Chromium Next GEM Single Cell 3' Kit v3.1	10x Genomics	Cat# PN-1000123
Qubit™ dsDNA HS and BR Assay Kits	Invitrogen Thermo Fischer	Cat# Q32851
High Sensitivity DNA Kit	Agilent Technologies	Cat# 5067-4626
Saline Solution (NaCl) 9mg/mL	B. Braun	Cat# 363 2202