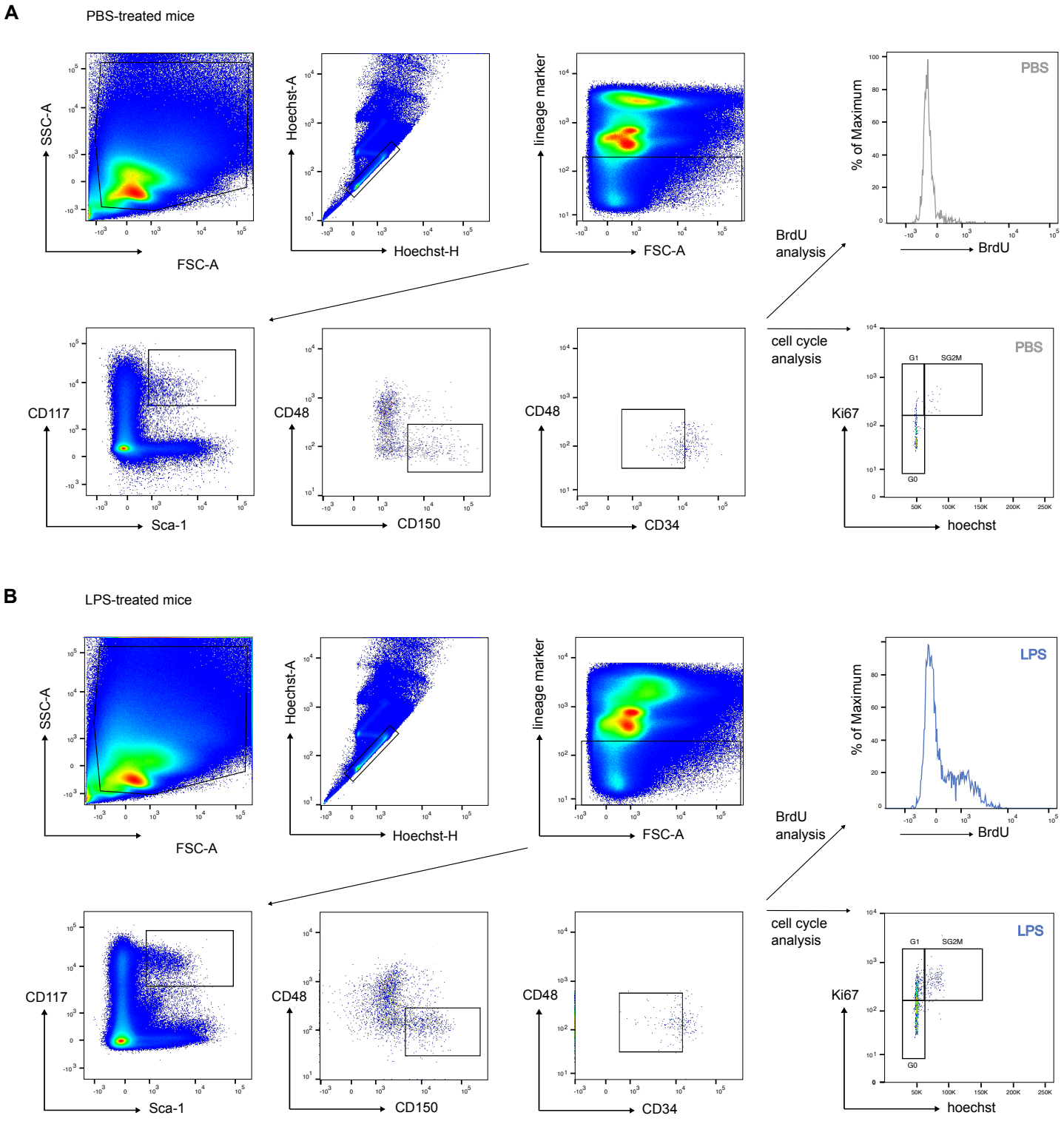
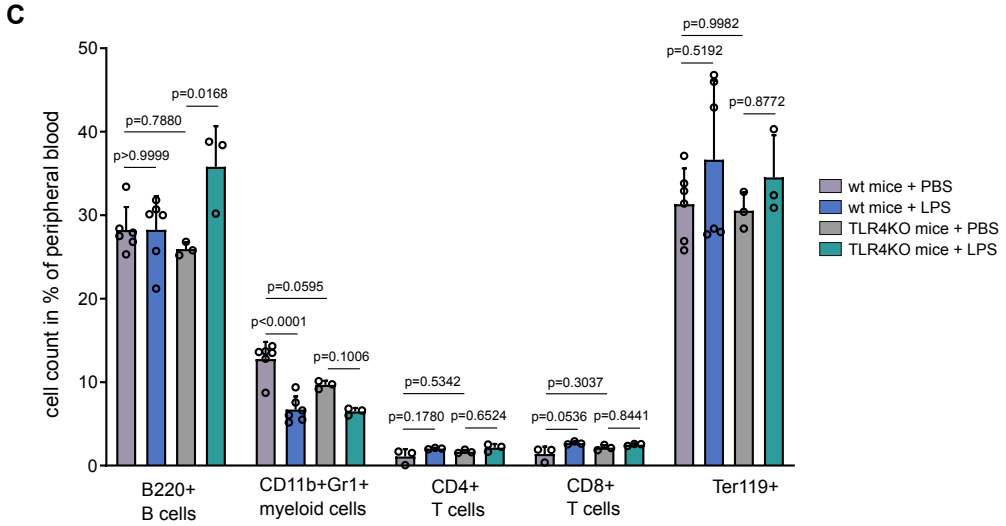




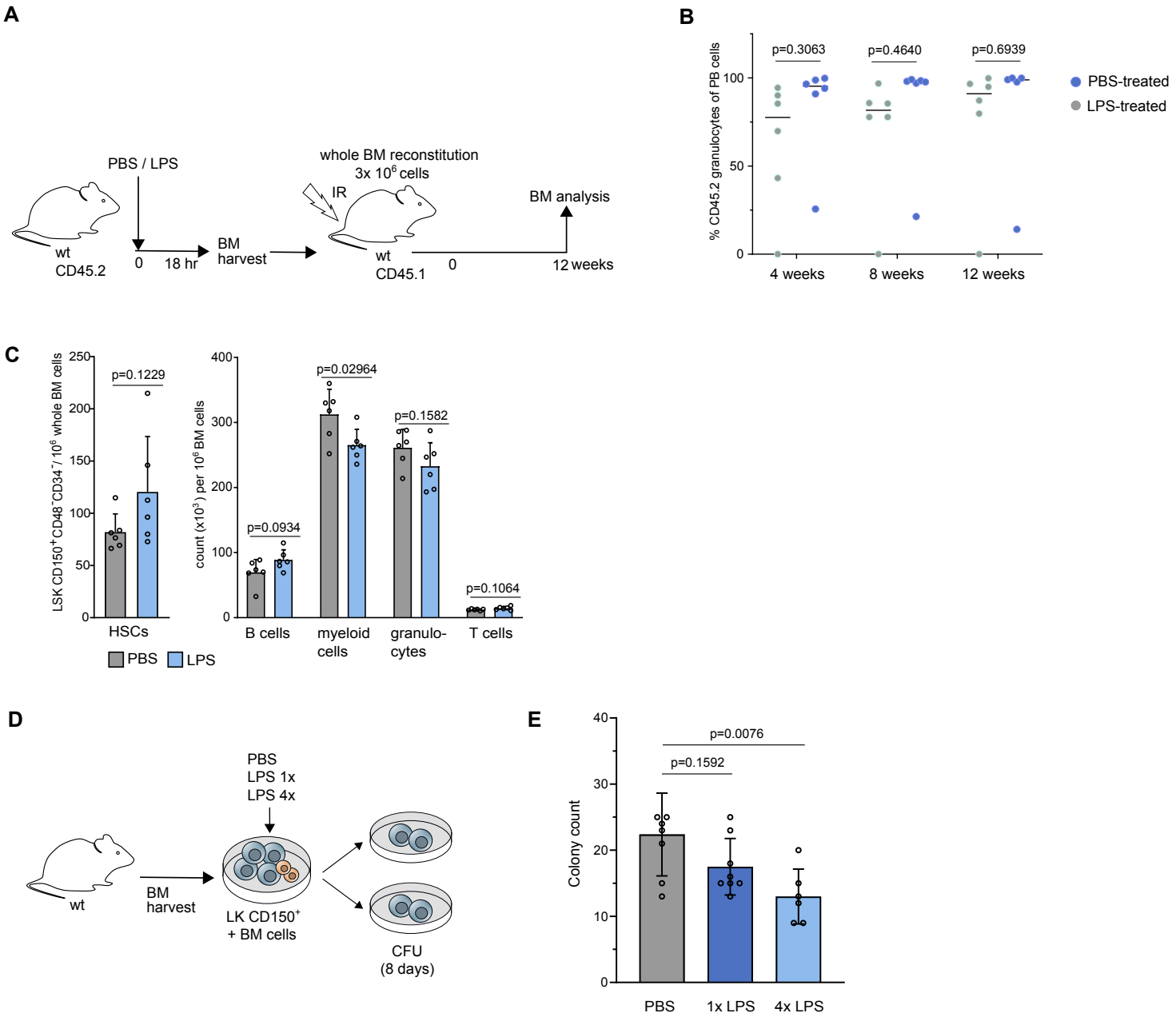
Supplementary Figure S1

Supplementary Figure S1.

(A) Representative FACS profiles illustrating gating scheme for HSCs from PBS-treated mouse; BrdU proliferation and cell cycle analysis (icKi67-Hoechst 33342).

(B) Representative FACS profiles illustrating gating scheme for HSCs from LPS-treated mouse; BrdU proliferation and cell cycle analysis (icKi67-Hoechst 33342).

(C) Relative count of indicated cell populations as percentage of peripheral blood cells after *in vivo* treatment of wt or *TLR4*$^{-/-}$ mice with PBS (control) or LPS (0.25 mg/kg) for 18h (n=6 for wt mice, n=3 for *TLR4*$^{-/-}$ mice). *P-values* were determined by ANOVA; Tukey`s post hoc test.



Supplementary Figure S2

Supplementary Figure S2.

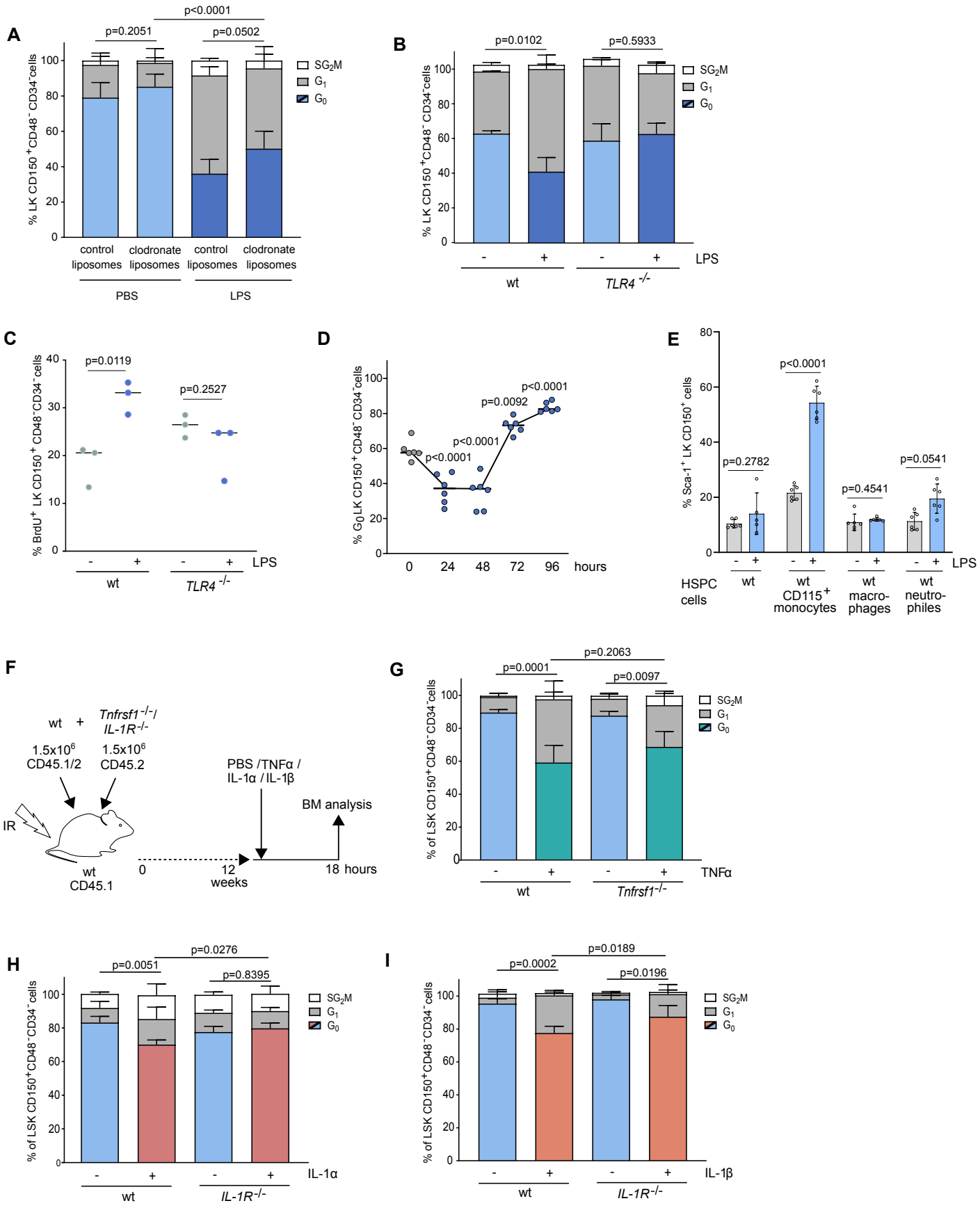
(A) Scheme indicating *in vivo* transplantation: BM was harvested from PBS (control) or LPS (0.25mg/kg, 18h) treated mice ($CD45.2^+$) and transplanted (3x 10^6 BM cells) into irradiated wt mice ($CD45.1^+$). Analysis was done 12 weeks post transplantation.

(B) Percentage of CD45.2 granulocytes of peripheral blood cells in recipient mice 4, 8 and 12 weeks post transplantation, transplantation set-up as indicated in Fig. 2SA (n=6); *P-values* were determined by unpaired t-test.

(C) Absolute numbers of HSCs (LSK $CD150^+CD48^-CD34^-$, per 10^6 BM cells) and mature blood cell types ($B220^+$ B-cells, $CD11b^+Ly6C^+$ myeloid cells, $CD11b^+Gr.1^+$ granulocytes, $CD3^+$ T-cells; $x10^3$ per 10^6 BM cells) in recipient mice 12 weeks post transplantation, as indicated in Fig. 2SA (n=6); *P-values* were determined by unpaired t-test and ANOVA; Tukey`s post hoc test.

(D) Scheme illustrating CFU assay set-up: $Lin^{neg}Kit^+CD150^+$ ($LKCD150^+$) (20.000) and $CD11b^+CD115^+$ (10.000) cells were sorted from wt mouse (n=4) into culture. Cells were treated with either PBS, LPS (single treatment vs. 4 treatments by refreshing medium every second day, 100ng/ml). After 7 days 2.000 cells out of each well were plated in duplicate for colony-forming unit (CFU) assay. Colonies were counted after 8 days.

(E) Absolute number of colonies counted in CFU assay. Experimental set-up as indicated in Fig. 2SD (n=8); *P-values* were determined by ANOVA; Tukey`s post hoc test.



Supplementary Figure S3

Supplementary Figure S3.

(A) Cell cycle analysis (icKi67-Hoechst 33342) of HSCs (LK $CD150^+CD48^-CD34^-$) from wt mice treated with PBS (control) or LPS (0.25 mg/kg, 18h) and pre-treated with control- or clodronate-loaded liposomes as indicated in Fig.3H (n=6). *P-values* refer to G_0 phase and were determined by ANOVA Tukey's post hoc test.

(B) Cell cycle analysis (icKi67-Hoechst 33342) of HSCs (LK $CD150^+CD48^-CD34^-$) from PBS or LPS (0.25 mg/kg, 18h) treated wt and *TLR4*$^{-/-}$ mice (n=3); *P-values* refer to G_0 phase and were determined by ANOVA; Tukey`s post hoc test.

(C) 14h BrdU (18mg/kg) uptake of HSCs (LK $CD150^+CD48^-CD34^-$) from PBS (control) or LPS (0.25 mg/kg, 18h) treated wt and *TLR4*$^{-/-}$ mice (n=3); *P-values* were determined by ANOVA; Tukey`s post hoc test.

(D) Percentage of HSCs (LK $CD150^+CD48^-CD34^-$) in G_0 phase (icKi67^{neg} Hoechst 33342^{low}) at indicated time points after treatment of wt mice with PBS (control, time point 0h, grey dots) or LPS (0.25 mg/kg, blue dots) (n=6); *P-values* were determined by ANOVA; Tukey`s post hoc test.

(E) Relative Sca-1 expression on sorted wt HSPCs (LK $CD150^+$) after *in vitro* culture for 18h in the presence of wt $Gr1^+CD115^+$ monocytes, $Gr1^+CD115^-F4/80^+$ macrophages or $Gr1^+CD115^-$ neutrophils. *P-values* were determined by unpaired t-test.

(F) Scheme indicating the *in vivo* transplantation: BM from wt ($CD45.1/2^+$) and *Tnfrsf1*$^{-/-}$ or *IL-1R*$^{-/-}$ mice ($CD45.2^+$) ($1.5x10^6$ BM cells each) was transplanted into irradiated wt mice ($CD45.1^+$). Mice were treated with PBS (control) or the respective cytokine TNFα (0.75 mg/kg, 18h), IL-1α or IL-1β (each 0.25 mg/kg, 18h) 12 weeks post transplantation.

(G) Cell cycle analysis (icKi67-Hoechst 33342) of wt ($CD45.1/2^+$) and *Tnfrsf1*$^{-/-}$ ($CD45.2^+$) HSCs (LSK $CD150^+CD48^-CD34^-$) in mixed BM chimeras as indicated in Fig.3SF, treated with PBS (control) or TNFα (0.75 mg/kg, 18h) (n=4 for PBS, n=6 for TNFα). *P-values* refer to G_0 phase and were determined by ANOVA; Tukey`s post hoc test.

(H) Cell cycle analysis (icKi67-Hoechst 33342) of wt ($CD45.1/2^+$) and *IL-1R*$^{-/-}$ ($CD45.2^+$) HSCs (LSK $CD150^+CD48^-CD34^-$) in mixed BM chimeras as indicated in Fig.3SF, treated with PBS (control) or IL-1α (0.25 mg/kg, 18h) (n=3). *P-values* refer to G_0 phase and were determined by ANOVA; Tukey`s post hoc test.

(I) Cell cycle analysis (icKi67-Hoechst 33342) of wt ($CD45.1/2^+$) and *IL-1R*$^{-/-}$ ($CD45.2^+$) HSCs (LSK $CD150^+CD48^-CD34^-$) in mixed BM chimeras as indicated in Fig.3SF,

treated with PBS (control) or IL-1β (0.25 mg/kg, 18h) (n=3). *P-values* refer to G_0 phase and were determined by ANOVA; Tukey`s post hoc test.

Supplementary Tables

Table 1. Flow-Cytometry Antibodies

Company	Antigen	clone	Channel	Cat number
eBioscience	cKit	2B8	PE	12-1171-82
eBioscience	cKit	2B8	APC	17-1171-82
Biolegend	ckit	2B8	BV711	105835
eBioscience	cKit	2B9	APC-eFluor 780	47-1171-82
eBioscience	Gr-1	RB6-8C5	PE	12-5931-82
eBioscience	Gr-1	RB6-8C6	PECy7	25-5931-82
eBioscience	B220	RA3- 6B2	PB	2016454
eBioscience	B220	RA3- 6B2	PECy5	15-0452-82
eBioscience	B220	RA3- 6B2	PECy7	25-0452-82
eBioscience	CD48	HM48-1	PE	12-0481-82
eBioscience	CD4	GK1.5	PECy7	25-0041-82
eBioscience	CD8a	53-6.7	PECy7	25-0081-82
eBioscience	CD11b	M1/70	PB	48-0112-82
eBioscience	CD11b	M1/70	PECy7	25-0112-82
eBioscience	TER-119	TER-119	PECy7	25-5921-82
eBioscience	CD45.1	A20.1	FITC	11-0453-82
eBioscience	CD115	AFS98	APC	17-1152-82
eBioscience	CD34	RAM34	Alexa700	56-0341-82
Biolegend	CD150	TC15-12F12.2	PECy5	115904
Biolegend	CD150	TC15-12F12.2	APC	115910
Biolegend	CD48	HM48-1	PE-CY7	103424
Biolegend	CD48	HM48-1	PB	103418
Biolegend	CD45.2	104	PB	109820
Biolegend	B220	RA3- 6B2	biotin	103204
Biolegend	CD11b	M1/70	biotin	101204
eBioscience	CD8a	53-6.7	PB	48-0081-82
Biolegend	CD8a	53-6.7	biotin	100704
eBioscience	CD4	GK1.5	PB	48-0041-82
Biolegend	CD4	GK1.5	biotin	100404
Biolegend	Gr-1	RB6-8C5	biotin	108404
eBioscience	Gr-1	RB6-8C5	PB	48-5931-82
eBioscience	TER-119	TER-119	PB	48-5921-82
Biolegend	TER-119	TER-119	biotin	116204
BD Pharmingen	ki67	B56	FITC	556026
BD Pharmingen	ki67	B56	Alexa Fluor 647	558615
BD Pharmingen	CD45.2	104	Alexa700	560693
BD Pharmingen	Sca-1	D7	APCCy7	560654

Table 2. qRT-PCR Primers

Gene	FW/RV	Sequence
IFNa	FW	CTGCTGGCTGTGAGGACATA
	RV	AGGAAGAGAGGGCTCTCCAG
IL-1a	FW	TTGGTTAAATGACCTGCAACA
	RV	GAGCGCTCACGAACAGTTG
IL-1b	FW	AGTTFACGGACCCCAAAAG
	RV	AGCTGGATGCTCTCATCAGG
TNFa	FW	CCACCACGCTCTTCTGTCTA
	RV	AGGGTCTGGGCCATAGAACT
sdha	FW	AAGTTGAGATTTGCCGATGG
	RV	TGGTTCTGCATCGACTTCTG
socs3	FW	CACACAAGGAGCCAAACACA
	RV	TAGCCACCTGGGTGAATCC