Supplemental Table S1. Antibody combinations used to isolate/identify cell populations

Isolated/Identified cell population	Antibody combinations
B cells	$CD45^+$ $B220^+$ $Gr1^-$ $CD18^-$ $CD8a^-$ $CD4^-$
T cells	$CD45^+$ $B220^-$ $Gr1^-$ $CD18^-$ $CD8a^+$ $CD4^+$
Myeloid cells	$CD45^+$ $B220^-$ $Gr1^+$ $CD18^+$ $CD8a^-$ $CD4^-$
CD11b +	$CD45^+$ $CD11b^{HI}$
Neutrophils (CD115 -)	$CD45^+$ $CD11b^{HI}$ $CD115^-$ $Ly6G^+$
Monocytes (CD115 +)	$CD45^+$ $CD11b^{HI}$ $CD115^+$ $Ly6G^-$
Ly6C -	$CD45^+$ $CD11b^{HI}$ $CD115^+$ $Ly6G^-$ $Ly6C^-$
Ly6C + (anti-inflammatory monocytes)	$CD45^+$ $CD11b^{HI}$ $CD115^+$ $Ly6G^-$ $Ly6C^{DIM}$
Ly6C ++(proinflammatory monocytes)	$CD45^+$ $CD11b^{HI}$ $CD115^+$ $Ly6G^-$ $Ly6C^{HI}$
Lineage neg (Lin-)	Lineage cocktail (Ter119, CD11b, Gr-1, CD3e, B220)$^-$
LK	Lin^- $cKit^+$
LKS	Lin^- $cKit^+$ $Sca\text{-}1^+$
LT HSC	Lin^- $cKit^+$ $Sca\text{-}1^+$ $CD135^-$ $CD48^-$ $CD150^{HI}$
ST HSC	Lin^- $cKit^+$ $Sca\text{-}1^+$ $CD135^-$ $CD48^-$ $CD150^{LO}$
MPP	Lin^- $cKit^+$ $Sca\text{-}1^+$ $CD135^-$ $CD48^+$
CLP	Lin^- $cKit^+$ $Sca\text{-}1^+$ $CD135^+$ $CD150^-$
CMP	Lin^- $cKit^+$ $Sca\text{-}1^-$ $CD34^+$ $CD16/32^-$
GMP	Lin^- $cKit^+$ $Sca\text{-}1^-$ $CD34^+$ $CD16/32^+$
MEP	Lin^- $cKit^+$ $Sca\text{-}1^-$ $CD34^-$ $CD16/32^-$

Bone Marrow Transplant (BMT)

Isolated/Identified cell population	Antibody combinations
B cells	($CD45.1^+$ or $CD45.2^+$) $B220^+$ $Gr1^-$ $CD18^-$ $CD8a^-$ $CD4^-$
T cells	($CD45.1^+$ or $CD45.2^+$) $B220^-$ $Gr1^-$ $CD18^-$ $CD8a^+$ $CD4^+$
Myeloid cells	($CD45.1^+$ or $CD45.2^+$) $B220^-$ $Gr1^+$ $CD18^+$ $CD8a^-$ $CD4^-$
CD11b +	($CD45.1^+$ or $CD45.2^+$) $CD11b^{HI}$
Neutrophils (CD115 -)	($CD45.1^+$ or $CD45.2^+$) $CD11b^{HI}$ $CD115^-$ $Ly6G^+$
Monocytes (CD115 +)	($CD45.1^+$ or $CD45.2^+$) $CD11b^{HI}$ $CD115^+$ $Ly6G^-$
Ly6C -	($CD45.1^+$ or $CD45.2^+$) $CD11b^{HI}$ $CD115^+$ $Ly6G^-$ $Ly6C^-$
Ly6C + (anti-inflammatory monocytes)	($CD45.1^+$ or $CD45.2^+$) $CD11b^{HI}$ $CD115^+$ $Ly6G^-$ $Ly6C^{DIM}$
Ly6C ++ (proinflammatory monocytes)	($CD45.1^+$ or $CD45.2^+$) $CD11b^{HI}$ $CD115^+$ $Ly6G^-$ $Ly6C^{HI}$

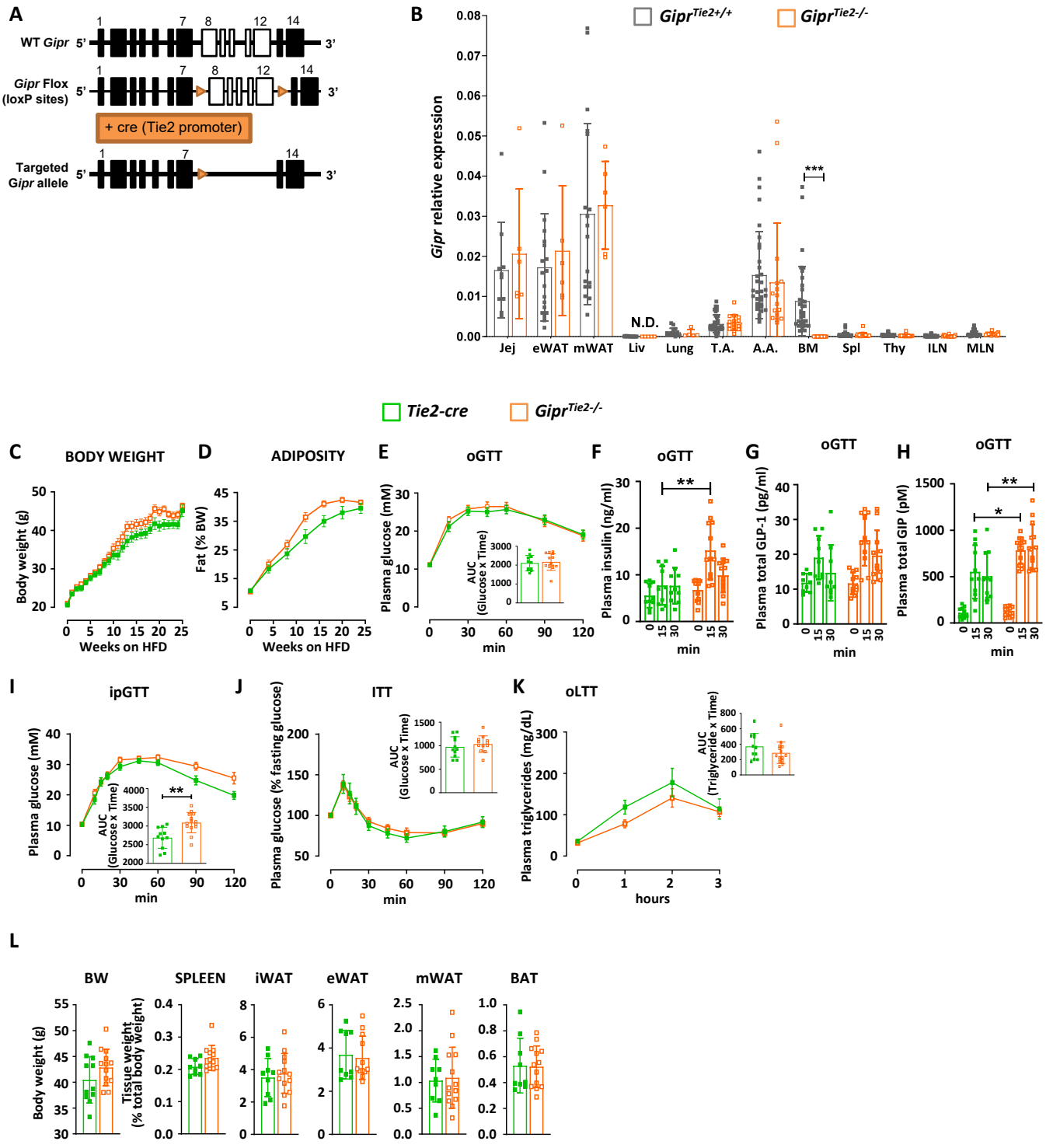
Supplemental Table S2. Antibodies information

Name	Clone	Cat#	Company
Alexa Fluor® 488 anti-mouse Ly-6A/E (Sca-1)	D7	108115	BioLegend
APC anti-mouse CD45	30-F11	103111	BioLegend
APC anti-mouse CD45.2	104	109814	BioLegend
APC anti-mouse CD48	HM48-1	103411	BioLegend
APC anti-mouse Ki-67	16A8	652405	BioLegend
APC anti-mouse Ly-6C	HK1.4	128015	BioLegend
APC/Cy7 anti-mouse CD11b	M1/70	101225	BioLegend
APC/Fire™ 750 anti-mouse CD117 (c-kit)	2B8	105837	BioLegend
Biotin anti-mouse Lineage Panel	145-2c11/RB6-8C5/RA3-6B2/Ter-119/M1/70	133307	BioLegend
Brilliant Violet 421™ anti-mouse CD135	A2F10	135313	BioLegend
Brilliant Violet 510™ anti-mouse CD16/32	93	101333	BioLegend
FITC anti-mouse CD18	M18/2	101405	BioLegend
FITC anti-mouse CD45	30-F11	103107	BioLegend
FITC anti-mouse CD45.2	104	109806	BioLegend
FITC anti-mouse Ly-6G/Ly-6C (Gr-1)	RB6-8C5	108405	BioLegend
FITC anti-mouse CD45R/B220	RA3-6B2	103205	BioLegend
Pacific Blue™ anti-mouse Ly-6G	1A8	127611	BioLegend
PE anti-mouse CD115 (CSF-1R)	AFS98	135505	BioLegend
PE anti-mouse CD34	SA376A4	152203	BioLegend
PE anti-mouse CD4	RM4-5	100511	BioLegend
PE anti-mouse CD8a	53-6.7	100707	BioLegend
PE anti-mouse CD45R/B220	RA3-6B2	103207	BioLegend
PE/Cy5 Streptavidin	-	405205	BioLegend
PE/Cy7 anti-mouse CD150 (SLAM)	TC15-12F12.2	115913	BioLegend
PE/Cy7 anti-mouse CD45.1	A20	110730	BioLegend
TruStain fcX™ (anti-mouse CD16/32)	93	101320	BioLegend
7-AAD Viability Staining Solution		420403	BioLegend
Brilliant Violet 510™ Rat IgG1, κ Isotype Ctrl	RTK2071	400435	BioLegend
Hamster IgG	biotin	400903	BioLegend
Hamster IgG	APC	400911	BioLegend
PE/Cy5 Rat IgG1, κ Isotype Ctrl	RTK2071	400410	BioLegend
PE/Cy7 Rat IgG1, κ Isotype Ctrl	RTK2071	400415	BioLegend
Rat IgG2a, κ	APC	400511	BioLegend
Rat IgG2a,k	biotin	400503	BioLegend
Rat IgG2a,k	Alexa Fluor 488	400525	BioLegend
Rat IgG2a,k	BV421	400535	BioLegend
Rat IgG2a,k	PE	400507	BioLegend
Rat IgG2a,k	FITC	400505	BioLegend
Rat IgG2b,k	biotin	400603	BioLegend
Rat IgG2b,k	APC/Fire750	400669	BioLegend
Rat IgG2b,k	APC	400611	BioLegend
Rat IgG2b,k	FITC	400605	BioLegend

Supplemental table S3. Taqman primer information

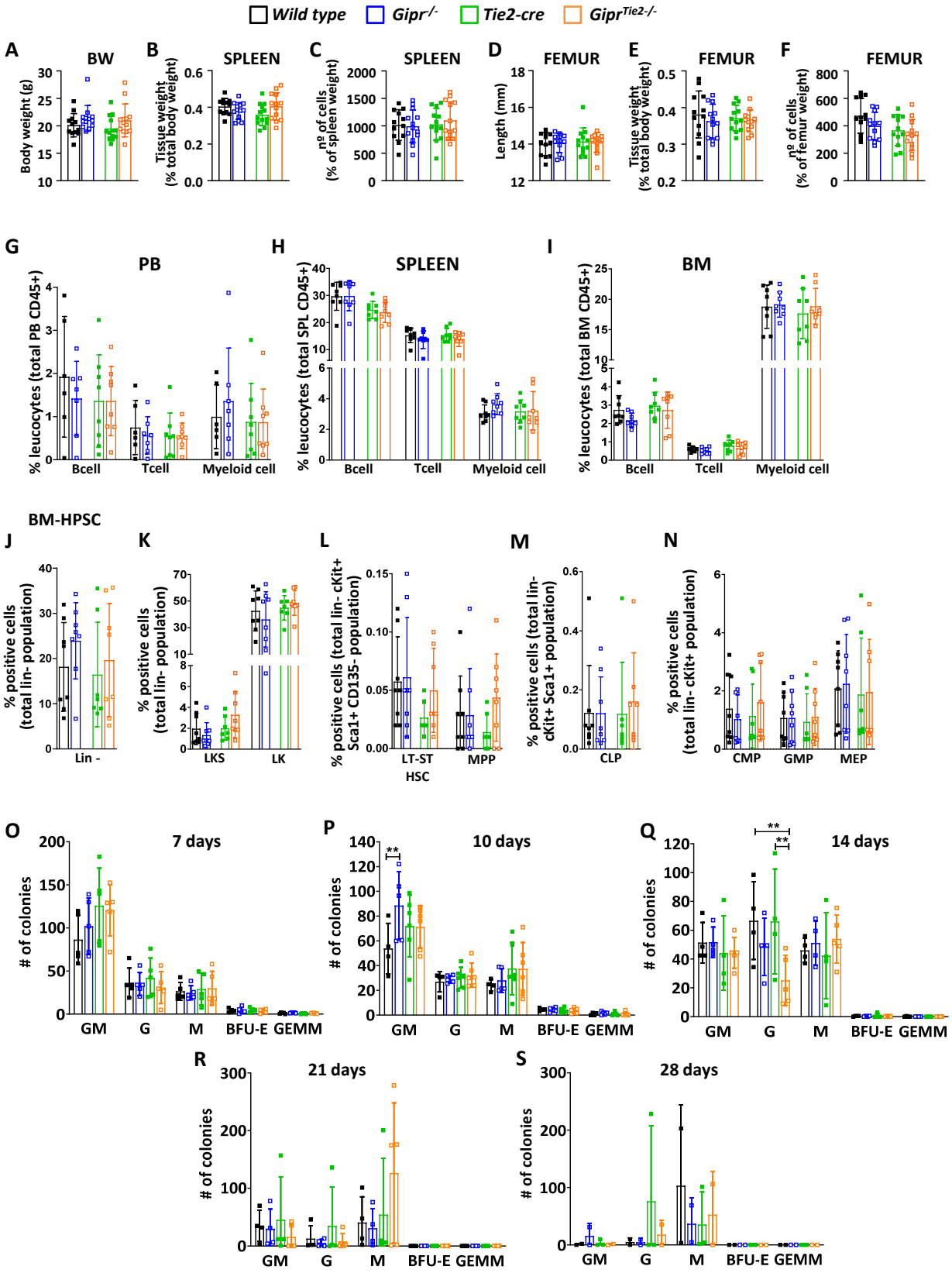
Gene symbol	Gene name	Assay ID
Adgre 1 (F4/80)	adhesion G protein-coupled receptor E1 (F4/80)	Mm00802529_m1
Ccl2 (Mcp-1)	chemokine (C-C motif) ligand 2	Mm00441242_m1
Cxcl1 (KC/GRO)	chemokine (C-X-C motif) ligand 1	Mm00433859
Cxcl2 (Mip-2a)	chemokine (C-X-C motif) ligand 2 (MIP-2a)	Mm00436450_m1
Dkk1	dickkopf homolog 1 (Xenopus laevis)	Mm00438422_m1
Gipr (ex.12-13)	gastric inhibitory polypeptide receptor	Mm01316344_m1
Gipr (ex.4-5)	gastric inhibitory polypeptide receptor	Mm01316349_g1
Hes1	hairy and enhancer of split 1 (Drosophila)	Mm01342805_m1
Hes3	hairy and enhancer of split 3 (Drosophila)	Mm01260283_g1
Il1b	interleukin 1 beta	Mm00434228_m1
Il6	interleukin 6	Mm00446190_m1
Jag1	jagged 1	Mm00496902_m1
Mgl2	macrophage galactose N-acetyl-galactosamine specific lectin 2	Mm00460844_m1
MyD88	myeloid differentiation primary response gene 88	Mm00440338
Notch1	notch 1	Mm00435249_m1
Notch2	notch 2	Mm00803077_m1
Notch3	notch 3	Mm01345646_m1
Notch4	notch 4	Mm00440525_m1
Ppia	Cyclophilin (peptidylprolyl isomerase A)	Mm02342430_g1
S100a8	S100 calcium binding protein A8 (calgranulin A)	Mm00496696_g1
S100a9	S100 calcium binding protein A9 (calgranulin B)	Mm00656925_m1
Ticam1	toll-like receptor adaptor molecule 1	Mm00844508
Tlr1	toll-like receptor 1	Mm00446095
Tlr11	toll-like receptor 11	Mm01701924
Tlr12	toll-like receptor 12	Mm01180204
Tlr13	toll-like receptor 13	Mm01233819
Tlr2	toll-like receptor 2	Mm00442346_m1
Tlr3	toll-like receptor 3	Mm00628112
Tlr4	toll-like receptor 4	Mm00445273_m1
Tlr5	toll-like receptor 5	Mm00546288_s1
Tlr6	toll-like receptor 6	Mm02529782
Tlr7	toll-like receptor 7	Mm00446590
Tlr8	toll-like receptor 8	Mm04209873_m1
Tlr9	toll-like receptor 9	Mm00446193
Tnf	Tumor necrosis factor alpha	Mm00443258_m1

Supplementary Figure 1



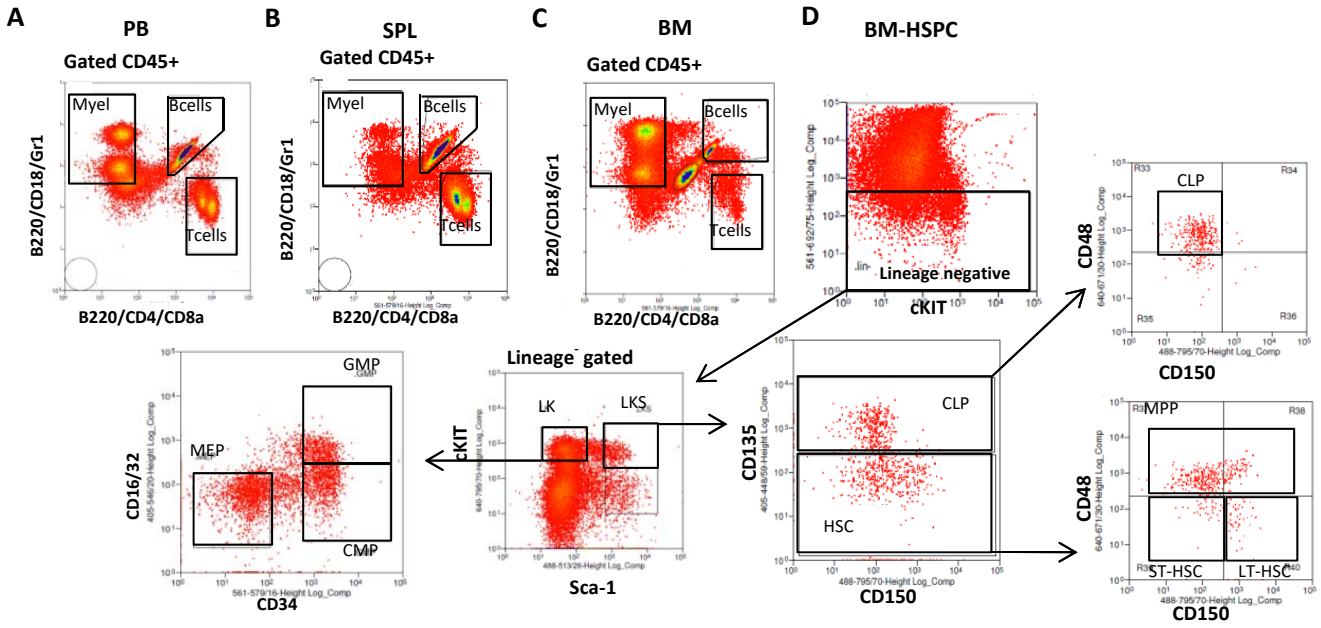
Supplementary Figure 1. Generation of *Gipr*$^{Tie2-/-}$ mice and related metabolic parameters. (A) Schematic of Cre LoxP targeting strategy to generate *Gipr*$^{Tie2-/-}$ mice. (B) *Gipr* mRNA levels, normalized to *Ppia*, in different tissues of 30-34 week-old *Gipr*$^{Tie2+/+}$ (pooled WT, *Gipr*$^{Flox/Flox}$ and *Tie2-cre* control mice) and *Gipr*$^{Tie2-/-}$ males fed a HFD (n=6-40/group). Data are presented as the mean ± SD. Body weight (C) and fat mass (D) of *Tie2-cre* and *Gipr*$^{Tie2-/-}$ males (starting at 6-8 weeks of age) fed a HFD for 25 weeks. (E) Glucose excursion and AUC (inset graph) following an oral glucose challenge (oGTT). (F) Plasma insulin, (G) total GLP-1 and (H) total GIP levels at baseline (0 min) and the indicated time points after oral glucose administration. Glucose excursion following (I) intraperitoneal glucose (ipGTT) or (J) insulin (ITT) administration (AUC as inset graph). (K) Plasma triglyceride excursion after oral olive oil administration (oLTT) and AUC as an inset graph. Data in E-K are from *Tie2-cre* and *Gipr*$^{Tie2-/-}$ male mice fed a HFD for 20-25 weeks (n= 11-14 /group). (L)Body and tissue weights relative to body weight in 30-34 week-old HFD-fed *Tie2-cre* and *Gipr*$^{Tie2-/-}$ males (n=6-19/group). Data are presented as the mean ± SD. * $P \leq 0.05$, ** $P \leq 0.01$ and *** $P \leq 0.001$. Jej=jejunum, eWAT=epididymal white adipose tissue, mWAT=mesenteric white adipose tissue, Liv=liver, T.A.=thoracic aorta, A.A.=aortic arch, BM=bone marrow, Spl=spleen, Thy=thymus, ILN=inguinal lymph nodes, MLN=mesenteric LN, AUC=area under the curve, oGTT=oral glucose tolerance test, ipGTT=intraperitoneal glucose tolerance test, ITT=insulin tolerance test, oLTT=oral lipid tolerance test, GLP-1=glucagon-like peptide 1, GIP=glucose-dependent insulinotropic polypeptide, BW=body weight, iWAT=inguinal white adipose tissue and BAT=brown adipose tissue.

Supplementary Figure 2



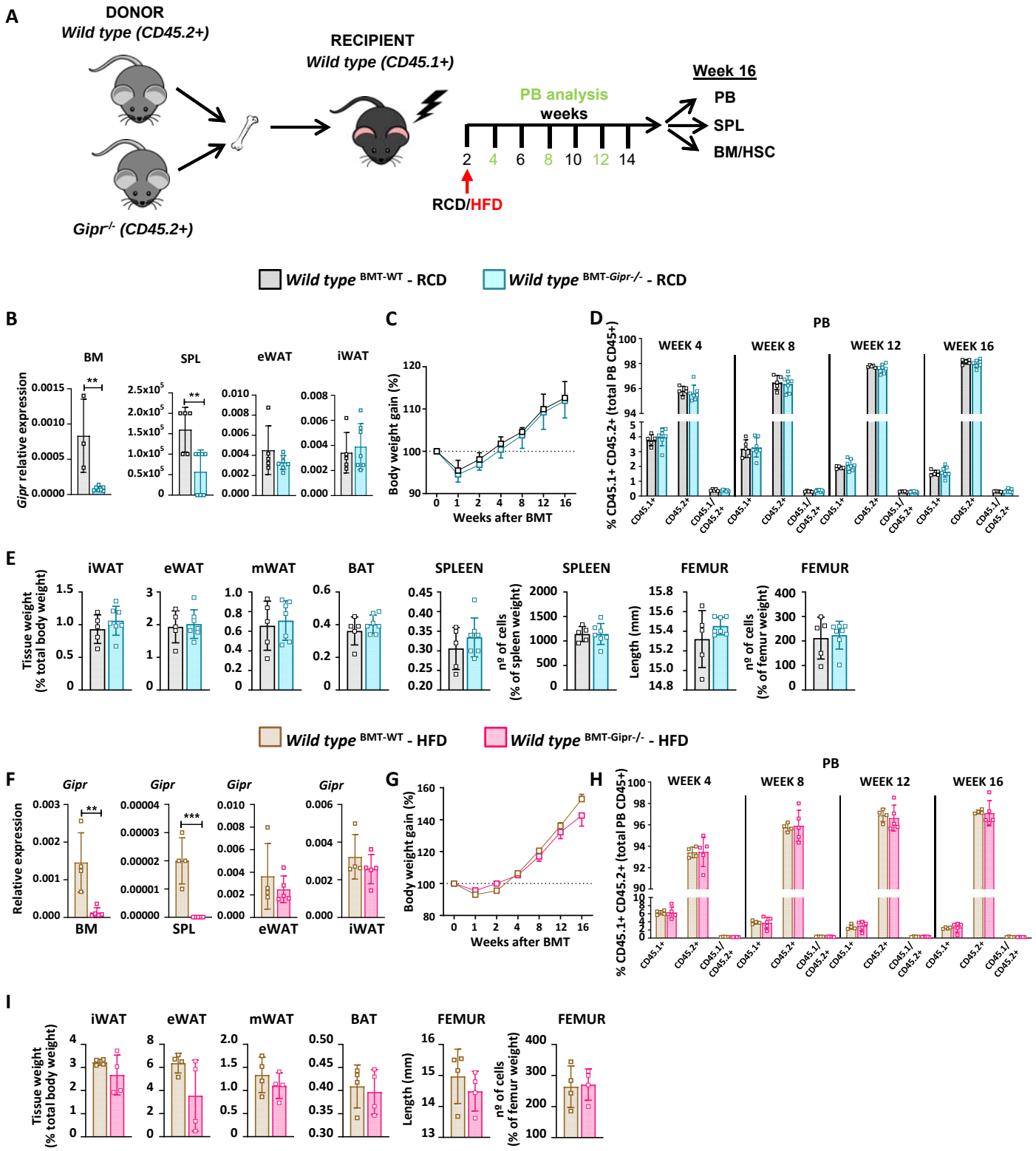
Supplementary Figure 2. Flow cytometry analysis of peripheral blood, spleen and bone marrow and colony forming unit (CFU) assay. Body weight (A), spleen weight relative to body weight (B), number of spleen cells relative to spleen weight (C), femur length (D), femur weight relative to body weight (E), and number of cells isolated from a single femur relative to femur weight (F). Frequency of isolated CD45+ cells relative to the total viable cell population in the peripheral blood (G), spleen (H) and bone marrow (I). Frequency of the total lineage negative cell population (J), LKS and LK populations (K), LT-ST HSC and MPP (L), CLP (M) and CMP, GMP and MEP (N) cells in bone marrow. Data are from 8 week-old WT, *Gipr*$^{-/-}$, *Tie2*-cre and *Gipr*$^{Tie2-/-}$ female mice (n=12-13/group). Colony-forming unit (CFU) assay analysis of bone marrow cells from 8 week-old WT, *Gipr*$^{-/-}$, *Tie2*-cre and *Gipr*$^{Tie2-/-}$ females (n= 5/group). Absolute colony numbers for primary cultures at 7 days (O) and 10 days (P), and for secondary cultures at 7 days after the first replating (day 14) (Q), 7 days after the second replating (21 days) (R), and 7 days after the third replating (28 days) (S). Data are presented as the mean ± SD. ** $P \leq 0.01$. BW= body weight, PB= peripheral blood, SPL=spleen, BM=bone marrow, BM-HSPC=bone marrow hematopoietic stem progenitor cells, LK= Lin-cKit+Sca1-, LKS= Lin-cKit+Sca1+, HSC=hematopoietic stem cells, ST-HSC=short term hematopoietic stem cells, LT-HSC=long term hematopoietic stem cells, MPP=multipotent progenitor, CLP=common lymphoid progenitor, CMP=common myeloid progenitor, GMP= granulocyte-monocyte progenitor, MEP=megakaryocyte-erythroid progenitors, GM= granulocyte-macrophage, G=granulocytes , M=macrophages, BFU-E=Burst-forming unit-erythroid, GEMM=multi-potential granulocyte, erythroid, macrophage, megakaryocyte.

Supplementary Figure 3



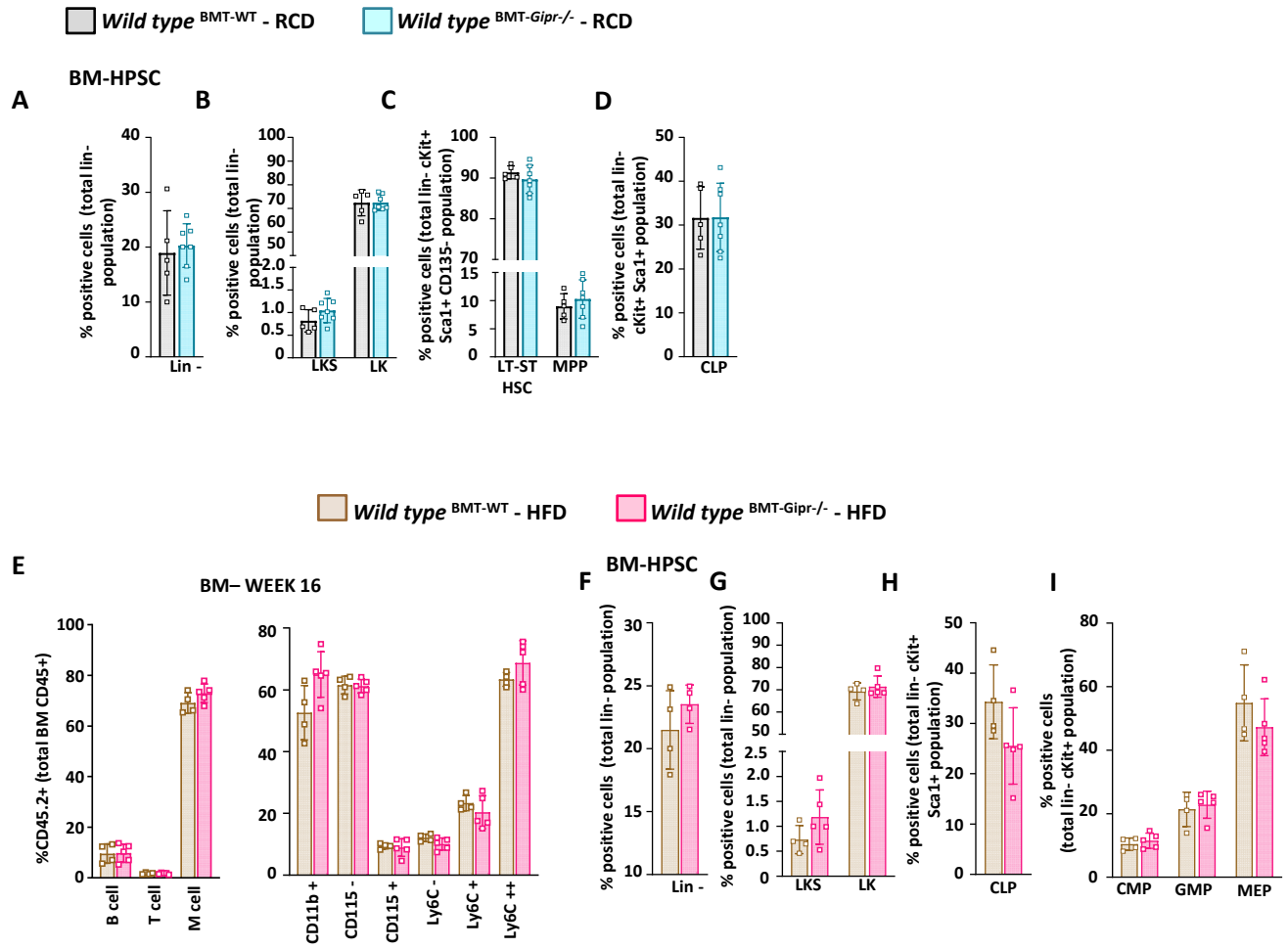
Supplementary Figure 3. Representative flow cytometry images showing the followed strategy. Representative flow cytometry images showing the strategy followed to define and sort mature immune cells in the peripheral blood (A), spleen (B), bone marrow (C), and bone marrow HSPC population (D).

Supplementary Figure 4



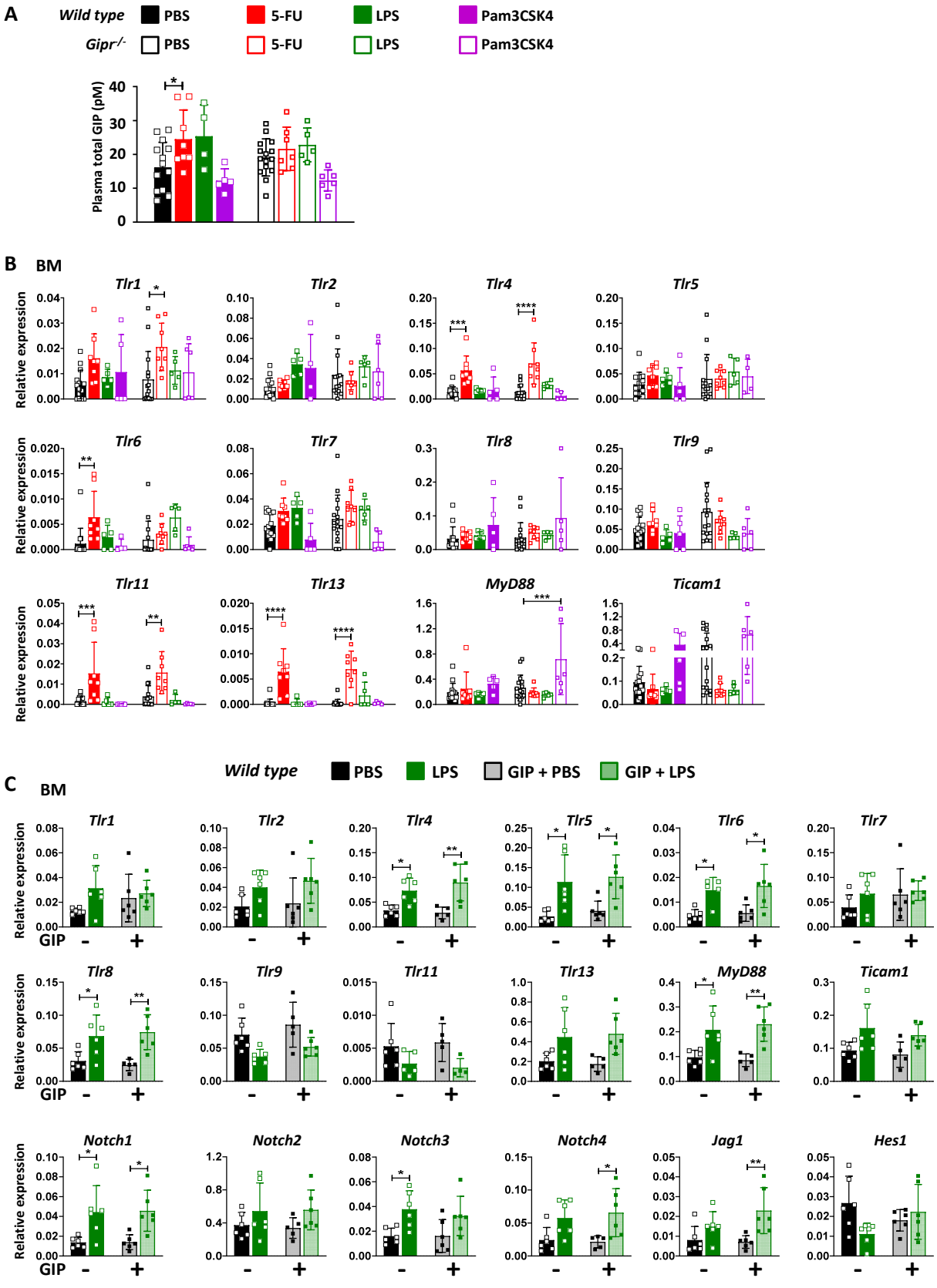
Supplementary Figure 4. Body and tissue weights and cell population frequencies in *Gipr*$^{-/-}$ BM recipients fed a RCD or a HFD. (A) Experimental schedule for BMT where WT male mice received WT (BMT-WT) or *Gipr*$^{-/-}$ (BMT-*Gipr*$^{-/-}$) bone marrow at 8 weeks-old and fed a RCD or HFD for the following 14 weeks. (B) *Gipr* mRNA levels, normalized to *Ppia* expression, in the indicated tissues, 16 weeks after receiving BMT. (C) Percent body weight gain in BMT recipient mice starting before BMT and continuing for up to 16 weeks post BMT and kept on a RCD. (D) Whole blood chimerism expressed as the percentage of residual recipient cells (CD45.1), donor repopulated cells (CD45.2), and cells co-expressing both (CD45.1 and CD45.2), versus the total CD45+ population at 4, 8, 12 and 16 weeks after BMT. (E) Tissue weights relative to body weight, femur length and spleen and femur cellularity in 26 week-old RCD-fed WT mice that received a BMT from WT (Wild type$^{BMT\text{-}WT}$) or *Gipr*$^{-/-}$ (Wild type$^{BMT\text{-}\ Gipr\text{-}/\text{-}}$) donors at 8 weeks-old (n= 5-7/group). (F) *Gipr* mRNA levels, normalized to *Ppia* expression, in the indicated tissues, in 26 week-old HFD-fed WT mice that received a BMT from WT (Wild type$^{BMT\text{-}WT}$) or *Gipr*$^{-/-}$ (Wild type$^{BMT\text{-}\ Gipr\text{-}/\text{-}}$). (G) Percent body weight gain in BMT recipient mice starting before BMT and continuing for up to 16 weeks post BMT and kept on a HFD. (H) Whole blood chimerism expressed as the percentage of residual recipient cells (CD45.1), donor repopulated cells (CD45.2), and cells co-expressing both (CD45.1 and CD45.2), versus the total CD45+ population at 4, 8, 12 and 16 weeks after BMT. (I) Tissue weights relative to body weight, femur lengt and cellularity in 26 week-old HFD-fed WT mice that received a BMT from WT (Wild type$^{BMT\text{-}WT}$) or *Gipr*$^{-/-}$ (Wild type$^{BMT\text{-}\ Gipr\text{-}/\text{-}}$) donors at 8 weeks-old (n= 4/group). Data are presented as the mean ± SD. ***P*≤ 0.01 and ****P* ≤ 0.001. BMT=bone marrow transplant, RCD=regular chow diet, HFD=high fat diet, BM=bone marrow, SPL=spleen, eWAT=epididymal white adipose tissue, iWAT=inguinal white adipose tissue, BAT=brown adipose tissue, mWAT=mesenteric white adipose tissue, BM/HPSC=bone marrow hematopoietic progenitor stem cells and PB=peripheral blood.

Supplementary Figure 5



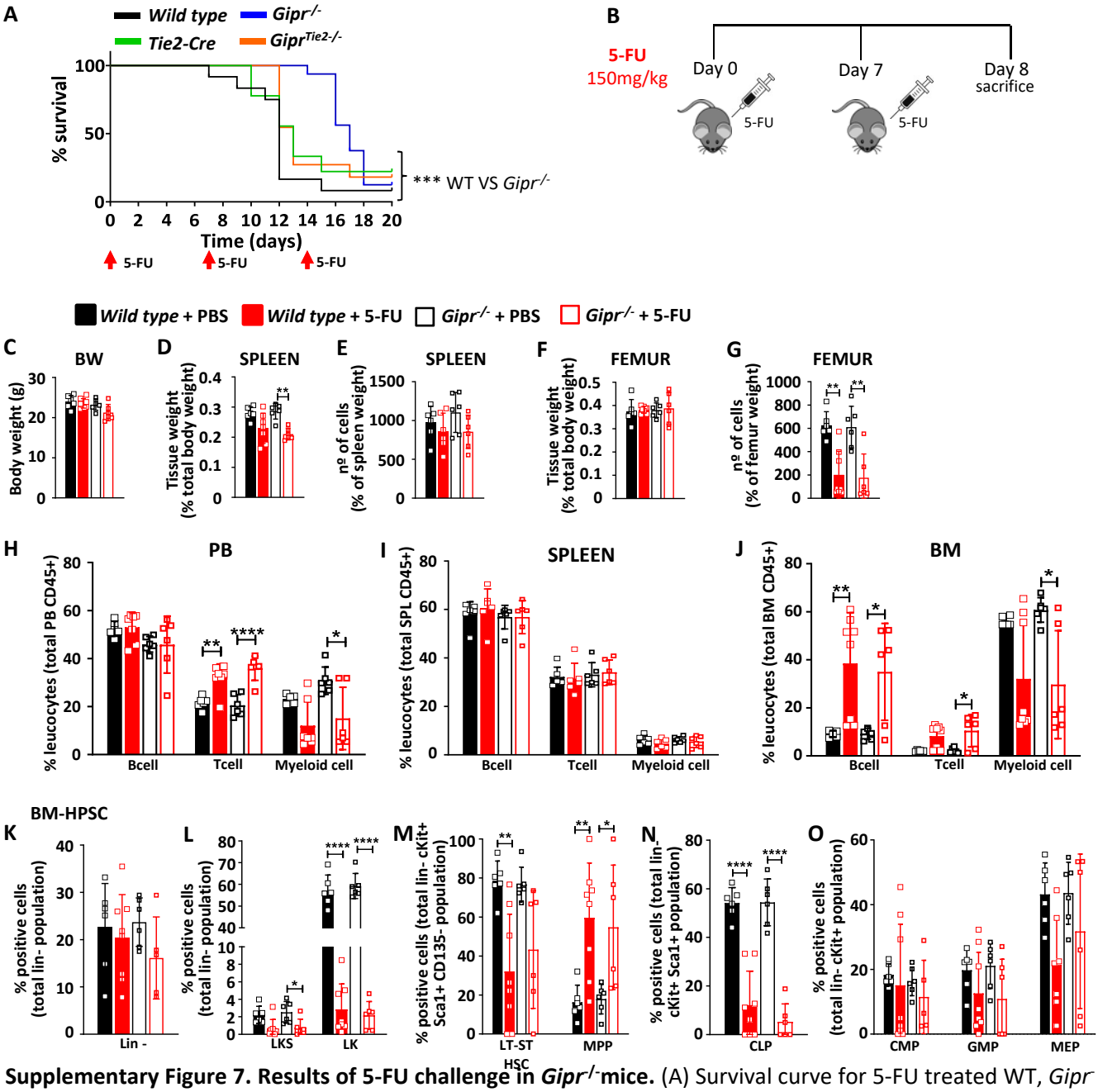
Supplementary Figure 5. Bone marrow cell frequencies in mice transplanted with *Gipr*$^{-/-}$ donor BM. Frequency of the total lineage negative cell population (A), LKS and LK (B), LT-ST HSC and MPP (C) and CLP (D) cells in bone marrow at 16 weeks after BMT from RCD-fed WT male mice that received a BMT from WT (Wild type$^{BMT\text{-}WT}$) or *Gipr*$^{-/-}$ (Wild type$^{BMT\text{-}Gipr\text{-}/\text{-}}$) donors (n=5-7/group). (E) Frequencies of B cells, T cells, M cells and monocyte lineage cells (neutrophils and monocytes) in bone marrow and frequency of the total lineage negative cell population (F), LKS and LK (G), CLP (H) and CMP, GMP and MEP (I) cells in bone marrow at 16 weeks after BMT from HFD-fed WT male mice that received a BMT from WT (Wild type$^{BMT\text{-}WT}$) or *Gipr*$^{-/-}$ (Wild type$^{BMT\text{-}Gipr\text{-}/\text{-}}$) donors (n=4/group). Data are presented as the mean ± SD. BMT=bone marrow transplant, RCD=regular chow diet, HFD=high fat diet, BM=bone marrow, BM-HPSC=bone marrow hematopoietic progenitor stem cells, M cell=myeloid cells, Lin-=lineage negative, LK=Lin-cKit+Sca1-, LKS=Lin-cKit+Sca1+, ST-HSC=short term hematopoietic stem cells, LT-HSC=long term hematopoietic stem cells, MPP=multipotent progenitor, CLP=common lymphoid progenitor, CMP=common myeloid progenitor, GMP=granulocyte-monocyte progenitor and MEP=megakaryocyte-erythroid progenitors.

Supplementary Figure 6



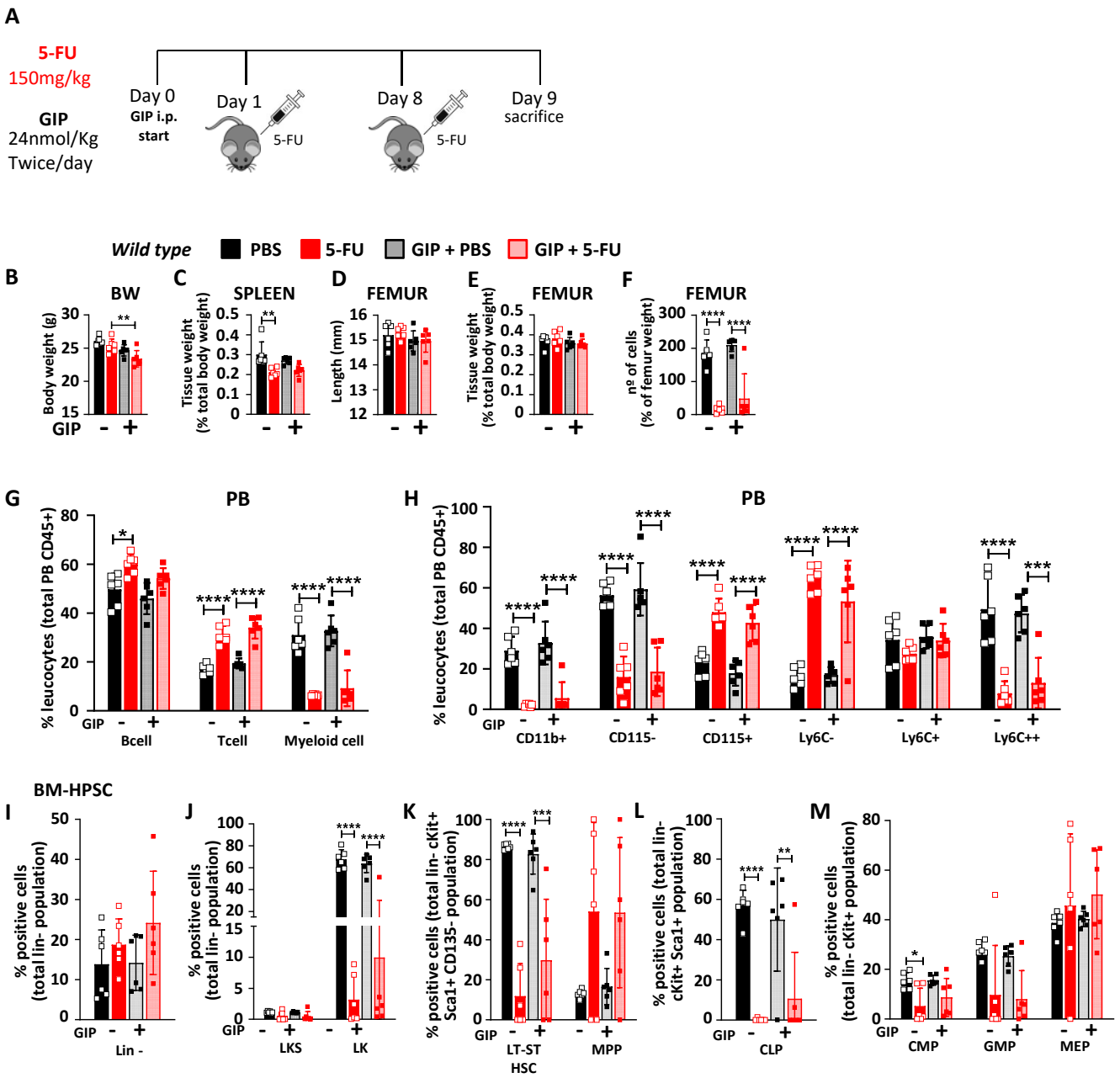
Supplementary Figure 6. Circulating GIP levels and bone marrow expression of TLR- and Notch signalling-related genes after 5-FU, LPS or Pam3CSK4 treatment. (A) Circulating GIP levels in 7 week-old WT and *Gipr*$^{-/-}$ male mice treated with PBS, 5-FU, LPS or Pam3CSK4 (n=4-15/group). (B-C) mRNA levels of the indicated Tlr and Notch-related genes, relative to *Ppia* gene expression, in isolated bone marrow cells from 7 week-old WT and *Gipr*$^{-/-}$ male mice that were treated with PBS, 5-FU, LPS or Pam3CSK4 ± GIP as indicated (n=4-15/group). Data are presented as the mean ± SD. **P*≤ 0.05, ***P*≤ 0.01, ****P* ≤ 0.001 and *****P* ≤ 0.0001. BM= Bone marrow, 5-FU=5-fluorouracil, PBS=Phosphate buffered saline, LPS=Lipopolysaccharide, Pam3CSK4=Pam3CysSerLys4 and GIP=glucose-dependent insulinotropic polypeptide.

Supplementary Figure 7



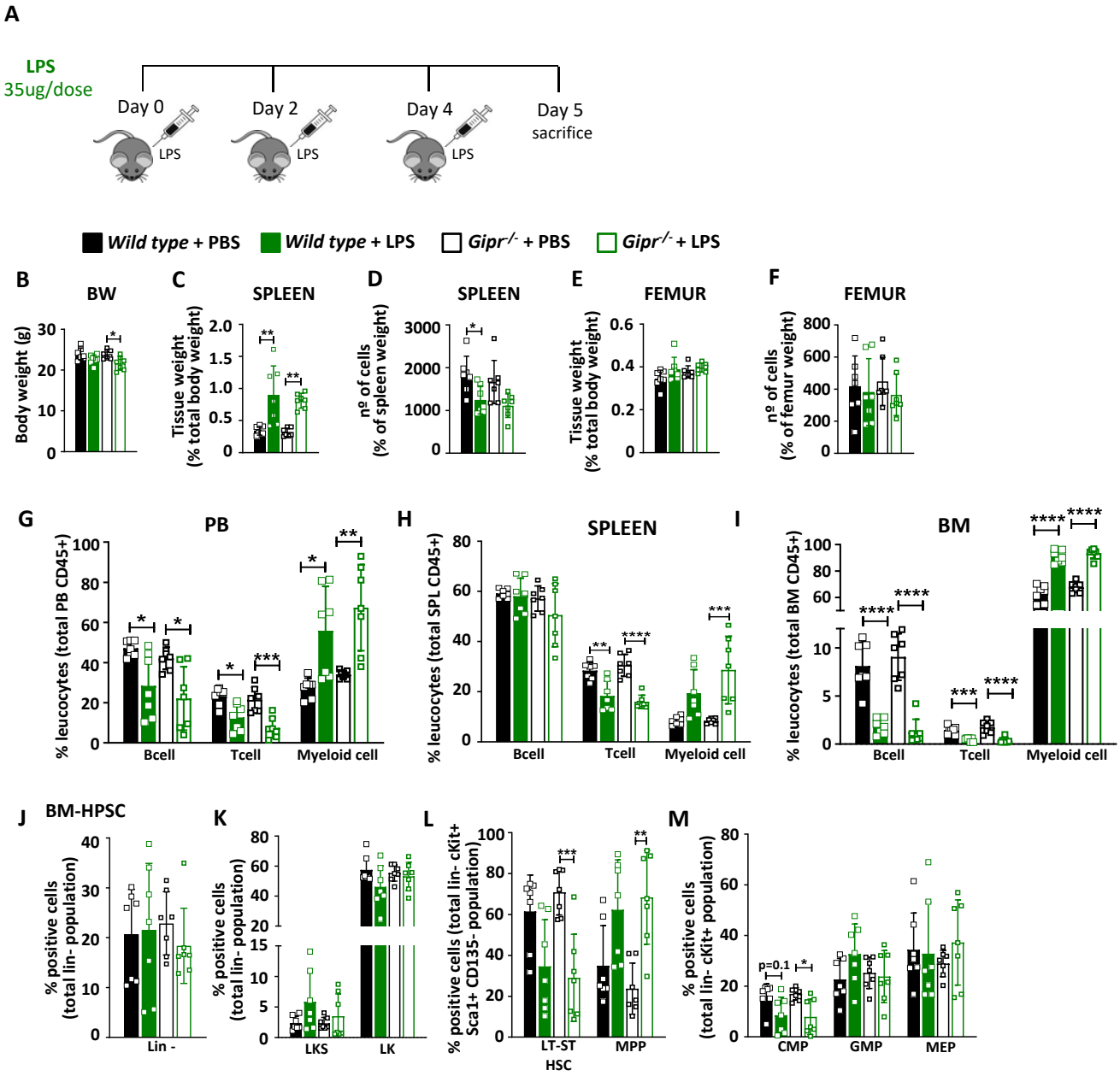
Supplementary Figure 7. Results of 5-FU challenge in *Gipr*$^{-/-}$mice. (A) Survival curve for 5-FU treated WT, *Gipr*$^{-/-}$, *Tie2*-cre and *Gipr*$^{Tie2-/-}$ male mice (n=9-16/group). (B) Treatment schedule for 5-Fluorouracil (5-FU) in *Gipr*$^{-/-}$ and WT males. Body weight (C), spleen weight relative to body weight (D), spleen cell numbers relative to spleen weight (E), femur weight relative to body weight (F), number of cells isolated from a single femur relative to femur weight (G) from 7week-old WT and *Gipr*$^{-/-}$ males, treated either with PBS or 5-FU as indicated (n=6-8/group). Frequencies of B cells, T cells and myeloid cells in peripheral blood (H), spleen (I) and bone marrow (J). Frequency of the total lineage negative cell population (K), LKS and LK population frequencies (L), LT-ST HSC and MPP (M), CLP (N) and CMP, GMP and MEP (O) cells in bone marrow from 7-week old WT and *Gipr*$^{-/-}$ males, treated either with PBS or 5-FU as indicated (n=6-8/group). PBS=Phosphate buffered saline, 5-FU=5-fluorouracil, BW=body weight, PB=peripheral blood, SPL=spleen, BM=Bone marrow, BM-HPSC=bone marrow hematopoietic progenitor stem cells, Lin-=lineage negative, LK=Lin-cKit+Sca1-, LKS=Lin-cKit+Sca1+, ST-HSC=short term hematopoietic stem cells, LT-HSC=long term hematopoietic stem cells, MPP= multipotent progenitor, CMP=common myeloid progenitor, GMP=granulocyte-monocyte progenitor and MEP=megakaryocyte-erythroid progenitors. *P≤0.05, **P≤0.01, ***P≤0.001 and ****P≤0.0001 is missing.

Supplementary Figure 8



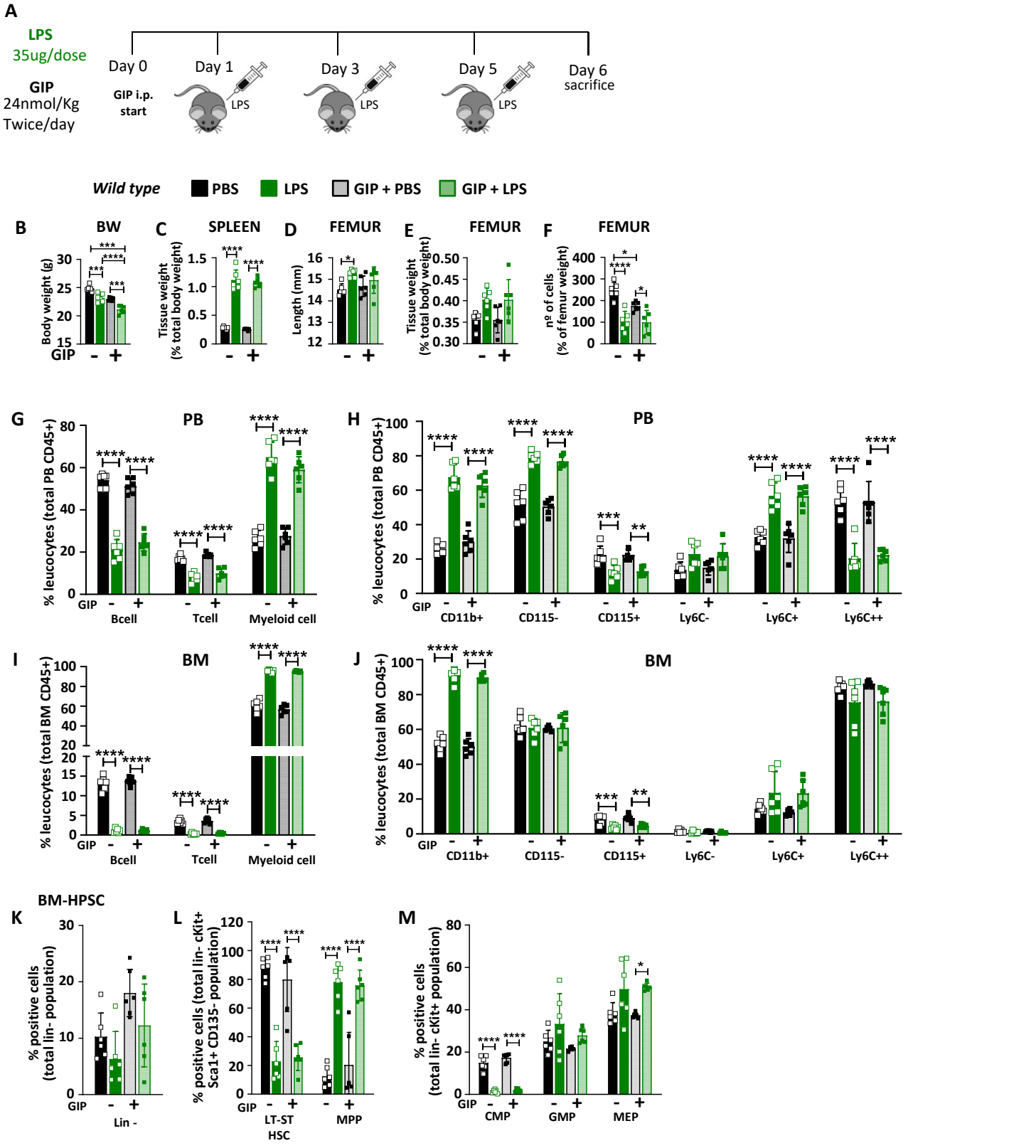
Supplementary Figure 8. Results of 5-FU challenge in WT mice treated with [DAla2]-GIP. (A) 5-FU treatment schedule in WT males treated with [DAla2]-GIP or PBS vehicle. Body weight (B), spleen weight relative to body weight (C), femur length (D), femur weight relative to body weight (E), and number of cells isolated from a single femur relative to femur weight (F). Frequencies of B cells, T cells, M cells (G) and monocyte lineage cells (neutrophils and monocytes) (H) in peripheral blood. Frequency of the total lineage negative cell population (I), LKS and LK populations (J), LT-ST HSC and MPP (K), CLP (L) and CMP, GMP and MEP (M) cells in bone marrow from 7-week old WT males treated with [D-Ala]-GIP and/or 5-FU and controls. Data are presented as the mean ± SD (n=6/group). *$P \leq 0.05$, **$P \leq 0.01$, *** $P \leq 0.001$ and ****$P \leq 0.0001$. 5-FU=5-fluorouracil, PBS=Phosphate buffered saline, GIP=glucose-dependent insulinotropic polypeptide, PB=peripheral blood, BM-HPSC=bone marrow hematopoietic progenitor stem cells, Lin-=lineage negative, LK=Lin-cKit+Sca1-, LKS=Lin-cKit+Sca1+, ST-HSC=short term hematopoietic stem cells, LT-HSC=long term hematopoietic stem cells, MPP= multipotent progenitor, CLP= common lymphoid progenitor, CMP=common myeloid progenitor, GMP=granulocyte-monocyte progenitor and MEP=megakaryocyte-erythroid progenitors.

Supplementary Figure 9



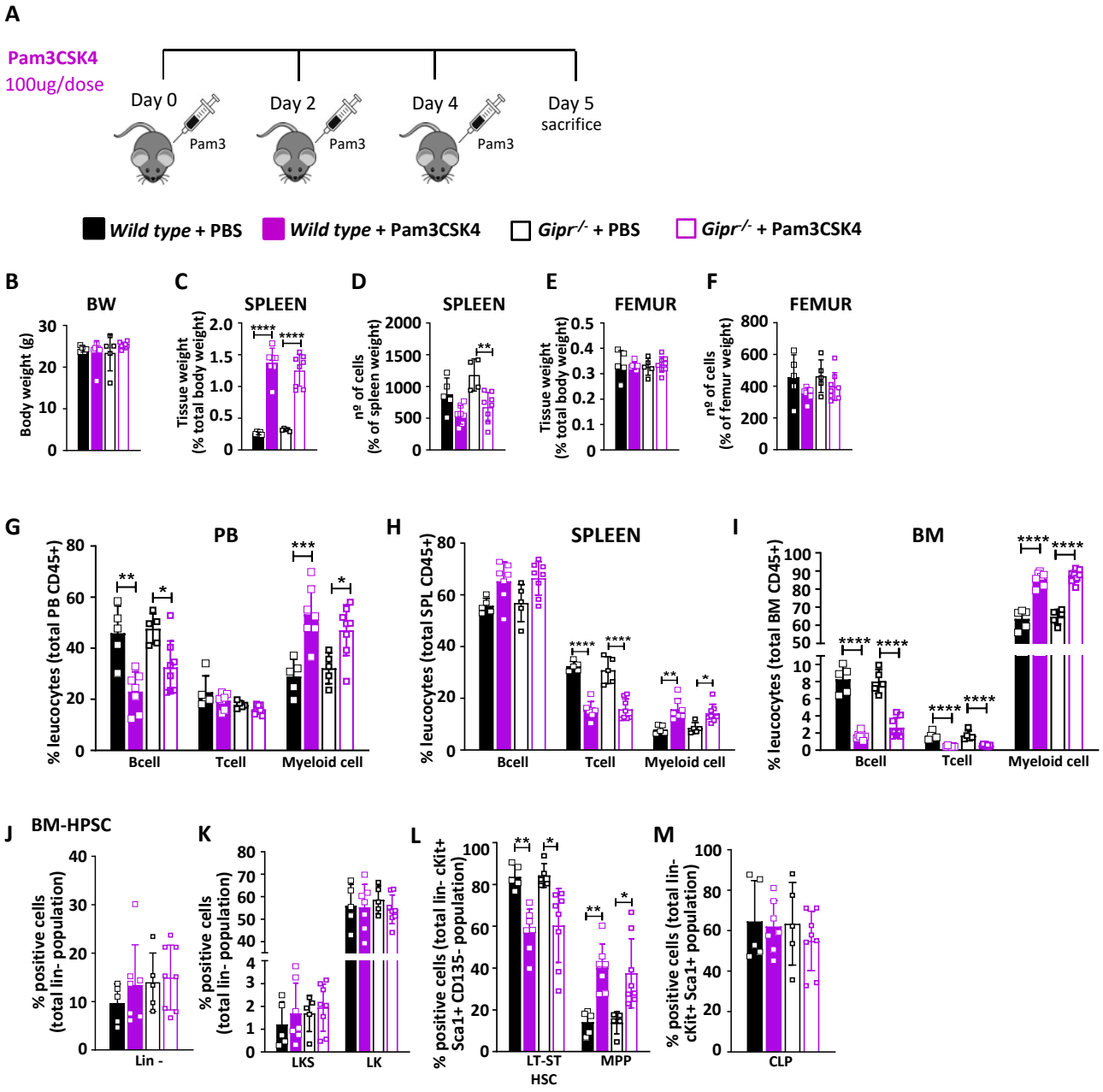
Supplementary Figure 9. Bone marrow responses to LPS in *Gipr*$^{-/-}$ mice. (A) Treatment schedule for LPS in *Gipr*$^{-/-}$ and WT males. Body weight (B), spleen weight relative to body weight (C), spleen cell numbers relative to spleen weight (D), femur weight relative to body weight (E), number of cells isolated from a single femur relative to femur weight (F) from 7 week-old WT and *Gipr*$^{-/-}$ males, treated either with PBS or LPS as indicated (n=6-7/group). Frequencies of B cells, T cells and myeloid cells in peripheral blood (G), spleen (H) and bone marrow (I). Frequency of the total lineage negative cell population (J), LKS and LK population frequencies (K), LT-ST HSC and MPP (L), and CMP, GMP and MEP (M) cells in bone marrow from 7-week old WT and *Gipr*$^{-/-}$ males, treated either with PBS or LPS as indicated (n=6-7/group). Data are presented as the mean ± SD (n=6-7/group). **P*≤ 0.05, ***P*≤ 0.01, *** *P* ≤ 0.001 and *****P* ≤ 0.0001. PBS=Phosphate buffered saline, LPS= Lipopolysaccharide, BW=body weight, PB=peripheral blood, BM=Bone marrow, BM-HPSC=bone marrow hematopoietic progenitor stem cells, Lin-=lineage negative, LK=Lin-cKit+Sca1-, LKS=Lin-cKit+Sca1+, ST-HSC=short term hematopoietic stem cells, LT-HSC=long term hematopoietic stem cells, MPP=multipotent progenitor, CMP=common myeloid progenitor, GMP=granulocyte-monocyte progenitor and MEP=megakaryocyte-erythroid progenitors.

Supplementary Figure 10



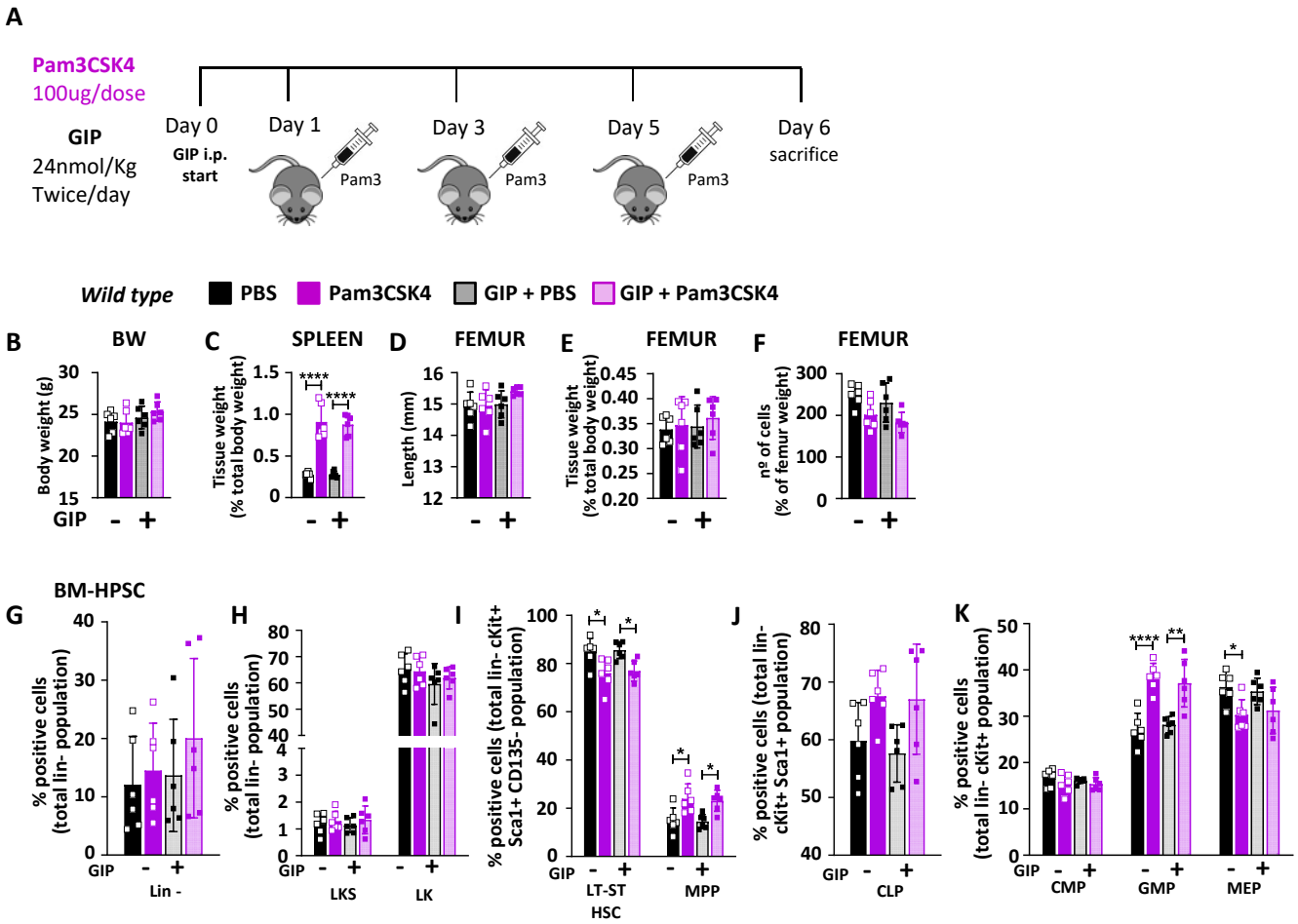
Supplementary Figure 10. Effect of LPS treatment alone or in combination with [DAla2]-GIP in WT mice. (A) LPS treatment schedule for WT males treated with [DAla2]-GIP or PBS vehicle. Body weight (B), spleen weight relative to body weight (C), femur length (D), femur weight relative to body weight (E) and number of cells isolated from a single femur relative to femur weight (F). Percentages of B cells, T cells, M cells and monocyte lineage cells (neutrophils and monocytes) in peripheral blood (G,H) and bone marrow (I,J). Frequency of the total lineage negative cell population (K), LT-ST HSC and MPP (L), and CMP, GMP and MEP (M) cells in bone marrow from 7-week old WT male mice treated with [D-Ala]-GIP and/or LPS and controls. Data are presented as the mean ± SD (n=6/group). *$P \leq 0.05$, *** $P \leq 0.001$ and ****$P \leq 0.0001$. LPS=Lipopolysaccharide, PBS=Phosphate buffered saline, GIP=glucose-dependent insulinotropic polypeptide, BW= body weight, PB=peripheral blood, BM=bone marrow, BM-HPSC=bone marrow hematopoietic progenitor stem cells, Lin-=lineage negative, ST-HSC=short term hematopoietic stem cells, LT-HSC=long term hematopoietic stem cells, MPP=multipotent progenitor, CMP= common myeloid progenitor, GMP=granulocyte-monocyte progenitor and MEP=megakaryocyte-erythroid progenitors.

Supplementary Figure 11



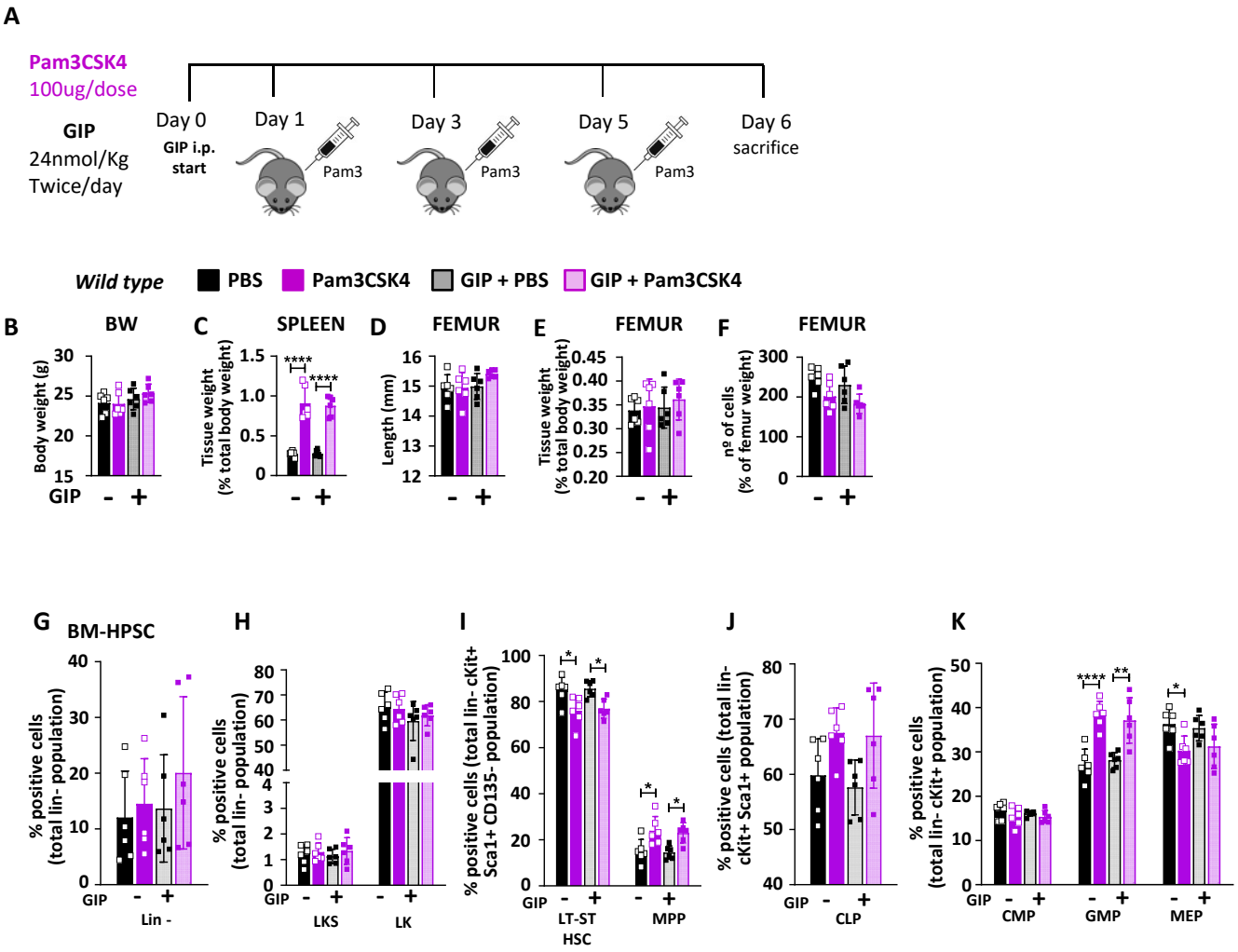
Supplementary Figure 11 Pam3CSK4 treatment has no impact on haematopoiesis in *Gipr*$^{-/-}$ mice. (A) Pam3CSK4 treatment schedule in WT and *Gipr*$^{-/-}$ males. Body weight (B), spleen weight relative to body weight (C), spleen cell numbers relative to spleen weight (D), femur weight relative to body weight (E), number of cells isolated from a single femur relative to femur weight (F) from 7 week-old WT and *Gipr*$^{-/-}$ males, treated either with PBS or Pam3CSK4 as indicated (n=5-8/group). Frequencies of B cells, T cells and myeloid cells in peripheral blood (G), spleen (H) and bone marrow (I). Frequency of the total lineage negative cell population (J), LKS and LK population frequencies (K), LT-ST HSC and MPP (L), and CLP (M) cells in bone marrow from 7-week old WT and *Gipr*$^{-/-}$ males, treated either with PBS or Pam3CSK4 as indicated (n=5-8/group). Data are presented as the mean ± SD. **P*≤ 0.05, ***P*≤ 0.01, *** *P* ≤ 0.001 and *****P* ≤ 0.0001. PBS=Phosphate buffered saline, Pam3CSK4=Pam3CysSerLys4, BW= body weight, PB=peripheral blood, BM=bone marrow, BM-HPSC=bone marrow hematopoietic progenitor stem cells, Lin-=lineage negative, LK=Lin-cKit+Sca1-, LKS=Lin-cKit+Sca1+, ST-HSC=short term hematopoietic stem cells, LT-HSC=long term hematopoietic stem cells, MPP=multipotent progenitor, and CLP= common lymphoid progenitor.

Supplementary Figure 12



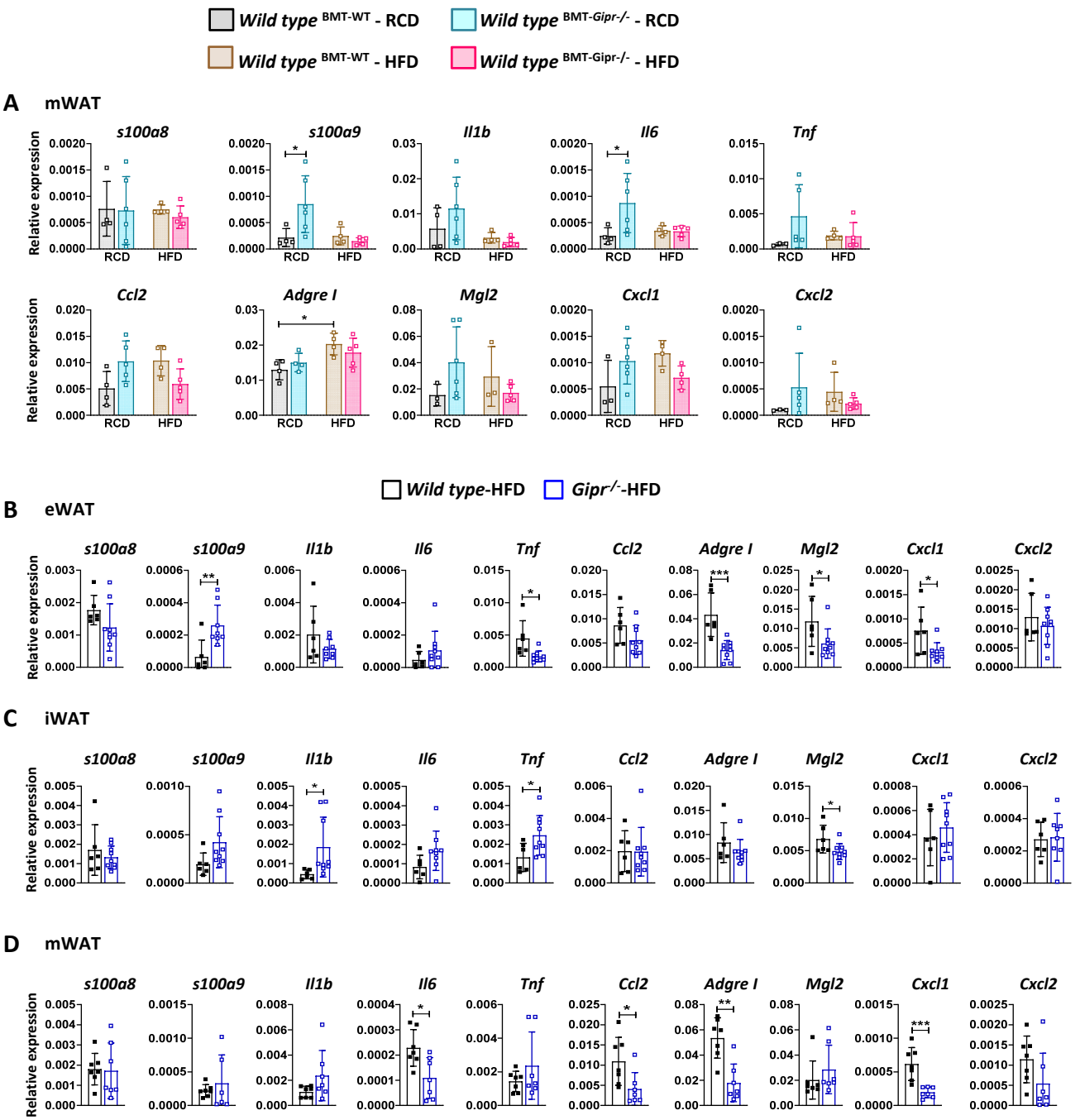
Supplementary Figure 12 (related to Main Figure 3 and 4). The haematopoietic response to Pam3CSK4 is not impaired in WT mice treated with [DAla2]-GIP. (A) Pam3CSK4 treatment schedule in WT males treated with [DAla2]-GIP or PBS vehicle. Body weight (B), spleen weight relative to body weight (C), femur length (D), femur weight relative to body weight (E), and number of cells isolated from a single femur relative to femur weight (F) from 7-week old WT male mice treated with [D-Ala]-GIP and/or Pam3CSK4 and controls (n=6/group). Frequency of the total lineage negative cell population (G), LKS and LK population frequencies (H), LT-ST HSC and MPP (I), CLP (J), and CMP, GMP and MEP (K) cells in bone marrow from 7-week old WT male mice treated with [D-Ala]-GIP and/or Pam3CSK4 and controls (n=6/group). Data are presented as the mean ± SD. *$P \leq 0.05$, ** $P \leq 0.01$ and ****$P \leq 0.0001$. PBS=Phosphate buffered saline, GIP=glucose-dependent insulinotropic polypeptide Pam3CSK4=Pam3CysSerLys4, BW=body weight, BM-HPSC=bone marrow hematopoietic progenitor stem cells, Lin-=lineage negative, LK=Lin-cKit+Sca1-, LKS=Lin-cKit+Sca1+, ST-HSC=short term hematopoietic stem cells, LT-HSC=long term hematopoietic stem cells, MPP=multipotent progenitor, CLP=common lymphoid progenitor, CMP=common myeloid progenitor, GMP=granulocyte-monocyte progenitor and MEP=megakaryocyte-erythroid progenitors.

Supplementary Figure 12



Supplementary Figure 12 The haematopoietic response to Pam3CSK4 is not impaired in WT mice treated with [DAla2]-GIP. (A) Pam3CSK4 treatment schedule in WT males treated with [DAla2]-GIP or PBS vehicle. Body weight (B), spleen weight relative to body weight (C), femur length (D), femur weight relative to body weight (E), and number of cells isolated from a single femur relative to femur weight (F) from 7-week old WT male mice treated with [D-Ala]-GIP and/or Pam3CSK4 and controls (n=6/group). Frequency of the total lineage negative cell population (G), LKS and LK population frequencies (H), LT-ST HSC and MPP (I), CLP (J), and CMP, GMP and MEP (K) cells in bone marrow from 7-week old WT male mice treated with [D-Ala]-GIP and/or Pam3CSK4 and controls (n=6/group). Data are presented as the mean ± SD. *$P \leq 0.05$, *** $P \leq 0.001$ and ****$P \leq 0.0001$. PBS=Phosphate buffered saline, Pam3CSK4=Pam3CysSerLys4, BW= body weight, PB=peripheral blood, BM=bone marrow, BM-HPSC=bone marrow hematopoietic progenitor stem cells, Lin-=lineage negative, LK=Lin-cKit+Sca1-, LKS=Lin-cKit+Sca1+, ST-HSC=short term hematopoietic stem cells, LT-HSC=long term hematopoietic stem cells, MPP=multipotent progenitor, CLP= common lymphoid progenitor, CMP= common myeloid progenitor, GMP=granulocyte-monocyte progenitor and MEP=megakaryocyte-erythroid progenitors.

Supplementary Figure 13



Supplementary Figure 13. Gene expression of inflammatory markers in fat depots after BMT and in *Gipr*$^{-/-}$ fed a HFD. Adipose tissue mRNA levels, relative to *Ppia* expression, of inflammatory genes. Data in A are from RCD-fed (n= 4-7/group) or HFD-fed (n= 4-5/group) WT mice 16 weeks after receiving a BMT from WT (wild type$^{BMT\text{-}WT}$) or *Gipr*$^{-/-}$ (wild type$^{BMT\text{-}Gipr\text{-}/\text{-}}$) donors. Data in B-D are from WT or *Gipr*$^{-/-}$ 30-34 weeks old males fed a HFD. Data are presented as the mean ± SD. **P*≤ 0.05, ***P* ≤ 0.01 and ****P* ≤ 0.001. BMT=bone marrow transplant, RCD=regular chow diet, HFD=high fat diet, mWAT=mesenteric white adipose tissue, eWAT=epididymal white adipose tissue, and iWAT=inguinal white adipose tissue.