Supporting Information

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LSD1^{-/-} **Fig. S2.** LSD1-deficient mice have acute expansion of hyperproliferative and hyperinflammatory myeloid progenitors in BM. (A) The representative expression of CD11b and GR-1 of BM cells from *LSD1^{fl/fl}*. Mx-Cre (*LSD1^{-/-}*) mice and the control mice are shown. (*B*) The representative expression of CD11b and TER119 of BM cells from *LSD1^{fl/fl}*. Mx-Cre (*LSD1^{-/-}*) mice and the control are shown. Numbers are indicated as the percentage of indicated quadrant population among total BM cells; (C) The representative expression of CD11b and CD90 of BM cells from *LSD1^{fl/fl}*. Mx-Cre (*LSD1^{-/-}*) mice and the control are shown. Sumbers are indicated as the percentage of indicated quadrant population among total BM cells. (*D*) The representative expression of CD11b and Sca1 of BM cells from *LSD1^{fl/fl}*. Mx-Cre (*LSD1^{-/-}*) mice and the control are shown. (*E*) Total BM cells were isolated from *LSD1^{fl/fl}*. Mx-Cre (*LSD1^{-/-}*) mice and the control are shown. (*E*) Total BM cells were isolated from *LSD1^{fl/fl}*. Mx-Cre (*LSD1^{-/-}*) mice and the control were cultured in methylcellulose-based medium supplement with a mixture of cytokines. The number of BFU colonies is shown after in vitro serial transfer into the methylcellulose-based medium. Data are shown as an average of triplicates, and error bar indicates the SD. (*F*) *LSD1*-deficient BM cells gain self-renewal (colonies at *Left*) and become SCF- and IL-3-independent (colonies at *Right*). (*G*) Total or CD11b-positive BM cells were determined from *LSD1^{-/-}* mice and the control mice.



Fig. S3. Altered HSC homeostasis in mice during sepsis. (A) Schematic experimental designs of endotoxin (LPS)-induced endotoxic shock. (B) The representative expression of CD11b, GR-1, and F4/80 on peritoneal cavity cells after indicated hours of LPS injection is shown. (C) Total BM cells and peritoneal cavity cells were isolated from sepsis-induced mice and cultured for 24 h in vitro, and expression of CFSE gated on lineage negative cKit positive cells is shown. (D) Expression of *iNOS* (*Upper*) and *TNF-α* (*Lower*) upon LPS treatment in control, inflammation, and sepsis conditions. (E) Recruitment of LSD1 (blue bar) and Nurr1 (orange bar) onto *iNOS* promoter (*Upper*) or *TNF-α* promoter (*Lower*) measured by ChIP assay.



Fig. S4. miRNA-mediated down-regulation of LSD1 during sepsis. (*A*) Luciferase report assays using 2-kb LSD1 promoter, revealing no effect of TNF- α or IL-1 β treatment on reporter activity. (*B*) Luciferase report assays using *LSD1* 3' UTR, revealing repressive effect of TNF- α or IL-1 β treatment on reporter activity. (*C*) Schematic diagram of miR-seq experiments. (*D*) Heat map of miRNAs induced upon treatment. (*E*) Western blot analysis, revealing LSD1 expression is regulated by miRNAs upon IL-1 β treatment. Seed sequences on LSD1 3' UTR are mutated accordingly, and LSD1 expression are measured in the presence or absence of IL-1 β treatment. (*F*) The representative expression of CD11b and GR-1 on BM cells during animal models of sepsis is shown. After indicated time of 24 mg/kg LPS injection, mice with BMT using anti-miR group A+B or control are analyzed based on expression of CD11b and GR-1 expression on BM cells.

			B			C
Term ID	Enrichment	Target Genes	Term ID	Enrichment	Target Genes	25 -
Chemokine signaling pathway	3.47e-10	40	Osteoclast differentiation	2.99e-05	27	
Pathways in cancer	8.66e-06	47	B cell receptor signaling pathway	0.00064713	18	20 LSD
Endocytosis	3.65e-05	35	MAPK signaling pathway	0.00182989	41	20
MAPK signaling pathway	0.00015295	37	Pathways in cancer	0.00346215	47	5 .c
Cytokine-cytokine receptor interaction	0.00044347	30	Nicotinate & nicotinamide metabolism	0.00673496	8	은 IPF
Chronic myeloid leukemia	0.00114942	14	Endocytosis	0.00735069	34	T
Natural killer cell mediated cytotoxicity	0.0039129	18	Natural killer cell mediated cytotoxicity	0.01332254	20	S 10-
Osteoclast differentiation	0.0062748	17	Lysine degradation	0.01661433	11	0
ErbB signaling pathway	0.00632638	14	Chronic myeloid leukemia	0.02495519	13	5-
T cell receptor signaling pathway	0.00781131	16	Leishmaniasis	0.03556745	11	
Melanogenesis	0.00792179	15	Valine, leucine & isoleucine degradation	0.03702186	11	0
Prion diseases	0.00900191	8	T cell receptor signaling pathway	0.03708328	17	S. AL
Leukocyte transendothelial migration	0.009974	16	Insulin signaling pathway	0.04165683	22	L. WI
Regulation of actin cytoskeleton	0.01036099	25	Cytokine-cytokine receptor interaction	0.04876916	28	4
Acute myeloid leukemia	0.01083483	10	Chemokine signaling pathway	0.05103261	24	
Graft-versus-host disease	0.01309585	7	Cell adhesion molecules (CAMs)	0.05316581	17	
VEGF signaling pathway	0.0143949	12	Fc gamma R-mediated phagocytosis	0.05710328	15	
Amoebiasis	0.01707352	14	Regulation of actin cytoskeleton	0.06299794	27	
Complement & coagulation cascades	0.01849339	10	NOD-like receptor signaling pathway	0.07749851	9	
Lysine degradation	0.01990634	9	Adherens junction	0.07766841	12	
Focal adhesion	0.02061521	23		A STREET AND ADDREET A DESCRIPTION		
Staphylococcus aureus infection	0.0288757	7				
Adherens junction	0.03201267	11				
Antigen processing & presentation	0.03653983	10				
Adipocytokine signaling pathway	0.04707331	10				

Fig. S5. LSD1 regulates gene expression. (A) Gene Ontology (GO) term analysis of up-regulated genes upon LSD1 deletion. (B) GO term analysis of downregulated genes upon LSD1 deletion. (C) ChIP-PCR analysis of histone modifications on Gfi1b locus.

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