Supplemental Figure legends

Supplemental Figure 1. Macrophage depletion affected the mortality in LPS-induced sepsis. (A) The ratio of F4/80⁺CD11b⁺ splenic macrophages after i.v. injection of clodronate liposome (CLOP, 0.1ml/10g, the left of A) and PBS-control liposome (CONT, 0.1ml/10g, the right of A) for 24 hours. (B) The C57BL/6J mice were pretreated with i.v. injection of CONT or CLOP for 24 hours before treated with i.p. injection of LPS (40 mg/kg) or LPS (40 mg/kg) plus 3×10⁷ peritoneal macrophages (n=8, *P<0.05, **P<0.01, CLOP vs. CONT; #P<0.05, CLOP vs. CLOP+Mφ). Survival analysis utilized Log-rank (Mantel-Cox) test.

Supplemental Figure 2. Swiprosin-1 deletion decreased macrophages recruitment after CLP treatment. Swiprosin-1 knockout mice showed impaired macrophages recruitment in the lung and kidney after CLP treatment for 18 hours (green fluorescence: F4/80⁺ macrophage, blue fluorescence: nucleus, scan bar=200μm).

Supplemental Figure 3. Effect of swiprosin-1 on macrophages migration after LPS treatment. (A) Cell viability of macrophages after LPS treatment for 6 hours (n=6), results depicted as mean ± SEM. (B) Wound healing analysis in macrophages after LPS treatment.

Supplemental Figure 4. Effect of swiprosin-1 on mRNA levels of pro-inflammatory cytokines in macrophages after LPS treatment. The mRNA
levels of IL-1β, IL-6, and TNF-α in macrophages after LPS treatment (n=3, *P<0.05, ***P<0.001, WT-LPS vs. WT-0 hour; ##P<0.01, ###P<0.001, KO-LPS vs. KO-0 hour; + + + P<0.001, WT-LPS vs. KO-LPS at the same time point), ANOVA (LSD test), results depicted as mean ± SEM.

**Supplemental Figure 5. Effect of swiprosin-1 on IL-10 expression in macrophages after LPS treatment.** IL-10 mRNA and protein expression in macrophages after LPS treatment (n=3-6, *P<0.05, **P<0.01, ***P<0.001 WT-LPS vs. WT-0 hour; #P<0.05, ###P<0.001, KO-LPS vs. KO-0 hour; +P<0.05, + + P<0.01, WT-LPS vs. KO-LPS at the same time point), ANOVA (LSD test), results depicted as mean ± SEM.

**Supplemental Figure 6. Activation of NF-κB and MAPKs pathways in macrophages after LPS treatment.** (A) Phosphorylation of IkBα, IKKα/β, and p65 in macrophages after LPS stimulation (n=3, *P<0.05, **P<0.01 WT-LPS vs. WT-0 hour; #P<0.05, ###P<0.01, KO-LPS vs. KO-0 hour), ANOVA (LSD test), results depicted as mean ± SEM. (B) Phosphorylation of p38, JNK, and ERK in macrophages after LPS stimulation (n=3, *P<0.05, **P<0.01 WT-LPS vs. WT-0 hour; #P<0.05, ###P<0.01, KO-LPS vs. KO-0 hour), ANOVA (LSD test), results depicted as mean ± SEM.
Supplemental Figure 7. Swiprosin-1 deletion attenuated IFN-γ expression in macrophages and T cells after LPS treatment. (A) mRNA and protein expression of IFN-γ in macrophages after LPS treatment for 12 hours (n=3-6, **P<0.01, WT LPS compared with WT 0h; +++P<0.01, ++++P<0.001, KO LPS compared with WT LPS at the same time point), ANOVA (LSD test), results depicted as mean ± SEM. (B) IFN-γ level in T cells after LPS treatment for 12 hours (n=6, ***P<0.001, WT-LPS vs. WT-CON; +++P<0.001, WT-LPS vs. KO-LPS), ANOVA (LSD test), results depicted as mean ± SEM.

Supplemental Figure 8. Effect of swiprosin-1 on mRNA levels of TLR4/CD14 in macrophages after LPS treatment. TLR4 and CD14 gene expression in macrophages after LPS treatment for 12 hours (n=3, **P<0.01, WT-LPS vs. WT-CON; ##P<0.01, KO-LPS vs. KO-CON), ANOVA (LSD test), results depicted as mean ± SEM.

Supplemental Figure 9. Effect of swiprosin-1 on pro-inflammatory cytokines and JAK-STAT pathway in THP-1 cells after LPS treatment. (A) Expression of swiprosin-1 in swiprosin-1-siRNA-treated THP-1 cells after LPS treatment for 12 hours (n=3, ***P<0.001, NC-LPS vs. NC-CON; ###P<0.001, siRNA-LPS vs. siRNA-CON; +++P<0.001, siRNA-LPS vs. NC-LPS), ANOVA (LSD test), results depicted as mean ± SEM. (B) Expression of pro-inflammatory cytokines in swiprosin-1-siRNA-treated THP-1 cells after LPS treatment for 12 hours (n=6,
**P<0.01, ***P<0.001, NC-LPS vs. NC-CON; #P<0.01, ###P<0.001, siRNA-LPS vs. siRNA-CON; ‡‡P<0.01, ‡‡‡P<0.001, siRNA-LPS vs. NC-LPS), ANOVA (LSD test), results depicted as mean ± SEM. (C) Activation of JAK-STAT pathway in swiprosin-1-siRNA-treated THP-1 cells after LPS treatment for 12 hours (n=3, **P<0.01, ***P<0.001, NC-LPS vs. NC-CON; #P<0.05, ###P<0.001, siRNA-LPS vs. siRNA-CON; ‡P<0.05, ‡‡P<0.01, ‡‡‡P<0.001, siRNA-LPS vs. NC-LPS), ANOVA (LSD test), results depicted as mean ± SEM.
Supplemental Methods

Swiprosin-1 siRNA Transfection. Plate $10^6$ THP-1 cells in 500µl RPMI-1640 medium without antibiotics. Dilute 2µl swiprosin-1 siRNA (sequence: 3’-UCAAGGAGUUCUCAGGAAATT’, 3’-UCCUGGAGAACUUUGATT-5’) oligomer in 50µl RPMI medium without serum and 1µl Lipofectamine 2000 in 50µl RPMI medium. Mix gently and incubate for 5 minutes at room temperature. After the 5-minute incubation, combine the diluted oligomer with the diluted Lipofectamine 2000. Mix gently and incubate for 20 minutes at room temperature. Add the oligomer-Lipofectamine 2000 complexes to each well containing cells and medium. Change the medium after 6 hours and incubate the cells with 100ng/ml PMA (Beyotime Biotechnology, Jiangsu, China) for 24 hours, and then detect the expression of RNA and protein.