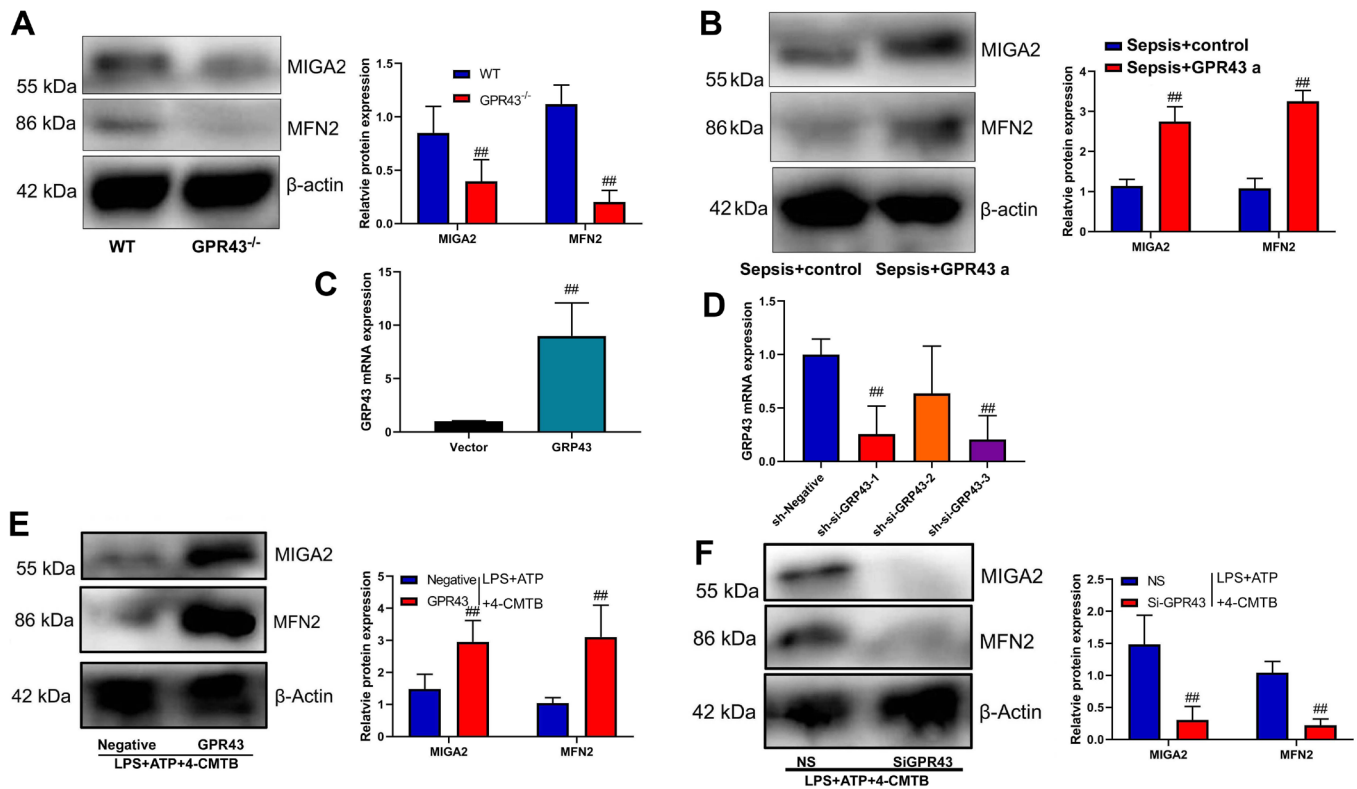
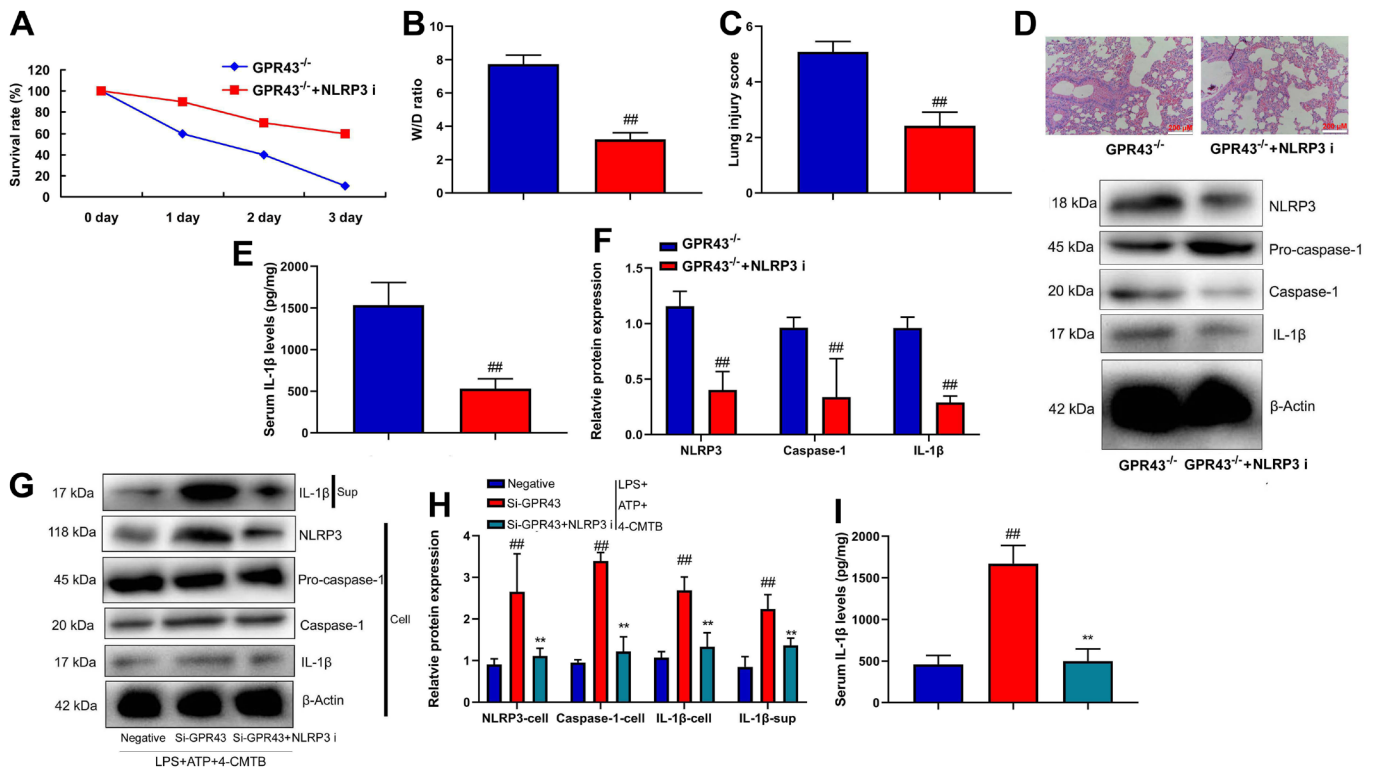


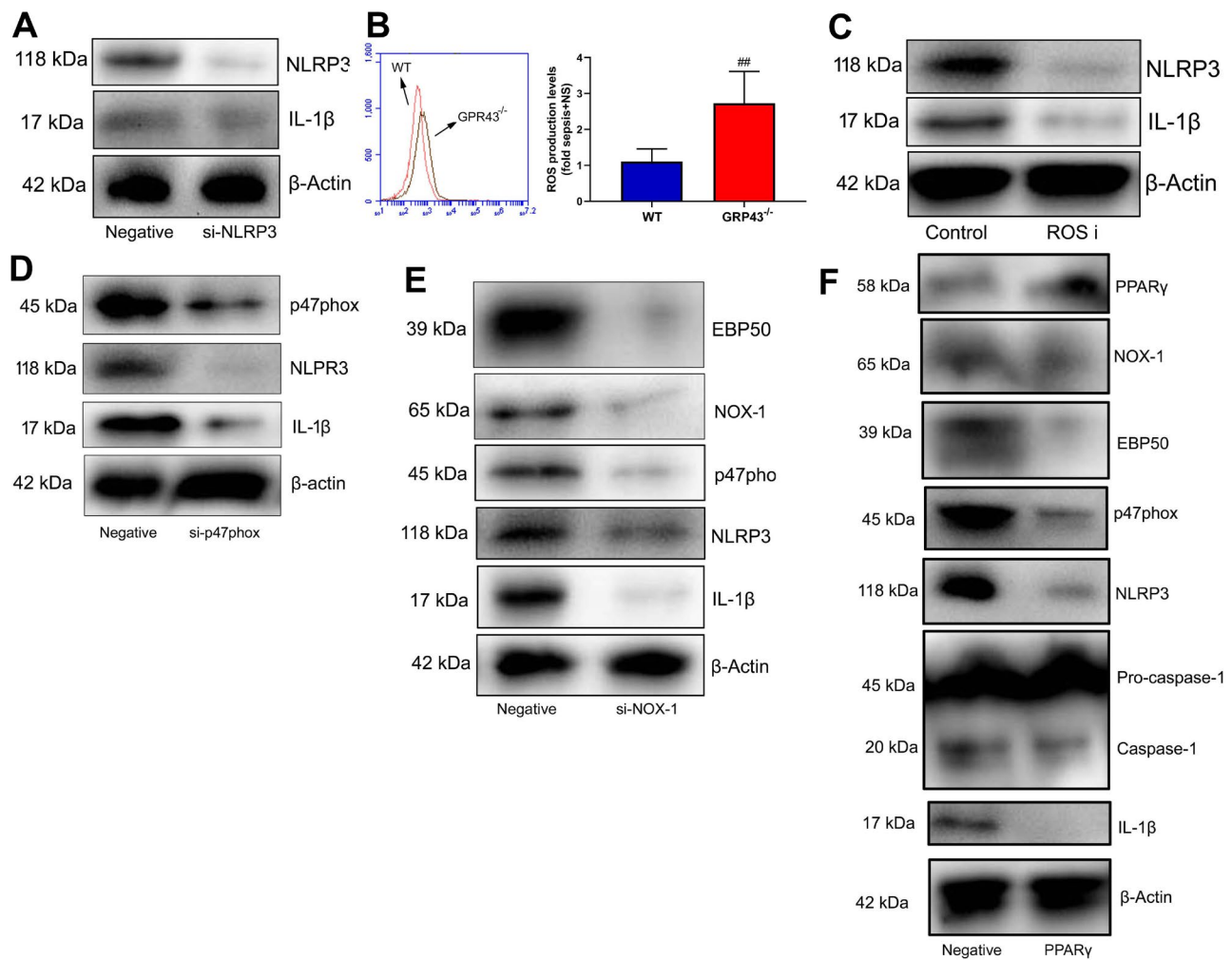
SUPPLEMENTARY FIGURES



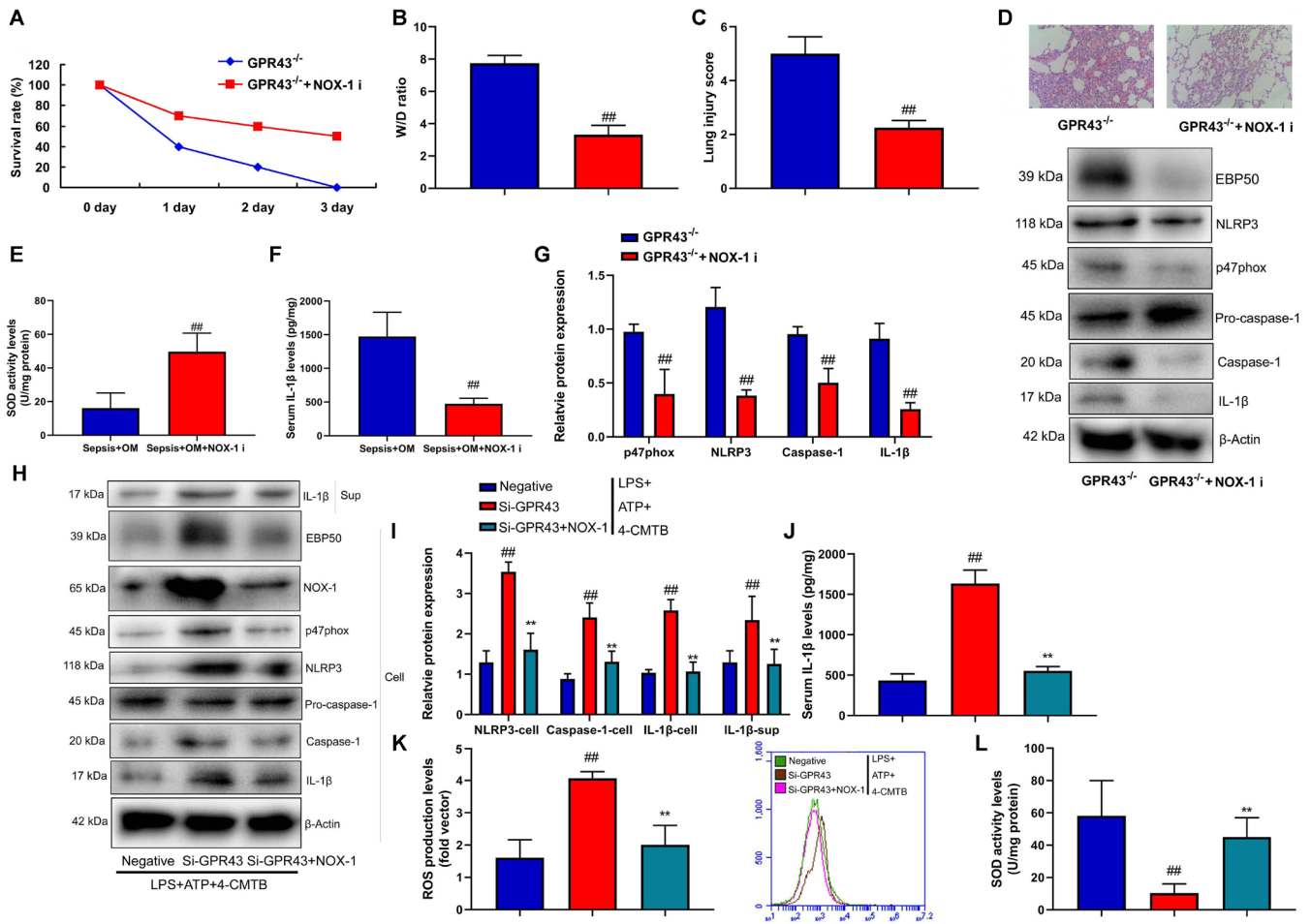
**Supplementary Figure 1. Mitochondrial fission and GPR43 expression *in vitro* model.** MIGA2 and MFN2 protein expressions in GPR43<sup>-/-</sup> mice with CLP (A) for 24 h; MIGA2 and MFN2 protein expressions in CLP mice with GPR43 agonist (B) for 24 h; GPR43 expression *in vitro* model by over-expression of GPR43 (C) for 24 h; GPR43 expression *in vitro* model by down-regulation of GPR43 (D) for 24 h; MIGA2 and MFN2 protein expressions in macrophage by up-regulation of GPR43 and LPS+ATP+GPR43 agonist (E) for 24 h; MIGA2 and MFN2 protein expressions in macrophage by down-regulation of GPR43 and LPS+ATP+GPR43 agonist (F) for 24 h; Sepsis+control, CLP mice with normal saline; Sepsis+GRP43 a, CLP mice with i GPR43 agonist (4-CMTB, 10 mg/kg, i.p.); WT, WT mice with CLP; GPR43<sup>-/-</sup>, GPR43<sup>-/-</sup> mice with CLP; Negative, negative control; Negative, negative control; GPR43, over-expression of GPR43; NS, si-negative control; Si-GPR43, down-regulation of GPR43; LPS+ATP+4-CMTB, macrophage by treated with LPS+ATP+4-CMTB. ##p<0.01 compared with WT mice with CLP or ###p<0.01 compared with CLP mice with normal saline; ###p<0.01 compared with negative control or si-negative control.



**Supplementary Figure 2. GPR43 is involved in the activation of NLRP3 Inflammasome in sepsis model.** Survival rate (A) in GPR43<sup>-/-</sup> mice of CLP with NLRP3 inhibitor for 72 h; W/D rate (B), lung injury score (C), lung tissue using HE staining (D), serum IL-1β levels (E), EBP50/GPR43/NLRP3/caspase-1/IL-1β protein expressions (F) in GPR43<sup>-/-</sup> mice of CLP with NLRP3 inhibitor for 24 h; NOX-1/EBP50, GPR43, NLRP3, Caspase-1 and IL-1β protein expressions in cells and IL-1β protein expression in supernatant (G, I), IL-1β levels (H) in macrophage by down-regulation of GPR43 and LPS+ATP+GPR43 agonist for 24 h. GPR43<sup>-/-</sup>, GPR43<sup>-/-</sup> mice with CLP; GPR43<sup>-/-</sup> + NLRP3 i, GPR43<sup>-/-</sup> mice of CLP with NLRP3 inhibitor; Negative, negative control; Si-GPR43, down-regulation of GPR43; NLRP3 i, NLRP3 inhibitor; LPS+ATP+4-CMTB, macrophage by treated with LPS+ATP+4-CMTB. ##p<0.01 compared with GPR43<sup>-/-</sup> mice with CLP or GPR43<sup>-/-</sup> mice with CLP; \*\*p<0.01 compared with down-regulation of GPR43.



**Supplementary Figure 3. Expression of protein *in vitro* model and ROS production.** NLRP3/ IL-1 $\beta$  protein expressions *in vitro* model by si-NLRP3 (A); ROS production levels in macrophage of CLP mice with OM (B) for 24 h; NLRP3/ IL-1 $\beta$  protein expressions *in vitro* model by ROS inhibitor (C); p47phox/NLRP3/ IL-1 $\beta$  protein expressions *in vitro* model by si-p47phox (D); EBP50/NOX-1/ p47phox/NLRP3/ IL-1 $\beta$  protein expressions *in vitro* model by si-NOX-1 (E); PPAR $\gamma$ /EBP50/NOX-1/ p47phox/NLRP3/ IL-1 $\beta$  protein expressions *in vitro* model by PPAR $\gamma$  (F). ## $p < 0.01$  compared with negative or control or DMSO group.



**Supplementary Figure 4. GPR43 is involved in the activation of NOX-1 in sepsis model.** Survival rate (A) in CLP mice with OM or NOX-1 inhibitor for 72 h; W/D rate (B), lung injury score (C), lung tissue using HE staining (D), SOD activity levels (E), serum IL-1 $\beta$  levels (F), EBP50/GPR43/NLRP3/caspase-1/IL-1 $\beta$  protein expressions (G) in CLP mice with OM or NOX-1 inhibitor for 24 h; NOX-1/EBP50, p47phox, NLRP3, Caspase-1 and IL-1 $\beta$  protein expressions in cells and IL-1 $\beta$  protein expression in supernatant (H, I), IL-1 $\beta$  levels (J), ROS production level (K), and SOD activity levels (L) in macrophage by down-regulation of GPR43 and LPS+ATP+GPR43 agonist for 24 h. GPR43<sup>-/-</sup>, GPR43<sup>-/-</sup> mice with CLP; GPR43<sup>-/-</sup>+NOX-1 i, GPR43<sup>-/-</sup> mice of CLP with NOX-1 inhibitor; Negative, negative control; Si-GPR43, down-regulation of GPR43; NOX-1 i, NOX-1 inhibitor; LPS+ATP+4-CMTB, macrophage by treated with LPS+ATP+4-CMTB. ##p<0.01 compared with GPR43<sup>-/-</sup> mice with CLP or GPR43<sup>-/-</sup> mice with CLP; \*\*p<0.01 compared with down-regulation of GPR43.