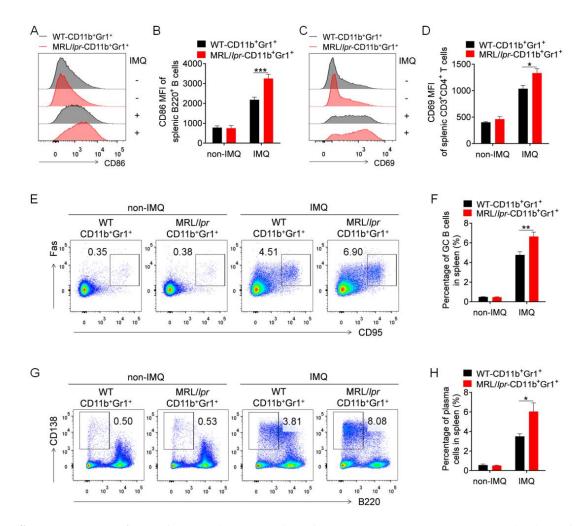
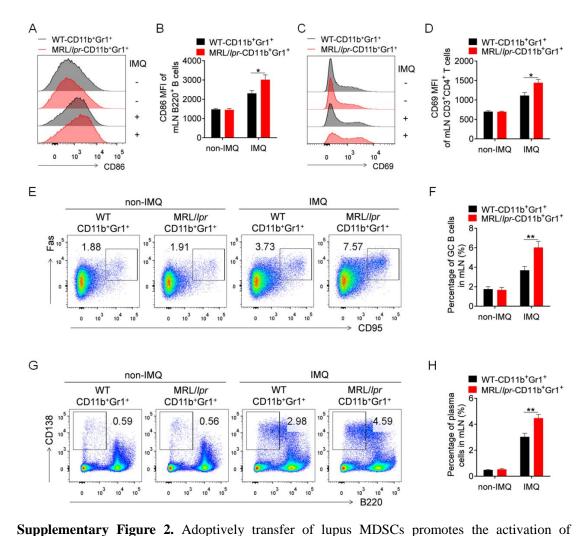
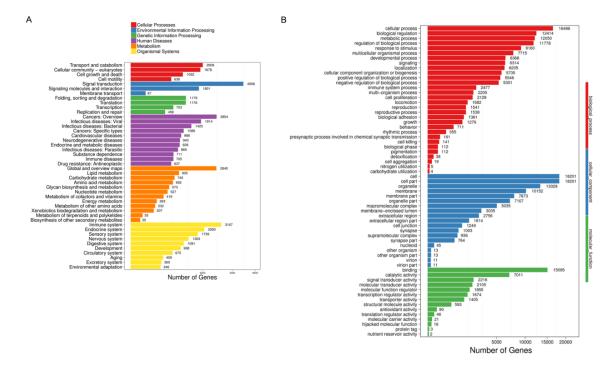
## **Supplemental Data**



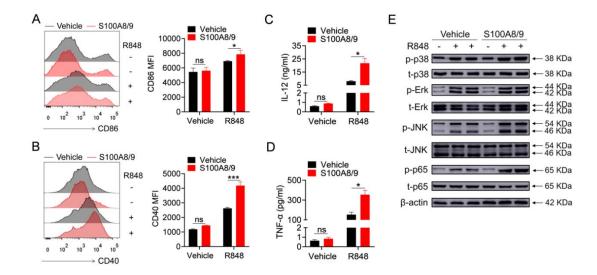
**Supplementary Figure 1.** Adoptively transfer of lupus MDSCs promotes the activation of immune cells in spleens of lupus mice. The splenic MDSCs isolated from 22-24 weeks old C57BL/6 mice or MRL/lpr mice were transferred into 8 weeks old C57BL/6 mice by caudal vein (n=6),  $2 \times 10^6$  cells/mice, once every 2 weeks. At the 10th week, mice were treated with IMQ to induce lupus model. After 10 weeks, the mice were sacrificed for further study. **A, B** Flow cytometric analysis of the expression of CD86 on splenic B220<sup>+</sup> B cells. **C, D** Flow cytometric analysis of the expression of CD69 on splenic CD4<sup>+</sup> T cells. **E, F** Flow cytometric analysis of the percentage of germinal center B cells (B220<sup>+</sup>GL7<sup>+</sup>CD95<sup>+</sup>) in splenic B220<sup>+</sup> B cells. **G, H** Flow cytometric analysis of the percentage of plasma cells (B220<sup>-/low</sup>CD138<sup>+</sup>) in splenocytes. \* p < 0.05, \*\*\* p < 0.01, \*\*\*\* p < 0.001.



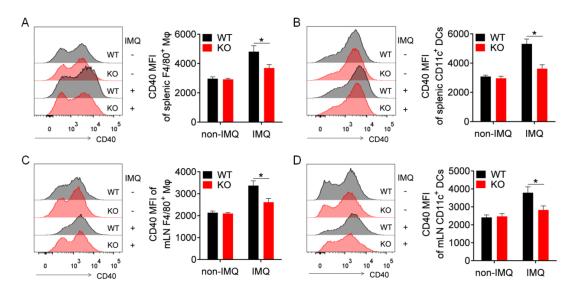
immune cells in mLN of lupus mice. The splenic MDSCs isolated from 22-24 weeks old C57BL/6 mice or MRL/lpr mice were transferred into 8 weeks old C57BL/6 mice by caudal vein (n=6),  $2 \times 10^6$  cells/mice, once every 2 weeks. At the 10th week, mice were treated with IMQ to induce lupus model. After 10 weeks, the mice were sacrificed for further study. **A, B** Flow cytometric analysis of the expression of CD86 on mLN B220<sup>+</sup> B cells. **C, D** Flow cytometric analysis of the expression of CD69 on mLN CD4<sup>+</sup> T cells. **E, F** Flow cytometric analysis of the percentage of germinal center B cells (B220<sup>+</sup>GL7<sup>+</sup>CD95<sup>+</sup>) in mLN B220<sup>+</sup> B cells. **G, H** Flow cytometric analysis of the percentage of plasma cells (B220<sup>-/low</sup>CD138<sup>+</sup>) in mLN. \* p < 0.05, \*\* p < 0.01, \*\*\* p < 0.001.



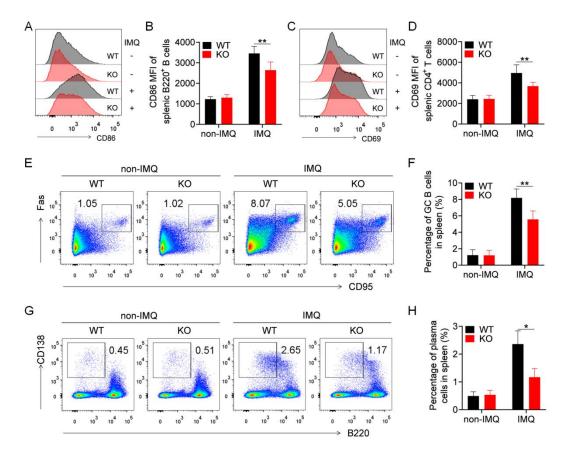
**Supplementary Figure 3.** Go analysis of up- and down-regulated DEGs. **A** GO analysis of represented biological pathways in the DEGs. **B** GO terms of Biological Process, Cellular Component, Molecular Function identified by Panther GO-slim analysis.



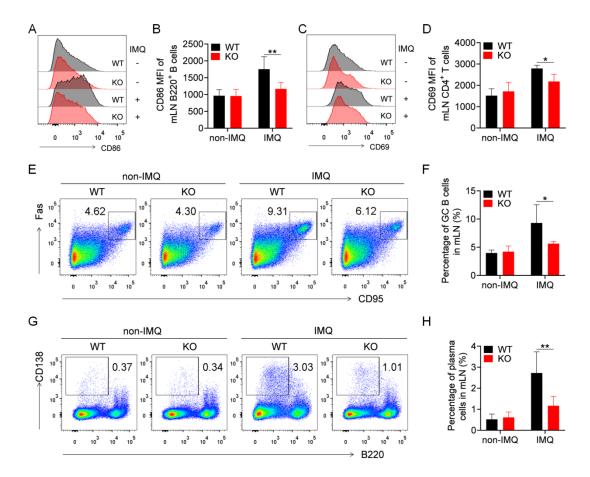
**Supplementary Figure 4.** S100A8/9 promotes TLR7-mediated BMDCs activation. BMDCs were pretreated with mouse recombinant S100A8/9 protein (1  $\mu$ g/mL) for 12 h, and then stimulated with R848 (1  $\mu$ g/mL). **A, B** Flow cytometric analysis of the expression of CD86 and CD40 at 24 h. **C, D** ELISA analysis of the levels of IL-12/IL-23 p40 and TNF- $\alpha$  in culture supernatant at 24 h. **E** Western blot analysis of the phosphorylation levels of p38, Erk, JNK and p65 at 30 and 60 min. \* p < 0.05, \*\*\* p < 0.001.



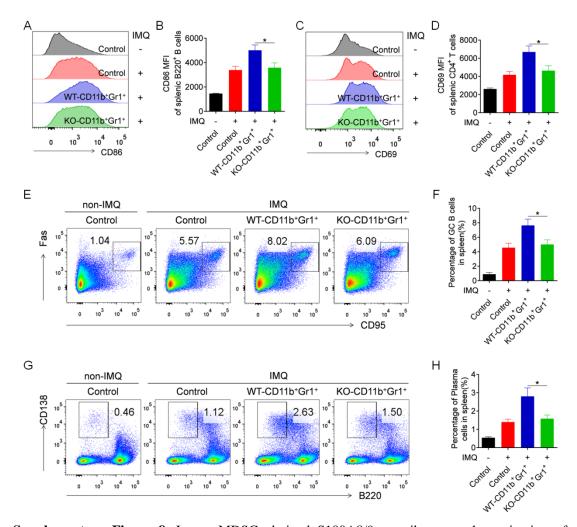
**Supplementary Figure 5.** S100A9 deficiency inhibits the expression of CD40 on macrophages and DCs in IMQ-induced lupus mice. S100A9<sup>-/-</sup> and WT mice at 8 weeks were treated with IMQ 3 times a week for 10 weeks, and sacrificed for further experiment. Flow cytometric analysis of the expression of CD40 on F4/80<sup>+</sup> macrophages and CD11c<sup>+</sup> dendritic cells in spleens (A, B) and mLN (C, D) of mice. \* p < 0.05.



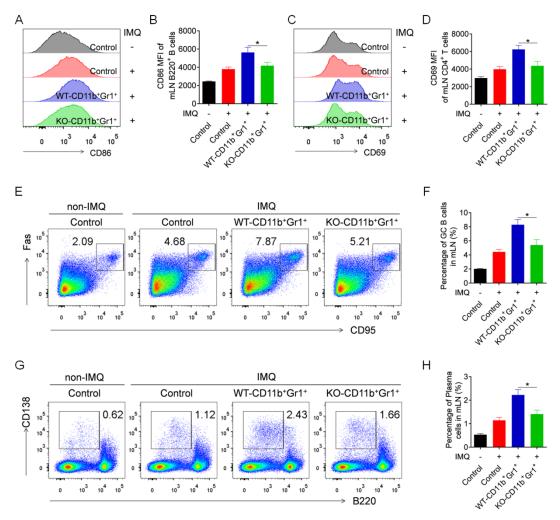
**Supplementary Figure 6.** S100A9 deficiency reduces activation of immune cells in spleens of lupus mice. S100A9<sup>-/-</sup> and wild-type mice (8 weeks old) were treated with IMQ for 10 weeks, and sacrificed for further experiment. **A, B** Flow cytometric analysis of the expression of CD86 on splenic B220<sup>+</sup> B cells. **C, D** Flow cytometric analysis of the expression of CD69 on splenic CD4<sup>+</sup> T cells. **E, F** Flow cytometric analysis of the percentage of germinal center B cells (B220<sup>+</sup>GL7<sup>+</sup>CD95<sup>+</sup>) in splenic B220<sup>+</sup> B cells. **G, H** Flow cytometric analysis of the percentage of plasma cells (B220<sup>-/low</sup>CD138<sup>+</sup>) in splenocytes. \* p < 0.05, \*\* p < 0.01.



**Supplementary Figure 7.** S100A9-deficiency reduces activation of immune cells in mesenteric lymph nodes of lupus mice. S100A9<sup>-/-</sup> and wild-type mice (8 weeks old) were treated with IMQ for 10 weeks, and sacrificed for further experiment. **A, B** Flow cytometric analysis of the expression of CD86 on mLN B220<sup>+</sup> B cells. **C, D** Flow cytometric analysis of the expression of CD69 on mLN CD4<sup>+</sup> T cells. **E, F** Flow cytometric analysis of the percentage of germinal center B cells (B220<sup>+</sup>GL7<sup>+</sup>CD95<sup>+</sup>) in mLN B220<sup>+</sup> B cells. **G, H** Flow cytometric analysis of the percentage of plasma cells (B220<sup>-/low</sup>CD138<sup>+</sup>) in mLN. \* p < 0.05, \*\* p < 0.01.



**Supplementary Figure 8.** Lupus MDSCs-derived S100A8/9 contributes to the activation of immune cells in spleens of lupus mice. The splenic MDSCs (S100A9<sup>-/-</sup>-MDSCs and WT-MDSCs) were isolated from S100A9<sup>-/-</sup> and wild-type mice which have been treated with IMQ for 10 weeks, and subsequently transferred into 8 weeks old C57BL/6 mice by caudal vein (n=6), 2×10<sup>6</sup> cells/mice, once every 2 weeks. At the 10th week, mice were treated with IMQ to induce lupus model. After 10 weeks, the mice were sacrificed for further study. **A, B** Flow cytometric analysis of the expression of CD86 on splenic B220<sup>+</sup> B cells. **C, D** Flow cytometric analysis of the expression of CD69 on splenic CD4<sup>+</sup> T cells. **E, F** Flow cytometric analysis of the percentage of germinal center B cells (B220<sup>+</sup>GL7<sup>+</sup>CD95<sup>+</sup>) in splenic B220<sup>+</sup> B cells. **G, H** Flow cytometric analysis of the percentage of plasma cells (B220<sup>-/low</sup>CD138<sup>+</sup>) in splenocytes. \* *p* < 0.05.



**Supplementary Figure 9.** Lupus MDSCs-derived S100A8/9 contributes to the activation of immune cells in mLN of lupus mice. The splenic MDSCs (S100A9<sup>-/-</sup>-MDSCs and WT-MDSCs) were isolated from S100A9<sup>-/-</sup> and wild-type mice which have been treated with IMQ for 10 weeks, and subsequently transferred into 8 weeks old C57BL/6 mice by caudal vein (n=6), 2×10<sup>6</sup> cells/mice, once every 2 weeks. At the 10th week, mice were treated with IMQ to induce lupus model. After 10 weeks, the mice were sacrificed for further study. **A, B** Flow cytometric analysis of the expression of CD86 on mLN B220<sup>+</sup> B cells. **C, D** Flow cytometric analysis of the expression of CD69 on mLN CD4<sup>+</sup> T cells. **E, F** Flow cytometric analysis of the percentage of germinal center B cells (B220<sup>+</sup>GL7<sup>+</sup>CD95<sup>+</sup>) in mLN B220<sup>+</sup> B cells. **G, H** Flow cytometric analysis of the percentage of plasma cells (B220<sup>-/low</sup>CD138<sup>+</sup>) in mLN. \* p < 0.05.