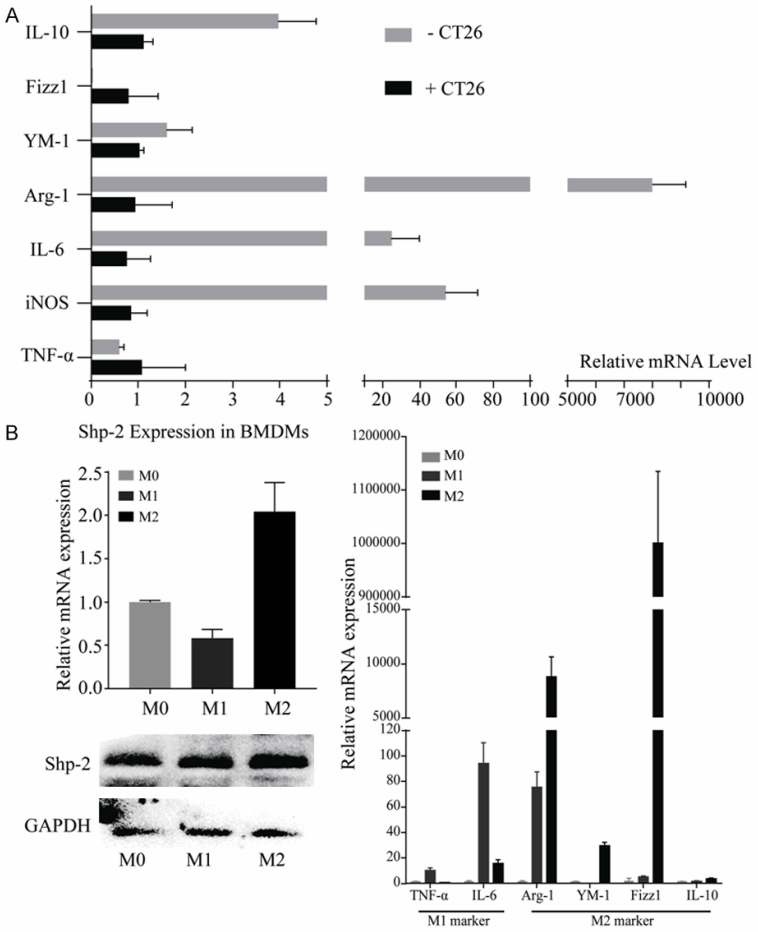
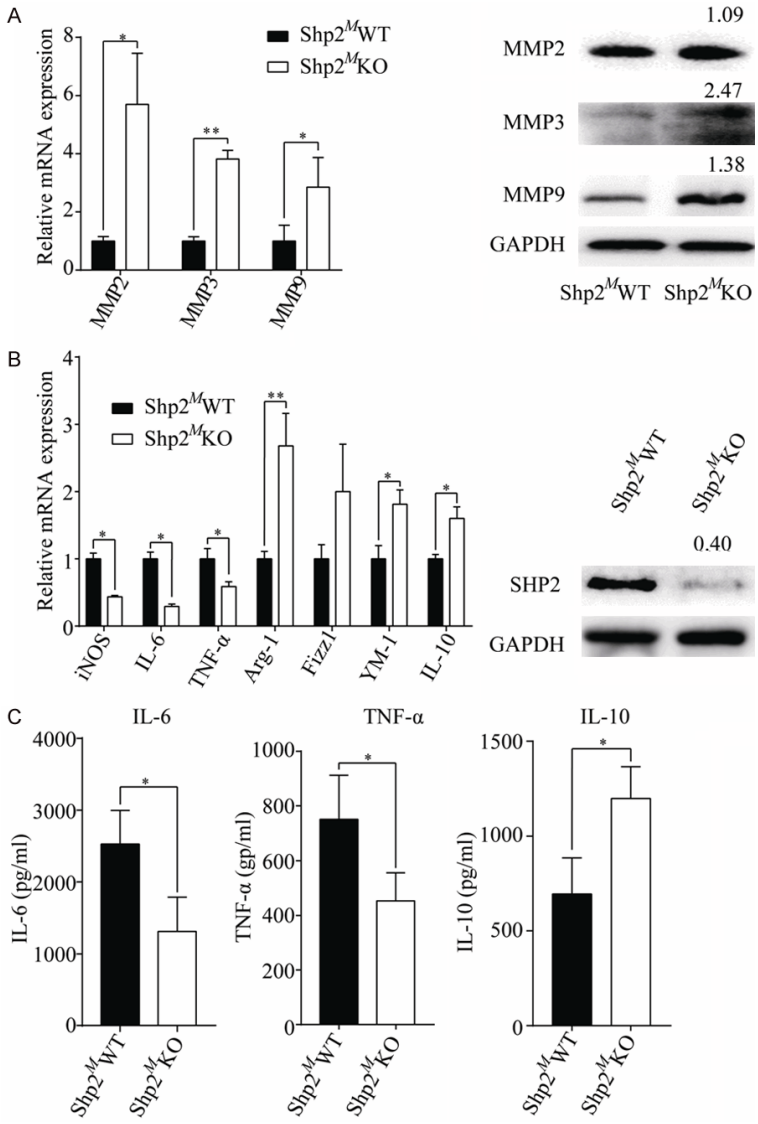
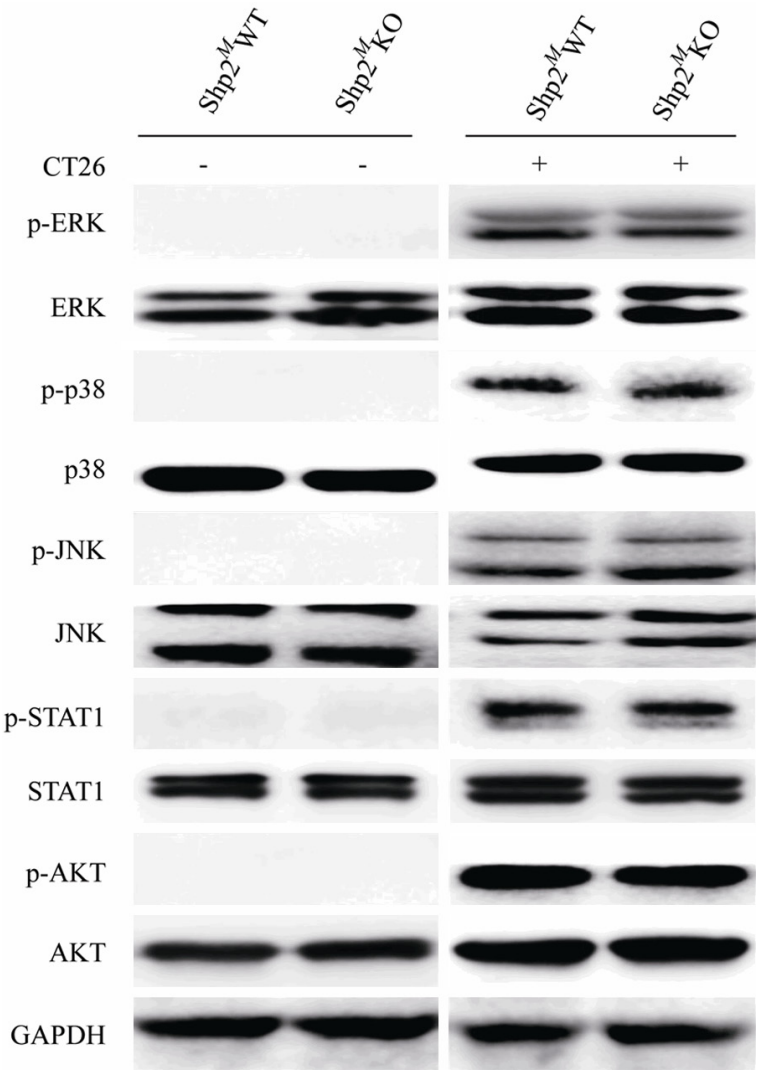


Supplementary Figure 1. There was no difference of Shp2 expression in M1 macrophages and M2 macrophages. A. BMDMs were co-cultured with CT26 cells for 24 hours before RNA was collected to determine the iNOS, IL-6, TNF-α, Arg-1, Fizz1, YM-1 and IL-10 expressions. B. BMDMs were stimulated with LPS (10 ng/mL) plus IFN-γ (20 ng/mL) (polarized to M1) or IL-4 (20 ng/mL) (polarized to M2) for 24 hours before RNA or proteins were extracted. The expressions of Shp2, IL-6, TNF-α, Arg-1, Fizz1, YM-1 and IL-10 were determined. Results were obtained from 3 independent experiments and are expressed as the means ± SEM.



Supplementary Figure 2. Knock out of Shp2 on macrophages promotes MMPs expressions on CT26 cells and M2-like polarization of TAMs in TME. (A) CT26 cells were direct co-cultured with Shp2^{M}WT or Shp2^{M}KO BMDMs for 24 hours before macrophages were isolated by anti-F4/80 microbeads and then CT26 cells were collected for RNA or protein extraction. The mRNA or protein expressions of MMP2, MMP3 and MMP9 were determined by RT-qPCR or western blotting, respectively. (B) CT26 cells were direct co-cultured with BMDMs isolated from Shp2^{M}WT or Shp2^{M}-KO mice for 24 hours, (B) BMDMs were collected for RNA extraction and mRNA expressions of iNOS, IL-6, TNF-α, Arg-1, Fizz1, YM-1 and IL-10 were determined by RT-qPCR. (C) Supernatants were collected for ELISA to determine the IL-6, TNF-α and IL-10 production. Results were obtained from 3 independent experiments and are expressed as the means ± SEM. *P < 0.05, **P < 0.01.



Supplementary Figure 3. Deletion of Shp2 on TAMs has no effects on the activation of MAPKs, STAT1 and AKT. CT26 cells were in-direct co-cultured with BMDMs isolated from Shp2^{M}WT or Shp2^{M}KO mice for 24 hours before proteins were extracted from BMDMs for western blot analysis to detect the p-ERK, ERK p-P38, P38, p-JNK, JNK, p-AKT, AKT, p-STAT1 and STAT1 expression levels. Results were representative of 3 independent experiments.