Supplementary Figures

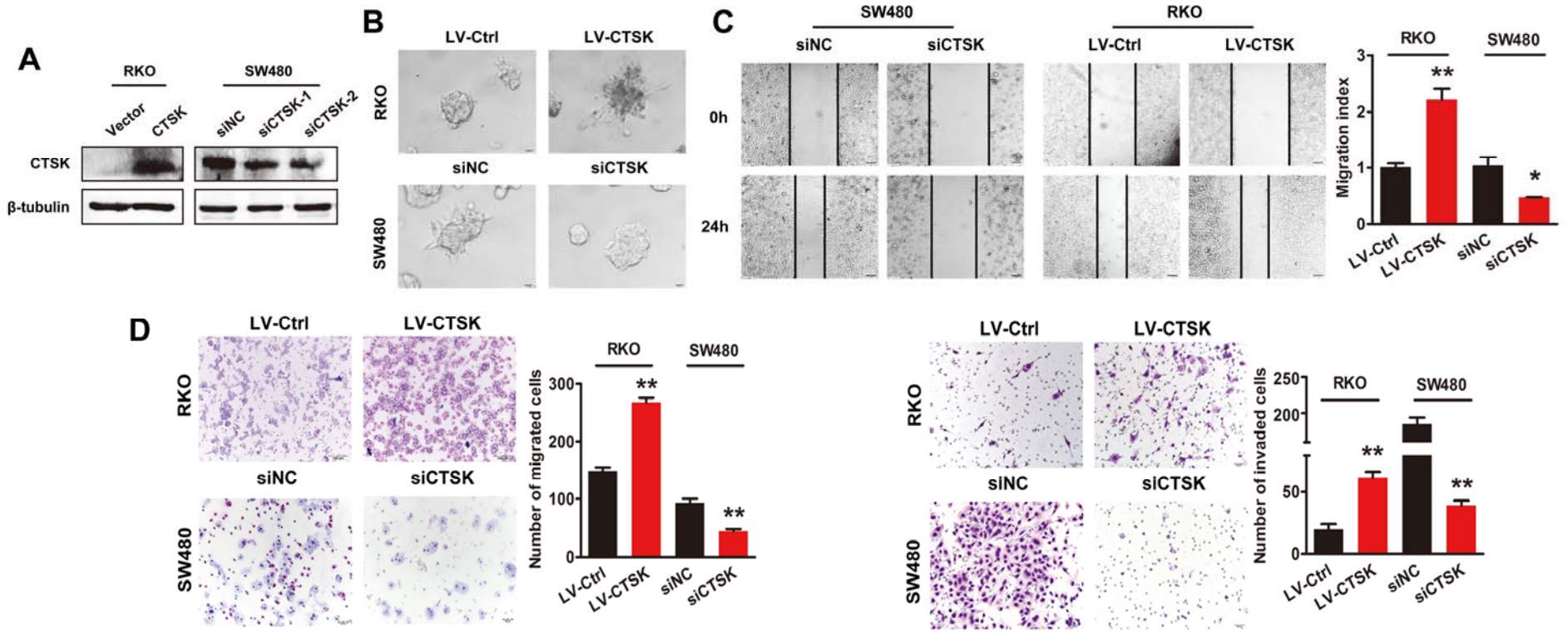

Figure S1. **CTSK contributes the aggressive phenotype of CRC cells. (A) Western blot analysis of CTSK in CTSK overexpression or silencing CRC cells. (B) 3-D invasion assay was applied to observe the morphology of CTSK**

overexpression or silencing CRC cells. (C) Representative images show the invaded cells in the transwell assay of CTSK overexpression or silencing CRC cells. Bar chart represents the number of invaded cells. (D) Wound healing assay was performed to evaluate the motility of indicated CRC cells. Bar chart represent the migration index of indicated CRC cells. Representative figures are shown. The asterisk (*) indicates $P<0.05$. The double asterisk (**) indicates $P<0.01$.

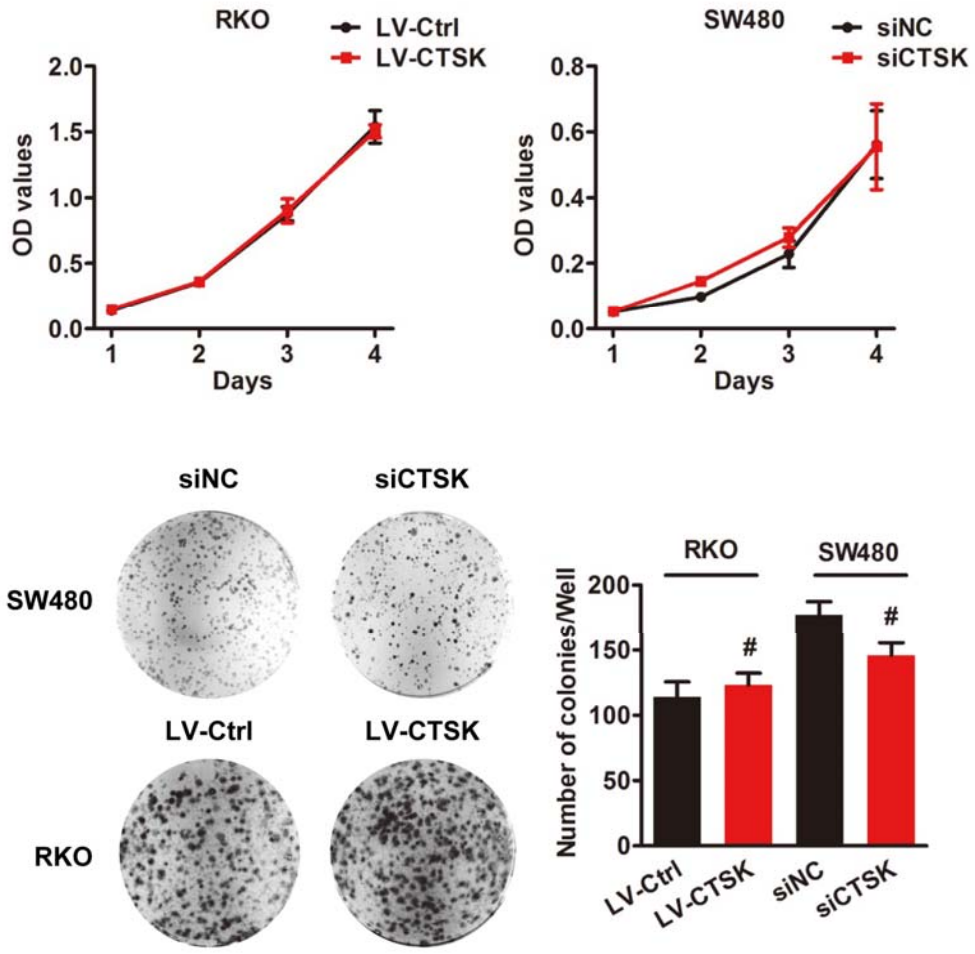

Figure S2. CCK-8 and colony formation assay shows the effects of CTSK on CRC cell proliferation.

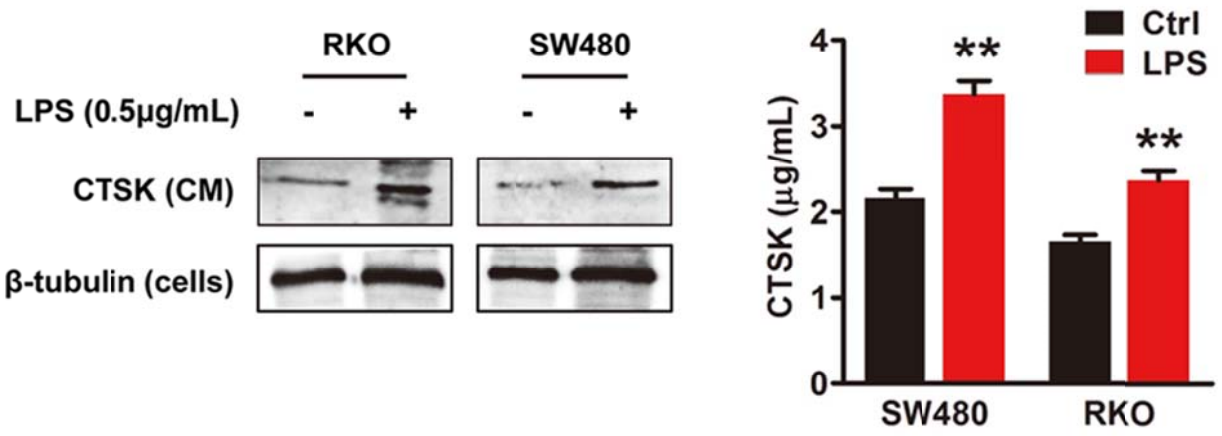

Figure S3. Western blot analysis (Left) and ELISA (Right) analysis of CTSK in the conditioned media (CM) and LPS treated CRC cell lines.

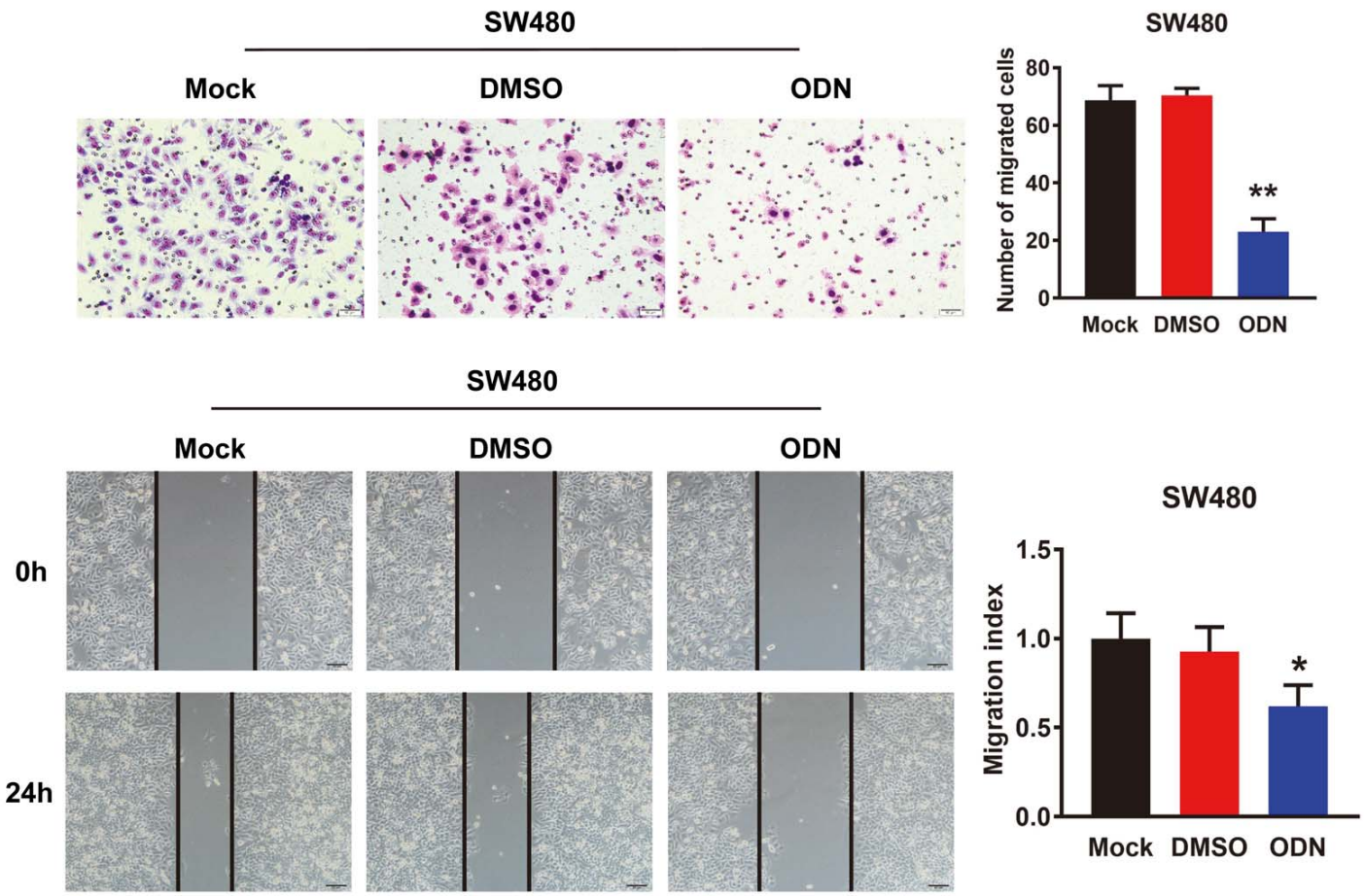

Figure S4. Transwell and wound healing assay was used to measure the migration of CRC cells with or without the treatment of Odanacatib (ODN).

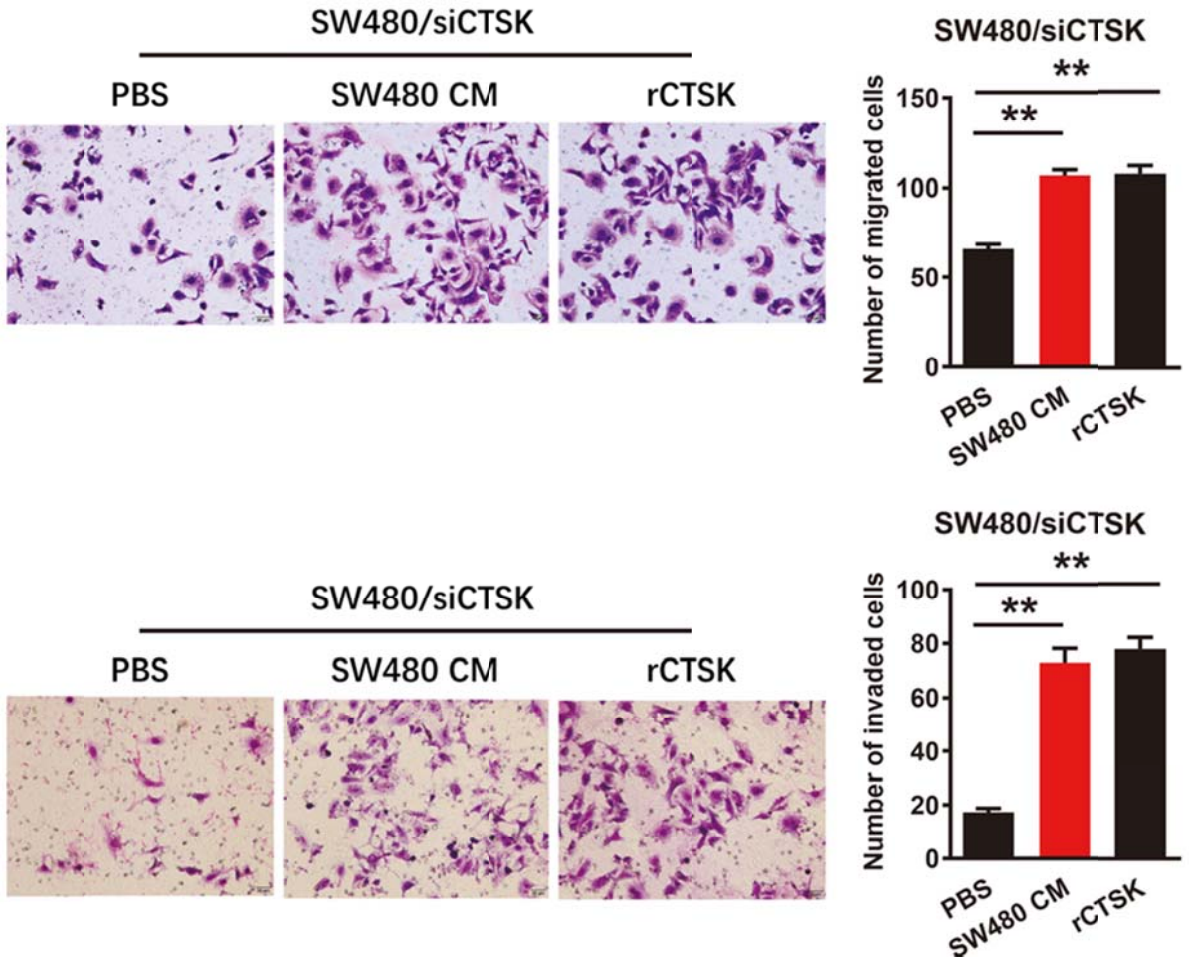

Figure S5. Transwell assay was applied to measure the migration and invasion of endogenous CTSK silencing CRC cells w/o the administration of rCTSK.

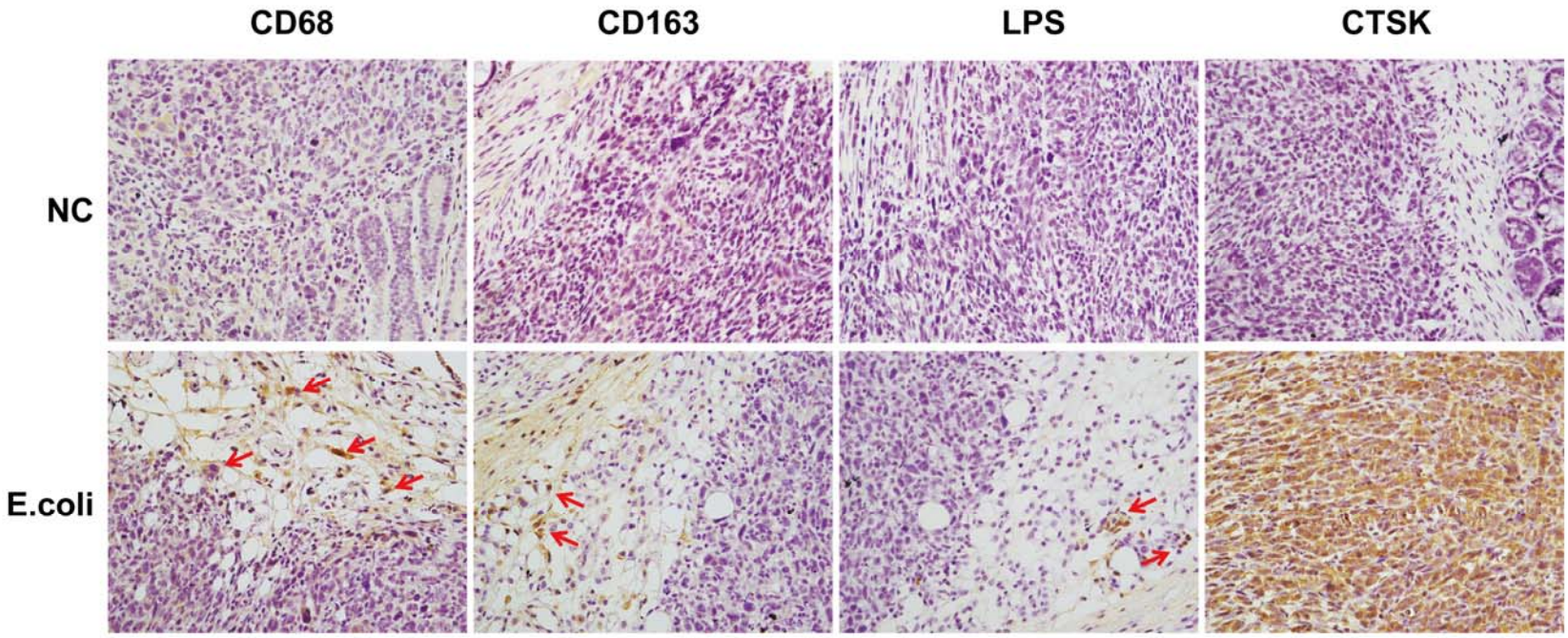

Figure S6. IHC shows the expression of LPS, CTSK and macrophage makers (CD68 and CD163) in primary tumors developed by MC38 cells implantation in antibiotic-treated mice w/o intragastrically administration of *E. coli*.

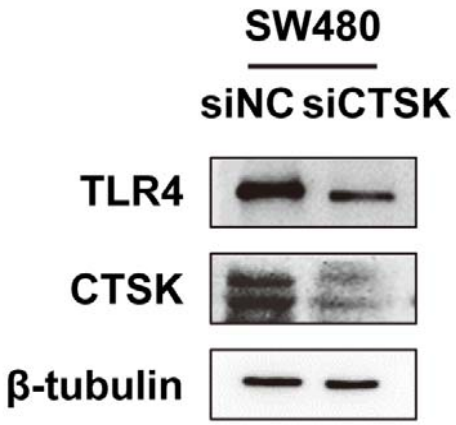

Figure S7. Western blot analysis shows the expression of TLR4 and CTSK in CTSK silencing CRC cells.

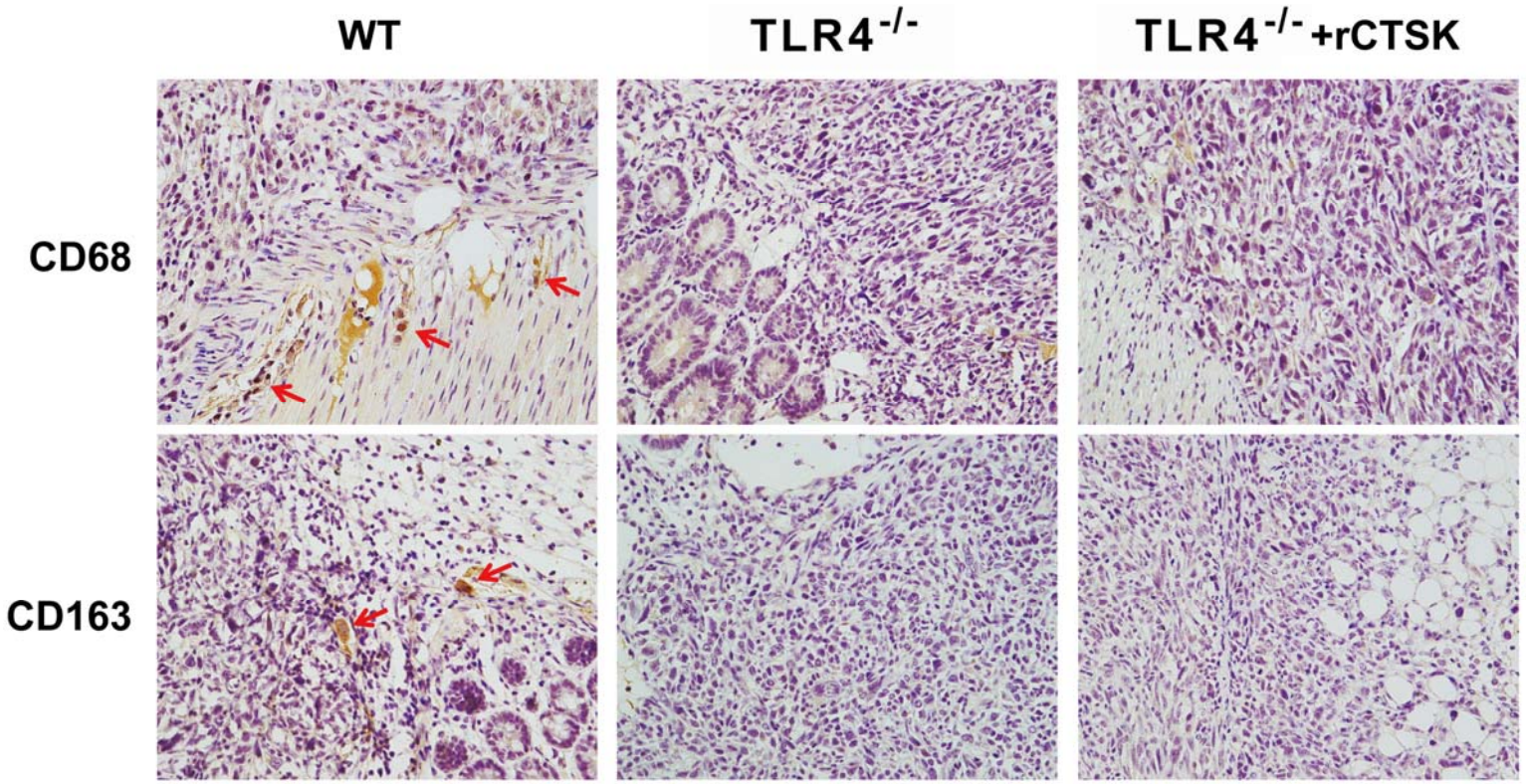

Figure S8. IHC showed the expression of the macrophage makers (CD68 and CD163) in WT and TLR4$^{-/-}$ mice treated w/o rCTSK.

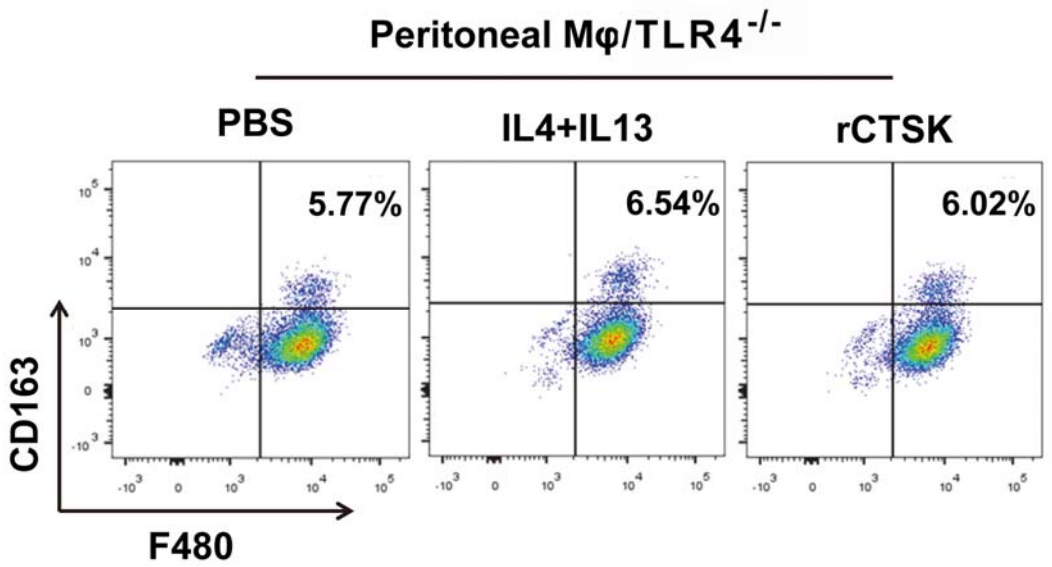

Figure S8. Flow cytometry analysis indicates the M2 polarization of peritoneal macrophages from TLR4$^{-/-}$ mice w/o the treatment of rCTSK.