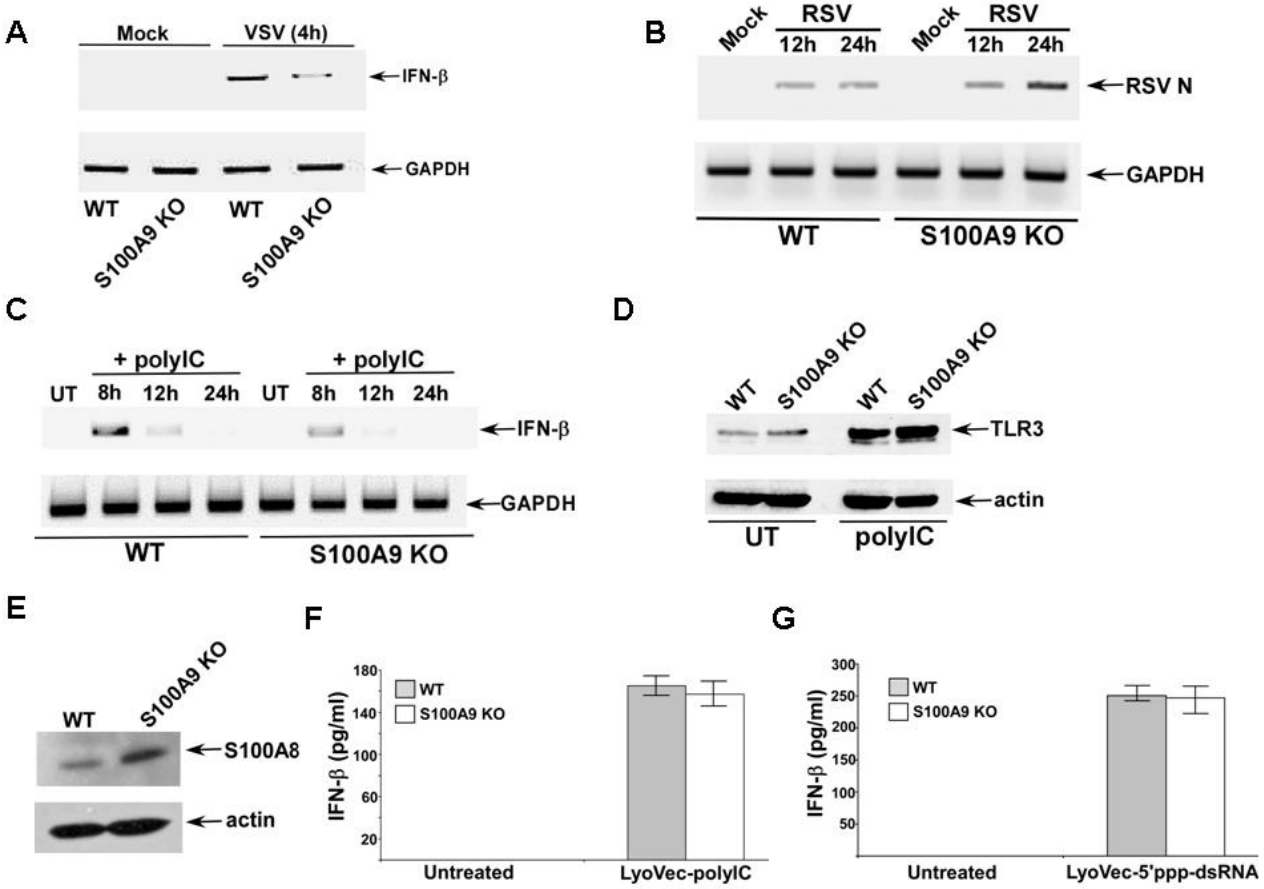
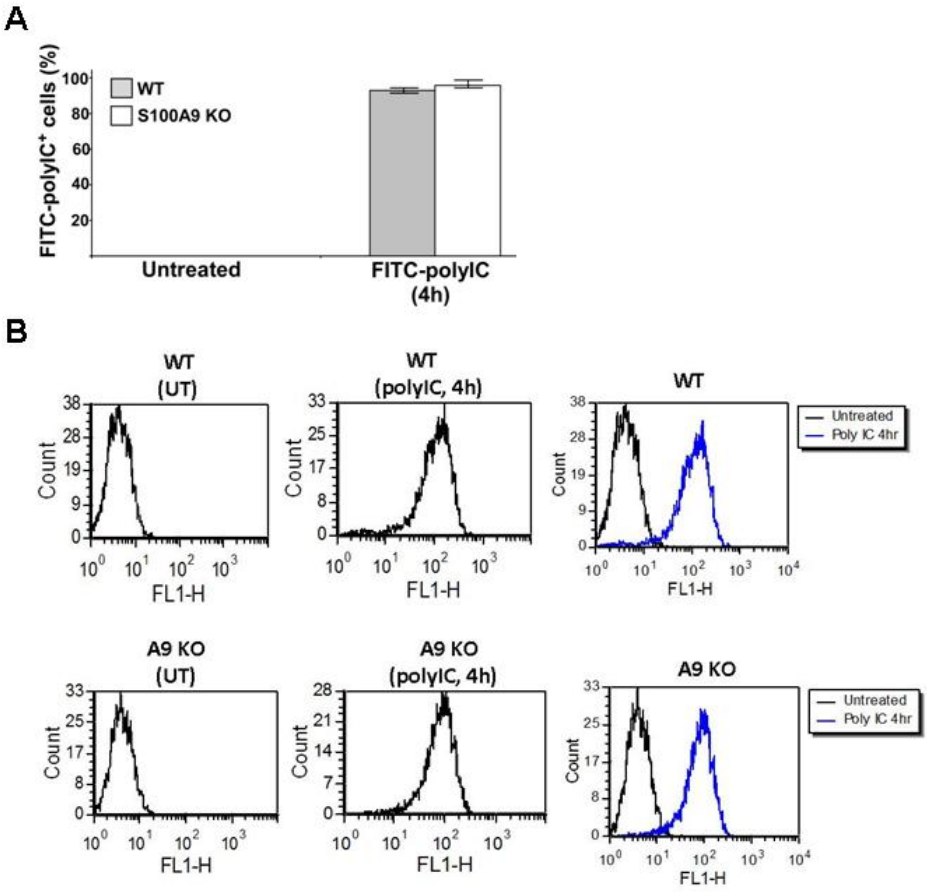
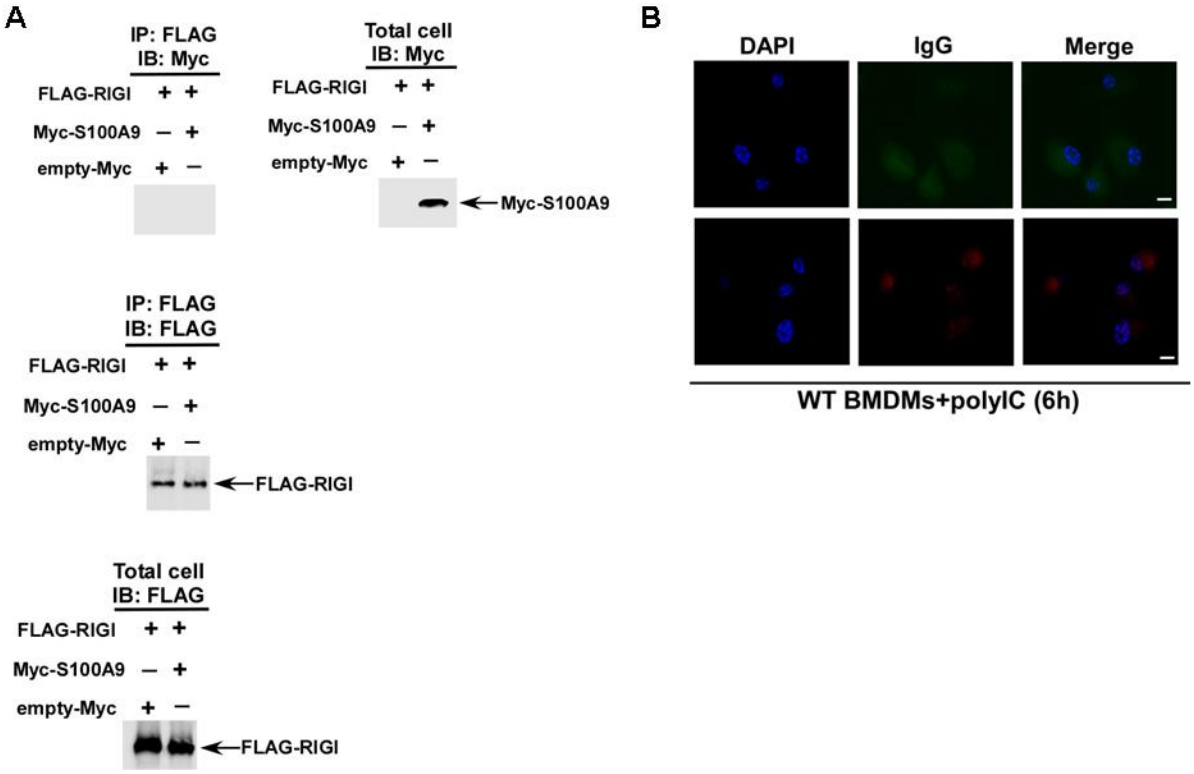
SUPPLEMENTAL DATA



Supplemental Figure 1. **(A)** Primary bone marrow derived macrophages (BMDM) isolated from wild-type (WT) and S100A9 knockout (KO) mice were infected with vesicular stomatitis virus (VSV). At 4h post-infection, RT-PCR analysis was performed to examine IFN-β induction. **(B)** WT and S100A9 KO BMDMs were infected with respiratory syncytial virus (RSV). At 12h and 24h post-infection, RT-PCR analysis was performed to examine the levels of RSV nucleocapsid (N) protein. **(C)** WT and S100A9 KO BMDMs were treated with polyIC for 8h, 12h and 24h. RT-PCR analysis was performed to examine IFN-β induction in polyIC treated cells. **(D)** Western blot analysis of TLR3 protein expression in polyIC treated WT and S100A9 KO BMDMs. **(E)** Western blot analysis of S100A8 protein expression in WT and S100A9 KO BMDMs. **(F)** WT and S100A9 KO BMDM were treated (transfected) with RIGI and MDA5 agonist LyoVec-polyIC (1 μg/ml) for 12h. Medium supernatant was collected to assess levels of mouse IFN-β by ELISA. **(G)** WT and S100A9 KO BMDM were treated (transfected) with RIGI and MDA5 agonist LyoVec-5'ppp-dsRNA (7.5 μg/ml) for 24h. Medium supernatant was collected to assess levels of mouse IFN-β by ELISA. LyoVec-PolyIC and LyoVec-5'ppp-dsRNA were purchased from Invivogen. UT; untreated cells.



Supplemental Figure 2. Primary bone marrow derived macrophages (BMDM) isolated from wild-type (WT) and S100A9 knockout (KO) mice were treated with FITC-labeled polyIC (FITC-polyIC) for 4h. Uptake of FITC-polyIC was examined by flow cytometry analysis. **(A)** Percentage of cells positive for FITC-polyIC was calculated based on the flow cytometry data. The data represents mean ± standard deviation. **(B)** A histogram derived from the flow cytometry analysis. A9 KO; S100A9 knockout BMDMs.



Supplemental Figure 3. **(A)** Cell lysate collected from HEK293 cells expressing FLAG-RIGI and Myc-S100A9 were immuno-precipitated (IP) with FLAG antibody, followed by immuno-blotting (IB) with either Myc antibody or FLAG antibody. Total lysate was also blotted with Myc and FLAG antibodies. **(B)** Wild type primary bone marrow derived macrophages (BMDM) were treated with polyIC for 6h. Fixed permeabilized cells were incubated with isotype control antibody (IgG) matching either TLR3 antibody or S100A9 antibody used in Fig. 5A. FITC conjugated and Texas-red conjugated secondary antibodies were used for S100A9 antibody and TLR3 antibody specific isotype control IgGs. The cells were also labeled with DAPI.