Supporting Information

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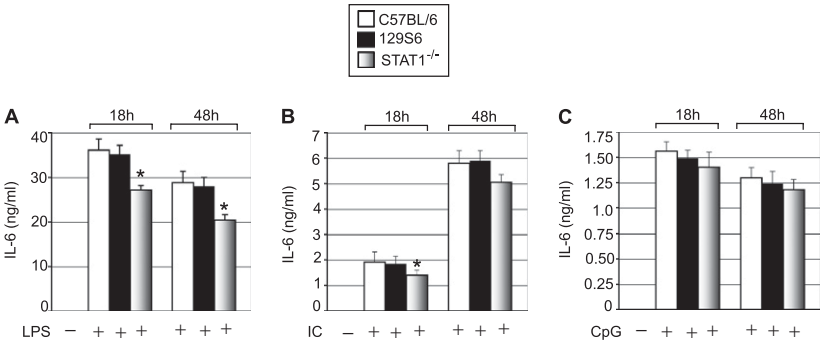

Fig. S1. TLR-induced IL-6 secretion in control and STAT1$^{-/-}$macrophages. Effect of LPS (*A*), Poly (I:C) (*B*), and CpG (*C*) on proinflammatory cytokine secretion in C57BL/6 (□), 129S6 (■), and STAT1$^{-/-}$(▨) macrophages. Cells were treated with TLR ligands for the indicated periods. Concentrations of IL-6 in the cell culture media were analyzed by ELISA. Data are mean ± SEM; $n = 3$. *$P < 0.05$ for STAT1$^{-/-}$ macrophages compared with control 129S6 macrophages.

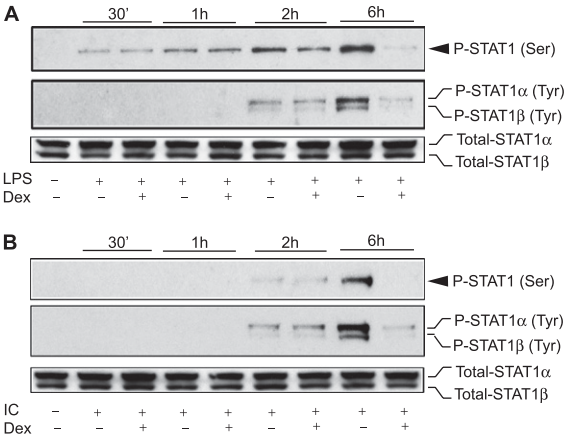

Fig. S2. Temporal effect of Dex on LPS- or Poly (I:C)-induced STAT1 phosphorylation. Macrophages were pretreated with or without Dex (100 nM), followed by treatment with LPS (100 ng/mL) (*A*) or Poly (I:C) (50 μg/mL) (*B*) for the indicated periods. Cell lysates were analyzed by Western blot analysis using anti-phospho STAT1 Ser^{727} (P-STAT1 Ser), phospho STAT1 Tyr^{701} (P-STAT1 Tyr), and total STAT1 (Total-STAT1) antibodies. Representative of two independent experiments.

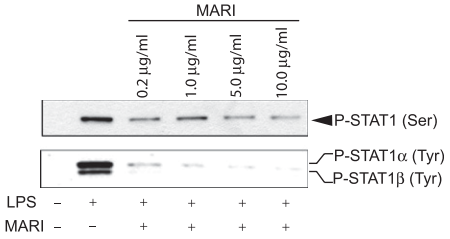

Fig. S3. Dose–response study with anti-IFNAR1 antibody (MARI) showing the effect of MARI on STAT1 phosphorylation. Macrophages were pretreated with varying doses of MARI, followed by treatment with LPS (100 ng/mL). Cell lysates were analyzed by Western blot analysis using anti-phospho STAT1 Ser^{727} (P-STAT1 Ser) and phospho STAT1 Tyr^{701} (P-STAT1 Tyr) antibodies. Representative of two independent experiments.

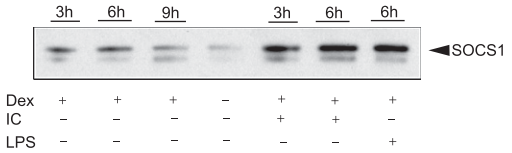

Fig. S4. Effect of GCs on SOCS1 expression. In the first three panels, macrophages were treated with Dex (100 nM) for the indicated periods. In the last three panels, macrophages were pretreated with Dex (100 nM) for 3 h, followed by treatment with LPS (100 ng/mL) or Poly (I:C) (50 μg/mL) for the indicated periods. Cell lysates were analyzed by Western blot analysis using anti-SOCS1 antibody. Representative of two independent experiments.

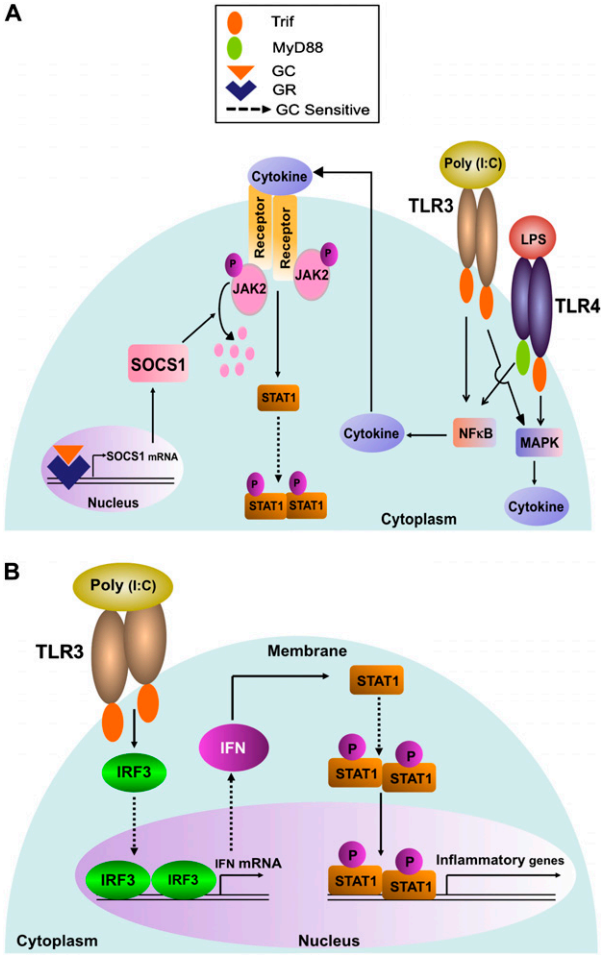

Fig. S5. (*A*) Shared mechanism for suppression of TLR3- or TLR4- induced STAT1 activation. Engagement of GR and TLR3 or TLR4 induces SOCS1 to degrade phosphorylated JAK2 and inhibit Poly (I:C)- or LPS-induced STAT1 phosphorylation. (*B*) A unique mechanism for suppression of TLR3-induced STAT1 activation. GCs impair TLR3-induced type I IFN secretion to suppress STAT1 phosphorylation.