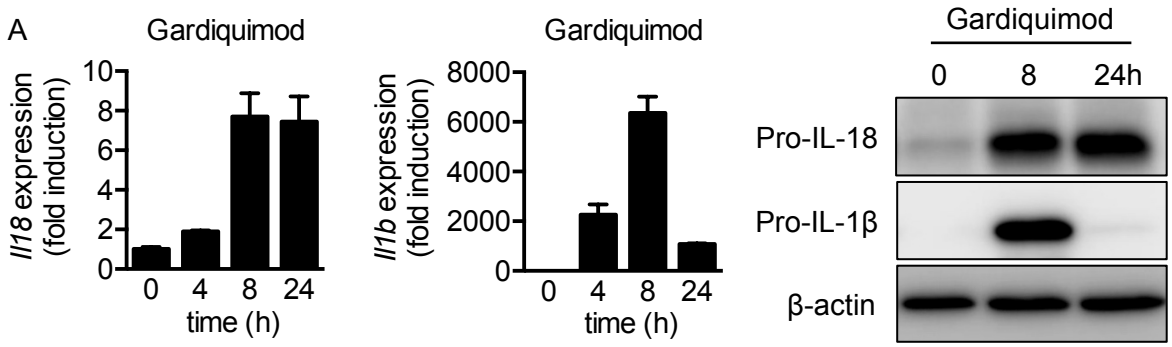
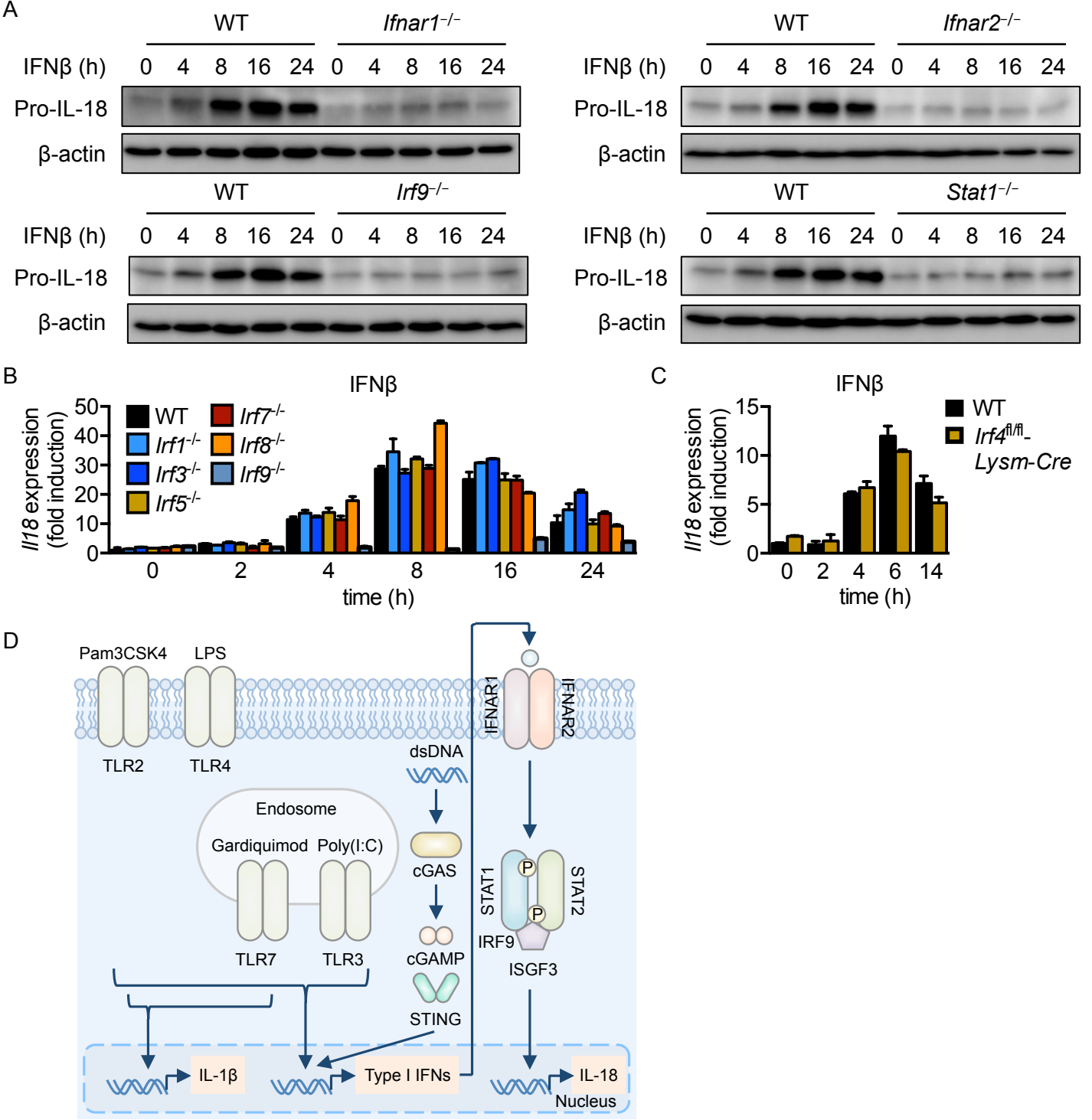



**Supplemental Figure 1. Kinetics of IL-18 and IL-1β expression stimulated by gardiquimod.**
(A) Real-time qPCR analysis of the genes encoding IL-18 and IL-1β and immunoblot analysis of pro-IL-18, pro-IL-1β and β-actin (loading control) in WT BMDMs at various times after treated with gardiquimod. Data are representative of 3 independent experiments.




**Supplemental Figure 2. Type I IFNs induce IL-18 expression via ISGF3 and a model of differential regulation of proinflammatory cytokines IL-18 and IL-1β.**

(A) Immunoblot analysis of pro-IL-18 and β-actin (loading control) in WT, *Ifnar2*$^{-/-}$, *Irf9*$^{-/-}$ or *Stat1*$^{-/-}$ BMDMs at various times after treated with IFNβ. (B) Real-time qPCR analysis of the gene encoding IL-18 in WT, *Irf1*$^{-/-}$, *Irf3*$^{-/-}$, *Irf5*$^{-/-}$, *Irf7*$^{-/-}$ or *Irf8*$^{-/-}$ BMDMs at various times after treated with IFNβ. (C) Real-time qPCR analysis of the gene encoding IL-18 in WT or *Irf4*$^{fl/fl}$-*Lysm-Cre* BMDMs at various times after treated with IFNβ. (D) Expression of IL-18 is induced and sustained by stimulations of TLR2, TLR4, or TLR7 ligand, while IL-1β expression declines soon after reaching its peak level. The TLR3 and cGAS–STING pathways also upregulate IL-18 expression but are modest at inducing IL-1β expression. Importantly, type I IFN signaling downstream of TLRs and cGAS–STING pathway is crucial in mediating IL-18 induction. Data are representative of 3 independent experiments.