



**Figure S3. Effects of the NLRP3 inflammasome on cytokine induction.** BMDCs ( $n = 3$ ) from C57BL/6 or *Nlrp3*<sup>-/-</sup> mice were pretreated with 25  $\mu$ g/ml of the IFNAR receptor blocking antibody MAR1-5A3 or an isotype control GIR-208 for 30 minutes prior to infection with WNV and at 48 hours cells were collected. **A.** Western blot showing the expression of STAT1, the ISG IFIT2, the WNV protein NS3, and IL-1 $\beta$  cleavage. **B.** Viral titers from the treated BMDCs were determined by a focus-forming assay. Data are shown as FFU per ml. Error bars indicate SD. **C.** Relative cytokine mRNA levels at 48 hours from WT or *Nlrp3*<sup>-/-</sup> BMDCs infected with WNV after

treatment with MAR1-5A3 or an isotype control MAb. Gene expression was measured by qRT-PCR and normalized to *Gapdh* levels. Data is displayed as the fold increase compared to untreated cells on a log2 scale. Data represent the average of three independent experiments. Error bars indicate SD. The limit of detection was assigned as a value log2  $\Delta\Delta C_t$  of -2. **D.** The concentration of IL-1 $\beta$ , IL-6 and TNF- $\alpha$  in serum from the treated WT and *Nlrp3*<sup>-/-</sup> mice was determined by cytokine bioplex assay. Mean values  $\pm$  SD are shown. **E-G.** WT, *Nlrp3*<sup>-/-</sup>, *caspase-1/11*<sup>-/-</sup> or *IL-1R*<sup>-/-</sup> mice were pretreated one day prior to WNV infection with 1 mg (40 mg/kg) of the IFNAR receptor blocking antibody MAR1-5A3 or isotype control MAb (GIR-208) prior. At 72 hours after infection, serum was collected and analyzed for ALT (**E**), AST (**F**), and glucose (**G**).