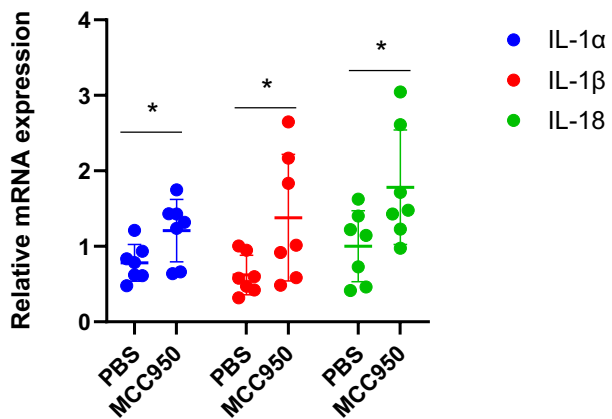
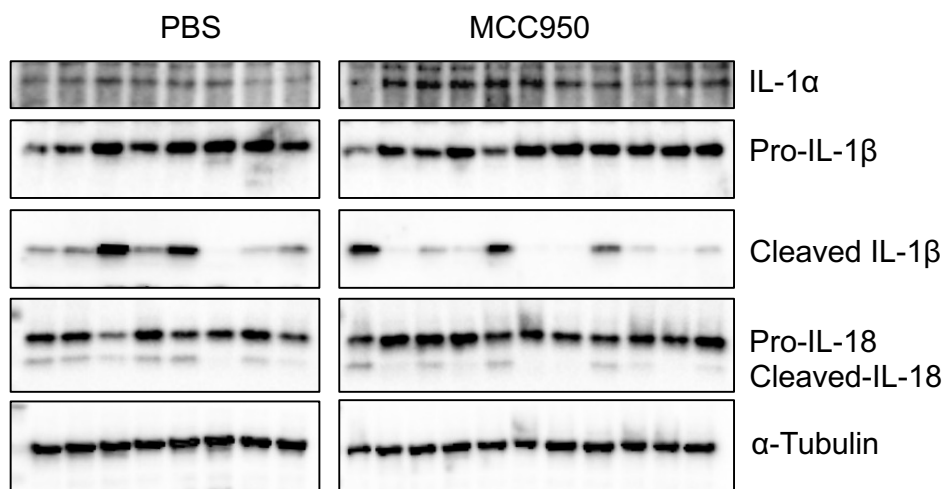
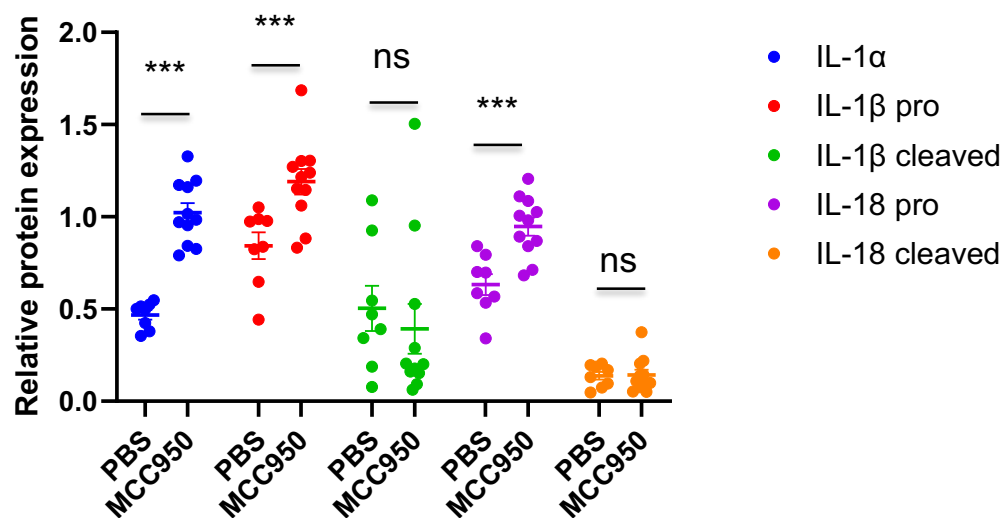
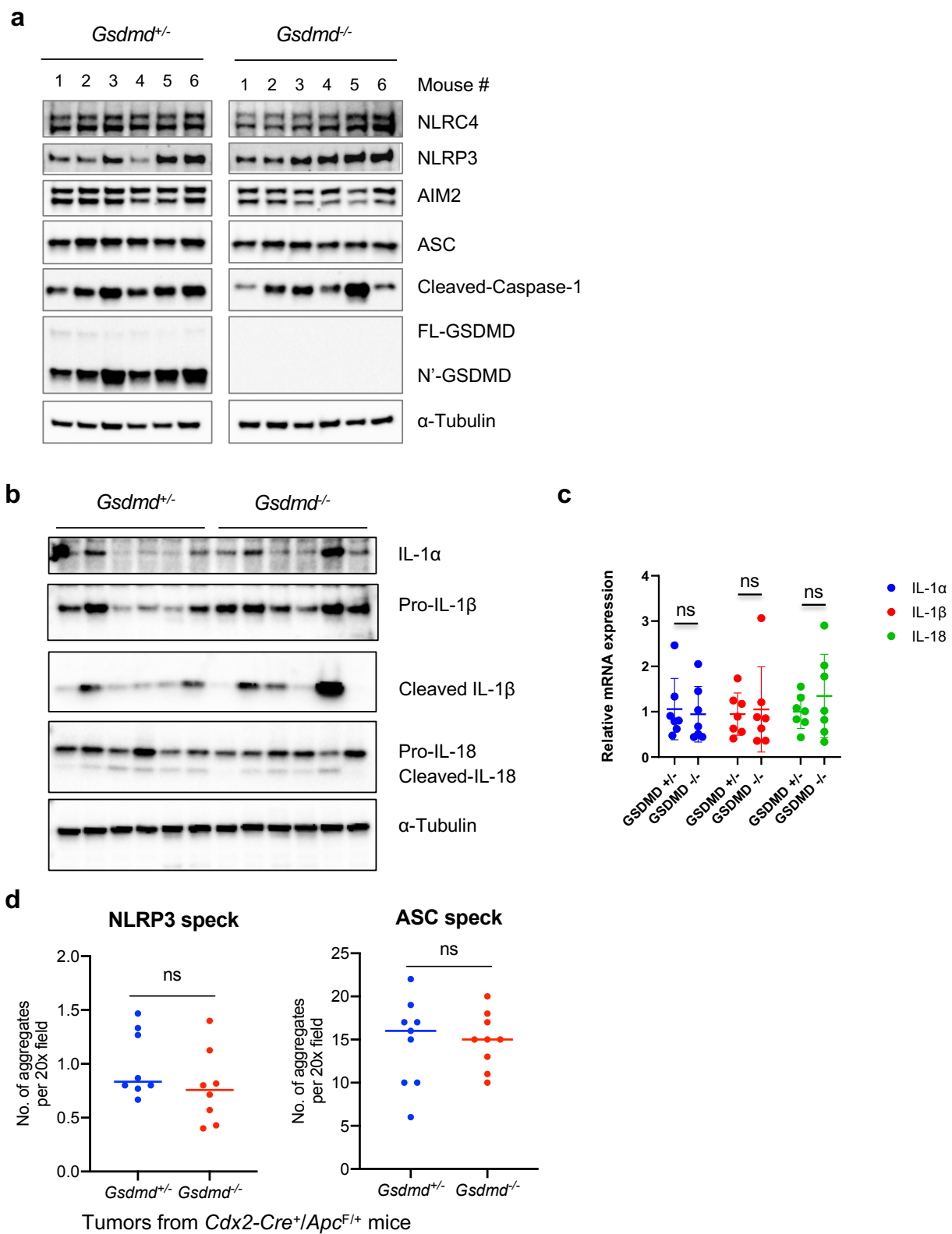


a**b**

Tumors from *Cdx2-Cre⁺/Apc^{F/+}* mice

c

Supplementary Figure 1: Level of IL-1 family cytokines following NLRP3 inhibition. 5-month-old *Cdx2-Cre⁺/Apc^{F/+}* mice bearing colorectal tumors were given *i.p.* injection of NLRP3 inhibitor MCC950 (10mg/kg) once every 2 days for 7 days. Mice were sacrificed 1 day after the last dose of MCC950 injection, and their colorectal tumors were harvested for analyses. **a:** Relative mRNA expression of IL-1 α , IL-1 β or IL-18 in colorectal tumors from PBS or MCC950 injected mice (n=7). GAPDH was used as an endogenous control. **b:** Tumors from the mice injected with MCC950 or PBS were dissected and analyzed by Western blotting. Each lane represents the pooled tumor lysate of one tumor-bearing mouse. **c:** Quantified levels of IL-1 α , IL-1 β (pro and cleaved) or IL-18 (pro and cleaved) in tumors. PBS: n=8, MCC950: n=11. Data are represented as mean $\pm$ SD. P values: ns = not significant, * $p < 0.05$, *** $p < 0.001$.



Supplementary Figure 2: GSDMD does not feedback regulate the NLRP3 pathway. a: 5-

month-old *Cdx2-Cre⁺/Apc^{F/+}* mice that harbor heterozygous (*Gsdmd^{+/-}*, as controls) or null (*Gsdmd^{-/-}*) alleles of GSDMD were sacrificed and subjected to Western blotting analysis for indicated inflammasome signaling molecules. **b:** 5-month-old *Cdx2-Cre⁺/Apc^{F/+}* mice that harbor heterozygous (*Gsdmd^{+/-}*, as controls) or null (*Gsdmd^{-/-}*) alleles of GSDMD were sacrificed and subjected to Western blotting analysis for indicated proteins. **c:** Relative mRNA expression of IL-1 α , IL-1 β or IL-18 in colorectal tumors from *Cdx2-Cre⁺/Apc^{F/+}* mice that harbor heterozygous (*Gsdmd^{+/-}*, as controls) or null (*Gsdmd^{-/-}*) alleles of GSDMD were analyzed by RT-qPCR (n=7). GAPDH was used as an endogenous control. **d:** Images of immunostaining were obtained from tumors harboring heterozygous (*Gsdmd^{+/-}*) or null (*Gsdmd^{-/-}*) alleles of GSDMD by confocal microscopy, and were analyzed for the numbers of NLRP3 (n=8) and ASC (n=8) aggregates per field. Data represented as mean $\pm$ SD. P values: ns = not significant.