

**Supplementary Figure 1.** cGAS-STING expression and signaling over time in total and acinar cells in AP. (*A*) Total pancreas homogenates were obtained from 7 hourly cerulein-injected C57BL/6J AP mice euthanized at the indicated time points (0–24 hours). cGAS and STING mRNA as determined by quantitative polymerase chain reaction (qPCR). Data are presented as mean  $\pm$  SEM from 2 independent experiments (n = 5 mice per group and per experiment). (*B*) Total pancreas tissue was used to determine cGAS, STING, and downstream proteins by Western blot. (*C*) Pancreas acinar cells were obtained from pancreas of control (saline-treated) and cerulein-treated C57BL/6J AP mice at 12 hours following first cerulein injection (50  $\mu$ g/kg, 7 hourly injections). cGAS and STING mRNA as determined by qPCR. Data are represented as mean  $\pm$  SEM from 2 independent experiment). (*D*) Acinar cells from experiments in (*C*) were used to determine cGAS, STING, and downstream potens by Western blot.



**Supplementary Figure 2.** STING signaling also plays an important role in AP induced with CDE diet feeding. (*A*) Representative hematoxylin-eosin (H&E) pancreas staining and histology scores of C57BL/6J WT and STING KO mice euthanized 72 hours following CDE diet feeding. (*B*) Serum levels of lipase in WT and STING KO mice. (*C*) Pancreas trypsin activity from WT and STING KO mice. (*D*, *E*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from WT and STING KO mice. (*F*) DMXAA treatment of AP mice induced with 72 hours of CDE diet feeding. DMXAA (10 mg/kg) or vehicle control (VE) was administered intraperitoneally at 6 hours and 36 hours post initiation of CDE diet feeding. (*G*) Representative H&E pancreas staining and histology scores of mice at 72 hours following CDE diet feeding. (*H*) Serum levels of lipase in VE and DMXAA-treated mice. (*I*) Pancreas trypsin activity from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and IFN $\beta$  from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and DMXAA-treated mice. (*J*, *K*) Bar graphs show pancreas TNF $\alpha$  and IFN $\beta$  from VE and DMXAA-treated mice.