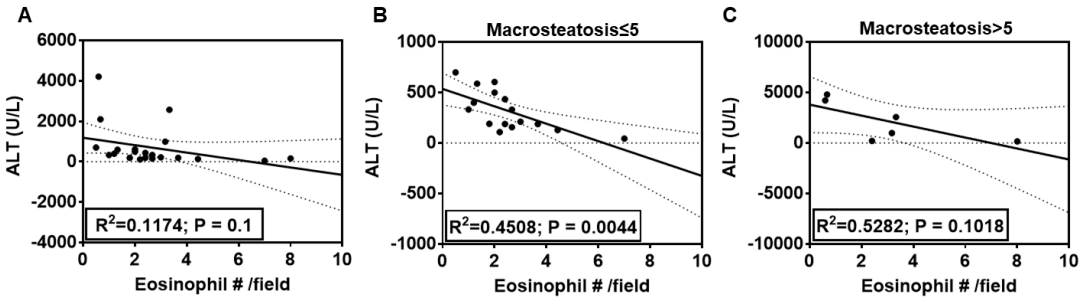

Fig. S1. Correlation between hepatic eosinophil frequency and ALT concentration after orthotopic liver transplantation. (**A**) The numbers of eosinophils in post-ischemia and reperfusion (IR) liver tissues were plotted against serum ALT concentration on day one after liver transplantation for all samples (*n* = 22). (**B**) The numbers of eosinophils were plotted against serum ALT concentration for samples with donor liver macrosteatosis equal to or less than 5% (*n* = 16). (**C**) The numbers of eosinophils were plotted against serum ALT concentration for samples with donor liver macrosteatosis greater than 5% (*n* = 6).

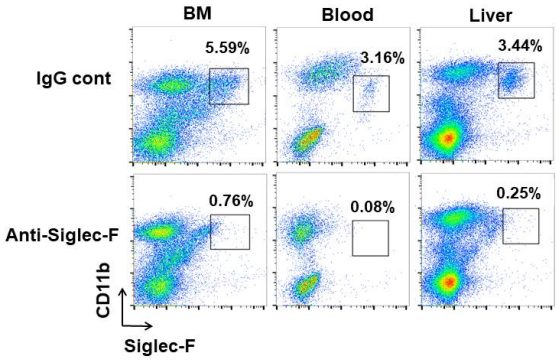

Fig. S2. Anti-Siglec-F antibody effectively depletes eosinophils from the bone marrow (BM), blood, and liver. Male C57BL/6 mice were injected with anti-Siglec-F antibody at 24 hours before liver ischemia. Control mice were injected with IgG. Eosinophils were measured by expression of CD11b and Siglec-F by flow cytometry at 4 hours post-reperfusion. Data represent results from 3 mice per group.

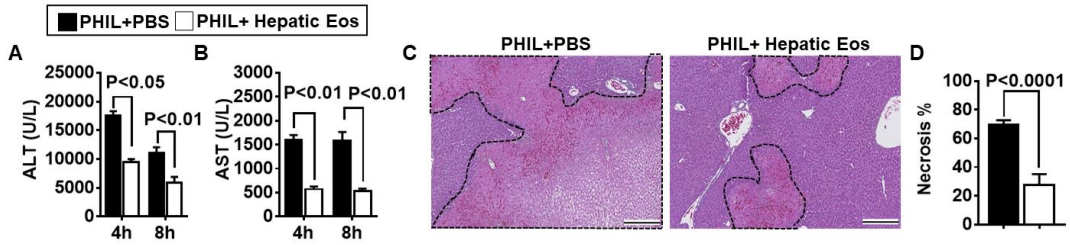

Fig. S3. Eosinophils from IR-injured livers of WT mice can attenuate IR injury in eosinophil-deficient PHIL mice. Liver eosinophils isolated from C57BL/6 mice at 24 hours after IR injury were adoptively transferred into PHIL mice (*n* = 3) at 24 prior to IR surgery. Control PHIL mice were injected with PBS (*n* = 3). Serum concentrations of ALT (**A**) and AST (**B**) were measured at 4 and 8 hours after reperfusion. Liver necrosis (scale bar, 200μm) was examined at 24 hours post-reperfusion (**C**) and quantified (**D**). A two-tailed unpaired Student's t tests with Welch's correction was performed in D. A two-way ANOVA was performed in A and B.

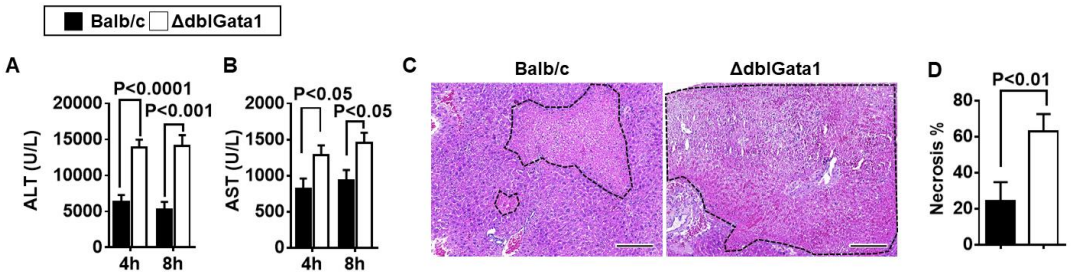

Fig. S4. ΔdblGata-1 mice develop exacerbated liver IR injury. WT male Balb/c and eosinophil-deficient male ΔdblGata-1 mice were subjected to hepatic IR surgery (*n* = 4 mice per group). Serum concentrations of ALT (**A**) and AST (**B**) were measured at 4 and 8 hours after reperfusion. Liver necrosis (scale bar, 200μm) was examined at 24 hours post-reperfusion (**C**) and quantified (**D**). A two-tailed unpaired Student's t tests with Welch's correction was performed in D. A two-way ANOVA was performed in A and B.

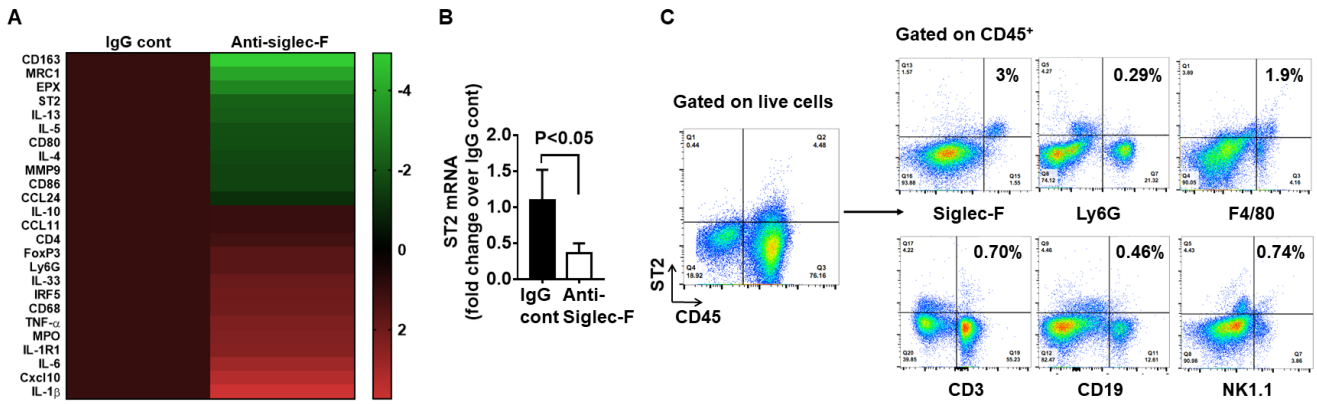

Fig. S5. Hepatic eosinophils express ST2 during IR injury. Male C57BL/6 mice were intraperitoneally injected with either IgG control or anti-Siglec-F antibody at 24 hours before liver ischemia. After 4 hours of reperfusion, liver non-parenchymal cells were isolated. (**A**) Microarray analysis was performed and a heatmap was generated by two-way hierarchical clustering. (**B**) mRNA expression of ST2 was measured by qPCR in male C57BL/6 mice 4 hours post IR injury (*n* = 4 mice per group). (**C**) Liver non-parenchymal cells were stained for ST2 and markers to identify eosinophils (Siglec-F$^+$), neutrophils (Ly6G$^+$), macrophages (F4/80$^+$), T lymphocytes (CD3$^+$), B lymphocytes (CD19$^+$), and NK or NKT cells (NK1.1$^+$) (*n* = 7 mice per group). A two-tailed unpaired Student's t tests with Welch's correction was performed in B.

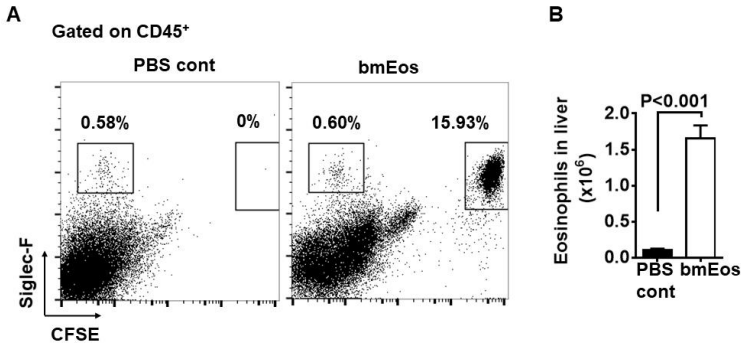

Fig. S6. Adoptively transferred eosinophils accumulate in the liver. ST2$^{-/-}$ mice received an adoptive transfer of CFSE-labeled WT-bone marrow derived eosinophils (bmEos) prior to IR surgery. At 4 hours post-reperfusion, eosinophil accumulation in the liver was measured by flow cytometry (**A**) and quantified (**B**) (*n* = 4 mice per group). A two-tailed unpaired Student's t tests with Welch's correction was performed in B.

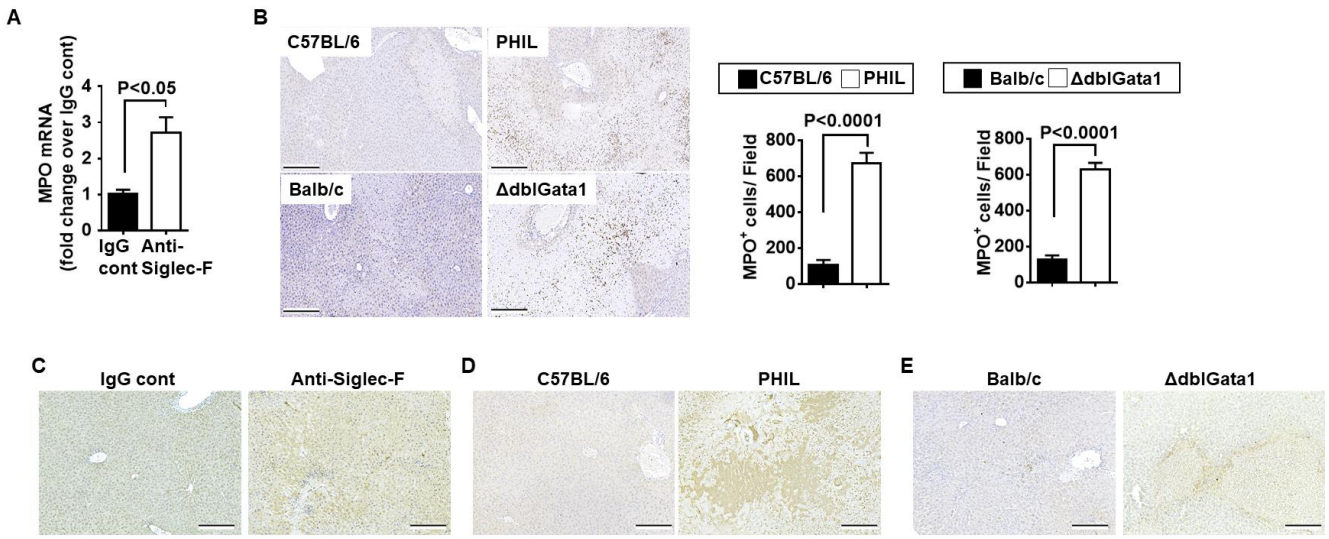

Fig. S7. Increase of hepatic neutrophil accumulation in the absence of eosinophils. (**A**) mRNA expression of myeloperoxidase (MPO) was measured by qPCR in liver non-parenchymal cells from anti-Siglec-F-treated and IgG-treated C57BL/6 mice after liver IR injury (*n* = 3 in IgG-treated group and *n* = 4 in anti-Siglec-F-treated group). (**B**) MPO immunohistochemical staining (scale bar, 200μm) was performed on liver sections to compare the numbers of neutrophils in eosinophil-deficient PHIL and ΔdblGata1 with their WT counterparts at 24 hours post-reperfusion. (**C-E**) Liver tissues (scale bar, 200μm) were collected at 4 hours post-reperfusion and stained for HOCl-protein adducts (brown) in anti-Siglec-F-treated mice (**C**), as well as in PHIL (**D**) and ΔdblGata1 mice (**E**). A two-tailed unpaired Student's t tests with Welch's correction was performed in E. A one-way ANOVA was performed in A and B.

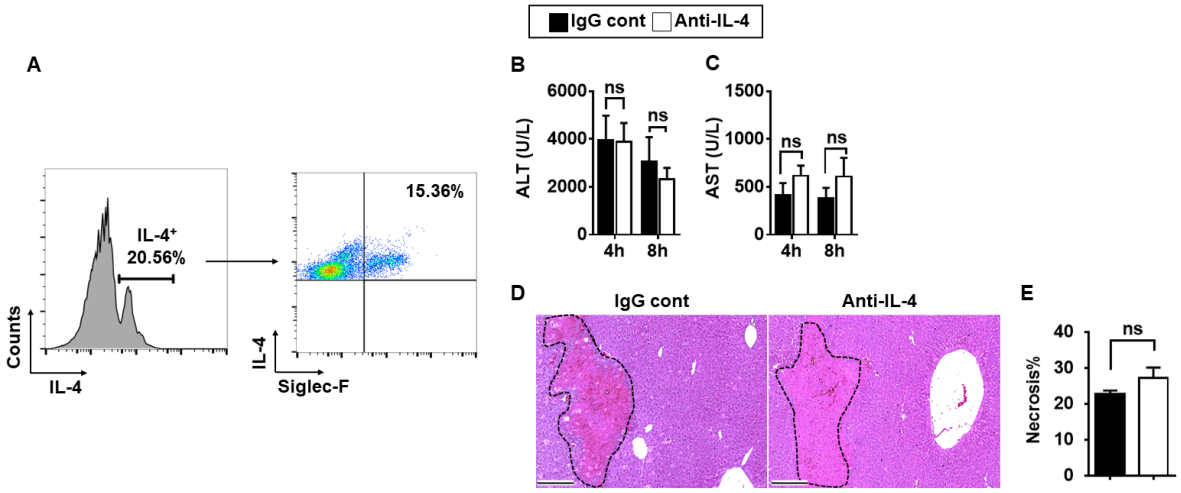

Fig. S8. IL-4 is not required for the hepatoprotective function of eosinophils. (**A**) Male C57BL/6 were subjected to ischemia and reperfusion. Liver non-parenchymal cells were isolated from WT mice at 4 hours post-reperfusion and stained for intracellular IL-4. IL-4-positive cells are gated, and the proportions of eosinophils (Siglec-F$^+$) that express IL-4 among total IL-4$^+$ cells are shown (*n* = 4 mice per group). (**B-E**) Male C57BL/6 (*n* = 3 mice per group) were intraperitoneally injected with anti-IL-4 at 1 hour prior to ischemia. Serum concentrations of ALT (**B**) and AST (**C**) were measured at 4 and 8 hours after reperfusion. (**D**) Liver necrosis (scale bar, 200μm) was examined at 24 hours post-reperfusion and quantified (**E**). A two-tailed unpaired Student's t tests with Welch's correction was performed in E. A two-way ANOVA was performed in B and C.

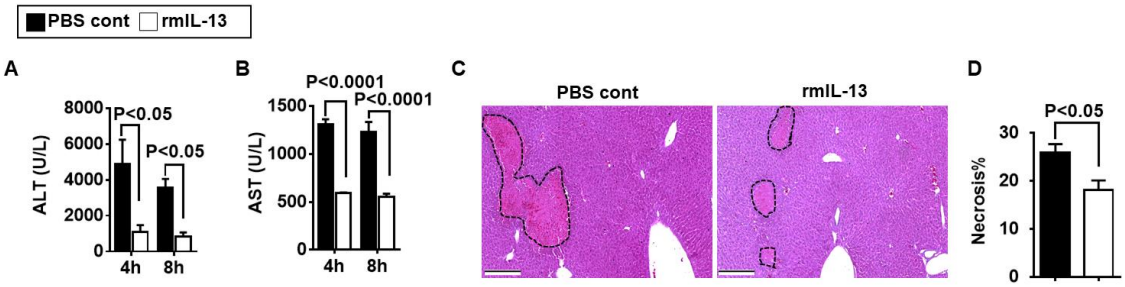

Fig. S9. Recombinant mouse IL-13 reduces hepatic IR injury. Male C57BL/6 mice were intravenously injected with recombinant mIL-13 at 1 hour prior to IR surgery (*n* = 3 mice per group). Serum ALT (**A**) and AST (**B**) concentrations were measured at 4 and 8 hours post-reperfusion. Liver necrosis (scale bar, 200μm) was determined at 24 hours post-reperfusion (**C**) and quantified (**D**). A two-tailed unpaired Student's t tests with Welch's correction was performed in D. A two-way ANOVA was performed in A and B.

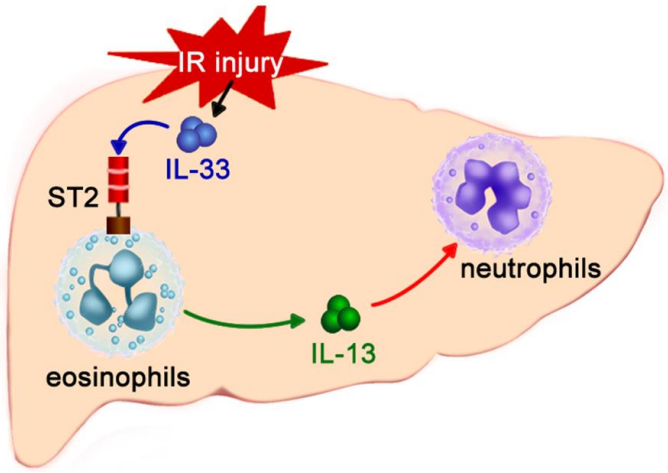

Fig. S10. Schematic summary of the main findings. Hepatic IR injury causes rapid accumulation of eosinophils in the liver. IL-33 signals through ST2 on eosinophils to induce IL-13 production. As the major source of IL-13, eosinophils suppress neutrophils and attenuate liver injury.