Supporting Information

Lee et al. 10.1073/pnas.1411679111

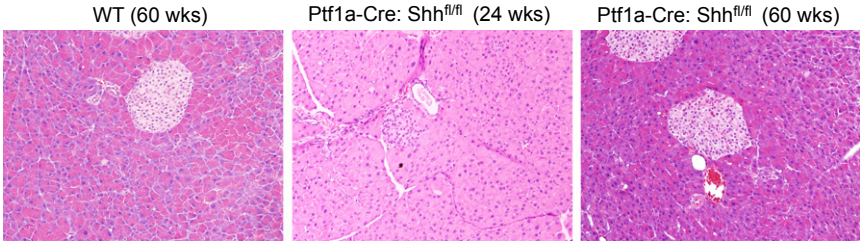

Fig. S1. Deletion of Shh is dispensable for normal pancreas development. Representative histology of pancreata from a 60-wk-old wild-type mouse (*Left*), 24-wk-old *Ptf1a-Cre:Shh$^{fl/fl}$* mouse (*Center*), and 60-wk-old *Ptf1a-Cre:Shh$^{fl/fl}$* mouse (*Right*).

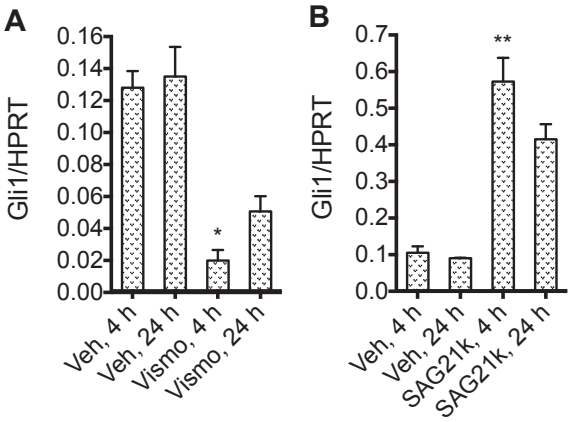

Fig. S2. Pharmacologic modulation of Hh pathway response in mice. (*A*) Normalized *Gli1* expression in pancreata of 9-wk-old male FVB mice given either MCT vehicle ($n = 3$) or vismodegib at 100 mg/kg ($n = 3$) by oral gavage daily for 5 d. Pancreata were harvested either 4 h or 24 h after the last dose of drug as shown. A 6.4-fold relative reduction of *Gli1* expression was observed in vismodegib-treated mice (Veh 4 h vs. Vismo 4 h, $*P = 0.0001$). (*B*) Normalized *Gli1* expression in pancreata of 9-wk-old male FVB mice given either MCT vehicle ($n = 3$) or SAG21k at 5 mg/kg ($n = 3$) by oral gavage daily for 5 d. Pancreata were harvested either 4 h or 24 h after the last dose of drug as shown. A 5.5-fold relative increase in *Gli1* expression was observed in SAG21k-treated mice (Veh 4 h vs. SAG21k 4 h, $**P = 0.002$). Error bars indicate SEM.

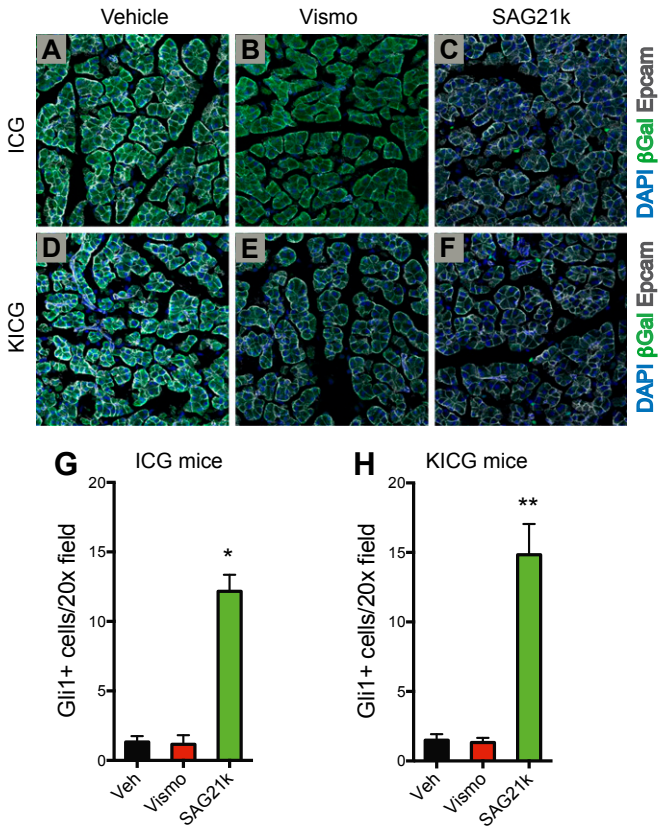

Fig. S3. Modulation of Hh response without concomitant cerulein controls the number of *Gli*$^+$ cells in pancreata. (*A–C* and *G*) ICG mice were treated as in Fig. 4, except that cerulein was not administered. Vismodegib does not alter significantly the number of *Gli1*$^+$ cells. However, SAG21k increases the number of *Gli1*$^+$ cells by 9.1-fold (*$P < 0.0001$, $n = 6$). Error bars indicate SEM. (*D–F* and *H*) KICG mice were similarly examined. Likewise, vismodegib does not alter the number of *Gli1*$^+$ cells whereas SAG21k increases the number by 9.9-fold (**$P < 0.0001$, $n = 6$). Error bars indicate SEM.

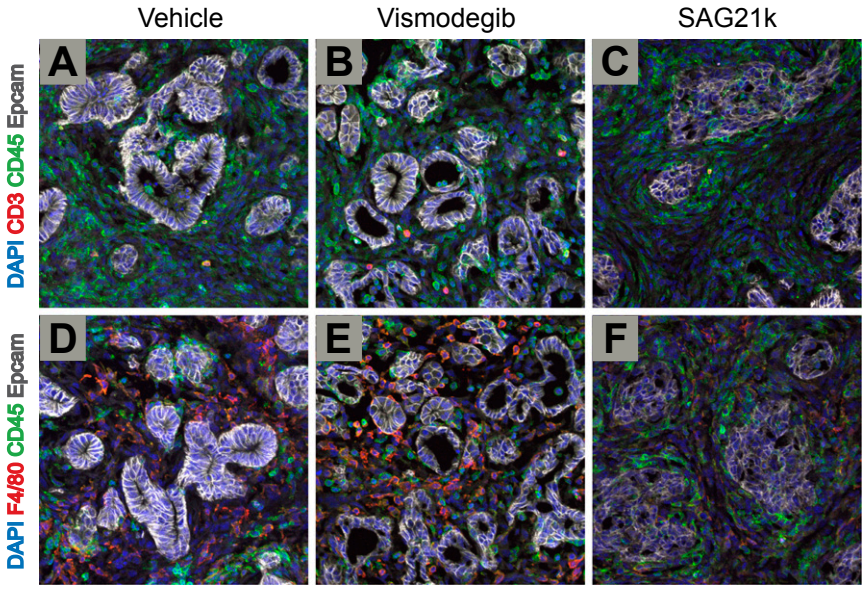

Fig. S4. Identity of CD45-positive hematopoietic cells during cerulein-enhanced oncogenesis. (*A–F*) Confocal images of pancreata of cerulein-treated KICG mice are shown. (*A–C*) CD3$^+$ T cells (orange or yellow) represent a minor fraction of the CD45$^+$ inflammatory infiltrate in vehicle-, vismodegib-, and SAG21k-treated mice. (*D–F*) F4/80$^+$ macrophages (orange or yellow) also represent a fraction of CD45$^+$ cells but appear more prevalent than CD3$^+$ cells under all three treatment conditions. (*C* and *F*) Notably, the zone of CD45$^+$ cells around globular epithelial structures in SAG21k-treated mice does not contain a predominance of either CD3$^+$ or F4/80$^+$ cells.