



**Figure S9:** Analysis of AP induced transcriptional changes in splenic  $T_{reg}$  and duodenal tissue samples. (A) Comparative pathway analysis of the transcriptome data showed similar immune pathway and disease pattern alterations in isolated  $T_{reg}$  (top) and duodenal tissue (bottom). (B-D) Comparative analysis of AP-associated predicted upstream regulators in  $T_{reg}$  (top) and duodenal tissue (bottom) of selected individual genes in the group of cytokines (B), transcriptional regulators (C) and downstream target genes (D). Important upstream regulators showed a similar activation pattern at the mRNA level in both sample sets. Whereas transcripts of the anti-inflammatory cytokines TGF $\beta$ 1, IL-4, and IL-13 were more abundant, type I cytokines IL-12 $\beta$ , IL-2 and IFN $\gamma$  mRNAs were decreased. Interestingly, gene expression of the IL-6 cytokine family like IL-6 or oncostatin M (OSM) was activated in both sample sets (B). The expression pattern of transcriptional regulator genes such as *Stat3* and *Stat6*, which were significantly induced, indicated a type 2 immune response. *Tbx21*, *Stat1* or *Irf1*, *Irf7* and *Irf3*, which were significantly repressed suggested a general pancreatitis-associated anti-inflammatory reaction (C). Gene expression alterations of other downstream regulators, such as CTLA4, IL10RA, IL6R, the IL-12 family pathway and the IFN $\gamma$  pathway support the notion of a general SAP-induced immune suppression, which is mediated by CD25<sup>+</sup>/FOXP3<sup>+</sup> Tregs (D). Heatmaps illustrate activation z-scores, whereas bar graphs depict Benjamini-Hochberg corrected  $p$ -values ( $-\log_{10}(pBH\text{-value})$ ).