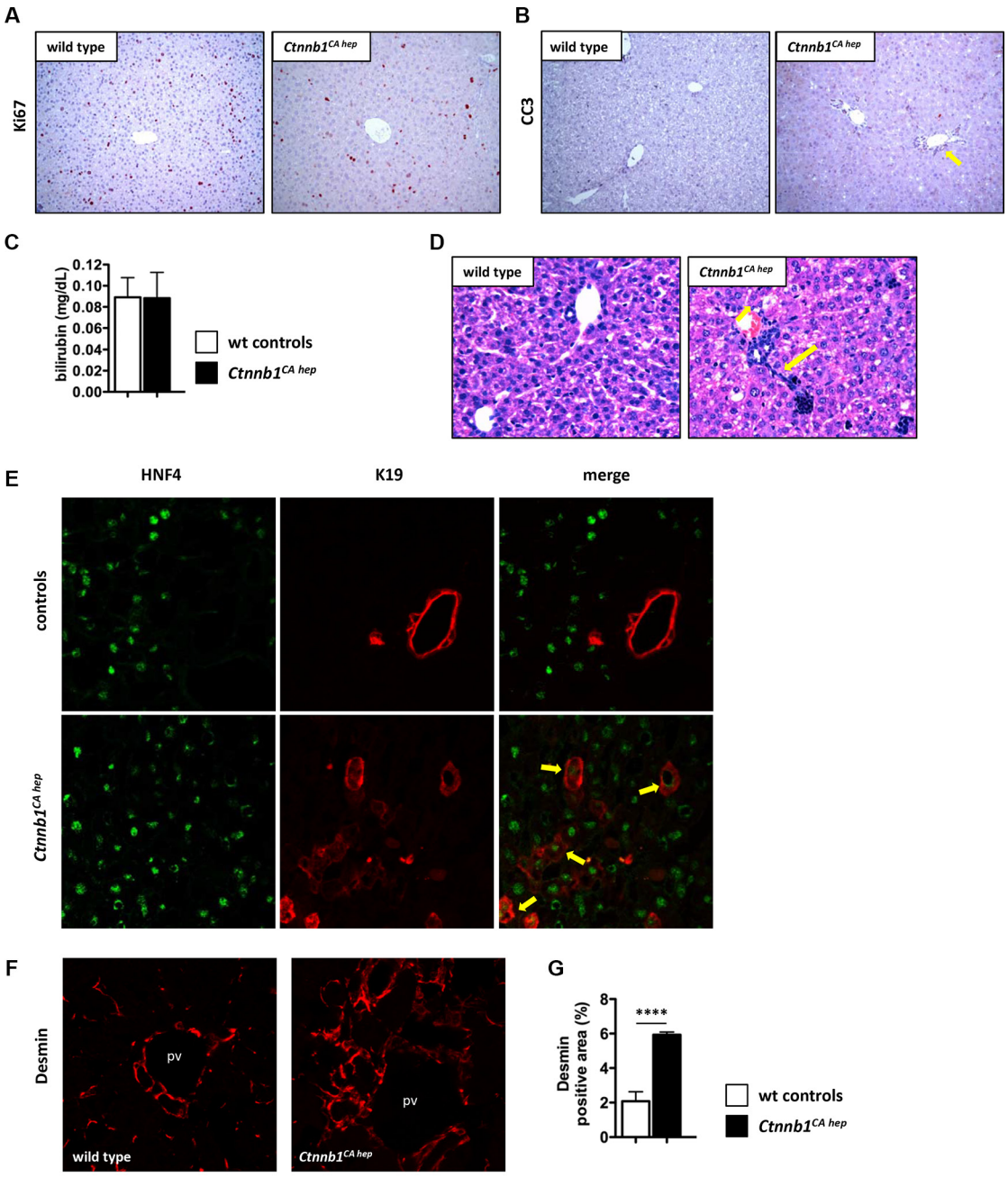
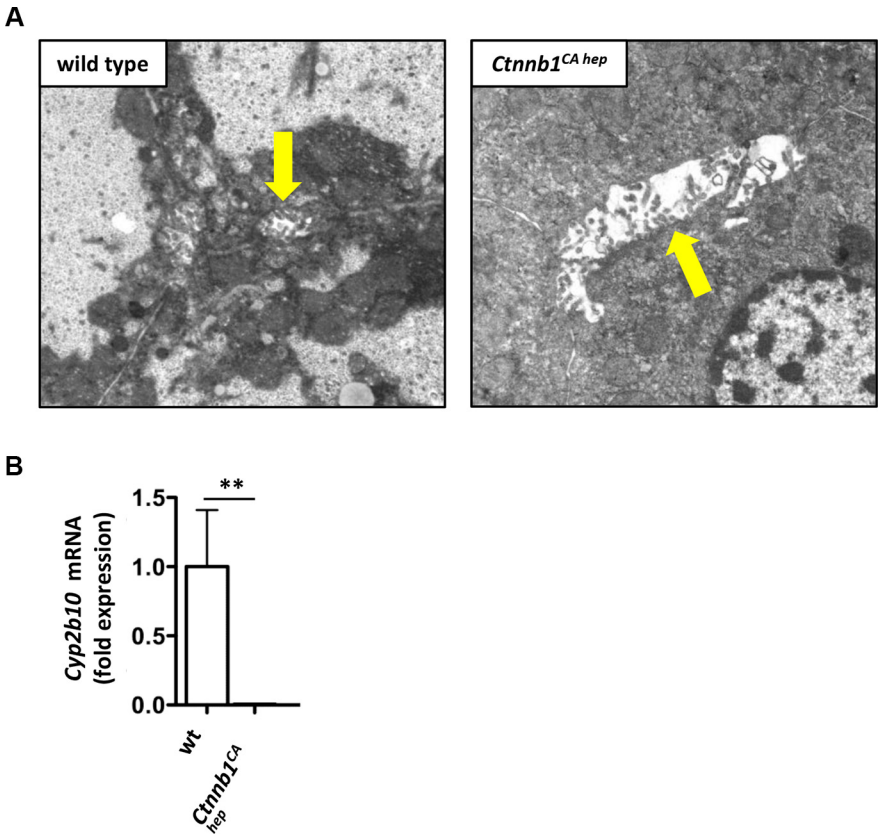
Hepatocyte specific expression of an oncogenic variant of β-catenin results in cholestatic liver disease

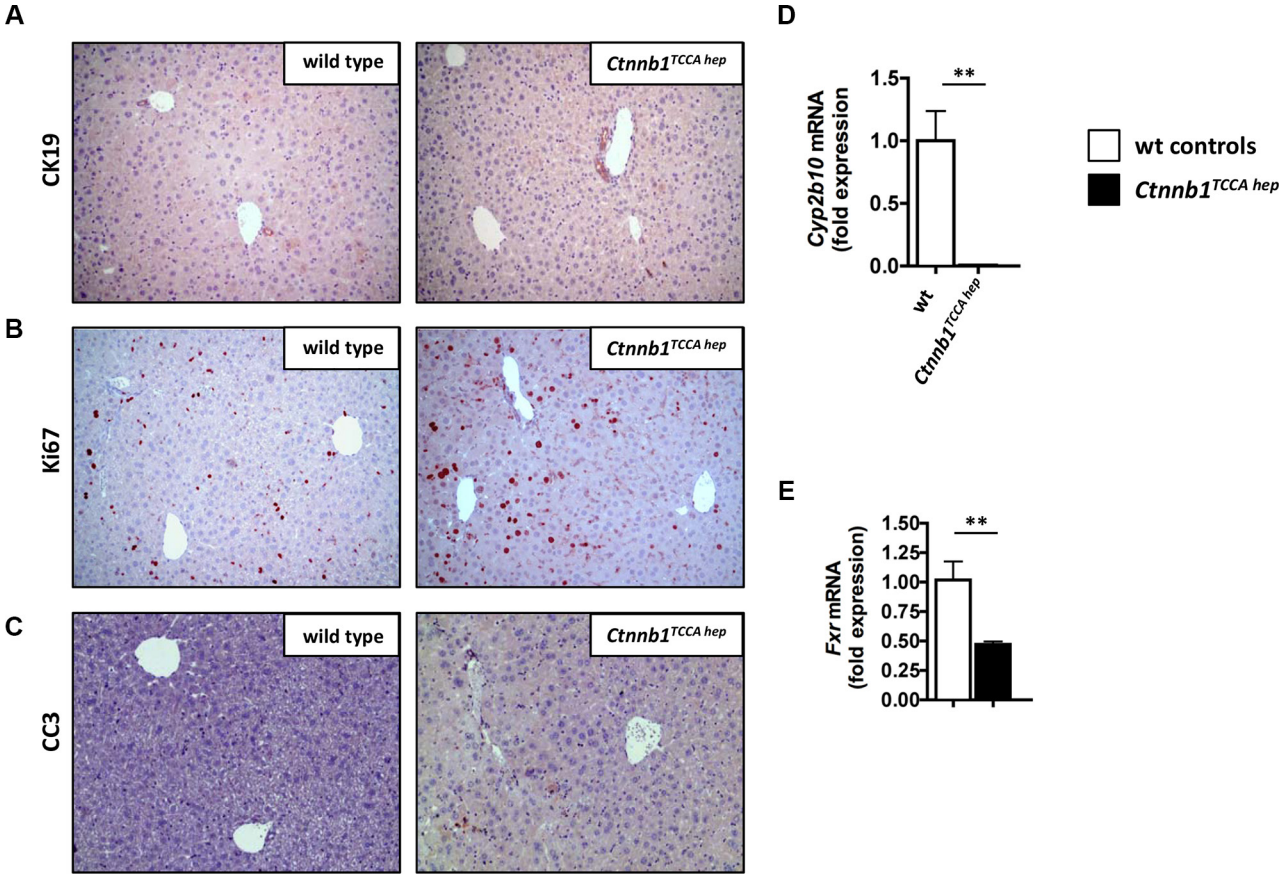
Supplementary Materials



Supplementary Figure S1: Histological analysis of livers of *Ctnnb1*$^{CA\ hep}$ mice. Livers of *Ctnnb1*$^{CA\ hep}$ mice show no changes in proliferation compared to wt controls as analyzed by immunohistochemical staining for the proliferation marker Ki67 (**A**). Cholangiocytes of bile ducts reveal apoptosis in *Ctnnb1*$^{CA\ hep}$ mice as detected by immunohistochemical staining for cleaved caspase 3 (CC3) (**B**). No changes in bilirubin could be detected (**C**). Increased cholangiocyte numbers are detected in H&E stained sections of *Ctnnb1*$^{CA\ hep}$ mice compared to wt controls (yellow arrows) (**D**). *Ctnnb1*$^{CA\ hep}$ mice displayed a dedifferentiation of hepatocytes, confirmed by double immunflourescence staining for HNF4 and Keratin 19 (K19). Double-positive cells are marked by arrows (**E**). *Ctnnb1*$^{CA\ hep}$ mice show significantly enhanced numbers of collagen producing hepatic stellate cells as analyzed by immunofluorescence staining for Desmin (**F**). Desmin positive areas were significantly increased as evaluated by morphometric quantification using Image J (pv = portal vein) (**G**).



Supplementary Figure S2: Evaluation of electron microscopy images revealed dilated bile canaliculi in *Ctnnb1*$^{CA\ hep}$ mice (yellow arrow) (A). mRNA levels of the CAR target gene *Cyp2b10* was completely abolished in livers of *Ctnnb1*$^{CA\ hep}$ mice (**B**).



Supplementary Figure S3: *Ctnnb1*$^{TCCA\ hep}$ mice display increased numbers of Keratin 19 positive cholangiocytes compared to wt controls. (**A**) Immunohistochemical staining for Ki67 and cleaved caspase 3 (CC3) revealed no significant changes in regards to proliferation (**B**) or apoptosis (**C**) in livers of *Ctnnb1*$^{TCCA\ hep}$ mice. mRNA levels of the CAR target gene *Cyp2b10* was completely abolished in livers of *Ctnnb1*$^{TCCA\ hep}$ mice (**D**). *Ctnnb1*$^{TCCA\ hep}$ mice displayed a significant decrease of *Fxr* levels in enterocytes of the terminal ileum compared to wt controls (**E**).