Supplementary Figures

Figure S1

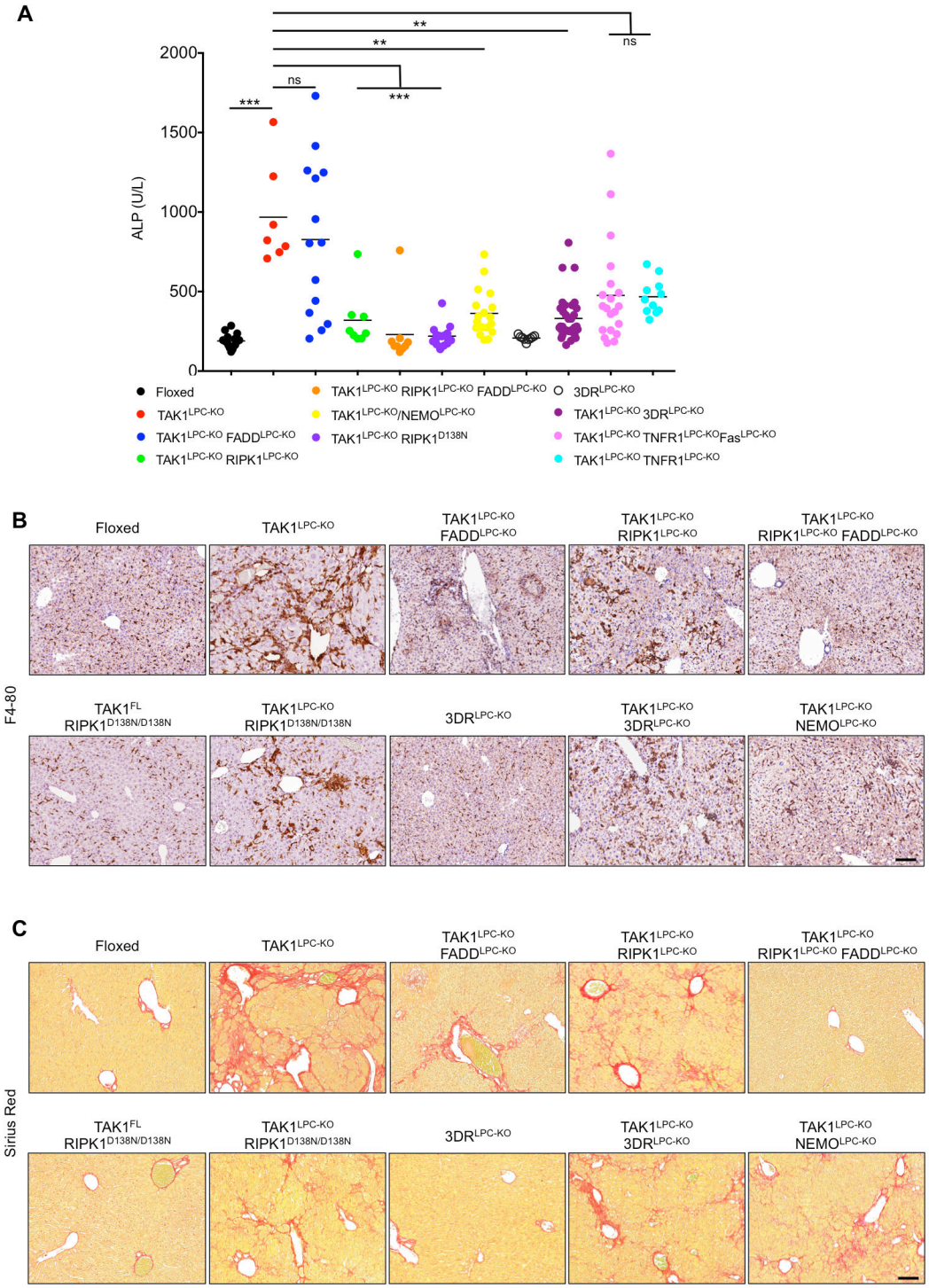

Figure S1: Biliary damage, inflammation and fibrosis in TAK1^{LPC-KO} mice. (A) Serum levels of alkaline phosphatase (ALP) in 6-week-old, sex-matched mice with the indicated genotypes. (B-C) Representative images of liver sections from 6-week-old mice with the indicated genotypes immunostained for the macrophage marker F4/80 (B) or stained with Picrosirius Red (C) to visualize liver inflammation and fibrosis, respectively. Bars: 100 µm.

Figure S2

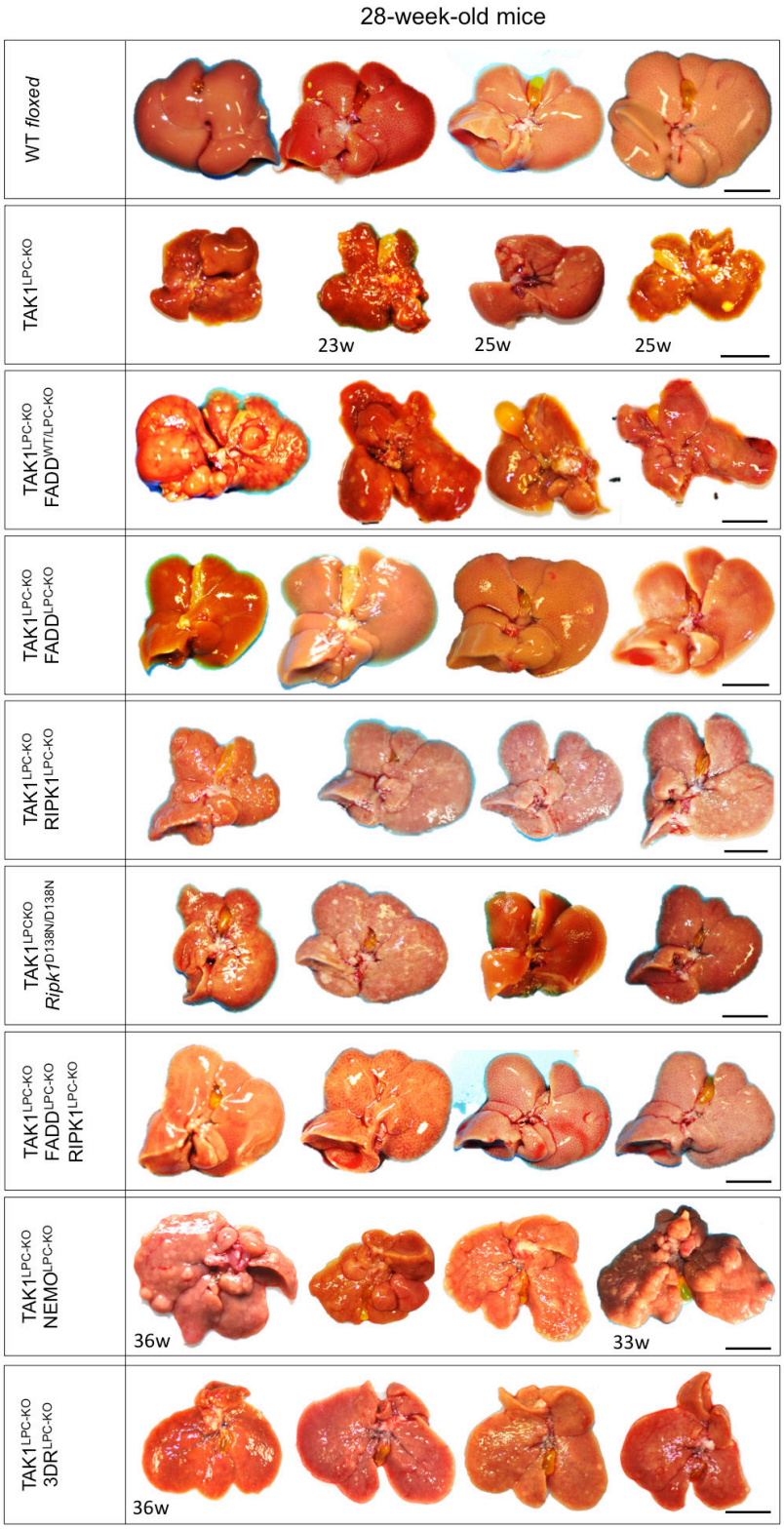

Figure S2: Collection of liver images from mice with the indicated genotypes at 28 weeks of age, unless otherwise stated. Bars: 1 cm.

Figure S3

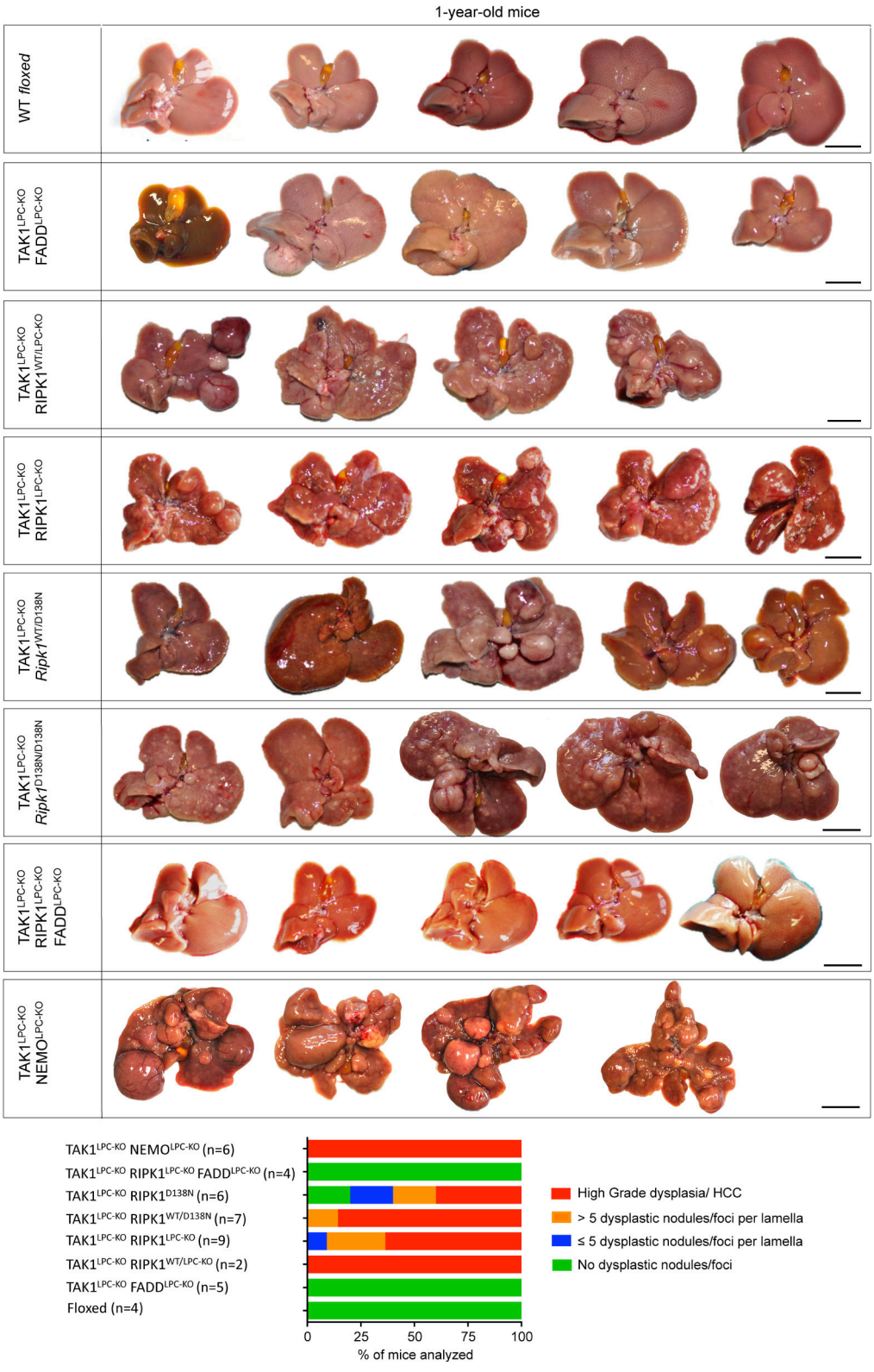

Figure S3: Collection of liver images from 1-year-old mice with the indicated genotypes and histopathological evaluation of hepatocarcinogenesis. Bars: 1 cm.

Figure S4

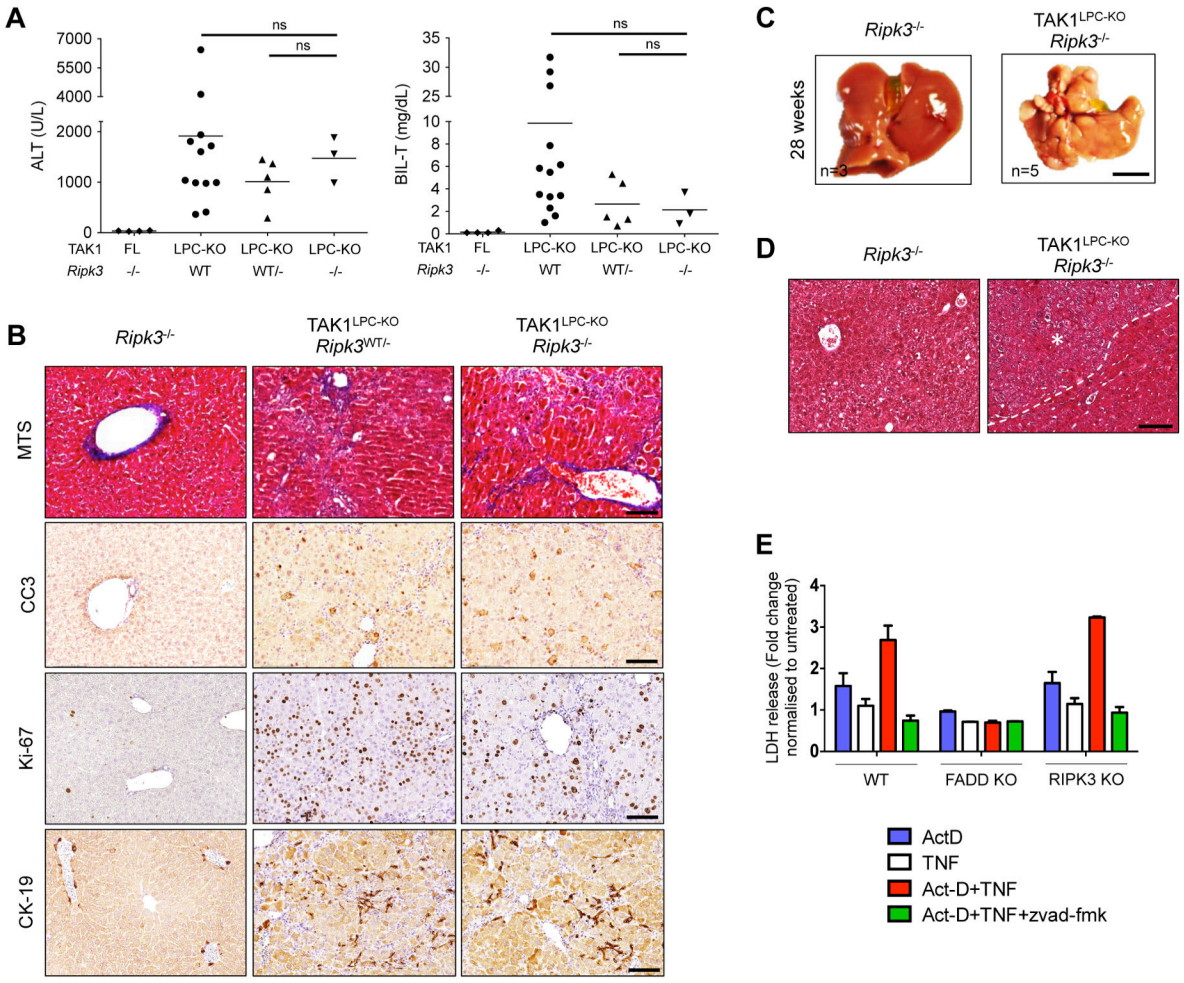

Figure S4: RIPK3 deletion reduces biliary but not hepatocellular damage in TAK1$^{LPC\text{-}KO}$ mice. (A) Serum levels of ALT and total Bilirubin in 6-week-old mice with the indicated genotypes (B) Representative images of liver sections from 6-week-old mice with the indicated genotypes stained with Masson's trichrome or immunostained for CC3, Ki-67 and CK19. (C-D) Representative liver photos (C) and images of liver sections stained with Masson´s trichrome (D) from 28-week-old mice with the indicated genotypes. A dysplastic nodule is outlined and marked with an asterisk. (E) Primary hepatocytes with the indicated genotypes were treated for 24 h with TNF, Actinomycin D and zVAD-fmk as indicated and cell death was measured using LDH release assay. The values are expressed as fold-change in LDH release after each treatment compared to respective non-treated cells for each genotype whose values were set at 1. Bars: (C) 1 cm; (B,D) 100 µm.

Figure S5

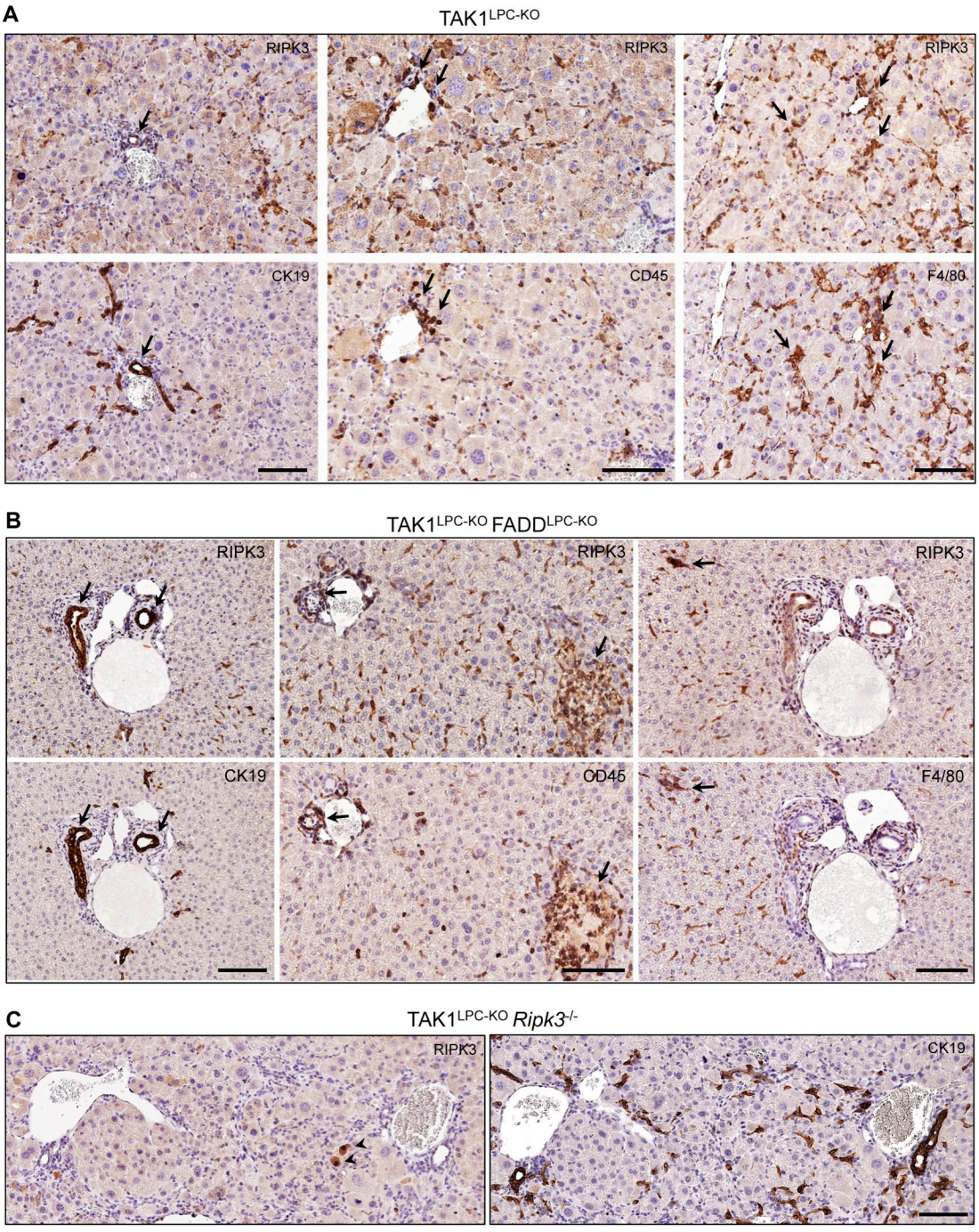

Figure S5: RIPK3 is expressed in liver macrophages, lymphocytes and cholangiocytes, but not in hepatocytes. Immunohistochemical localisation of RIPK3 and CK19 (cholangiocyte and liver progenitor cell marker), CD45 (immune cell marker with higher expression in liver lymphocytes) or F4/80 (macrophage marker) on serial sections from TAK1^{LPC-KO} (A), TAK1^{LPC-KO} FADD^{LPC-KO} (B) and TAK1^{LPC-KO} *Ripk3*$^{-/-}$ mice (C). Arrows indicate cholangiocytes, lymphocytes and macrophages expressing high levels of RIPK3 in contrast to hepatocytes, which are largely negative for RIPK3. Note the background RIPK3 staining in some apoptotic hepatocytes (arrowheads) in TAK1^{LPC-KO} *Ripk3*$^{-/-}$ mice. Bars: 100 µm.