

## **Supplemental Material and Methods**

### **Histochemical staining**

Immediately after euthanasia, a portion of liver tissue from WT, *Tlr5*KO, *Fxr*KO, and DKO mice was preserved in 10% neutral buffered formalin (NBF, Fisher Scientific) for 24 h. Samples were submitted to the University of Toledo Microscopy Facility for paraffin-embedded sectioning and hematoxylin and eosin (H&E) staining to describe liver tumors and cells found in surrounding liver tissue. Histology images were captured from the VS120 Virtual Slide Microscope (Olympus) through the OlyVIA software. Histological scoring was conducted by a board-certified pathologist in a blinded fashion.

### **Oil red O staining**

Immediately after euthanasia, a portion of liver from WT, *Tlr5*KO, *Fxr*KO, and DKO mice was embedded in optical cutting temperature (OCT) compound in a cryomold, snap-frozen on dry-ice, and stored at -80°C. Frozen sections (10 microns) generated using Cryostat (Leica Biosystems CM3050 S) were used for Oil red O staining to monitor steatosis. In brief, sections were kept in PBS for 10 min and briefly washed with 60% isopropanol. Liver sections were placed in Oil red O (Sigma-Aldrich, St. Louis, MO) solution (0.5% in 60% isopropanol) for 30 min. Afterward, sections were briefly rinsed with 60% isopropanol to remove the non-specific staining and counterstained with Mayer's hematoxylin (Sigma-Aldrich, St. Louis, MO). Images were captured from the VS120 Virtual Slide Microscope (Olympus) through the OlyVIA software.

### **Picrosirius red staining**

Picrosirius red staining was used to observe the collagen accumulation in the liver. Briefly, deparaffinized liver (5 microns) sections were incubated with picrosirius red (0.1% sirius red in saturated picric acid) solution for one hour and quickly washed with acidified water (0.5% acetic acid). Images were captured using the VS120 Virtual Slide Microscope (Olympus) through the OlyVIA software.

### **Immunohistochemical staining**

Immunohistochemical staining was performed on paraffin-embedded liver sections (5 microns) for the hepatobiliary tract marker [Cytokeratin 19 (1:400)] (Abcam, Cat# ab52625). Immunoreactivity was revealed by using Vectastain Elite ABC kit and peroxidase substrate kit (Vector Laboratories, Burlingame, CA). Similar exposure time for each section was used to acquire the image. The sections were imaged and analyzed by Olympus OlyVIA.