Supplemental Methods:

Hepatocyte isolation: Primary mouse HPCs were isolated as previously described [1]. Mice were given a single i.p. injection of 50 mg/kg sodium pentobarbital (Nembutal) or avertin (250 mg/kg) to achieve deep anesthesia. The caudal vena cava was canulated, the portal vein cut, and the liver perfused initially with 50 mL of 37°C sterile calcium- and magnesium-free Hanks' Balanced Salt Solution (HBSS, Sigma-Aldrich, St. Louis, MO) supplemented with 0.5 mM EGTA, 5.5 mM glucose, and penicillin/streptomycin (P/S, Sigma-Aldrich) followed by 40 mL of 37°C sterile HBSS supplemented with 1.5 mM calcium chloride, 5.5 mM glucose, P/S, and 0.039 g of Type IV Collagenase (920 collagen digestion units [CDU]/mg, Sigma). Livers were then surgically removed and gently agitated in William's medium E (medium) containing 10% fetal bovine serum (FBS, Sigma) and P/S, and the solution passed through sterile gauze to separate undigested liver. The medium containing digested liver was adjusted to 50 mL with FBS-containing medium and subjected to centrifugation at 50xg for 2 minutes. The supernatant was aspirated and the cell pellet (HPCs) was washed 3 times with 50 mL of FBS-free medium. HPC viability was evaluated by trypan blue exclusion and a viability of $\geq$85% was set as the minimum criteria for HPC utilization. HPCs were resuspended at a density of 2.5×10^5 viable cells/ml in FBS-containing medium and were immediately used for experimentation or were plated on 6-well culture plates at a density of 5×10^5 cells/well or on 24-well culture plates (Xa generation assay) at a density of 1.25×10^5 cells/well (Becton Dickinson and Company, Franklin Lakes, NJ) and incubated at 37°C at 5% CO_2.

Single-stage clotting assay: Cellular PCA was determined using a single-stage clotting assay as described previously [2]. Isolated HPCs or approximately 100 mg of whole liver were lysed or homogenized, respectively, in 15 mM N-octyl-β-D-glucopyranoside and incubated at 37°C for 15 minutes. Lysate was then adjusted to a final concentration of 5 mM N-octyl-β-D-glucopyranoside. PCA was assessed using 50 µl of citrated plasma (10% mouse plasma/90% human normal pooled plasma; George King Bio-Medical Inc., Overland Park, KS) and 50 µl of lysed mouse sample were clotted in a

Start4 coagulation analyzer (Stago, Parsippany-Troy Hills, New Jersey) after the addition of 50 µl of 20 mM calcium chloride (Sigma). For select studies, 100% normal human pooled plasma, or factor VII-deficient human plasma (George King Bio-Medical Inc.) were utilized. The concentration of protein in each sample was determined using a commercial kit (Bio-Rad D_C). PCA was adjusted per mg protein for whole liver or per cell input for hepatocytes

References:

1. Kim ND, Moon JO, Slitt AL, Copple BL. Early growth response factor-1 is critical for cholestatic liver injury. *Toxicol Sci*. 2006;90(2):586-595.

2. Morrissey JH, Fair DS, Edgington TS. Monoclonal antibody analysis of purified and cell-associated tissue factor. *Thromb Res*. 1988;52(3):247-261.