



Supplemental Fig 1. Effect of PHx on expression of Cyp7a1, 7b1, 8b1, 27a1, and BAT and FABP5 mRNA in mouse liver. Bars represent means of unit (RLU) 10 μg total RNA ± SEM of 5–8 mice. Asterisks indicate a significant difference (p < 0.05) from the respective value of sham-operated mice. Daggers indicate a statistically significant changes (p < 0.05) in sham operated mice 24 to 48 hrs.

Activation of FXR in response to BA accumulation causes repression of the key bile-acid synthetic enzyme Cyp7a1 through the small heterodimer protein (SHP). Cyp7a1 mRNA is reduced 50% in mice 24 and 48 hrs after PHx. Similar to Cyp7a1, Cyp8b1 and 27a1 decreased, changes which were only significant at 48 hrs after PHx. In contrast, PHx did not influence the mRNA expression of Cyp7b1. Cyp7b1 catalyses the conversion of 27-hydroxycholesterol to bile acid in the alternative pathway; however, production of its substrate, the 27-hydroxycholesterol, is probably compromised because the expression of Cyp27a1 decreased. Taken together, we conclude that the gene expressions of key classical and alternative BA synthetic enzymes are down-regulated in mice following PHx.

The conjugation of bile acids with glycine or taurine is a two-step process: BAs are first converted into their coenzyme A (CoA) thioesters by bile acid CoA ligase (BAL). These activated intermediates then become substrates for a second enzyme, bile acid CoA:amino acid N-acyltransferase (BAT), which conjugates BAs with either glycine or taurine. Fatty acid transport protein (Fatp5) is considered to be the major BAL in mice (Hubbard et al., 2006), however its exact role has not been clarified. PHx tended to decrease the mRNA expression of BAL at 24 hrs, but significantly decreased it at 48 hrs compared to sham operated mice. Interestingly, the expression of Fatp5 increased 42% in sham control mice from 24 to 48 hrs after PHx. This latter phenomenon in sham-operated mice is probably attributable to the recovery after operation. In contrast to BAL, PHx did not influence BAT mRNA levels. These data indicate that BA conjugation is not compromised in PHx-ed mice; however, the BA activation with CoA probably decreased. It is known that probably other enzymes such as Fatp2 might also activate bile acids. Since the bile acid conjugation enzymes of mice are not well characterized, further targeted studies are need to clarify the regulation of BA conjugation in PHx mice.