Supplemental Figure 1: Characteristics of GF/ SPF *mdr2*$^{-/-}$ and WT mice with and without broad-spectrum antibiotics. Akaline phosphatase (ALP), total cholic acid (CA) and α&β murichlolic acid (MCA) in GF v SPF in 6-8wk old *mdr2*$^{-/-}$ and WT mice (A-C). Pooled serum TB, ileal expression of apical sodium dependent bile acid transporter (ASBT), farsenoid-X receptor (FXR), fibroblast growth factor 15 (FGF-15), along with liver cyp7a1 in GF *mdr2*$^{-/-}$ vs WT mice (D-H). Survival in untreated SPF WT and *mdr2*$^{-/-}$ mice (WT= 13, *mdr2*$^{-/-}$ 23) (I-J). Representative photomicrographs of 6-8wk old GF, SPF, or post-FMT GF mdr2-/- murine liver stained by myeloperoxidase (MPO) (K, 100X) along with composite automated scoring of % MPO positive cells (L). Serum ALT (M), ALP(N) and 14d change in weight (O) following broad-spectrum antibiotics (vancomycin, neomycin and metronidazole) ad libitum compared to water controls. Results are expressed as means +/- SEM. Survival data analyzed by Log-rank (Mantel-Cox) test, group or pairwise comparisons performed by ANOVA or Student t-test, respectively. PCoA of the beta were analyzed by permanova analysis. P-value*P < .05, **P < .01, ***P <.001, ****P < .0001.

Supplemental Figure 2: Efficacy of putative hepatoprotective resident bacteria in *mdr2*$^{-/-}$ mice. Experimental design of accelerated antibiotic treatment model: SPF *mdr2*$^{-/-}$ mice were treated with broad-spectrum antibiotics (vancomycin, metronidazole and neomycin) for 7d vs. 14d (A) resulting in aggressive liver inflammation and injury: the 7d antibiotic regimen had increased histologic inflammation (B) and serum alkaline phosphatase (C), but not liver fibrosis (D), and increasing trend of serum total bile acids (E) (7d, N=3, 14d, N=3, 2 experiments). Experimental design of ad libitum exposure in drinking H2O of ASBT inhibitor (GSK23306,10mg/kg) for 14d in setting of 7d broad antibiotic pretreatment in 4–5-week-old SPF mdr2-/- mice vs no ASBTi group (N=5-7mice/group). Effect of ASBT inhibition on: alkaline phosphatase (F), Liver dehydxylation ratio (total secondary/primary liver BA) (G), total liver cholic acid (H), total liver α&β muricholic acid (MCA)(I), and liver taurine conjugated ursodiol

(UDCA) (J). *q*PCR amplified results of fecal samples from *mdr2*$^{-/-}$ mice with and without broad-spectrum antibiotics (vancomycin, neomycin, and metronidazole) using the 16s (K) and Clostridial cluster primers (cluster IV, XIVa, and XVIII) (L) normalized to 18s. Experimental desi3n of treatment of 3-4wk old SPF *mdr2*$^{-/-}$ mice treated with 7 day treatment of broad antibiotic cocktail followed by a 1d washout period, then the inoculation of 17-strain of Clostridium (M) and assessing 14 weight change (N), ALP & ALT (O-P). (n=4 mice in each treatment and control groups). Following Lachnospiraceae treatment of *mdr2*$^{-/-}$ mice outlined in Fig4E (lachno, N=13, H2O ctrl, N=12), we assessed pooled data from 2 separate experiments of ALT (Q) and total BA (R). qPCR assessment of orphan receptor FXR pathway by look at liver cyp7a1 (S), ileal FGF15 (T), fecal TBA (U), and fecal *bsh* activity (ratio of total unconjugated/conjugated fecal BA), (V) in *mdr2*$^{-/-}$ exposed to Lachnospiraceae. Group or pairwise comparisons performed by ANOVA or Student t-test, respectively. *P < .05, **P < .01, ***P <.001, ****P < .0001.

Supplemental Figure 3: Comparison of amplification and melt curves of DNA isolated from E. faecalis translocated *mdr2*$^{-/-}$ murine liver isolates from four different *mdr2*$^{-/-}$ mice by assessing small cytolysin subunits, cylLS, genomic DNA along with experiements on effect of Lachnospiraceae reconstitution in GF mdr2$^{-/-}$ mice. . E. faecalis cytolysin+ strain and deletion cytolysin mutant from the Schnabl lab were used as controls. Fold change (relative to Ef null control) of cylLS (A-D). Melting curve and amplification curves of control E. faecalis rpoB and Universal 16s primers of controls and murine E. faecalis isolates (E). Experiment design (F) and Kaplan-Meyer survival curves (G) of orally inoculated GF mdr2-/- or mdr2+/- mice with 10^8 of 21-strain Lachnospiraceae (Lachno) or H2O controls in (H2O, N=5, Lachno, N=4/group) and measure histologic hepatic fibrosis and inflammation(C-D).

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Group or pairwise comparisons performed by ANOVA or Student t-test, respectively. *P < .05, **P < .01, ***P <.001, ****P < .0001.

Table S1: Primers for qPCR

List of primers utilized in study.