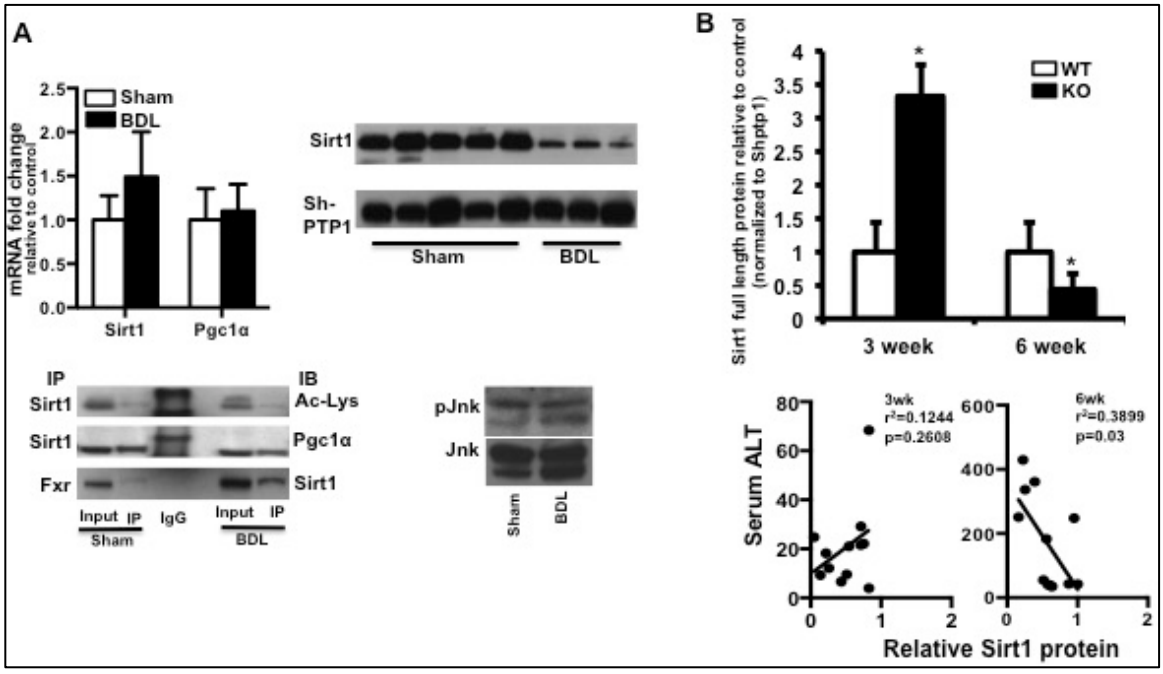
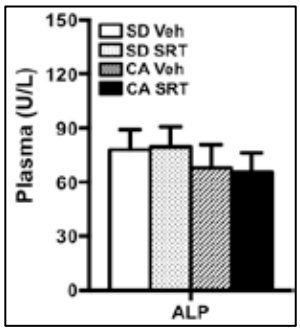
Supplementary Figure- 1: Mouse models of cholestatic liver injury demonstrate compromised hepatic Sirt1 protein expression along with Fxr hyper acetylation.

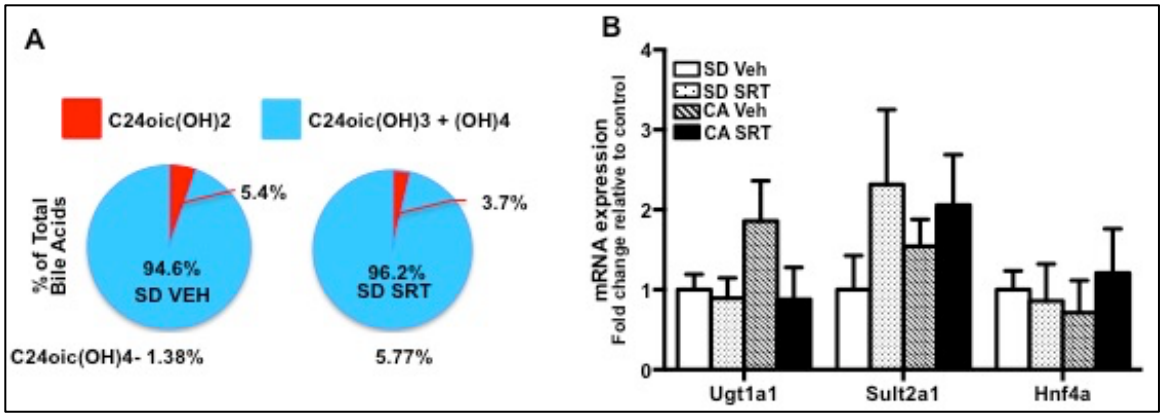
(A) Sirt1 mRNA and protein expression in livers of Sham and Bile duct ligated mice. Lower left panel represents immunoprecipitation data from sham and BDL livers using Sirt1 or Fxr and immunoblotted using Ac-Lys, Pgc1a or Sirt1 antibodies. (B) Hepatic Sirt1 protein expression in WT and Mdr2$^{-/-}$ (KO) at 3 and 6 weeks of age. Lower right graphs represent correlation plots of Sirt1 protein expression vs plasma ALT values Mdr2 wild type and KO mice (n=6 per genotype). Data is presented as average ± SD fold change in mRNA or protein expression relative to standard sham or WT controls. $p< 0.05$ was considered to be significant. "*" denotes a significant difference between sham and BDL (A) groups or WT and KO groups (B).



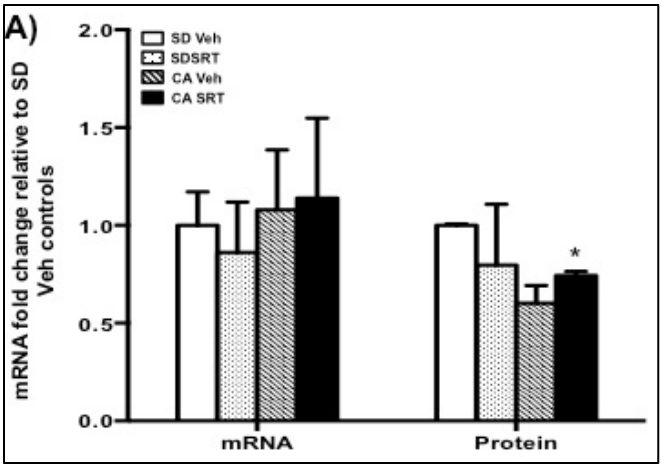
Supplementary Figure- 2: SRT1720 administration does not alter plasma ALP levels in mice fed 1%CA supplemented chow.
C57Bl/6 mice (n= 5-7/group) were fed standard chow or 1% CA supplemented chow with concurrent oral administration of vehicle or SRT1720 (50mg/kg body wt) for 5 days and plasma ALP (U/L) was quantified. Data is presented as average ± SD, Units/L or μM values.



Supplementary Figure- 3: SRT1720 administration increases hepatic tri- and tetra-hydroxylated BA fraction in standard rodent chow fed mice while BA conjugation enzymes remain unchanged.
C57Bl/6 mice (n= 5-7/group) were fed standard chow or 1% CA supplemented chow with concurrent oral administration of vehicle or SRT1720 (50mg/kg body wt) for 5 days. **(A)** hepatic di-, tri- and tetra- hydroxylated BA composition in WT SD vehicle and SRT1720 administered mice. The data is presented as % total bile acids present in mice fed standard diet and treated with vehicle or SRT1720, **(B)** hepatic BA metabolic gene expression measured by qPCR. Data is presented as average ± SD fold change in mRNA or protein expression relative to standard chow fed controls.

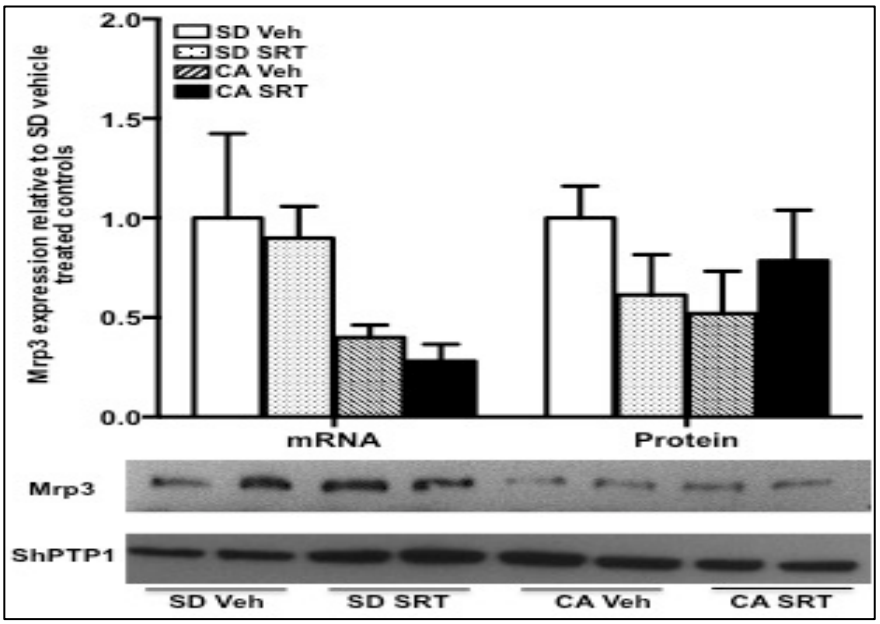


Supplementary Figure- 4: SRT1720 administration induces hepatic Bsep protein expression slightly while mRNA expression remains unchanged.
C57Bl/6 mice (n= 5-7/group) were fed standard chow or 1% CA supplemented chow with concurrent oral administration of vehicle or SRT1720 (50mg/kg body wt) for 5 days. Hepatic Bsep mRNA and protein expression was quantified by qPCR and western blotting respectively. Data is presented as average ± SD fold change in mRNA or protein expression relative to standard chow fed controls. $p < 0.05$ was considered to be significant. "*" denotes a significant difference between CA SRT1720 treated group as compared to the CA vehicle fed group.



Supplementary Figure- 5: SRT1720 administration does not alter renal Mrp3 expression upon CA feeding.

C57Bl/6 mice (n= 5-7/group) were fed standard chow or 1% CA supplemented chow with concurrent oral administration of vehicle or SRT1720 (50mg/kg body wt) for 5 days. Renal mRNA and protein expression was quantified by qPCR and western blotting respectively. Data is presented as average ± SD fold change in mRNA or protein expression relative to standard chow fed controls.



Supplementary Table 1: Antibodies and sources used for western blotting.

Antibody	Source
Sirt1	Cell Signaling, MA, USA
FXR	Santa Cruz, CA, USA
pJNK	Santa Cruz, CA, USA
JNK	Cell Signaling, MA, USA
Pgc1a	Santa Cruz, CA, USA
Ac-Lys	Cell Signaling, MA, USA

Supplementary Table 2: SRT1720 does not alter total bile acid pool or hepatic bile acid content. C57Bl/6 mice (n= 5-7/group) were fed standard chow or 1% CA supplemented chow with concurrent oral administration of vehicle or SRT1720 (50mg/kg body wt) for 5 days and total bile acid pool, fecal, hepatic, ileal bile acid content was quantified. Data is presented as average bile acid content ± SD (n=5-7/group).

PARAMETERS	SD-Vehicle	SD- SRT1720	1% CA- Vehicle	1% CA-SRT1720
Total bile acid pool (µmol/100g BW)	23.11 ± 5.55	23.21 ± 0.48	106.2 ± 11.6	97.75 ± 6.42
Fecal total bile acids (µM)			2965 ± 184	3385 ± 620
Hepatic bile acids (µmol/100gm)	7.37 ± 6.12	7.57 ± 4.55	23.86 ± 4.04	30.47 ± 7.65
Ileal bile acids (µmol/100gm)	4.04 ± 2.04	20.14 ± 3.41	6.39 ± 3.59	25.71 ± 6.46