

Supplementary Figure Legends

Sup Fig 1.

- A.** Representative image of gallbladder catheterization under the microscope. Under microscopic visualization, the common bile duct was double-ligated proximal to the duodenum to obstruct endogenous bile drainage. A polyethylene (PE-5) catheter was carefully inserted into the gallbladder and secured with two ligatures to allow continuous bile flow for collection and measurement.
- B.** Detailed dynamic bile volume comparison at indicated time points in WT and *Aqp8* KO mice with or without EtOH gavage (n=7-8 per group)

Sup Fig 2.

- A.** Isolated primary hepatocytes were incubated with 1mM AcH for 5,15,30 mins. Hepatocytes and supernatant AcH levels, and hepatocytes/supernatant (Hep/Sup) AcH ratio at each time point of *Aqp8* KO and WT isolated primary hepatocytes (The experiment was repeated 4 times independently).

Sup Fig 3.

- A.** EtOH consumption in male and female WT and *Aqp8* KO mice at each percentage (n=9-10 per group).
- B.** Sweetness 2-Bottle Choice: saccharine liquid consumption and preference in WT (n=12) and *Aqp8* KO mice (n=11) with 2 saccharine concentrations. Values represent

means $\pm$ SD or SEM. * $P < 0.05$, ** $P < 0.01$, ns=no significance. A two-sided Student's t-test was used for the comparison between the two groups.

C. D. WT and *Aqp8* KO received 5 g/kg EtOH binge (by gavage), and samples were collected 3/6/9 hours later. Liver, bile, and blood AcH levels were measured. (n=4-6)

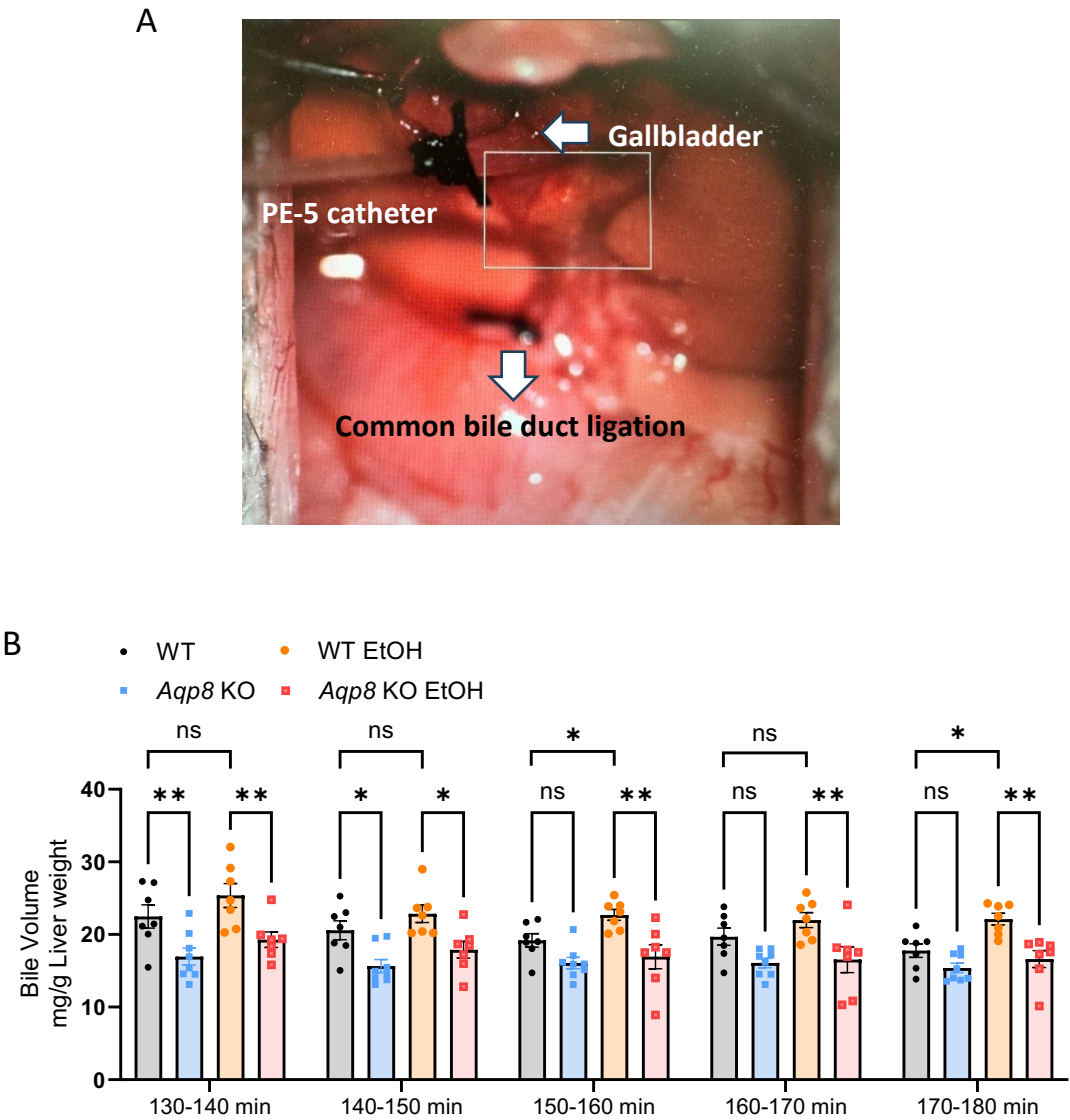
Sup Fig 4.

- A.** Serum ALT levels in WT and *Aqp8* KO mice in two sexes with pair-fed or 5% EtOH diet.
- B.** The liver/body weight ratio in WT and *Aqp8* KO mice with pair-fed or 5% EtOH diet.
- C.** Food consumption in WT and *Aqp8* KO mice with pair-fed or 5% EtOH diet.
- D.** Liver *Aqp8* mRNA expression in WT and *Aqp8* KO mice with pair-fed or 5% EtOH diet.
- E.** Representative liver H&E staining in WT and *Aqp8* KO mice with pair-fed or 5% EtOH diet.
- F.** Representative IBA1, and MPO IHC staining and IBA and MPO positive cell counts in WT and *Aqp8* KO mice with 5% EtOH diet.

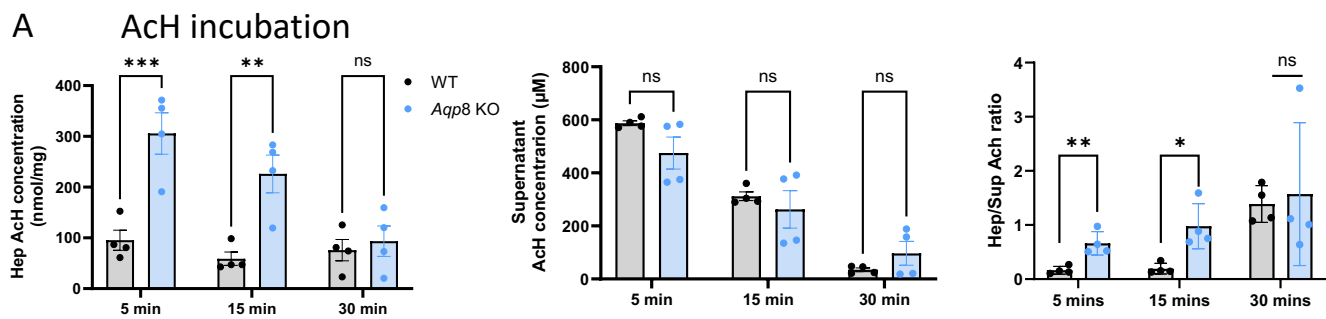
Sup Fig 5.

- A.** Food consumption in *Aqp8* KO GFP control mice (*Aqp8* KO^{Ad-GFP}) and liver AQP8 overexpression in *Aqp8* KO mice (*Aqp8* KO^{Ad-Aqp8}) with 5% EtOH diet.
- B.** Serum ALT levels in *Aqp8* KO^{Ad-GFP} and *Aqp8* KO^{Ad-Aqp8} mice.
- C.** Liver *Aqp8* mRNA expression in *Aqp8* KO^{Ad-GFP} and *Aqp8* KO^{Ad-Aqp8} mice.
- D.** Bile volume in *Aqp8* KO^{Ad-GFP} and *Aqp8* KO^{Ad-Aqp8} mice.

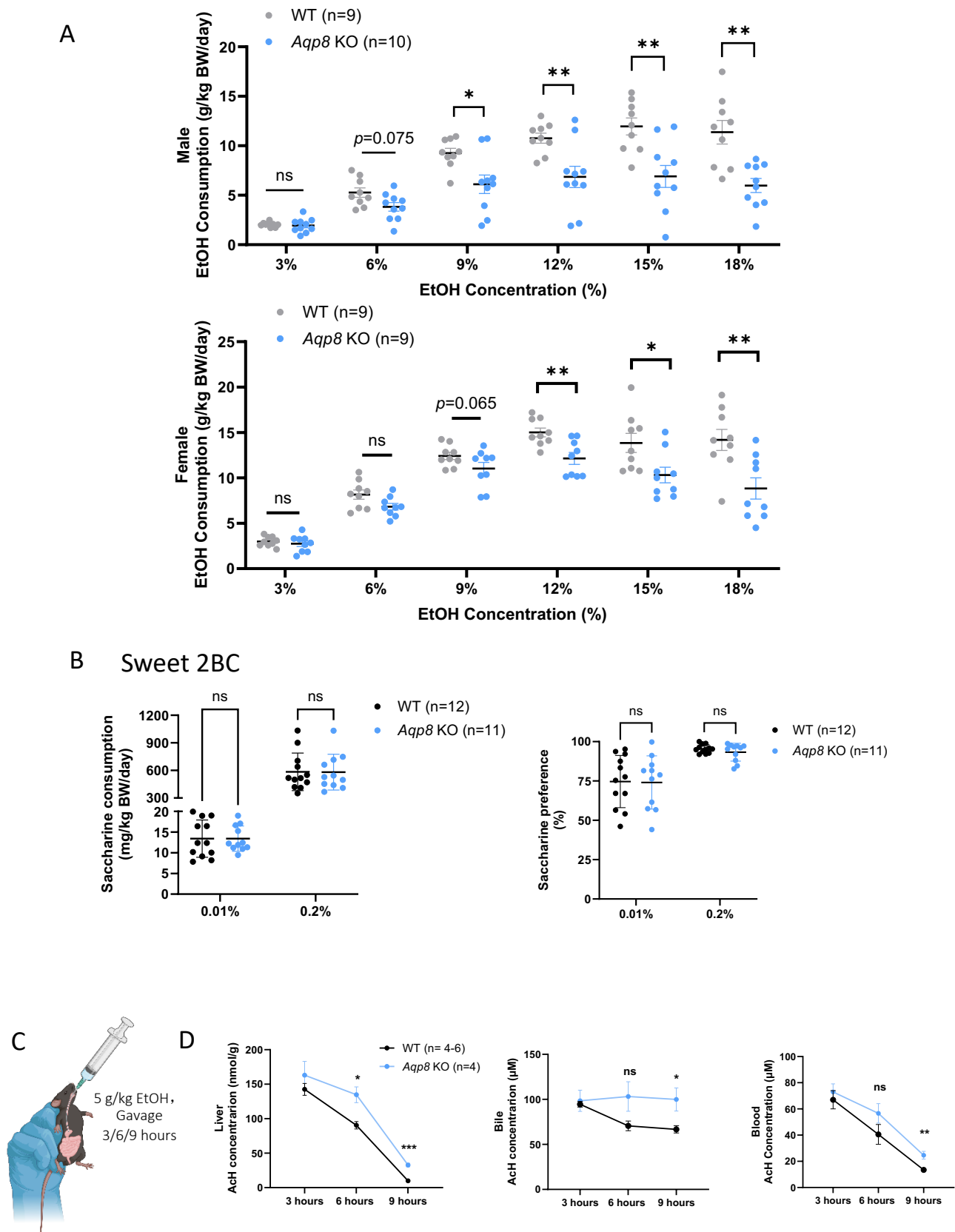
Sup Fig. 1



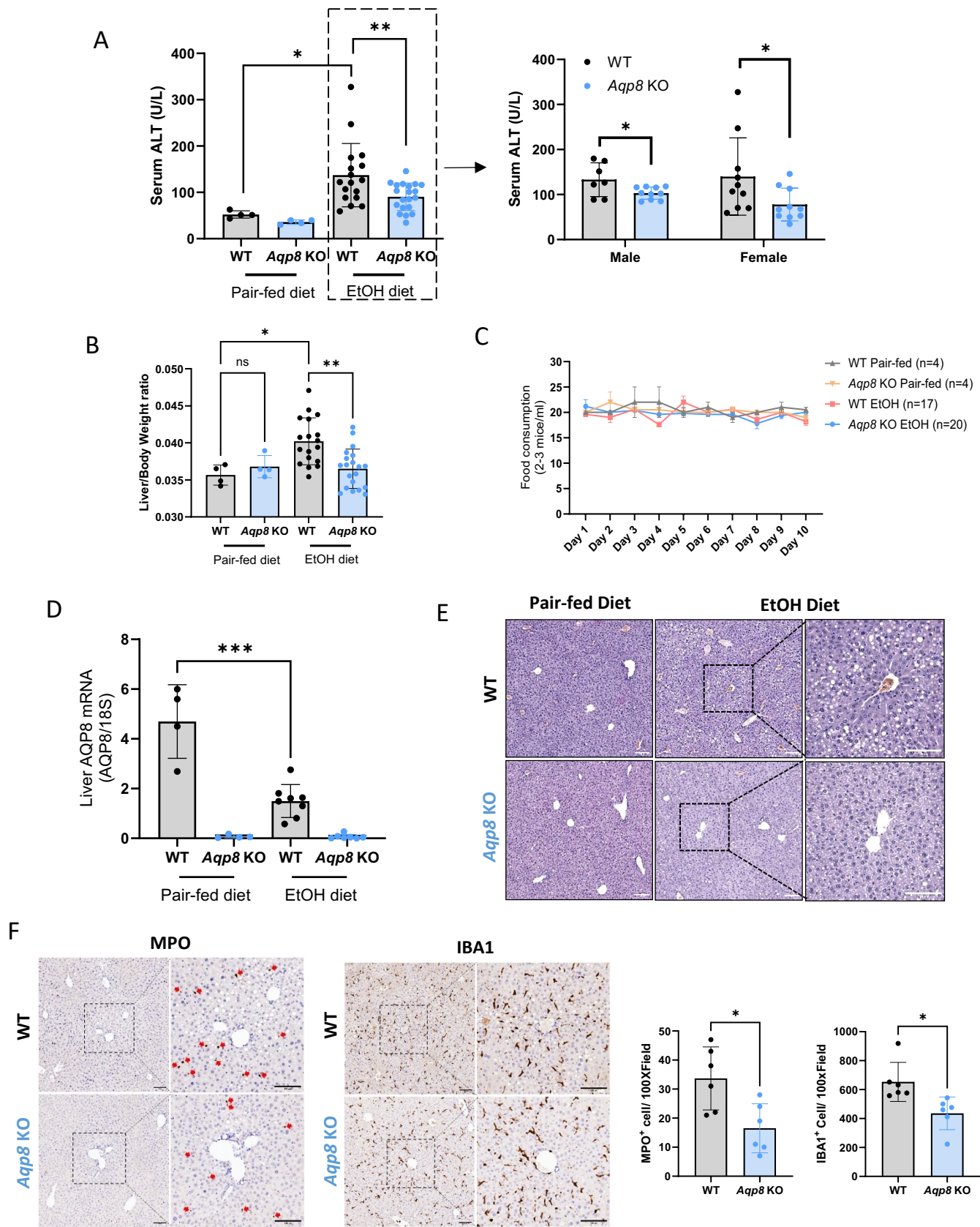
Sup Fig. 2



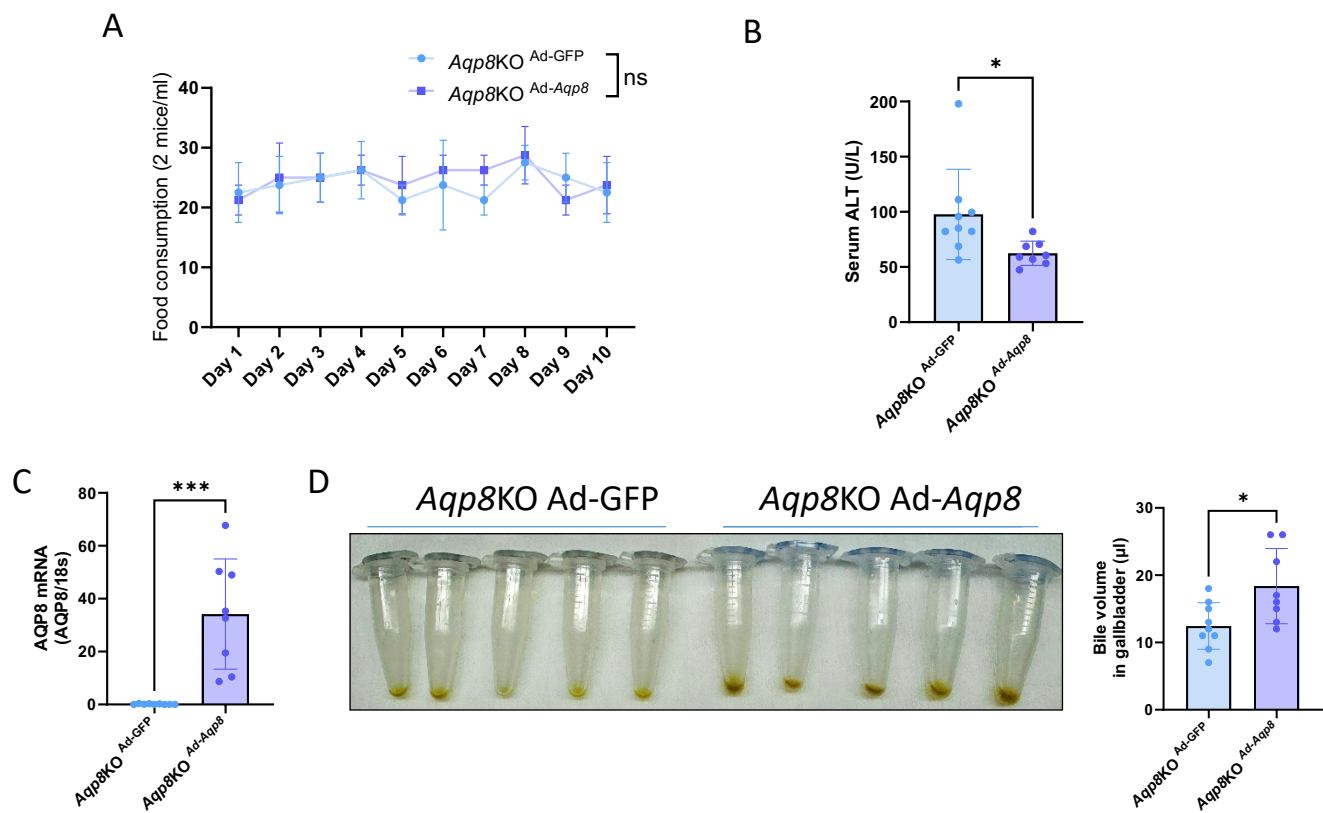
Sup Fig. 3



Sup Fig. 4



Sup Fig. 5



Sup Table 1. Primer list

Gene	Forward Primer (5'-3')	Reverse Primer (5'-3')
<i>Aqp8</i>	aacatcagcgggtggacactt	cagccctccaaatagctggg
<i>Lxr-β</i>	ctcccacccacgcttacac	gccctaacctctctccactca
<i>Abcg1</i>	gctgtgcgttttgtgctgtt	tgcagctccaatcagtagtcctaa
<i>Fas</i>	attgcatcaagcaagtgcag	gagccgtcaaacaggaagag
<i>Cd163</i>	tgggtggggaaagcataact	aagttgtcgtcacacaccgt
<i>Scd-1</i>	ttcttgcgatacactctggtgc	cgggattgaatgttcttgcgt
<i>Il-1β</i>	tcgctcagggtcacaagaaa	ctcagaggcaaggaggaaac
<i>Il-10</i>	atcgatttctcccctgtgaa	tgtcaaattcattcatggcct
<i>Ccl5</i>	gtgcccacgtcaaggagtat	ccacttcttctctgggttgg
<i>Ho-1</i>	aggctaagaccgccttcct	tgtgttcctctgtcagcatca
<i>Il-6</i>	acaagtcggaggcttaattacacat	ttgccattgcacaactcttttc
<i>Srebp1c</i>	ggcccgggaagtcaactgt	ggagccatggattgcacatt
<i>Sod-1</i>	tactgatggacgtggaaccc	gaaccatccacttcgagca
<i>18s</i>	acggaagggcaccaccagga	caccaccacccacggaatcg
<i>Ccl2</i>	ttaaaaacctggatcggaaccaa	gcattagcttcagatttacgggt
<i>Ccl20</i>	tctggacctcaaaatcctgc	tggagtagcttcttcacca