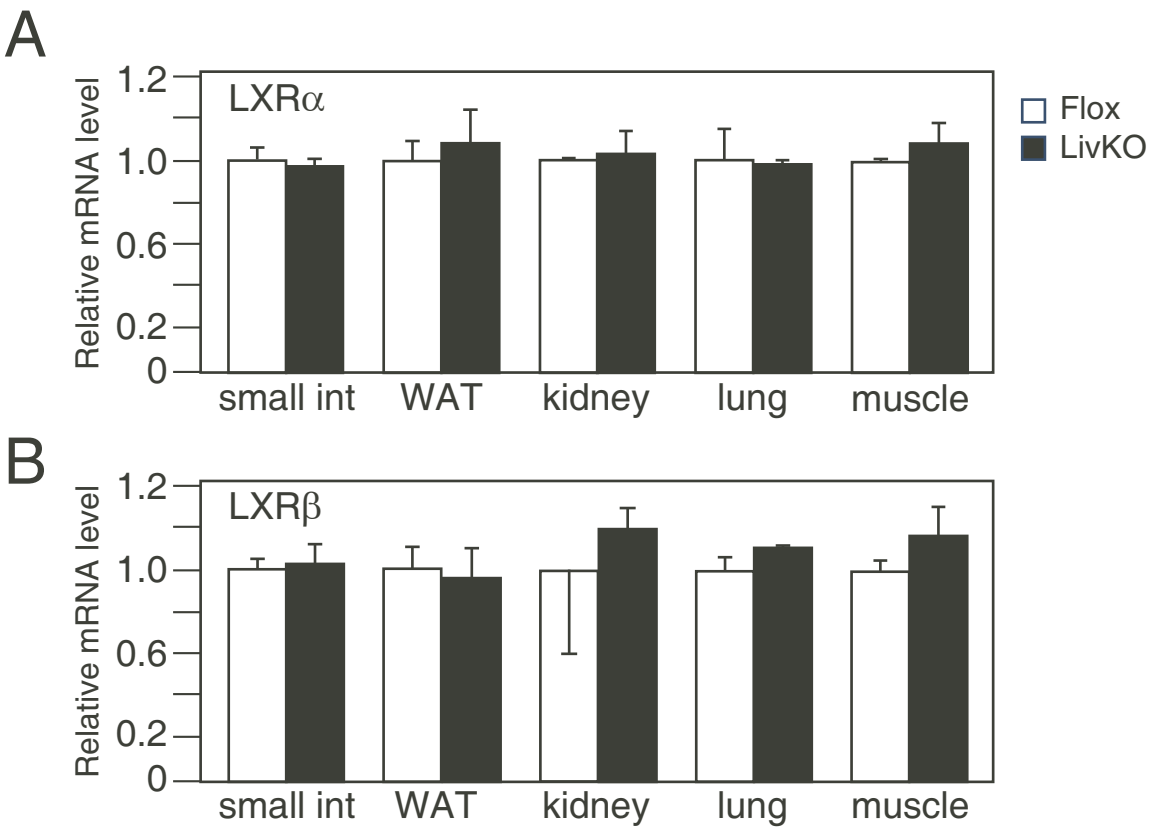
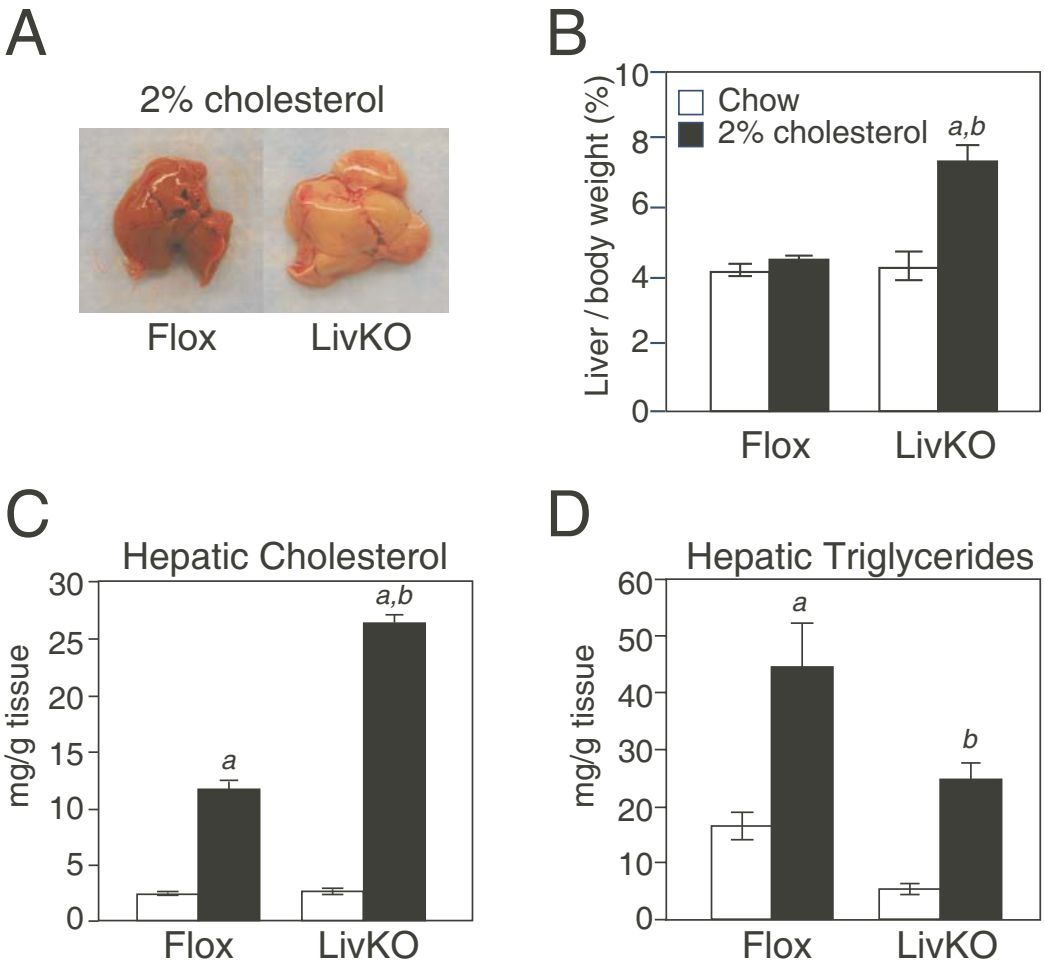
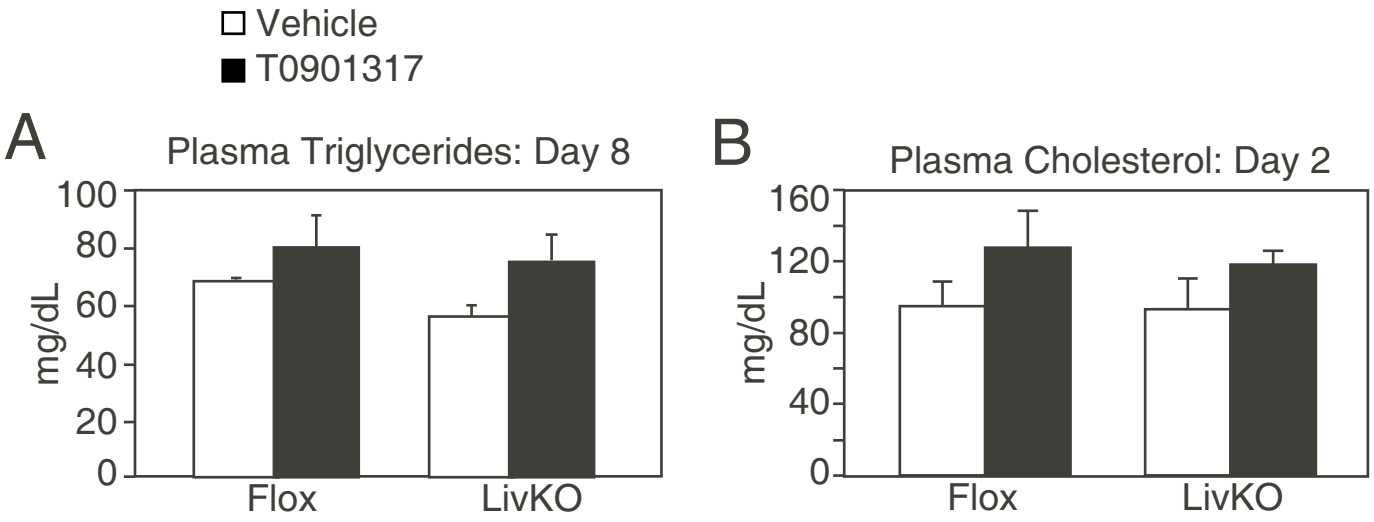


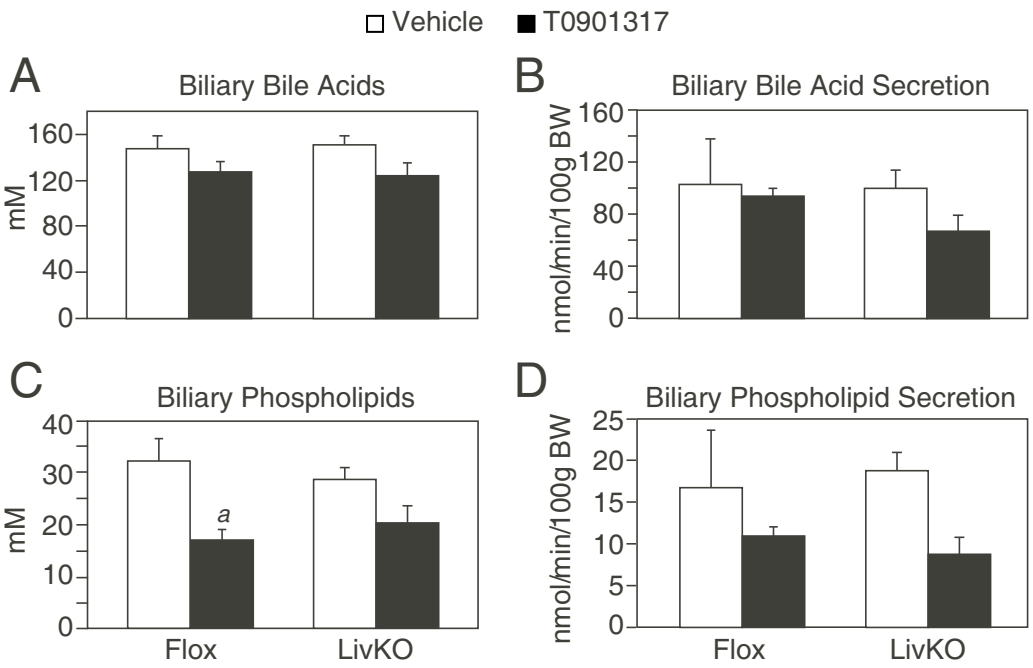
Supplemental Figure 1. LXR expression in LivKO mice. The mRNA levels of (**A**) LXRα and (**B**) LXRβ were determined by quantitaive real-time PCR in tissues isolated from 2-4 month old mice maintained on a normal chow diet (n = 2-5). Expression of LXRs in floxed mice was set at 1 for each tissue.



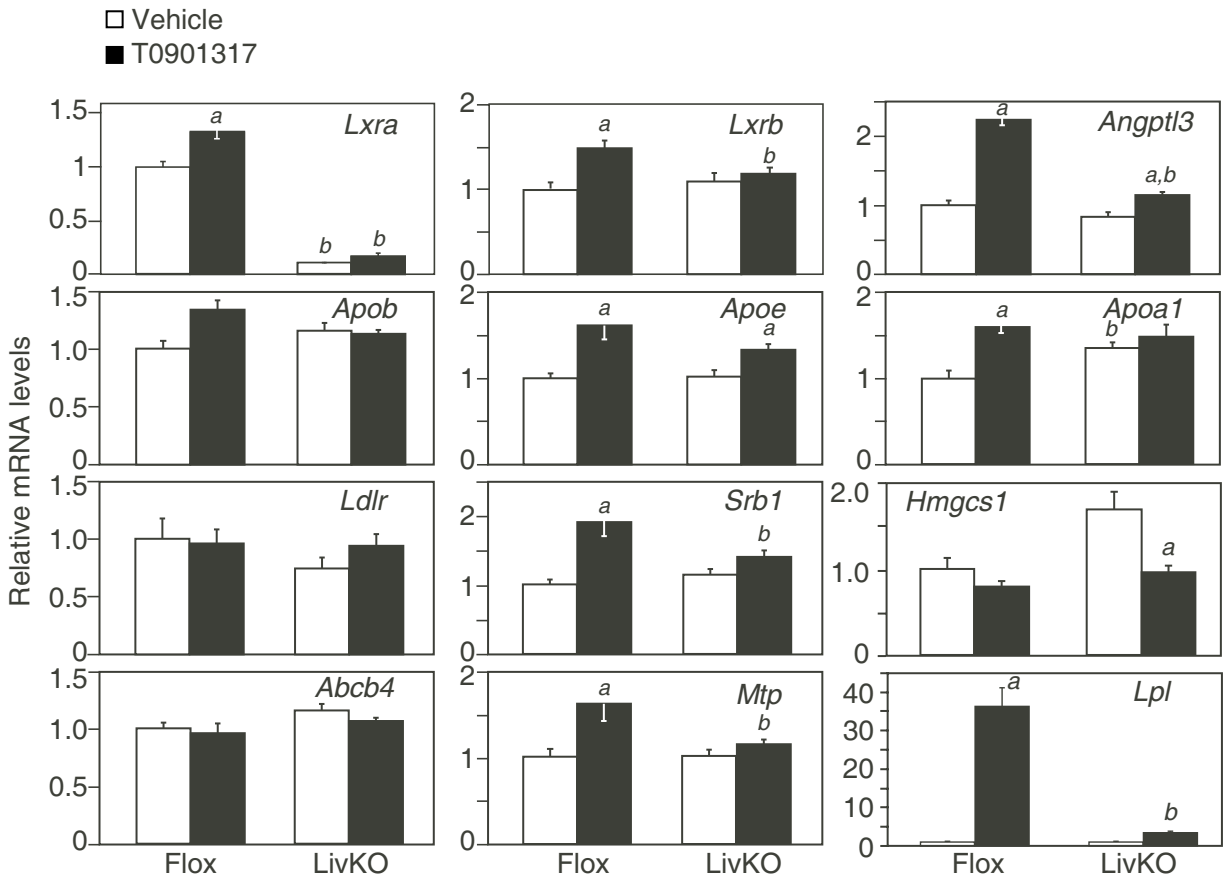
Supplemental Figure 2. Hepatic lipid levels in LivKO mice. Floxed and LivKO male mice 3 months old (n = 5) were fed a 2% cholesterol diet for 30 days. (**A**) Representative appearance of the livers. (**B-D**) At completion of the study liver weights, hepatic cholesterol, and hepatic triglycerides levels were determined. Data are the mean ± SEM. *a*, statistically significant difference between vehicle and T0901317 treated animals of the same genotype ($p \leq 0.05$). *b*, statistically significant difference between Flox and LivKO mice with the same treatment ($p \leq 0.05$).



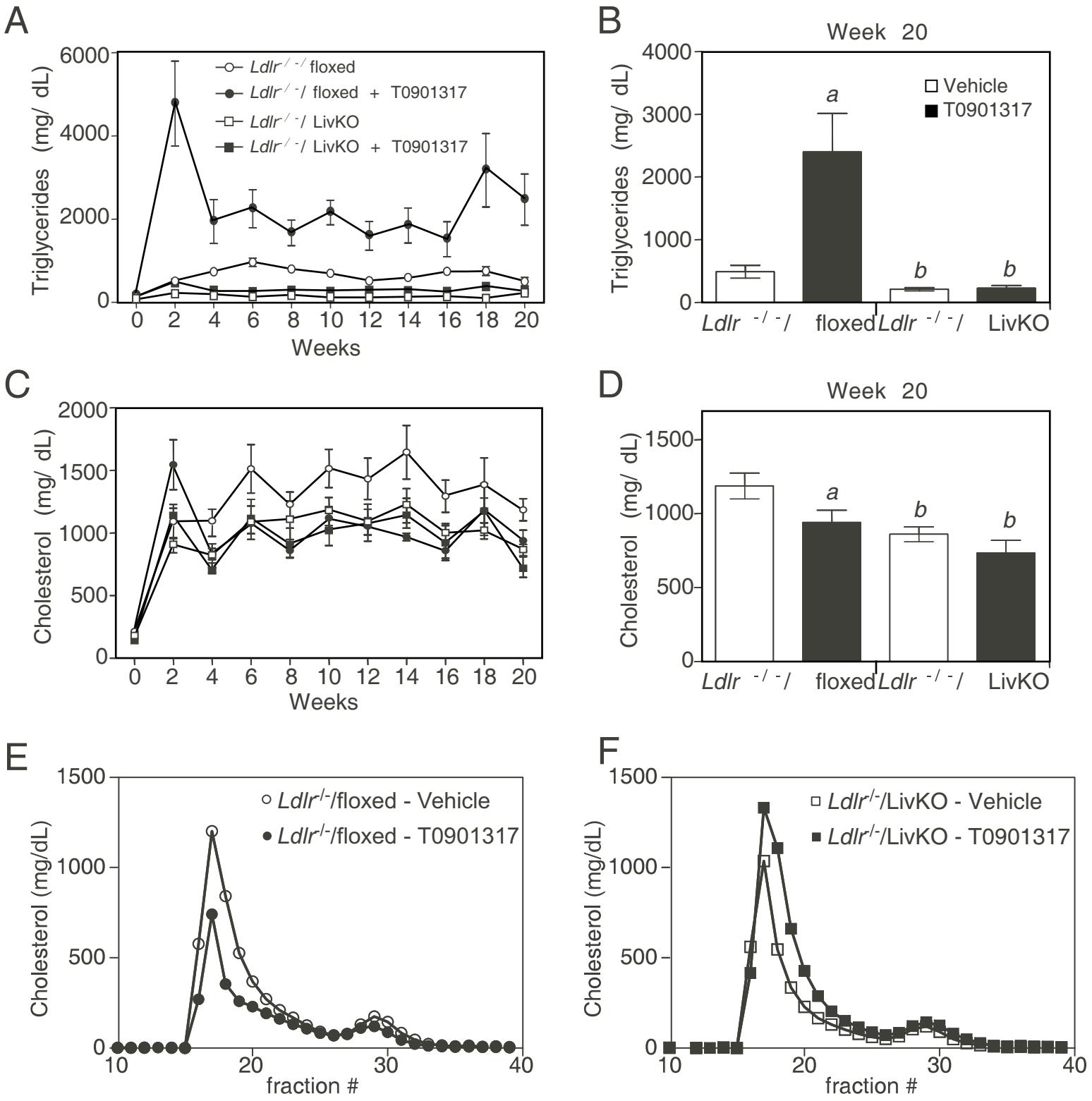
Supplemental Figure 3. Plasma lipid levels. Floxed and LivKO female mice 4-6 months old (n = 5-6) were fed a chow diet containing vehicle or T0901317 (40 mpk) for 8 days. Plasma triglycerides (**A**) at day 8 and cholesterol (**B**) at day 2 were determined enzymatically as described in the Methods. Data are the mean ± SEM. No significant differences among groups were detected.



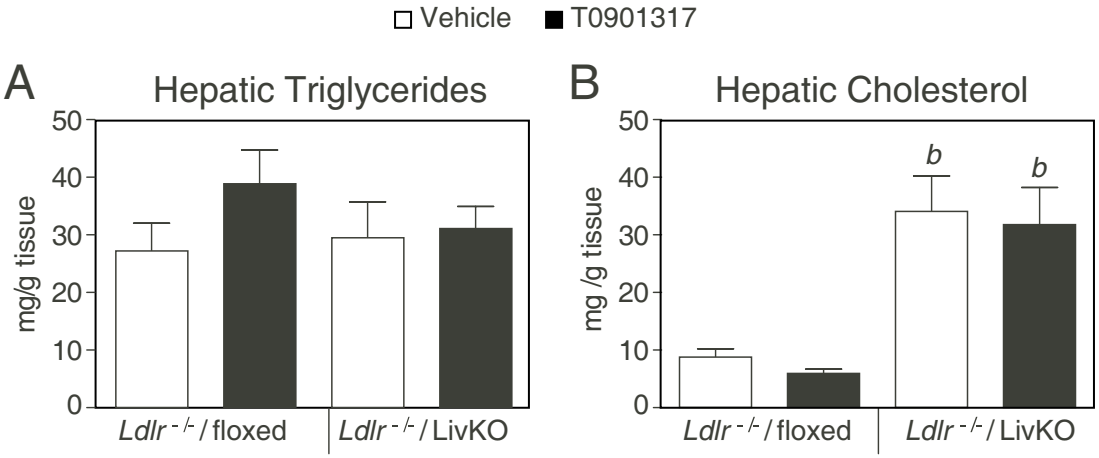
Supplemental Figure 4. Biliary bile acids and phospholipids in LivKO mice. Floxed and LivKO female mice 5-6 months old were fed a chow diet containing vehicle or T0901317 (40 mpk) for 3 days. (**A** and **C**) Gallbladder bile was collected and the concentration of bile acids (**A**) and phospholipids (**C**) were determined (n = 5-6). (**B** and **D**) Mice were anesthetized, the common bile duct was cannulated and bile flow was collected for 30 minutes. Biliary bile acids (**B**) and phospholipids (**D**) were measured (n = 3-6) and the secretion rate determined from measurement of the bile flow. Data are the mean ± SEM. *a*, statistically significant difference between vehicle and T0901317 treated animals of the same genotype ($p \leq 0.05$). BW, body weight.



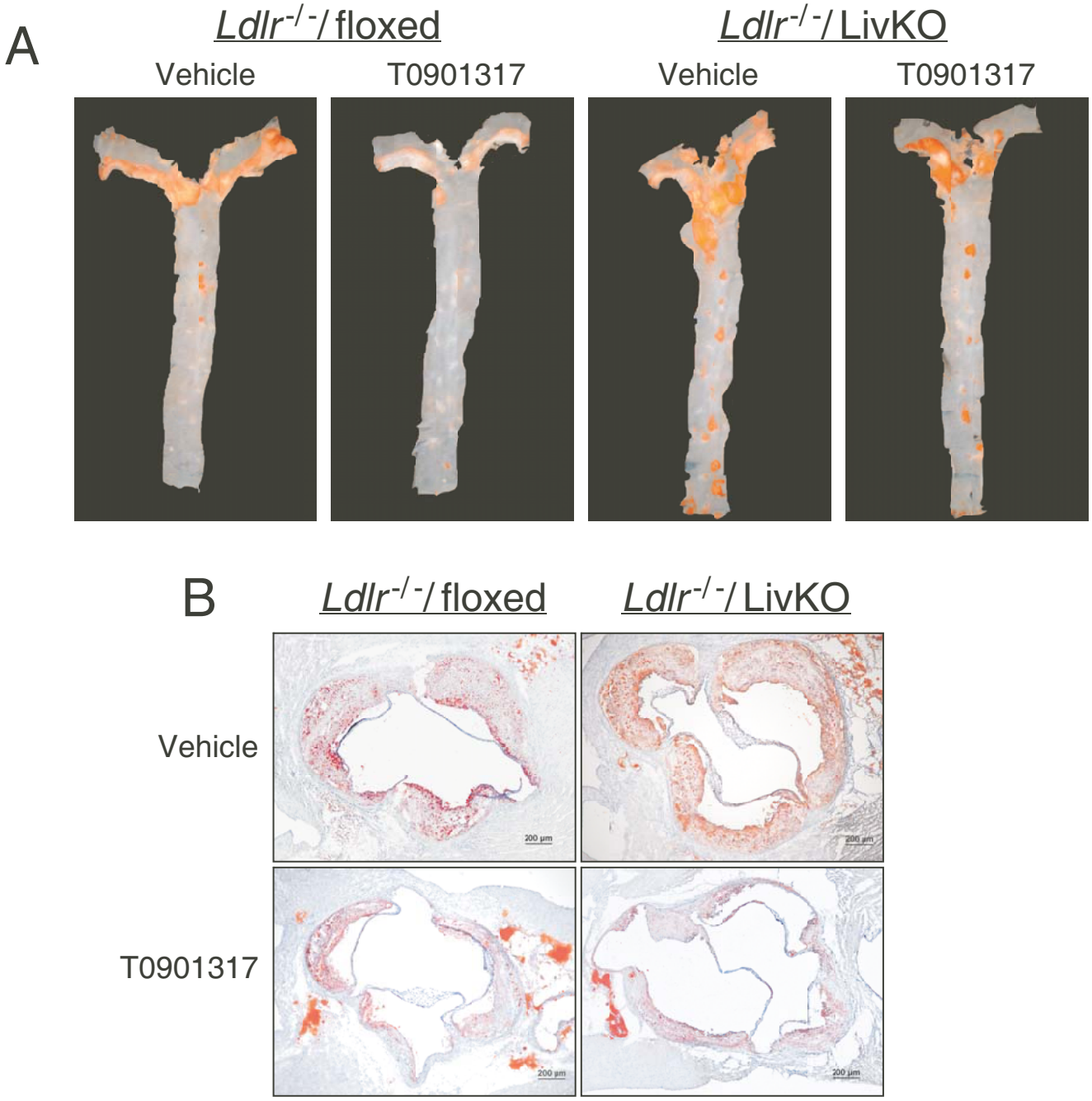
Supplemental Figure 5. Liver gene expression. Floxed and LivKO female mice 4-6 months old (n = 5-6) were fed a chow diet containing vehicle or T0901317 (40 mpk) for 8 weeks. Liver samples were harvested at completion of the experiment and mRNA levels assayed by quantitative real-time PCR. Data are the mean ± SEM. *a*, statistically significant difference between vehicle and T0901317 treated animals of the same genotype ($p \leq 0.05$). *b*, statistically significant difference between Flox and LivKO mice with the same treatment ($p \leq 0.05$).



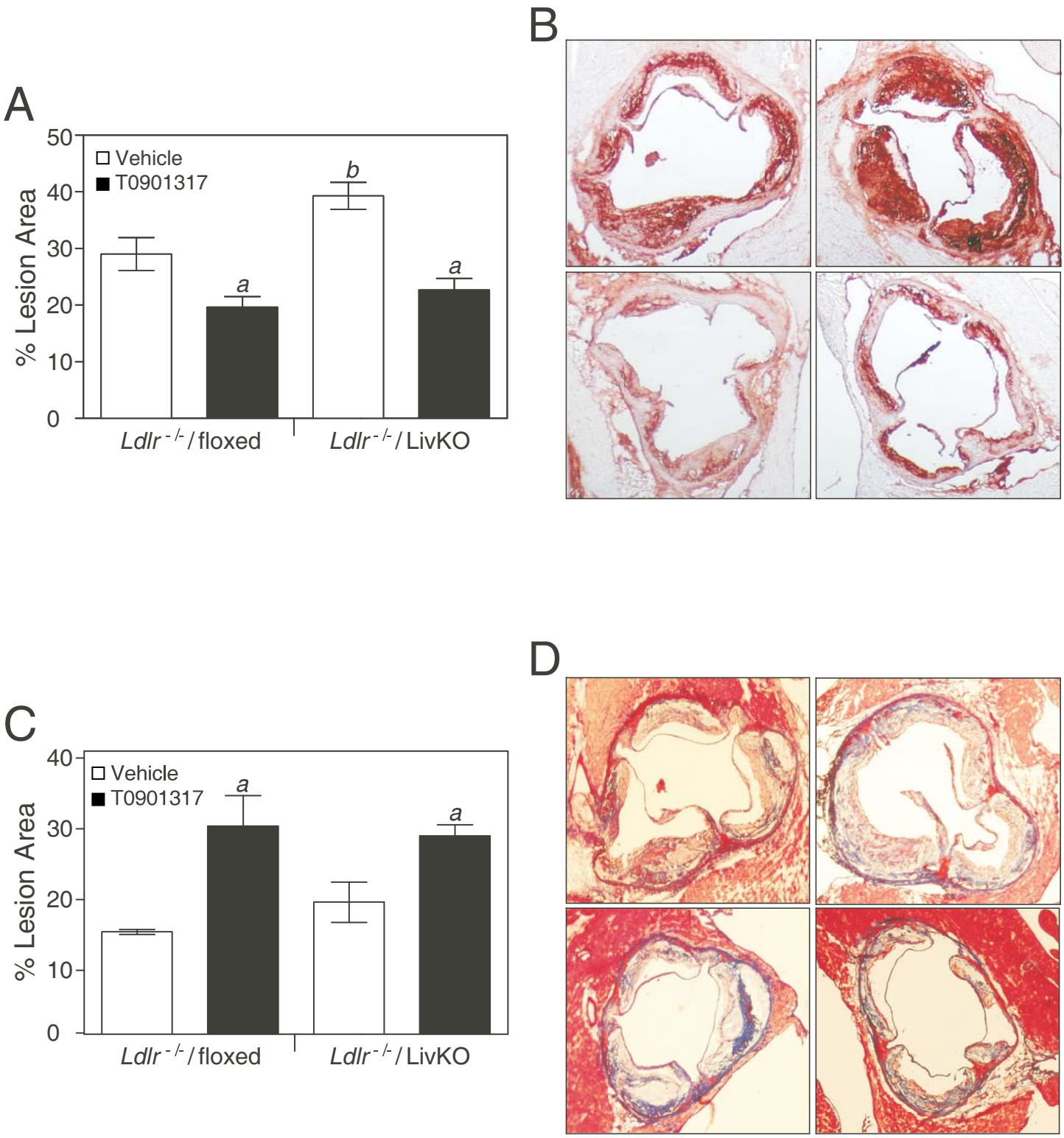
Supplemental Figure 6. Plasma lipid levels in *Ldlr*$^{-/-}$/LivKO mice. *Ldlr*$^{-/-}$/floxed and *Ldlr*$^{-/-}$/LivKO mice were fed a Western diet with or without 0.01% T0901317 for 20 weeks and (**A, B**) plasma triglycerides and (**C, D**) plasma total cholesterol levels were determined at 2 week intervals (n = 5/group). Data are the mean ± SEM. *a*, statistically significant difference between vehicle and T0901317 treated animals of the same genotype ($p \leq 0.05$). *b*, statistically significant difference between Flox and LivKO mice with the same treatment ($p \leq 0.05$) . *Ldlr*$^{-/-}$/floxed (**E**) and *Ldlr*$^{-/-}$/LivKO (**F**) mice were fed a Western diet with or without 0.01% T0901317 for 10 weeks and FPLC analysis was carried out using pooled plasma (n = 6/group) obtained from mice that had been fasted overnight. Elevated plasma triglycerides in samples from *Ldlr*$^{-/-}$/floxed mice treated with T0901317 resulted in a significant amount of non-HDL aggregating when samples were centrifuges to pellet particulate matter prior to loading the FPLC column. herefore the non-HDL cholesterol levels measured by FPLC for *Ldlr*$^{-/-}$/floxed mice treated with T0901317 is likely an underestimate.



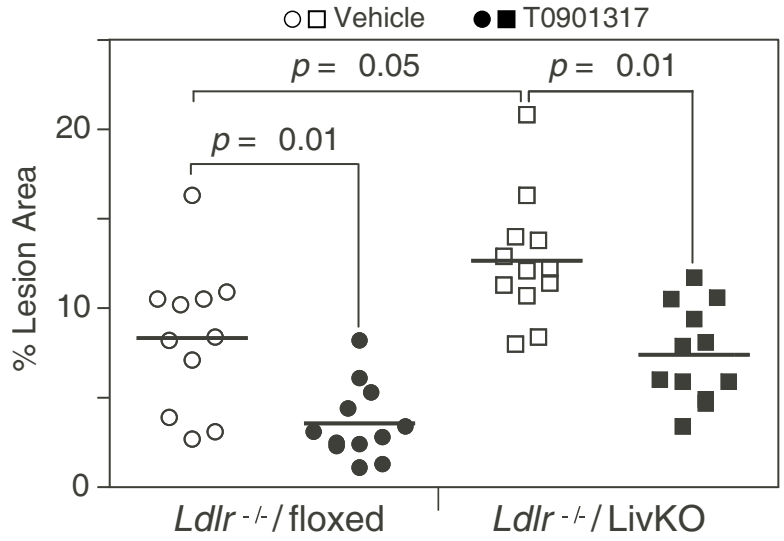
Supplemental Figure 7. Hepatic lipid levels in *Ldlr*$^{-/-}$/ LivKO mice. *Ldlr*$^{-/-}$/ floxed and *Ldlr*$^{-/-}$/ LivKO mice were fed a Western diet with or without 0.1% T0901317 for 20 weeks and hepatic (**A**) triglycerides and (**B**) cholesterol levels were determined at completion of the study (n = 5/ group; 3 male, 2 female). Data are the mean ± SEM. *b*, statistically significant difference between Flox and LivKO mice with the same treatment ($p \leq 0.05$).



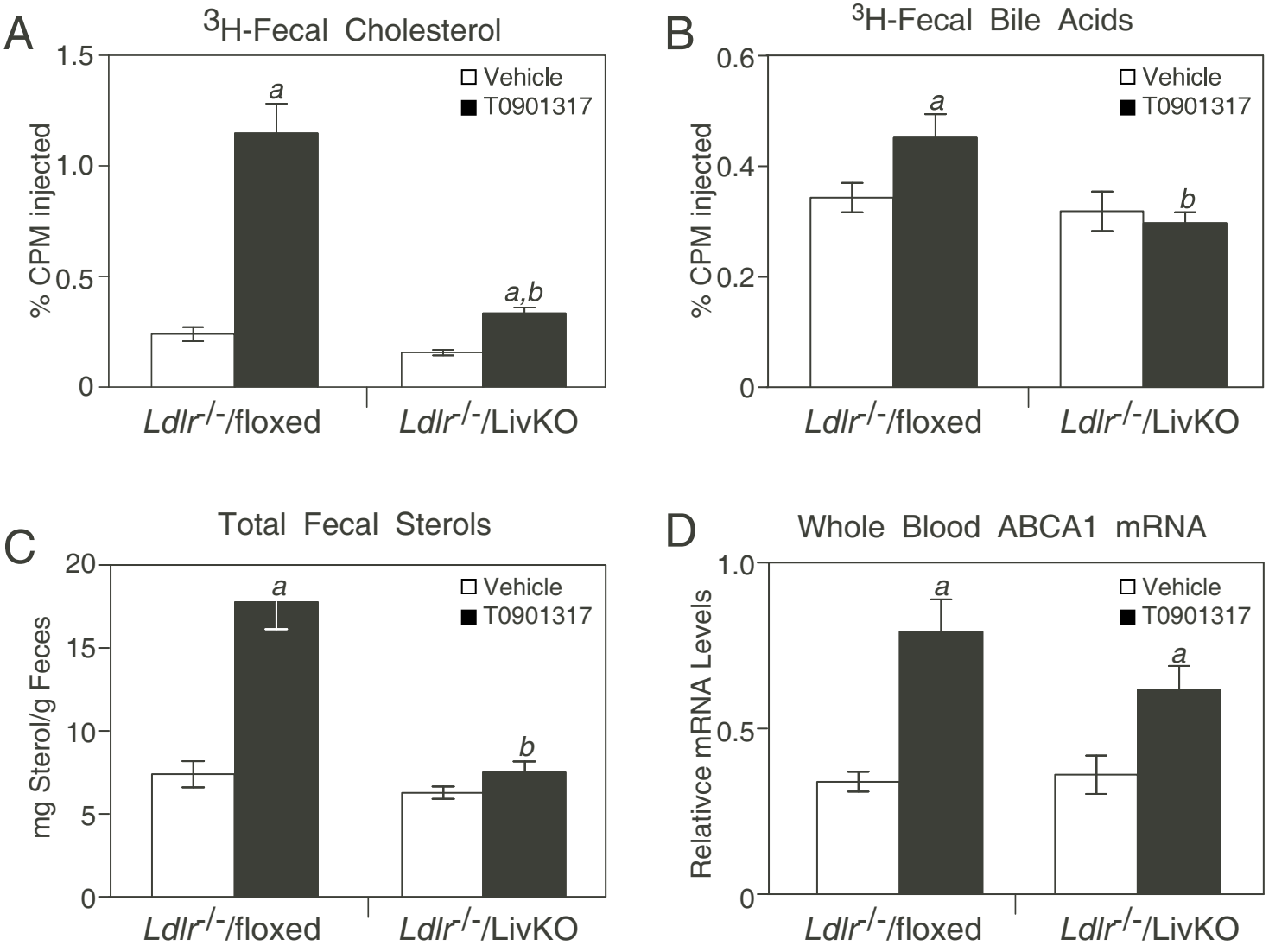
Supplemental Figure 8. Representative en face and root section images. Representative Sudan IV stained aortas (**A**) and oil red O stained aortic root sections (**B**).



Supplemental Figure 9. Macrophage and collagen staining. Aortic root sections from *Ldlr*$^{-/-}$/floxed and *Ldlr*$^{-/-}$/LivKO mice fed a Western diet with or without 0.01% T0901317 for 20 weeks were stained with antibodies to MOMA-2 to detect macrophages (**A, B**) or with trichrome to detect collagen (**C, D**). Quantitation was carried out as described in the methods. Date are mean ± SEM. *a*, statistically significant difference between vehicle and T0901317 treated animals of the same genotype ($p \leq 0.05$). *b*, statistically significant difference between floxed and LivKO mice with the same treatment ($p \leq 0.05$).



Supplemental Figure 10. Atherosclerosis in *Ldlr*$^{-/-}$/LivKO mice. Mice were fed a Western diet with or without 0.01% T0901317 for 10 weeks and atherosclerosis was quantitated by *en face* analysis as described in the Methods. *Ldlr*$^{-/-}$/floxed (vehicle n = 11; T0901317 n = 12). *Ldlr*$^{-/-}$/LivKO (vehicle n = 12; T0901317 n = 12).



Supplemental Figure 11. *In vivo* RCT, total fecal sterols and whole blood gene expression. Mice were fed a Western diet with or without 0.01% T0901317 for 9 weeks. (**A, B**) *In vivo* RCT analysis was carried out as described in the methods (n =6.group) and the levels of ^{3}H-cholesterol (**A**) and ^{3}H-bile acids (**B**) was determined. (**C**) Total fecal sterols were determined as described in the methods from feces collected just prior to initiating the *in vivo* RCT experiment. (**D**) Total RNA was isolated from whole blood as described in the methods and the mRNA levels of ABCA1 was measured by quantitative real-time PCR. Date are mean ± SEM. *a*, statistically significant difference between vehicle and T0901317 treated animals of the same genotype ($p \leq 0.05$). *b*, statistically significant difference between floxed and LivKO mice with the same treatment ($p \leq 0.05$).