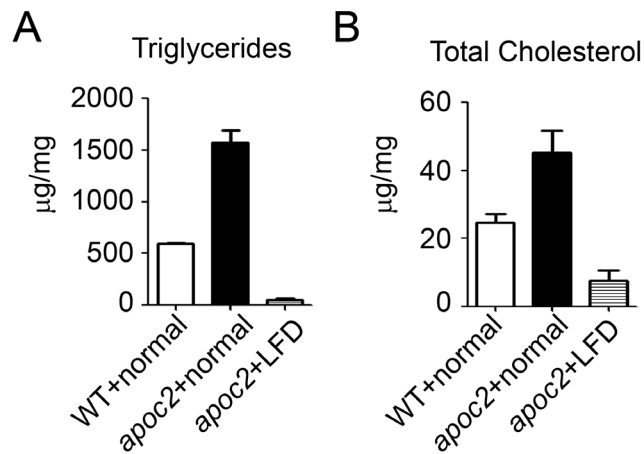
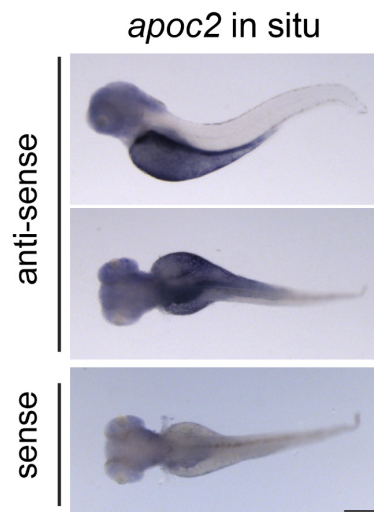


Supplementary Information Figures



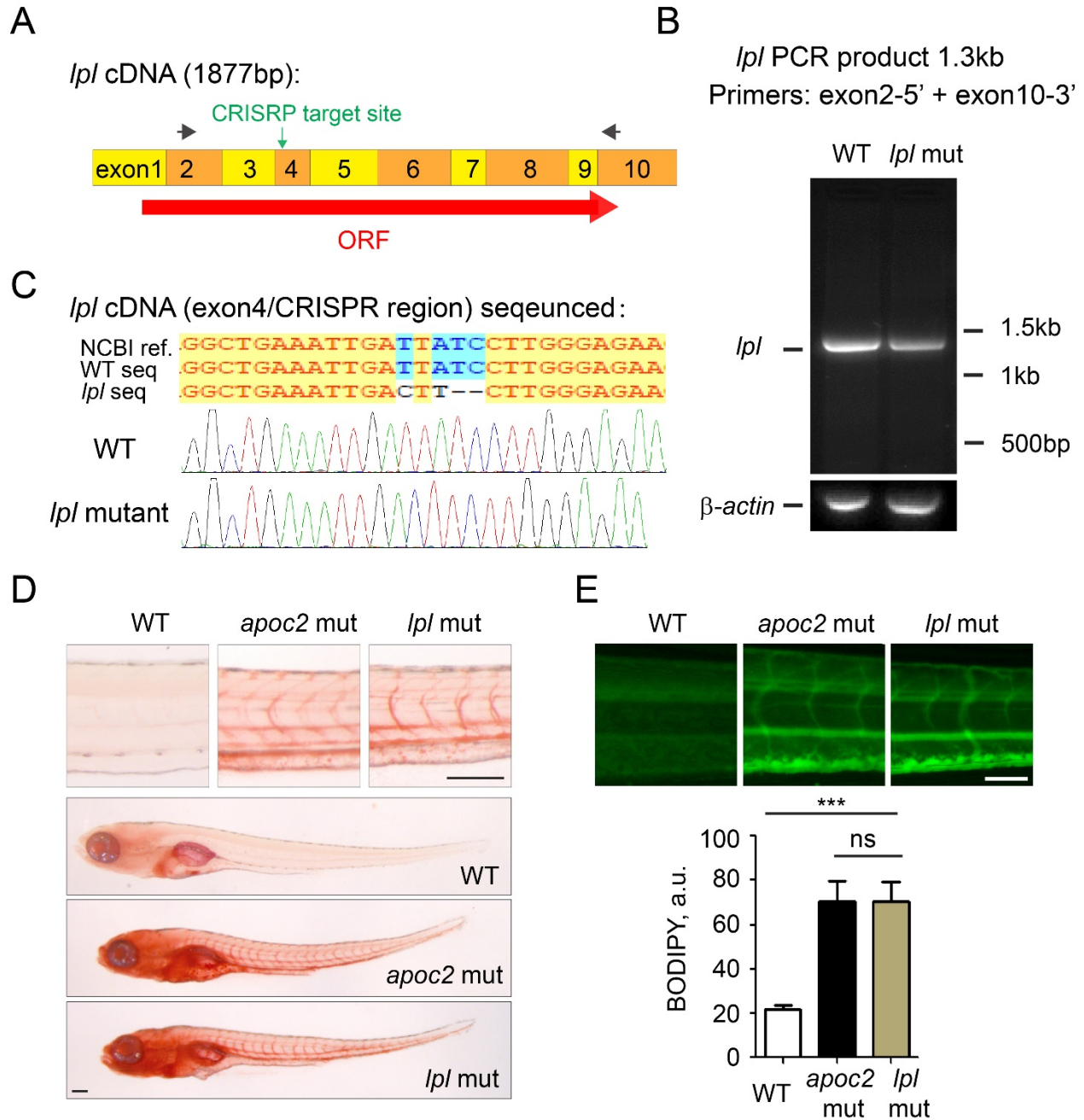
Supplementary Figure 1. Feeding a low-fat diet reduces hyperlipidemia in *apoc2* mutants.

Triglycerides (A) and total cholesterol (B) levels were measured in homogenates of 14 dpf larvae and normalized to total protein. Feeding normal or low-fat diet (LFD) started on 5th dpf. Triglycerides and total cholesterol were measured in a homogenate of 5 pooled larvae in each group. Mean±SD; n=3 (technical replicates).

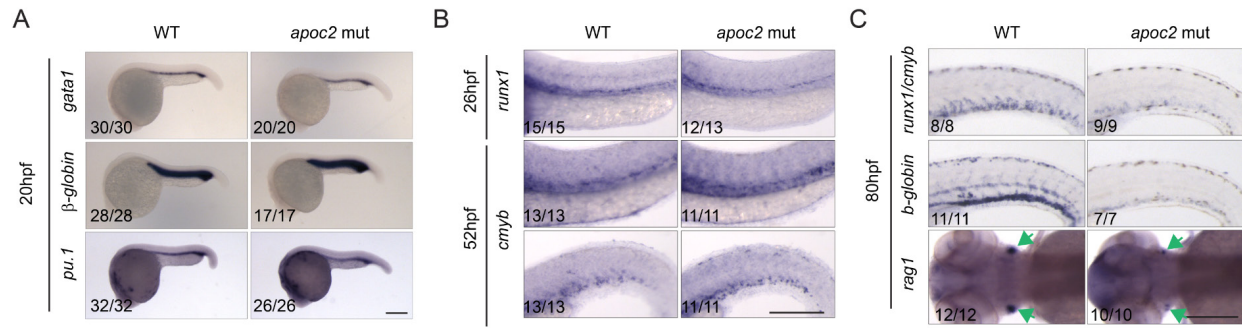


Supplementary Figure 2. *In situ* hybridization with *apoc2* antisense and sense probes.

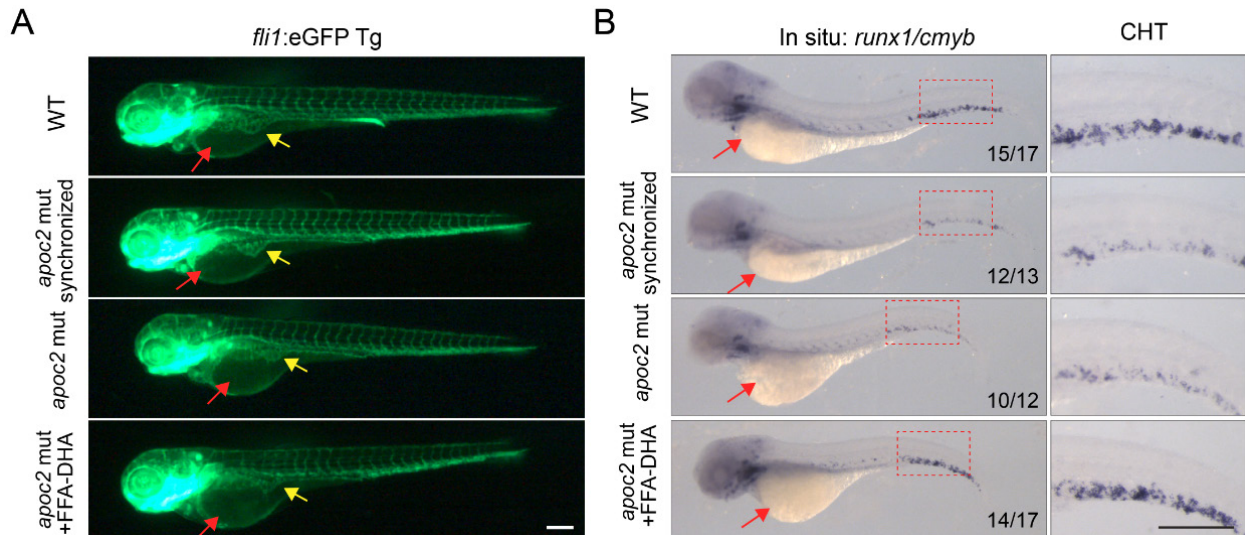
In 2 dpf zebrafish, *apoc2* is mainly expressed in the intestine and the yolk.



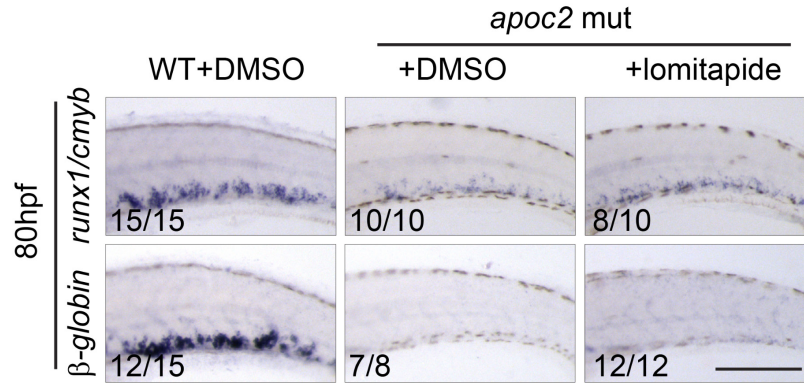
Supplementary Figure 3. *lpl* mutants develop hyperlipidemia. (A) Primers, flanking exon 4, the site of CRISPR target, are used to amplify *lpl* cDNA. (B) Single *lpl* cDNA band of the same size in WT and *lpl* mutant embryos indicates that no alternative splicing occurs in the mutant. (C) Sequence results indicate a 2nt deletion in cDNA from *lpl* mutants. (D) ORO staining of WT, *apoc2* and *lpl* mutants at 6 dpf. (E) Representative images and quantitative results of BODIPY neutral lipid staining of WT, *apoc2* and *lpl* mutants at 6 dpf. Results are mean±SEM; n=5 (WT and *apoc2* mut) and n=6 (*lpl* mut); *** P <0.001 (Student's t -test). Scale bars, 100 μ m in D, and 50 μ m in E.



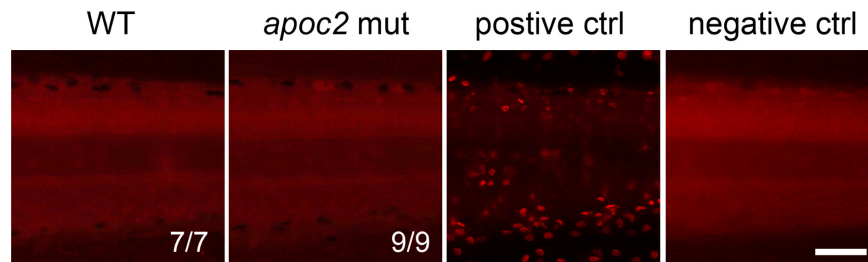
Supplementary Figure 4. Expression of hematopoietic markers in *apoc2* mutants at different developmental stages. (A) *In situ* hybridization with *gata1*, β -globin and *pu.1* probes in WT and *apoc2* mutants at 20 hpf. (B) *In situ* hybridization with *runx1* at 26 hpf (top) and *cmyb* at 52 hpf in WT and *apoc2* mutants' VDA (middle images) and CHT (bottom) regions. (C) *In situ* hybridization with *cmyb/runx1*, β -globin and *rag1* probes in WT and *apoc2* mutants at 80 hpf. *rag1* signals in the thymus are indicated with green arrows. Scale bars, 200 μ m.



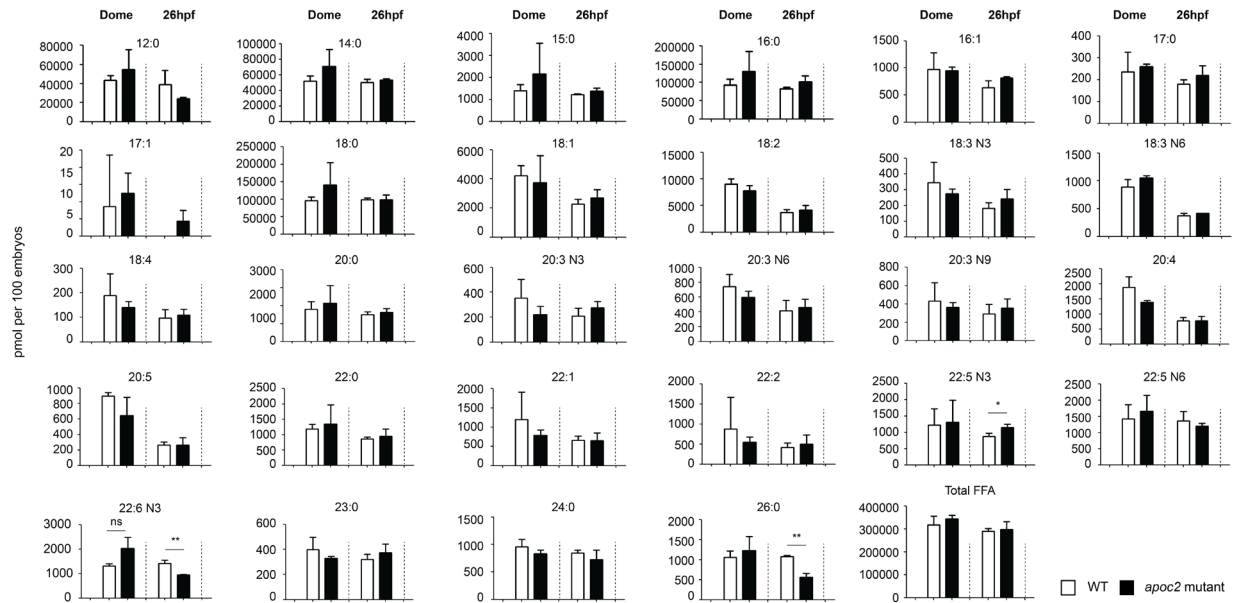
Supplementary Figure 5. Hematopoietic defect in *apoc2* mutants is not due to delayed angiogenesis. (A) Angiogenesis in *fli1:eGFP* WT, *apoc2* mutant, the *apoc2* mutant synchronized with WT, and the *apoc2* mutant injected with DHA, all imaged at 80 hpf. *apoc2* mutant synchronization was achieved by maintaining the embryos at 30°C from 72 to 80 hpf, while WT embryos were kept at 28°C. DHA was injected at 48 hpf. Yellow arrows point to sub-intestinal vessels. Red arrows point to the yolk. (B) *In situ* hybridization with *runx1/cmyb* primers in the same groups as in panel A, at 80 hpf. The CHT regions traced with red dashed quadrangles are enlarged in right-hand panels. Scale bars, 200 μ m.



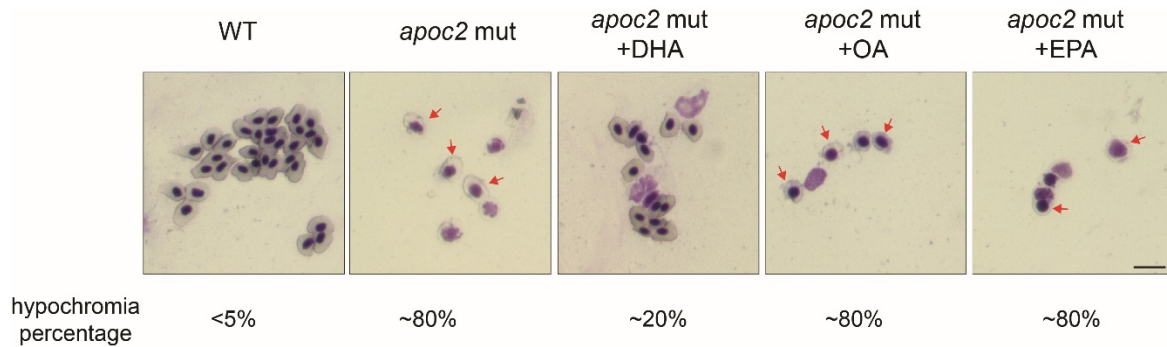
Supplementary Figure 6. Lomitapide does not rescue the hematopoietic defect in *apoc2* mutants. *In situ* hybridization with *cmyb/runx1* and β -globin probes in WT, *apoc2* mutants and the *apoc2* mutants treated with 5 μ M lomitapide. Lomitapide treatment was started at 2 dpf and continued until the embryos were fixed at 80 hpf for *in situ* hybridization. Scale bar, 200 μ m.



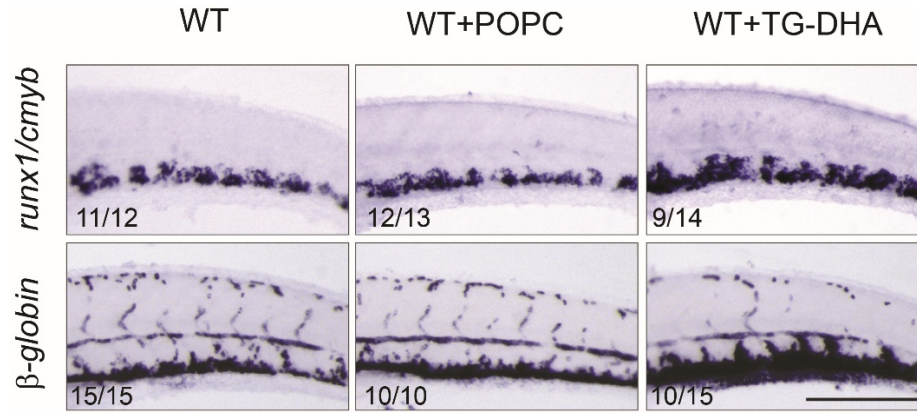
Supplementary Figure 7. *apoc2* mutants show no increase in apoptosis in the CHT region. TUNEL staining in the CHT region of 3.3 dpf WT and *apoc2* mutant embryos. Embryos incubated with Dnase I for 15 min at room temperature were used as a positive control. Embryos incubated with a labeling solution only, without terminal transferase, were used as a negative control. Scale bar, 50 μ m.



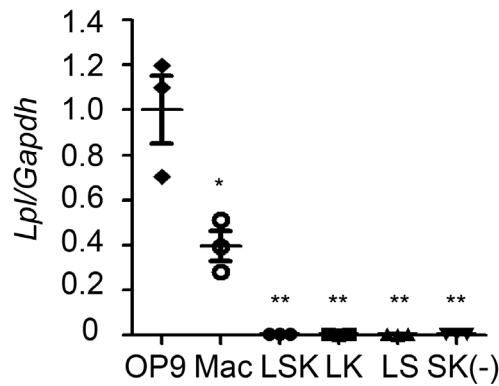
Supplementary Figure 8. GC-MS analysis of FFAs in zebrafish homogenates. Each replicate is a pool of 20 embryos. Results are mean $\pm$ SEM; n=3 in each group, * $P < 0.05$ and ** $P < 0.01$ (Student's t -test).



Supplementary Figure 9. DHA but not oleic or eicosapentaenoic acid rescues hypochromia in *apoc2* mutants. (A) *apoc2* mutant embryos were injected with free fatty acid DHA, OA or EPA at 48 hpf. Wright-Giemsa staining of peripheral blood cells in 6.3 dpf zebrafish. Red arrows point to immature erythrocytes containing larger and less condensed nuclei. Scale bar, 10 μ m.



Supplementary Figure 10. TG-DHA but not the vehicle increases hematopoietic markers in WT zebrafish. *In situ* hybridization with *cmyb/runx1* and β -globin probes in WT and WT injected with POPC or TG-DHA:POPC micelles. Embryos were injected at 2 dpf and fixed at 80 hpf for *in situ* hybridization. Left- and right-hand side images are the same as in Fig. 8B. Images in the middle were obtained from the same experiment as those shown in Fig. 8B. Scale bar, 200 μ m.



Supplementary Figure 11. *lpl* expression in murine OP9 stromal cells, macrophages (Mac) and lineage negative cells. LSK (Lineage negative, Sca1 and c-Kit positive), LK, LS and SK(-) cells were isolated from bone marrow of C57Bl6 mice. Results are mean $\pm$ SEM; n=3 in each group, * $P < 0.05$ and ** $P < 0.01$ (Student's *t*-test).