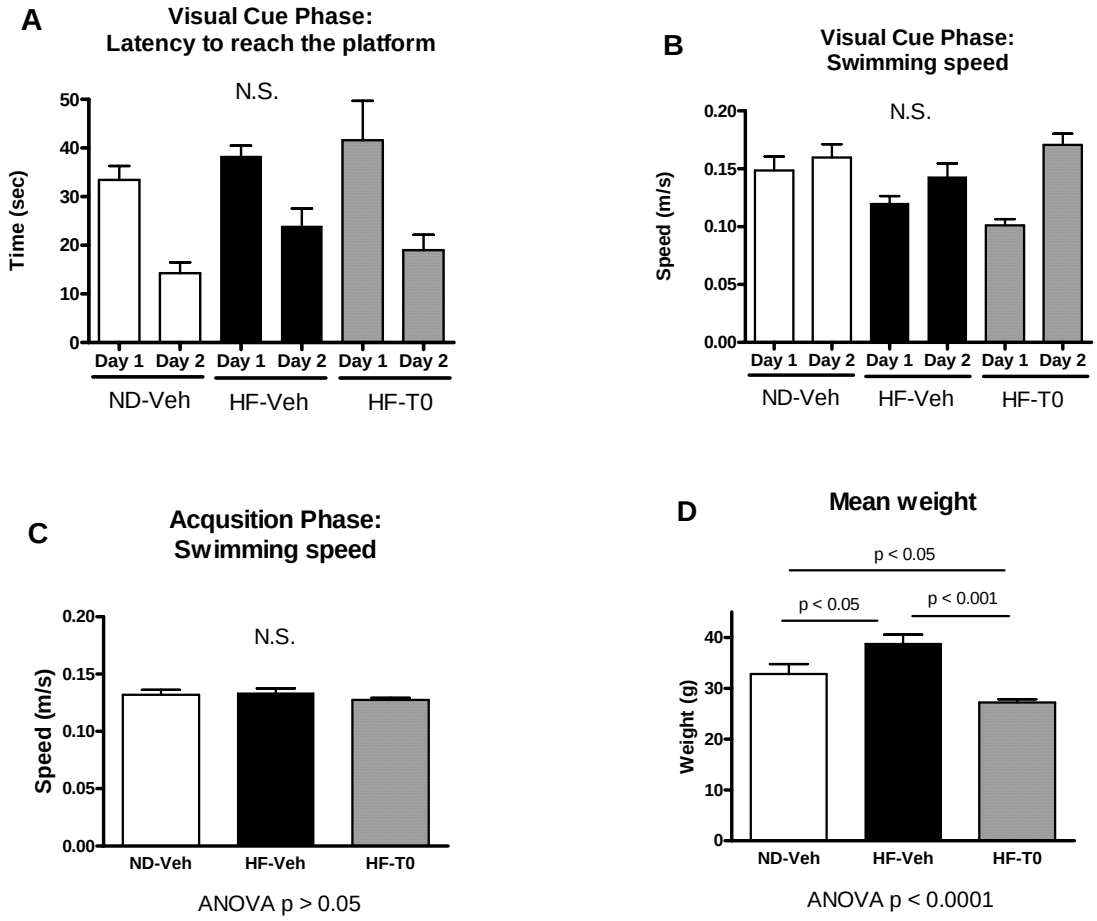
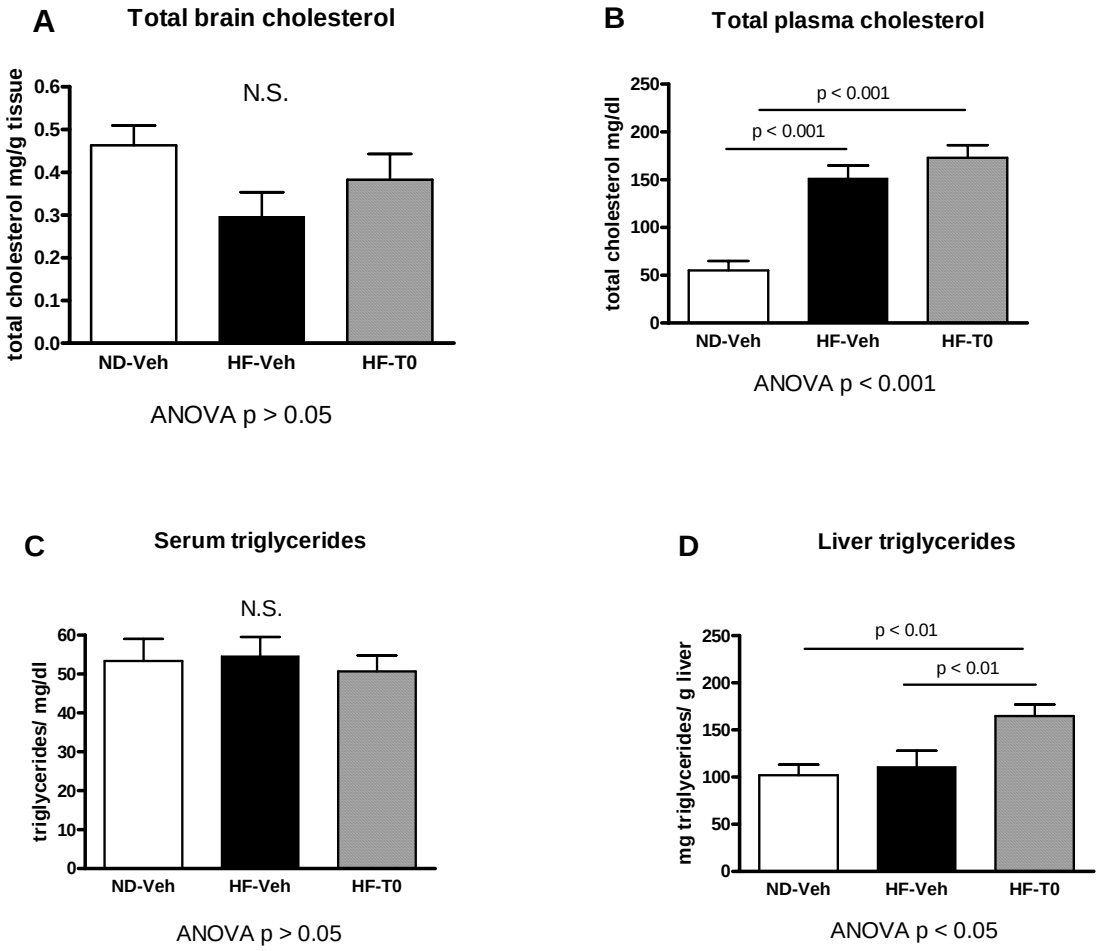
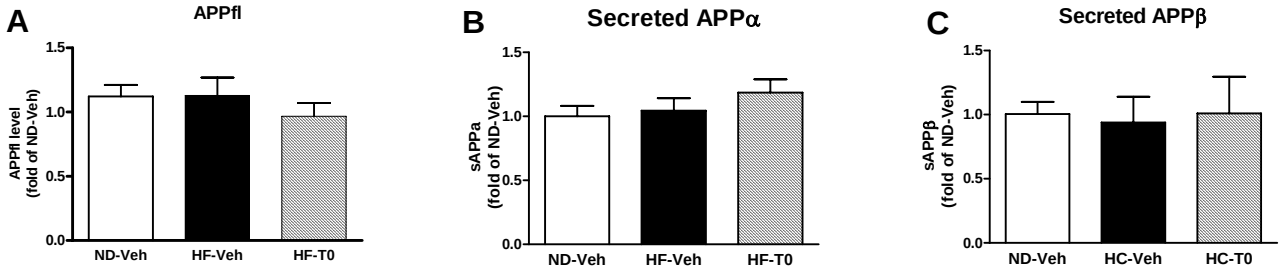


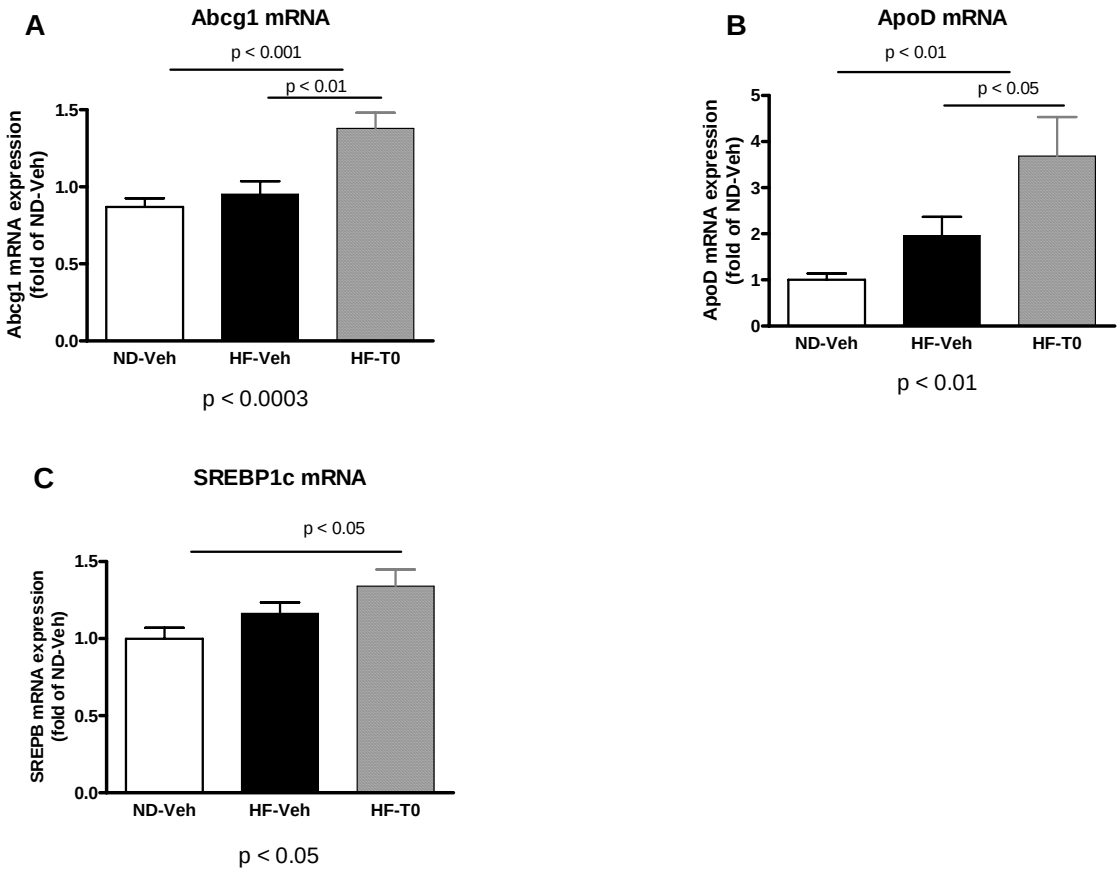
Supplementary Figure 1: High fat diet and T0 treatment did not affect the motivation or swimming speed but changed the weight of treated APP23 mice. A and B, High fat diet and T0 treatment did not affect the performance of APP23 mice during the visual cue phase of training in the MWM. **A**, There is no difference in the latency to reach the visual platform suggesting that motivation of the treated mice is not affected. **B and C**, Swimming speed during the visual cue phase (**B**) and during the acquisition phase of training in the MWM (**C**) suggests that there is no effect of treatment on locomotor activity of APP23 mice. **D,** High fat diet increases body weight in vehicle treated mice compared to mice on normal diet ($p < 0.05$). T0 treatment significantly decreases weight compared to HF-Veh and normal diet (for both $p < 0.05$). ND-Veh, normal diet vehicle; HF-Veh, high cholesterol/high fat diet vehicle; HF-T0, high cholesterol diet supplemented with T0. Analysis by one-way ANOVA followed by Tukey's post-test. Bars represent means ± S.E.M. N=8-14 mice per group. N.S.,no significance.



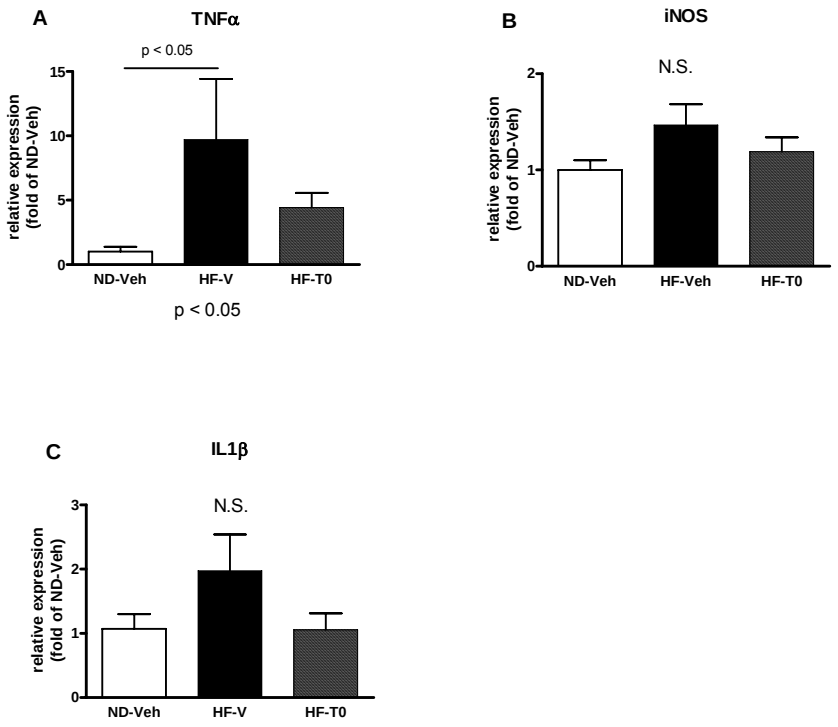
Supplementary Figure 2: High fat diet increases the level of total cholesterol in plasma but not in the brain. A, Total brain cholesterol is unchanged as a result of high fat/high cholesterol diet. **B**, Total plasma cholesterol is increased as a result of high fat/high cholesterol diet. **C**, Serum triglycerides are not affected by LXR ligand treatment; **D**, Liver triglycerides are increased after T0 treatment. ND-Veh, normal diet vehicle; HF-Veh, high cholesterol/high fat diet vehicle; HF-T0, high cholesterol diet supplemented with T0. Analysis by one-way ANOVA and Newman-Keuls post-test. Bars represent means ± S.E.M.N=12-19 mice per group. N.S., no significance.



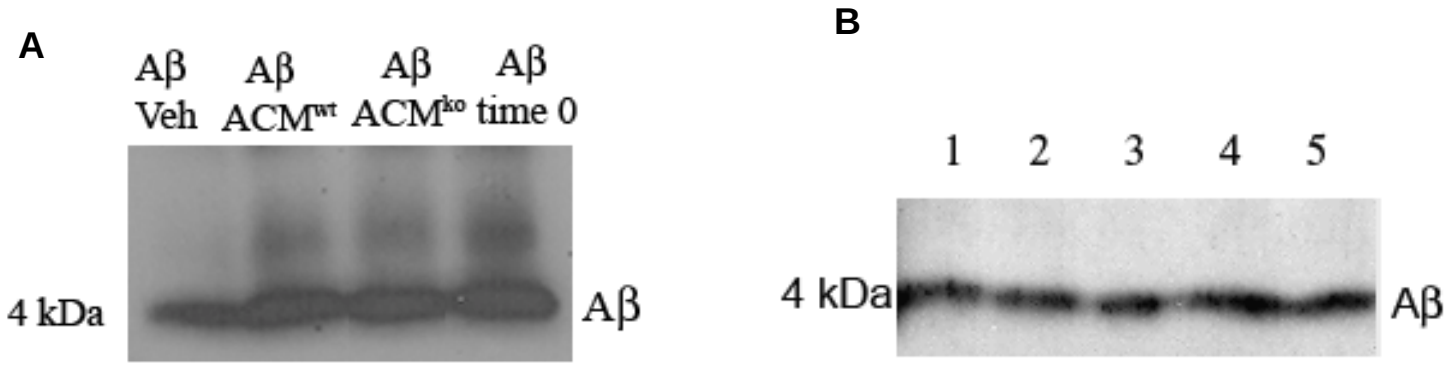
Supplementary Figure 3: High fat diet does not affect APP processing. Soluble proteins were extracted from cortices and hippocampi of APP23 mice on normal diet plus vehicle (ND-Veh) and mice on HF diet treated with vehicle (HF-Veh) or T0 (HF-T0) and APP processing was determined by WB as described in the text. **A**, Full length APP (APPfl); **B** and **C**, soluble fragments result of α- and β-secretase cleavage (sAPPα and sAPPβ). N=8-10 mice per group. Analysis by one-way ANOVA and Newman-Keuls post-test. Bars represent means ± S.E.M.



Supplementary Figure 4: HF diet and LXR ligand T0 increase mRNA expression of LXR responsive genes in hippocampus of APP23 mice. A, T0 increases Abcg1 mRNA in hippocampus. **B**, T0 increases ApoD mRNA in hippocampus. **C**, T0 increases SREBP1c in the hippocampus of mice on HF diet. ND-Veh, normal diet vehicle; HF-Veh, high cholesterol/high fat diet vehicle; HF-T0, high cholesterol diet supplemented with T0. Analysis by one-way ANOVA and Newman-Keuls post-test. Bars represent means ± S.E.M. N=6-12 mice per group.



Supplementary Figure 5: HF diet increase mRNA expression of some pro-inflammatory genes in cortex of APP23 mice. A, HF increases TNFα mRNA compared to ND-Veh ($p < 0.05$). HF-T0 shows a trend toward decrease versus HF-Veh but the difference is not statistically significant. **B**, iNOS mRNA level is not statistically different in all mice regardless of diets; **C**, IL1β mRNA level is not statistically different (N.S.) in mice on a ND and HF diets. Note that IL1β mRNA levels were very low in all samples and undetectable in few of the samples. Analysis by one-way ANOVA and Newman-Keuls post-test. Bars represent means ± S.E.M. N=6-11 mice per group.



Supplementary Figure 6: In the absence of microglia, ACM incubation does not increase $A\beta_{42}$ degradation. A, 0.5 μM $A\beta_{42}$ was incubated for 24 hours in the presence or absence of ACM from WT (ACM^{WT}) or Abca1ko (ACM^{KO}) astrocytes as described in the text. 6 μl aliquots of Aβ were resolved on a 4-12% Bis Tris NuPAGE gel and WB performed with 6E10 antibody. For comparison, on the right is shown Aβ at the start of the incubation (time 0). Representative picture of one experiment in triplicate. **B**, 0.5 μM $A\beta_{42}$ was incubated for 24 hours in the presence of ACM^{WT} treated with vehicle (2) or T0 (3); or ACM^{KO} treated with vehicle (4) or T0 (5) as described in the text. $A\beta_{42}$ incubated for 24 hours without ACM and only with vehicle is shown on lane 1. Representative picture of two experiments in duplicate. For **A** and **B**, note the lack of difference between $A\beta_{42}$ incubated only with vehicle and $A\beta_{42}$ incubated with ACM.