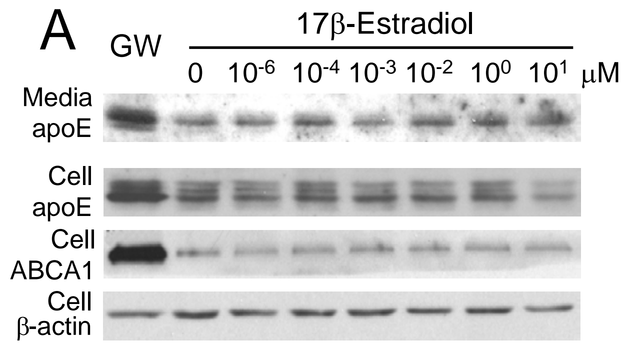
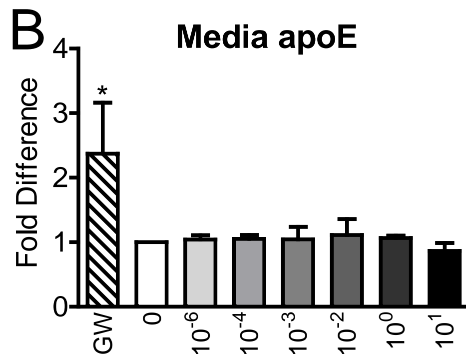
Supplemental Figure 1. 17β-estradiol does not exhibit LXR agonist activity. CCF-STTG1 cells were seeded in 12-well plates at 450K cells/well and treated with 17β-estradiol at 1 pM, 100 pM, 1 nM, 10 nM, 1μM and 10 μM for 24h, along with DMSO alone (0) as a negative control and 1μM of GW3965 (GW) as a positive control. (***A****)* Representative Western blots of media apoE, cellular apoE, cellular ABCA1, and β-actin as a loading control. Band intensity was quantitated by densitometry and expressed as fold change relative to the DMSO control. Data represent mean and SD of fold differences of media apoE (***B***), cellular apoE (***C***) and cellular ABCA1 (***D***). Graphs illustrate two independent experiments, each in duplicate, analysed by one-way ANOVA with a Tukey's post test. * represents $p<0.05$.

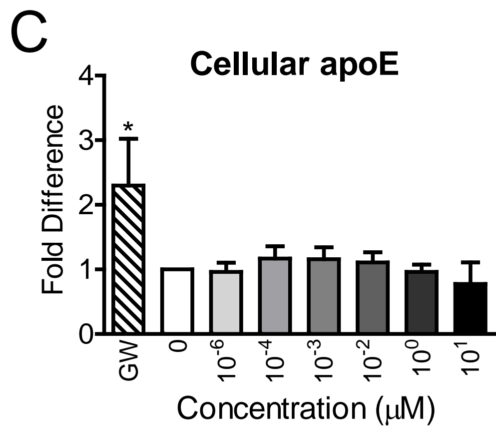
Supplemental Figure 2. Effects of progesterone and lynestrenol in primary murine mixed glia. Primary mixed glial cells were re-seeded in 12-well plates and pre-treated with 5 μM of RU486 or DMSO alone for 1h, followed by treatment of DMSO alone (Ctrl), 10 μM of progesterone (Prog), 10 μM of lynestrenol (Lyn) or 1 μM of GW3965 (GW), with or without 5 μM RU486 for another 72h. Western blotting (***A***) was used to measure media apoE (***B***), cellular protein levels of apoE (***C***) and ABCA1 (***D***) in whole cell lysates. Band intensity was quantitated by densitometry and expressed as fold change relative to the DMSO control without RU486 co-treatment. Real-time quantitative PCR was used to measure apoE (***E***) and ABCA1 (***F***) mRNA levels in whole cell lysates. Data represent mean and SD of fold differences from six independent experiments for B, five experiments for C and D, three experiments for E and F. Drug effect of progestins and GW3965 was analysed by two-way ANOVA with a Tukey's post test. Effect of RU486 was analysed by two-way ANOVA with a Sidak's column comparison. * represents $p<0.05$, ** represents $p<0.01$, and *** represents $p<0.0001$.

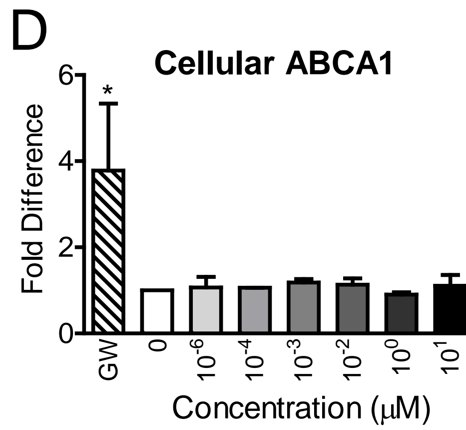
Supplemental Figure 3. Effects of progesterone and lynestrenol in apoE3- and apoE4-expressing immortalized astrocytes. Immortalized astrocytes from human apoE3 and apoE4 knock-in mice were seeded in 12-well plates and pre-treated with 5 µM of RU486 or DMSO alone for 1h, followed by treatment of DMSO alone (Ctrl), 1 µM of progesterone (Prog), lynestrenol (Lyn) or GW3965 (GW) with or without 5 µM RU486 for another 24h. Western blotting (***A, B***) was used to measure media apoE (***C, D***), cellular protein levels of apoE (***E, F***) and ABCA1 (***G, H***) in whole cell lysates. Band intensity was quantitated by densitometry and expressed as fold change relative to the DMSO control without RU486 co-treatment. Data represent mean and SD of fold differences from three independent experiments for C-F, four experiments for G and H. Drug effect of progestins and GW3965 was analysed by two-way ANOVA with a Tukey's post test. Effect of RU486 was analysed by two-way ANOVA with a Sidak's column comparison. * represents $p<0.05$ and *** represents $p<0.0001$.

Supplemental Figure 1

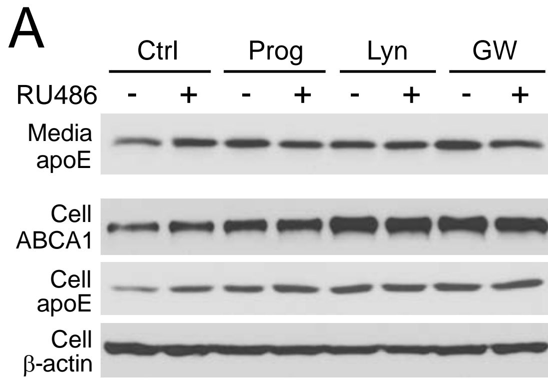


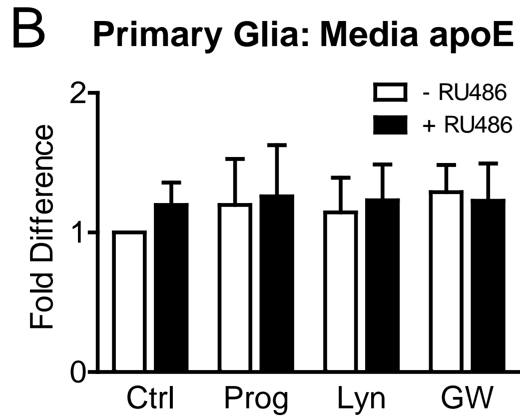


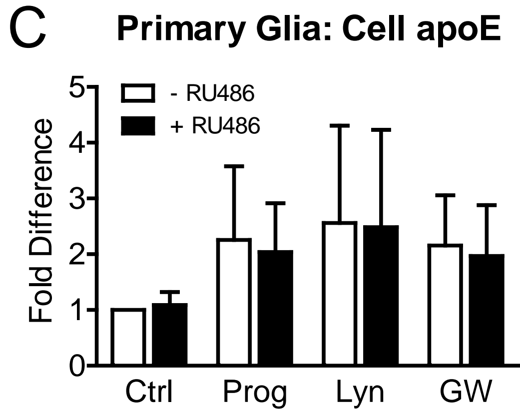


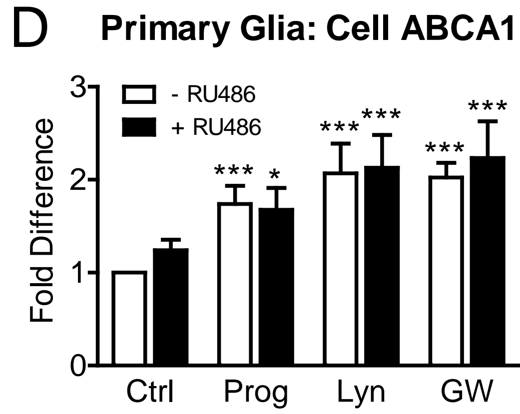


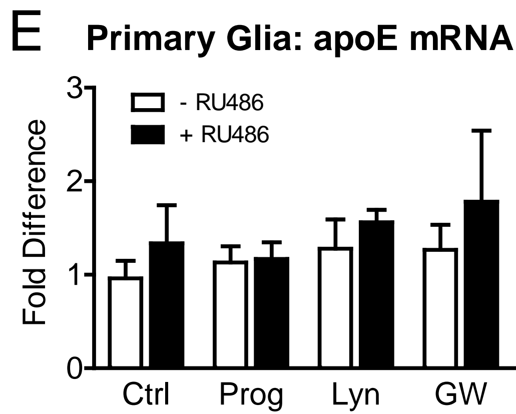
Supplemental Figure 2

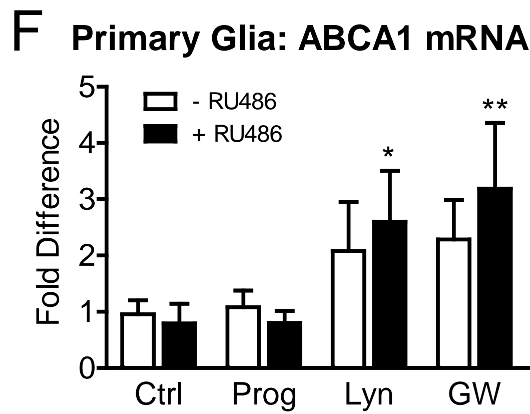












Supplemental Figure 3