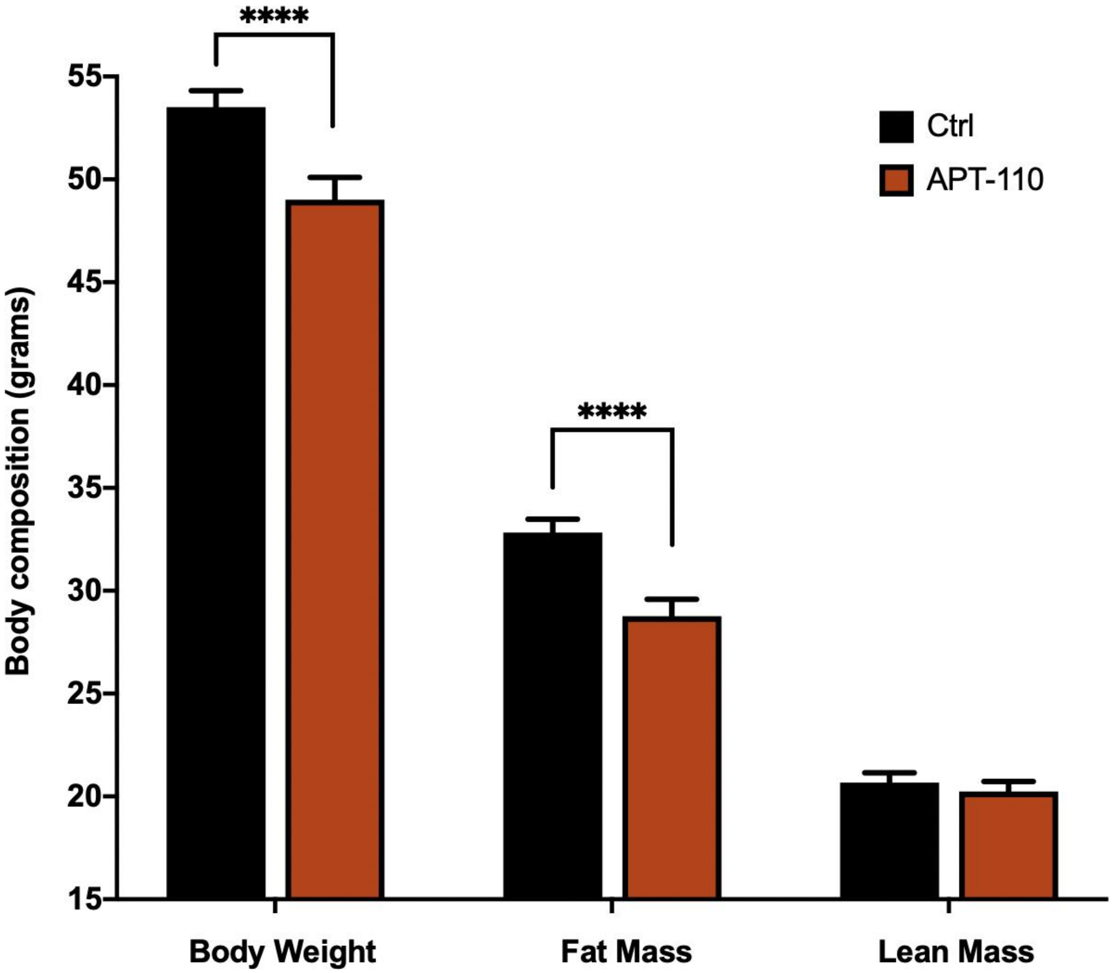
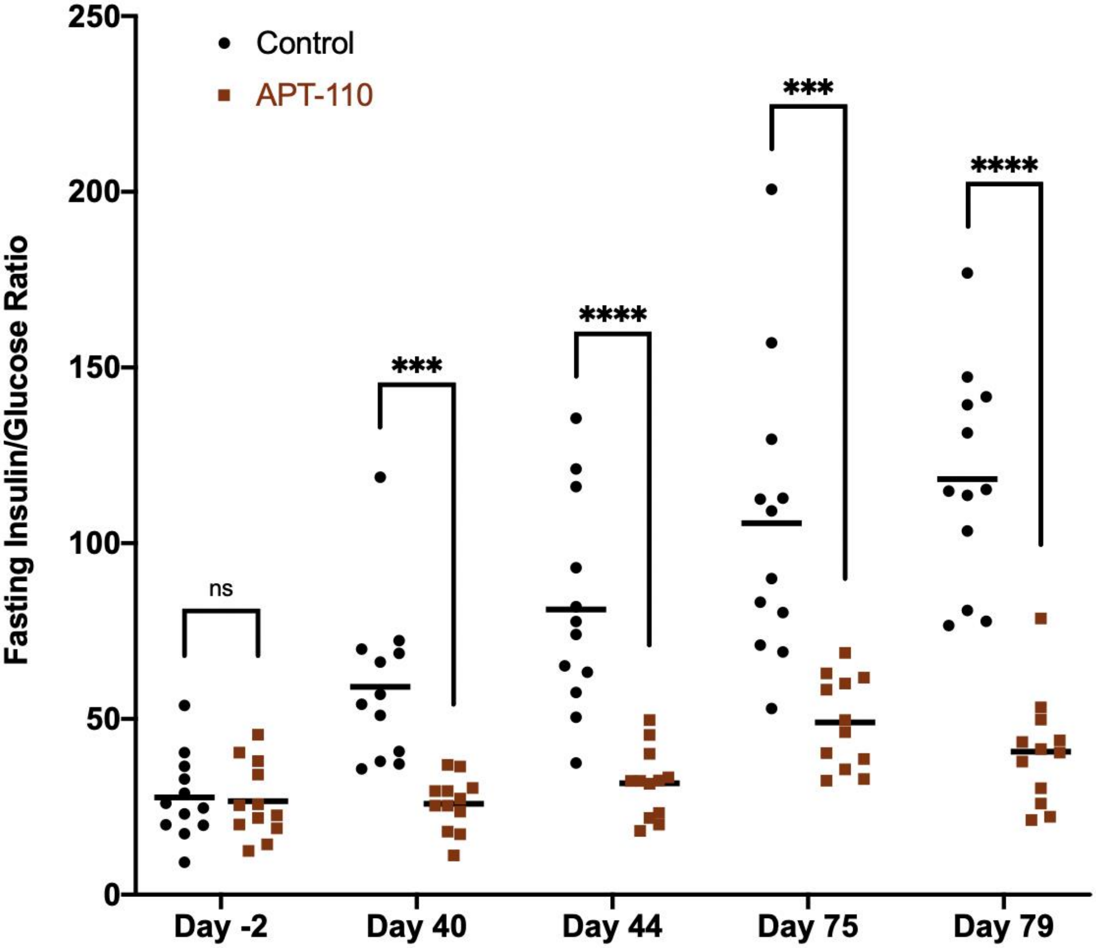
Supplementary Figure 1: Body composition by NMR analysis at week 12 of treatment (27 weeks of age) in mice receiving saline injections (black columns) or the APT-110 miR-22-3p antagomir (brown columns).



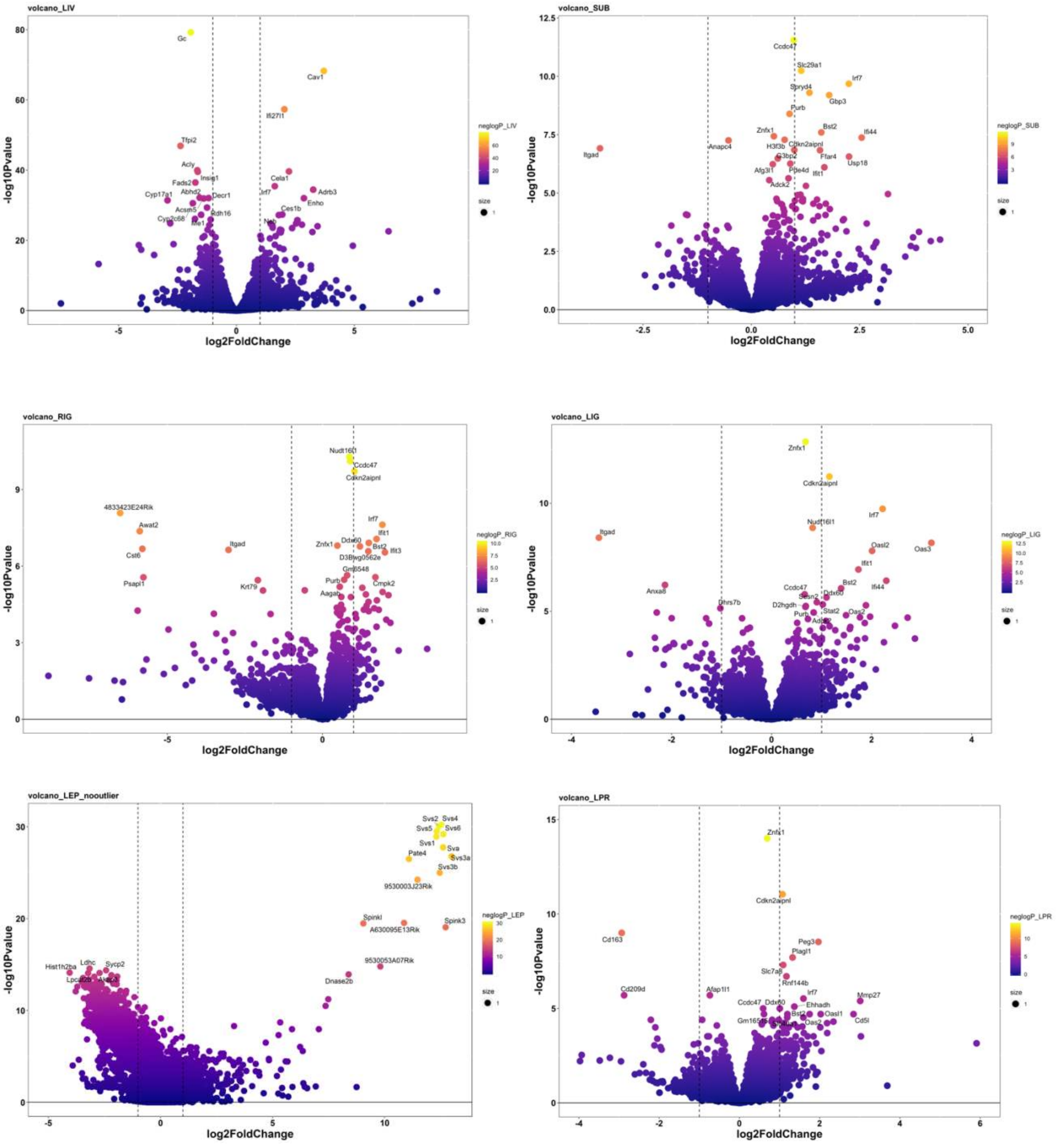
**** : $p \leq 0.0001$

Supplementary Figure 2: Fasting Plasma Insulin/Glucose ratio in mice receiving saline injections (black circles) or the APT-110 miR-22-3p inhibitor (brown squares) at baseline, in the middle and at the end of 12 weeks of treatment.

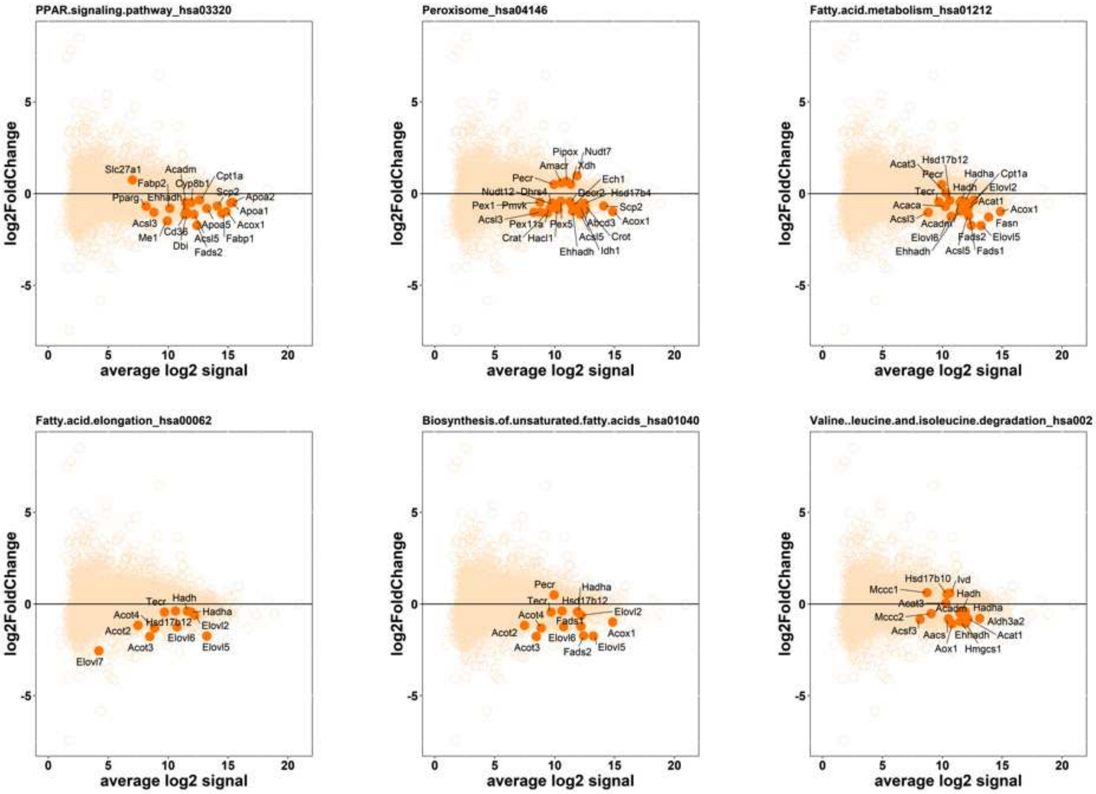


*** : p = 0.0001; **** : p ≤ 0.0001

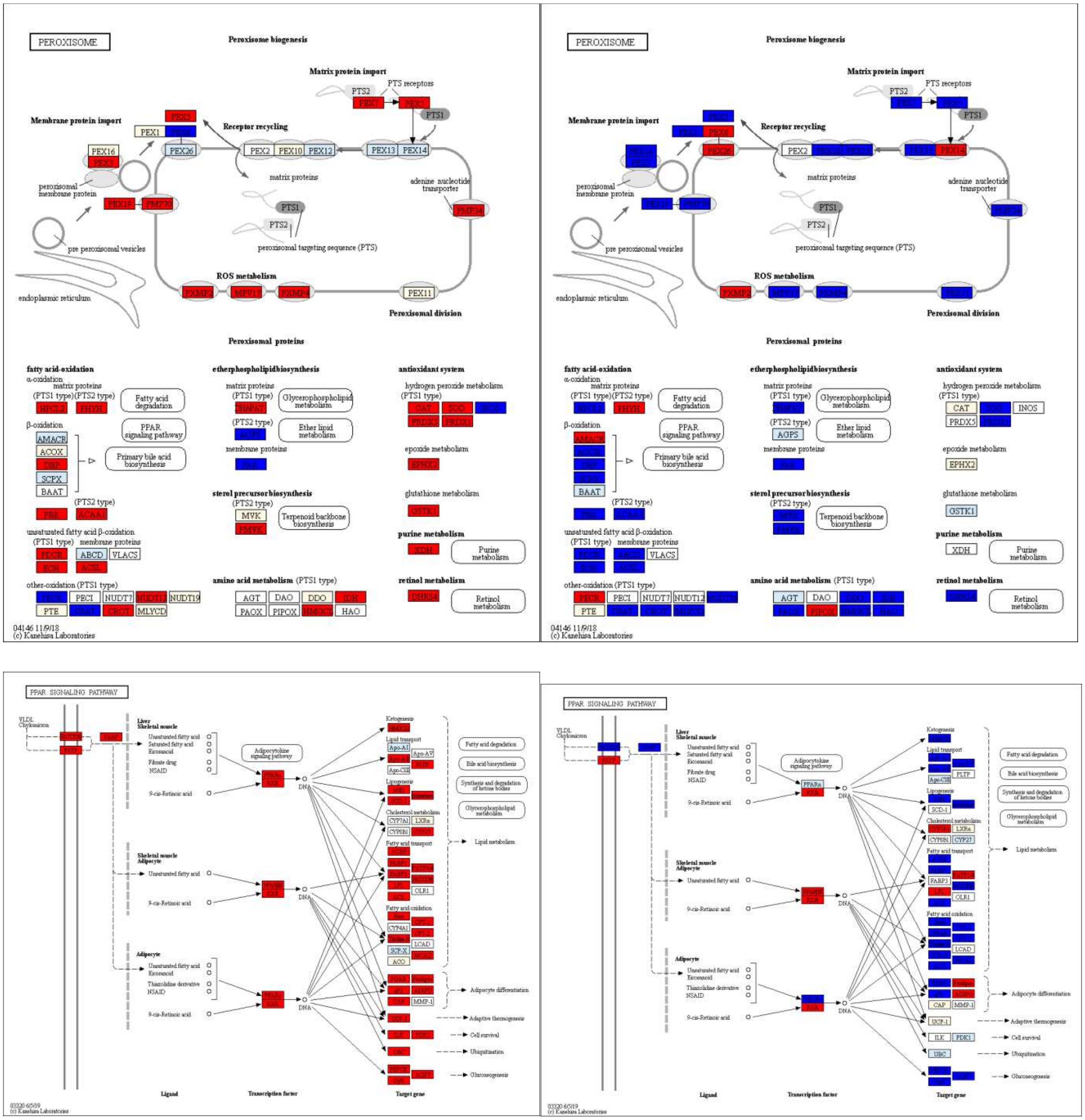
Supplementary Figure 3A: RNA-Seq Volcano Plots in liver (LIV), subscapular fat (SUB), right inguinal fat (RIG), left inguinal fat (LIG), left epididymal fat (LEP) and left perirenal fat (LPR) samples.



Supplementary Figure 3B: RNA-Seq Data Pathway Enrichment Analysis in liver samples. Pathway names are indicated on the top of each Mean-Average (MA) plot. In each plot, pathway genes are shown as filled orange circles. All other non-pathway genes from the RNAseq study are shown as tan, open circles (background).

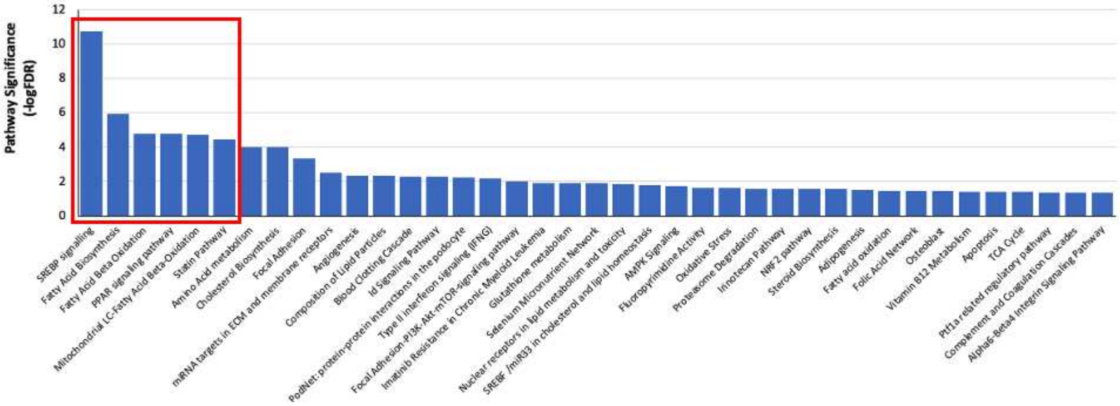


Supplementary Figure 3C: RNA-Seq Data Pathway Enrichment Analysis in inguinal and liver samples



Differentially expressed genes from fat (nominal p < 0.01) and liver (nominal p <0.001) RNA sequencing data were overlaid onto KEGG pathways via the KEGG pathway mapping tool (https://www.genome.jp/kegg/tool/map_pathway3.html). Up-regulated genes (logFC>=0.1) are colored in red and down-regulated genes (logFC<=-0.1) are colored in blue.

Supplementary Figure 3D: RNA-Seq Data Pathways analysis of liver samples of mice treated with the APT-110 miR-22-3p inhibitor (pathways with adjusted P-value (FDR) ≤5%).



Supplementary Figure 4: miR-22-3p target genes involved in lipid oxidation, mitochondrial functions, thermogenesis, glucose metabolism, adipocyte differentiation, inflammation and anti-oxidation.