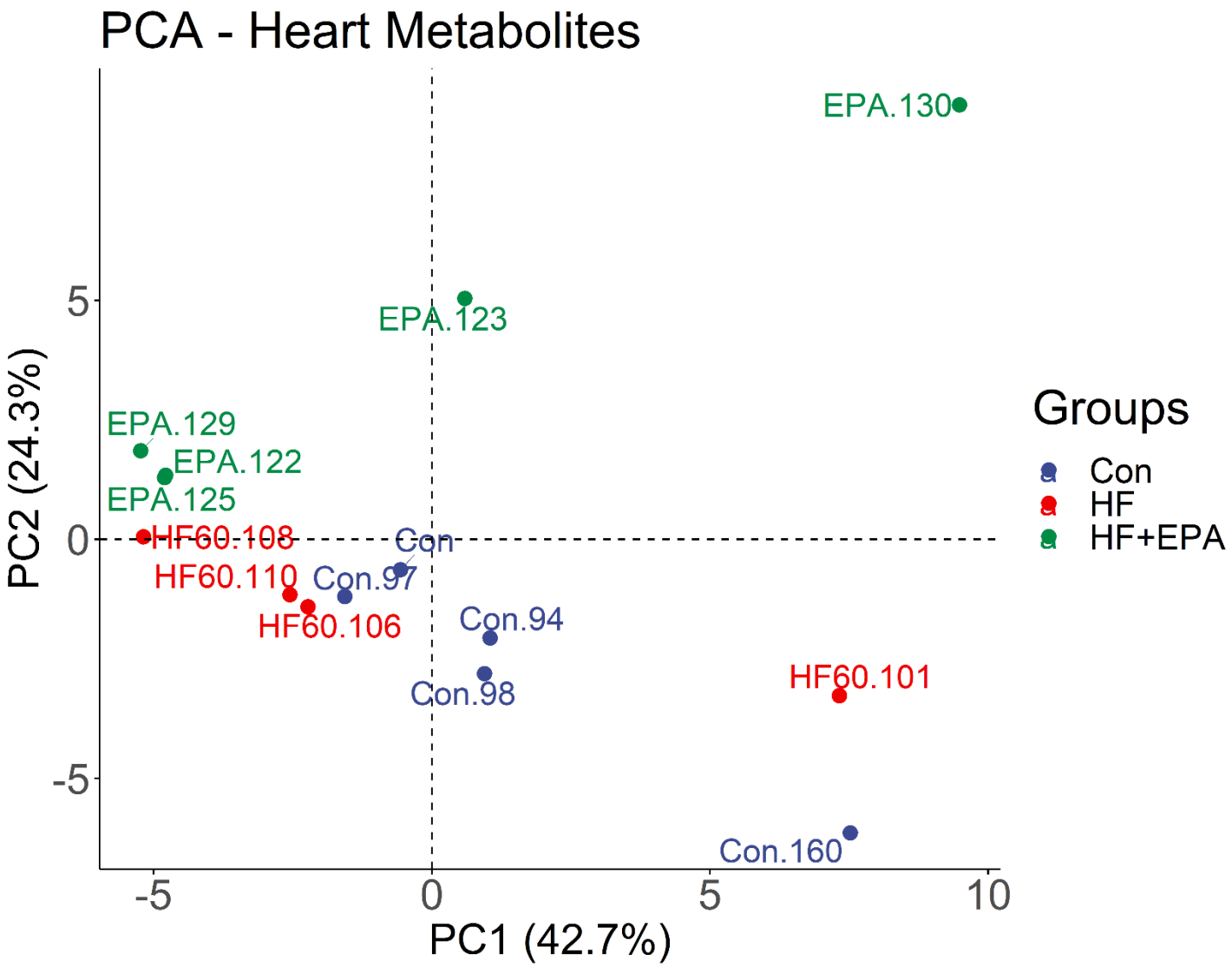
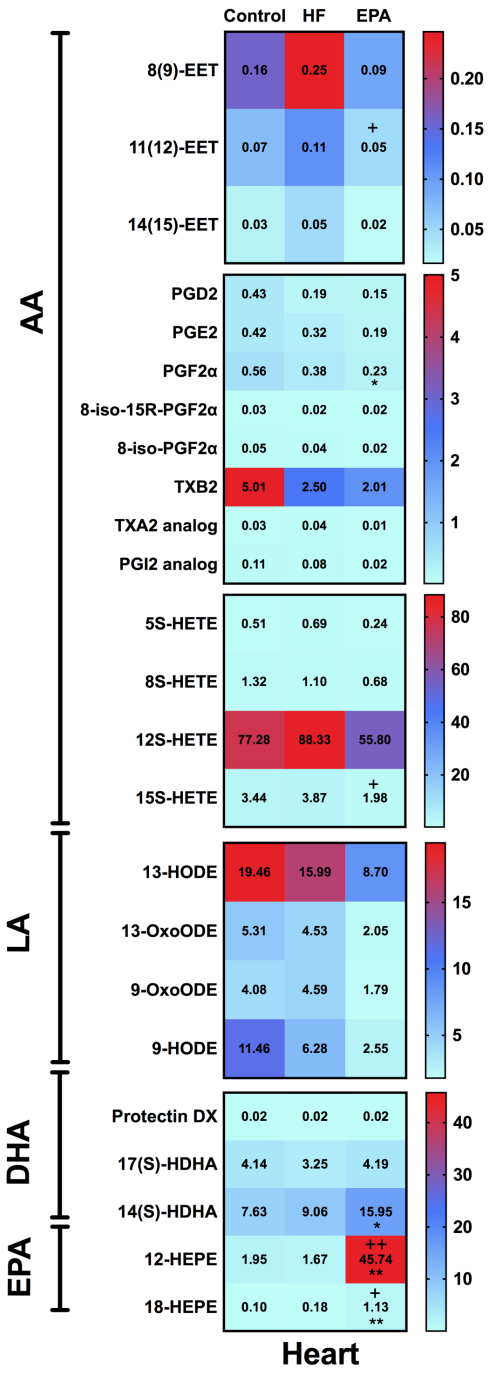
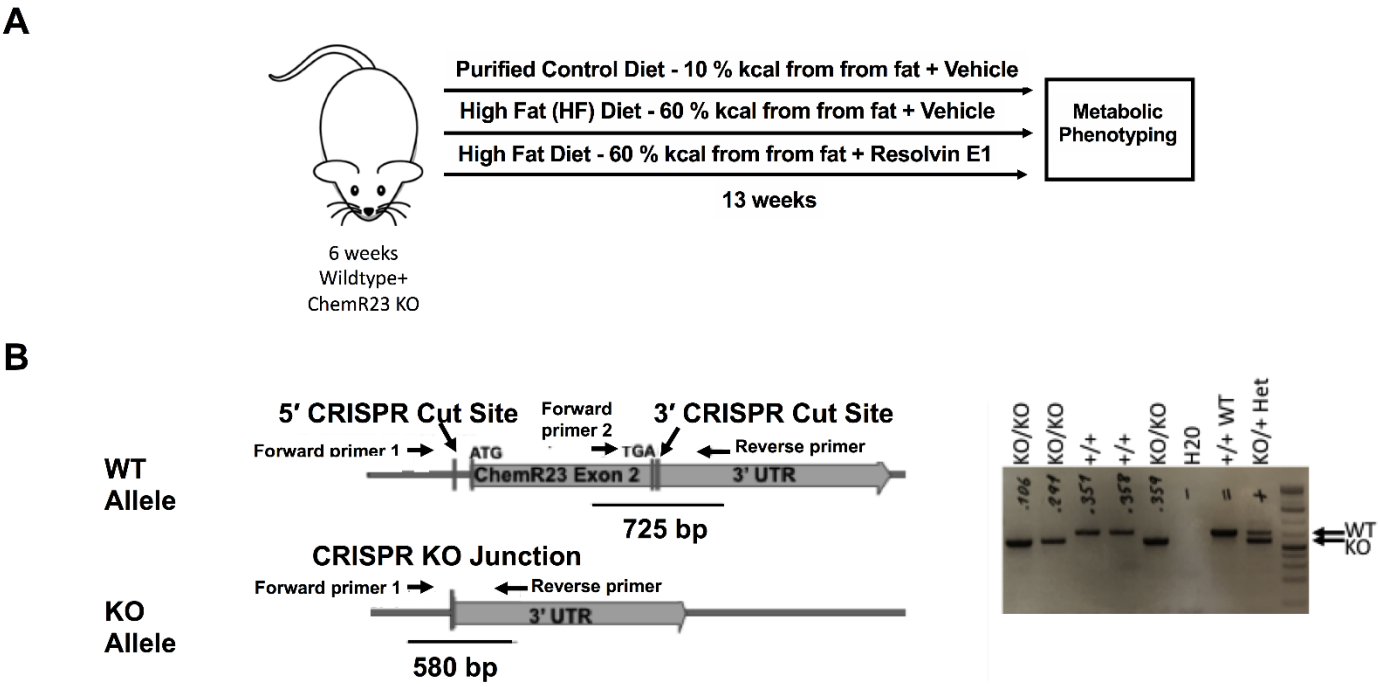


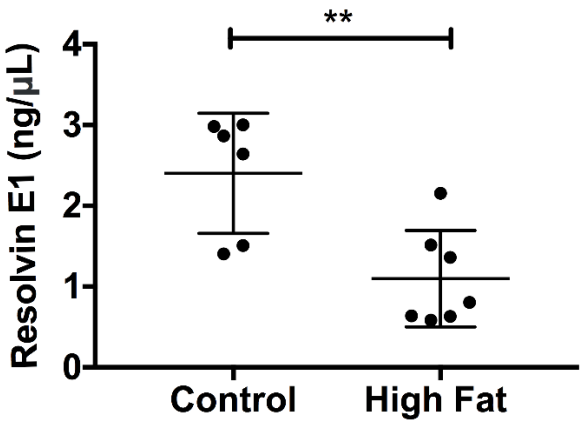
Supplemental Figure 1. Principal component analysis of untargeted metabolomic profiling in cardiac tissue. PCA plot of validated heart tissue metabolites for C57BL/6J male mice consuming a control diet, high fat (HF) or HF+EPA.



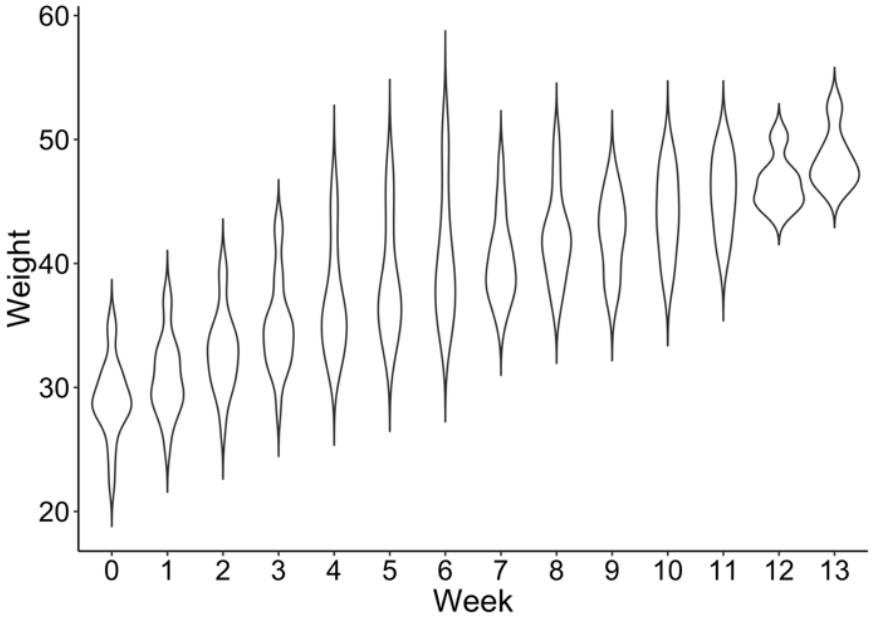
Supplemental Figure 2. EPA ethyl esters increase levels of EPA derived lipid metabolites 12-HEPE and 18-HEPE. Mass spectrometry based metabololipidomic analyses of cardiac tissue. Metabolites from eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), linoleic acid (LA) and arachidonic acid (AA) are depicted in the heat map. Male mice consumed experimental diets for 15 weeks. N=4-5 mice per diet. Data are average. *p<0.05, **p<0.01 as compared to a control diet and $^{+}$p<0.05, $^{++}$p<0.01 as compared to a high fat diet.



Supplemental Figure 3. Schematic representation of studies with ERV1/ChemR23 wild type and knockout mice. (A) Study design with ERV1/ChemR23 knockout mice and their wildtype littermates administered RvE1 or vehicle control for four days after being fed a high fat diet or lean control diet. (B) Illustration of ChemR23 deletion allele and genotyping.



Supplemental Figure 4. RvE1 levels of lean and obese mice. C57BL/6J obese mice were purchased from Jackson Laboratories. Mice consumed a control or high fat diet for 15 weeks. Serum RvE1 levels were measured with an ELISA. Data are average ± S.D. **p<0.01 with a two-tailed t test. N=6-7 mice per diet.



Supplemental Figure 5. Body weights of DO mice consuming a high fat diet. Violin plots of body weights as a function of time for DO mice at the completion of the first experimental design. This protocol entailed using DO mice that achieved approximately 14 grams of fat mass prior to RvE1 administration.