**Supplemental Figures:**

**Supplemental Figure 1. PPARγ deacetylation inhibits aortic arch lesion in early stage of atherogenesis.** Male mice were fed a WTD for 8 weeks. n=15 for *WT:Ldlr****–/–*** (referred as WT), n=15 for *2KR:Ldlr****–/–*** (referred as 2KR). (**A**) Representative images of aortic arches, and (**B**) *en face* plaque analysis with Oil Red O staining. The quantified arch lesion areas were squared. (**C**) Quantification of *en face* aortic arch plaque area. (**D**) Representative H&E staining of aortic root sections, with plaque outlined in black. (**E**) Quantification of total lesion area and (**F**) necrotic core of aortic root sections. N.S.: not significant, \*: P<0.05 by Mann-Whitney U test. Data are presented as mean ± SEM.

**Supplemental Figure 2. PPARγ deacetylation inhibits aortic arch atherosclerosis in female mice.** Female animals on *Ldlr****–/–*** background were fed a WTD for 12 weeks. (**A**) Representative images of aortic arches. (**B**) Representative images of en face aortic plaque analysis with Oil Red O staining. (**C**) Quantification of en face aortic plaque. n=10 for WT, n=14 for 2KR. Not significant by Mann-Whitney U test. (**D**) Body weight curve on WTD feeding. (**E**) Body composition and (**F**) tissue composition after 12 weeks of WTD. Mice were sacrificed after overnight fasting and 4-hour refeeding. (**G-J**) Plasma triglycerides (TG), non-esterified fatty acid (NEFA), total cholesterol, and high-density lipoprotein (HDL-c). (**K**) FPLC analysis of lipoproteins. \*: P<0.05, \*\*: P<0.01 for WT vs. 2KR by 2-tailed t-test; n=10 for WT, n=14 for 2KR. (**L**) GTT on WTD for 9 weeks; (**M**) ITT on WTD for 8 weeks; **(L-M)** Data are presented as mean ± SEM. (**N**) Plasma insulin levels determined by ELISA. n=15 for WT, n=15 for 2KR. Data are presented as mean ± SEM.

**Supplemental Figure 3.**

Male mice on *Ldlr****–/–*** background were fed a WTD for 12 weeks, n=11 for WT, and n=14 for 2KR. (**A**) Liver TG (B) Representative images of Liver after H&E staining. Data are presented as mean ± SEM.

**Supplemental Figure 4. 3D structure of PPARg showing the clustering of K268, K293 and K395.**

The 3D structure of PPARg (PDB ID: 3GBK) were generated by using Cn3D macromolecular structure viewer. (A) and (B) are the different views of the structures with K268, K293, and K395 marked in yellow.