Data S1.

Animal diet compositions.

Two primary diets were used as the nutritional basis for the animal experiments. The standard chow diet (cat. no. XTI01SL-002, Jiangsu Synergy Bio-engineering Co., Ltd.) was a gamma-irradiated, nutritionally complete regimen formulated to meet Chinese National Standards (GB/T 14924.1-3 and GB 13078). Its nutritional profile included ≥200 g/kg crude protein, ≥40 g/kg crude fat, ≤50 g/kg crude fiber, ≤80 g/kg crude ash, and ≤100 g/kg moisture. It contained calcium (10-18 g/kg), phosphorus (6-12 g/kg), magnesium (2.6 g/kg), potassium (7.1 g/kg), and sodium (2.5 g/kg). Amino acid composition (g/kg) was as follows: lysine (14.1), methionine + cystine (8.8), arginine (14.1), histidine (5.9), tryptophan (2.9), phenylalanine + tyrosine (15.3), threonine (9.3), leucine (17.8), isoleucine (10.9), and valine (11.8). Trace minerals (mg/kg) included iron (229), manganese (107), copper (17), zinc (59.2), iodine (0.75), and selenium (supplied as yeast selenium; exact concentration unspecified). This diet was fortified with organic zinc and natural vitamin E to support reproductive health. By contrast, the high-fat diet (cat. no. D12492i, Research Diets, Inc.) was also gamma-irradiated and formulated to derive 60% of its total caloric content from fat, 20% from protein, and 20% from carbohydrate, with an elevated energy density of 5.21 kcal/g. Its formulation per kilogram consisted of casein (200.0 g), L-cystine (3.0 g), maltodextrin (125.0 g), sucrose (72.8 g), cellulose (50.0 g), lard (245.0 g), soybean oil (25.0 g), mineral mix S10026B (50.0 g), vitamin mix V10001C (1.0 g), choline bitartrate (2.0 g), and FD&C Blue #1 dye (0.05 g).

Figure S1. AK induces hepatic lipid deposition. (A) Hematoxylin and eosin staining of liver tissue of all individuals in the WT groups (magnification, x100). (B) Hematoxylin and eosin staining of liver tissue of all individuals in the WT-AK groups (magnification, x100). (C) Hematoxylin and eosin staining of liver tissue of all individuals in the KO groups (magnification, x100). (D) Hematoxylin and eosin staining of liver tissue of all individuals in the KO-AK groups (magnification, x100). AK, acesulfame-K; WT, wild-type; KO, PPARα-null.

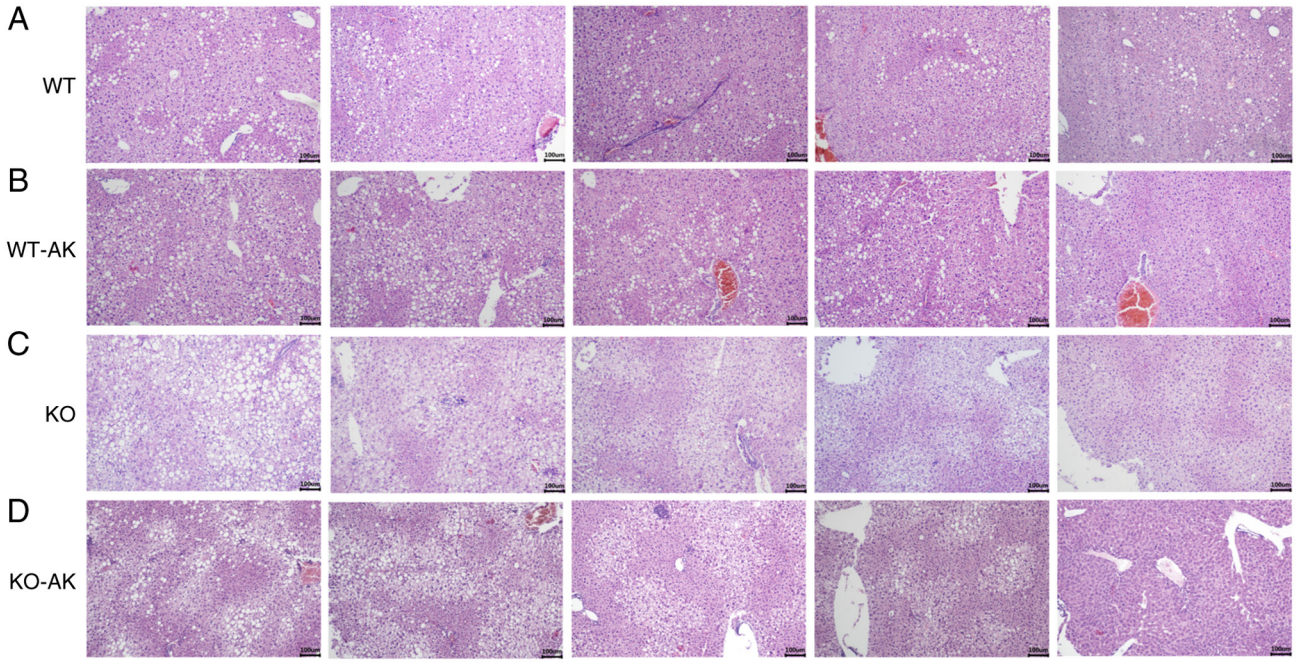

Figure S2. AK exhibits no significant impact on hepatic inflammation. (A) Plasma ALT levels in the 4 experimental groups. (B) Plasma AST levels in the four experimental groups. The mRNA expression levels of inflammatory genes (C) *Tnfα*, (D) *Il6*, (E) *Ccl2* (F) *Il1β*) in liver tissues of the four experimental groups. Data were expressed as mean ± SEM. *P<0.05, **P<0.01, ns, not significant. AK, acesulfame-K; ALT, alanine aminotransferase; AST, aspartate aminotransferase; *Ccl2, C-C motif chemokine ligand 2*; *Il1β, interleukin 1 beta*; *Il6, interleukin 6*; KO, PPARα-null; *Tnfα, tumor necrosis factor*; WT, wild-type.

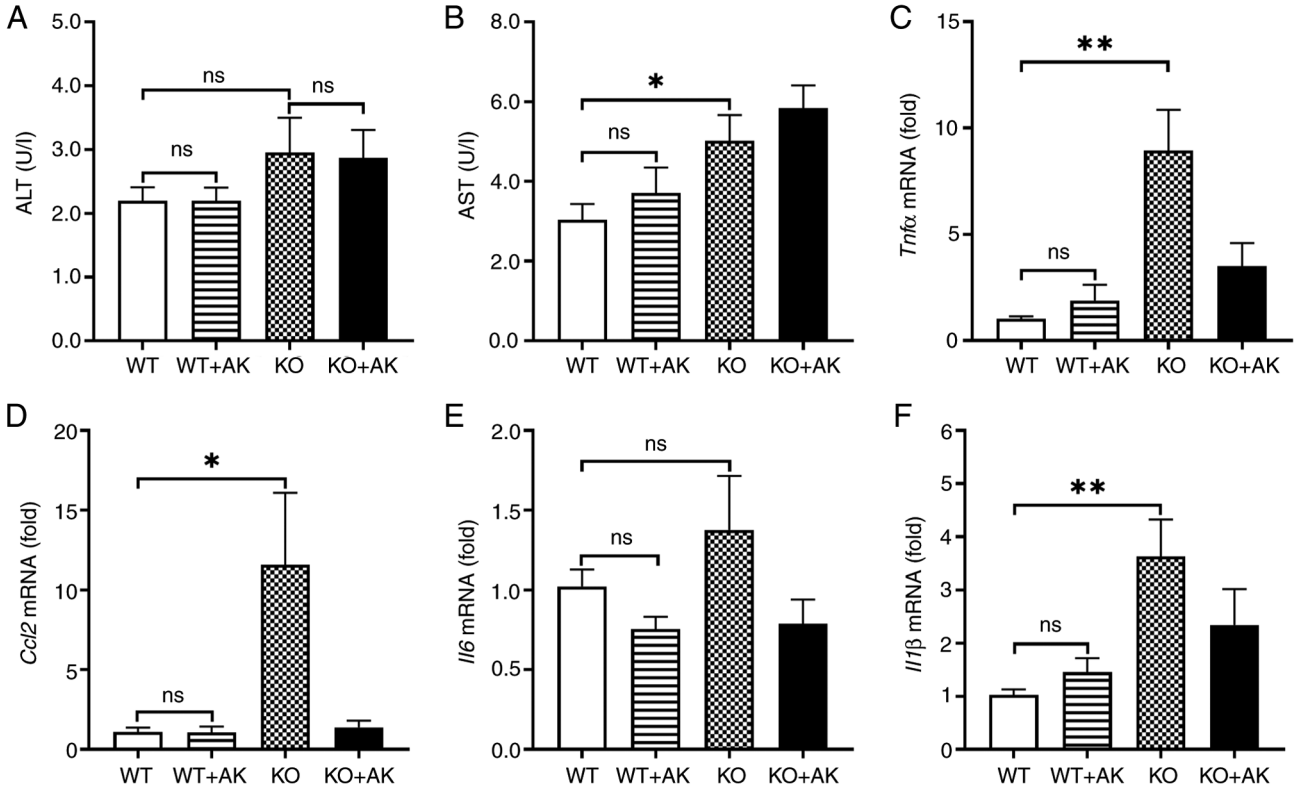

Figure S3. AK administration upregulated hepatic lipid synthesis genes. (A-D) The mRNA expression levels of lipid metabolism-related genes (A) *Acaca*, (B) *Elovl6*, (C) *Srebf1* and (D) *Acox1* in liver tissues from the four experimental groups. The mRNA expression levels of lipid transport genes (E) *Dgat2* and (F) *Cd36* in liver tissues of the four groups. The mRNA expression levels of gluconeogenesis genes (G) *Pck* and (H) *Pgm2* in liver tissues from each group. Data were expressed as mean ± SEM. $^{*}P<0.05$ ns, not significant. AK, acesulfame-K; *Acaca, acetyl-Coenzyme A carboxylase alpha*; *Elovl6, ELOVL fatty acid elongase 6*; *Srebf1, sterol regulatory element binding transcription factor 1*; *Acox1, acyl-Coenzyme A oxidase 1, palmitoyl*; *Dgat2, diacylglycerol O-acyltransferase 2*; *Cd36, CD36 molecule*; *Pck1, phosphoenolpyruvate carboxykinase 1, cytosolic*; *Pgm2, phosphoglucomutase 2*; KO, PPARα-null; WT, wild-type.

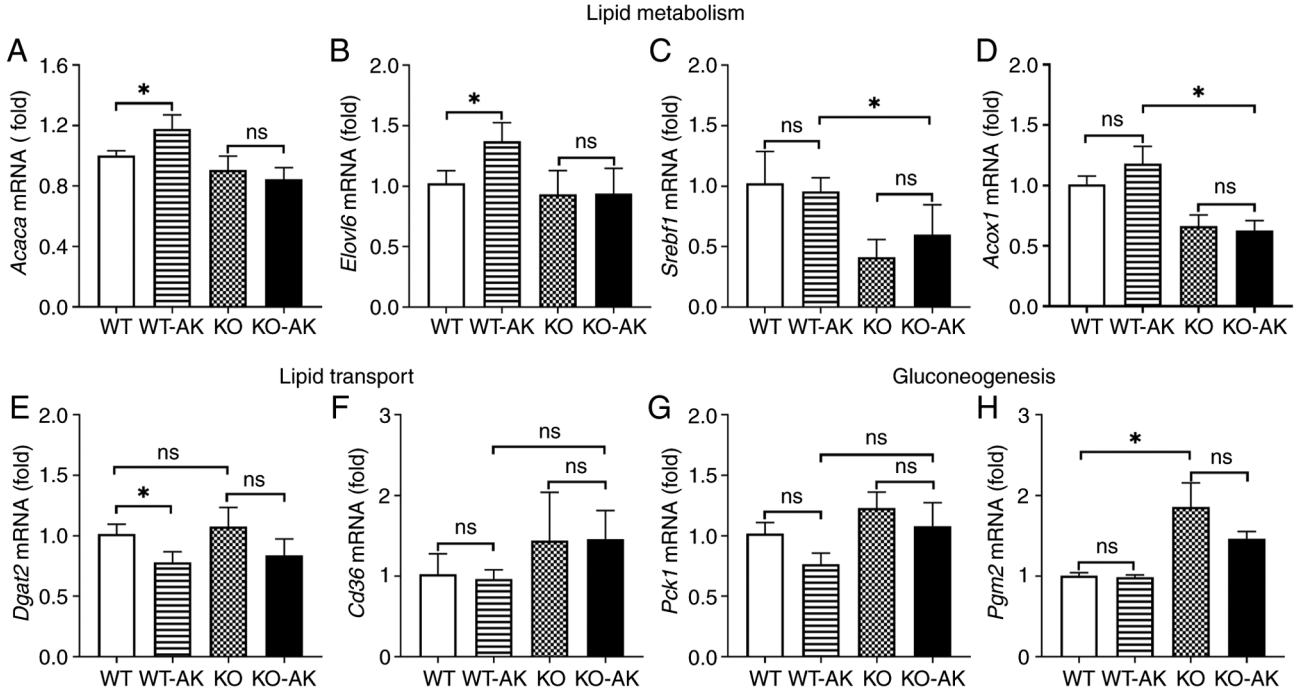

Figure S4. PPARα activation does not markedly regulate transcription of STR signaling pathway genes. (A) Volcano plot depicting hepatic transcriptomic profiles of Wy14,643-treated mice vs. vehicle controls. Red dots: significantly upregulated transcripts (log2 fold-change >1.5, FDR-corrected P<0.01); green dots: significantly downregulated transcripts (log2 fold-change <-1.5, FDR-corrected P<0.01); gray dots represent non-significant genes. (B) Heatmap of genes involved in the STR signaling pathway. Color scale ranges from blue (low expression) to red (high expression). PPARα, peroxisome proliferator-activated receptor alpha; STR, sweet taste receptor; Wy, Wy-14,643, a peroxisome proliferator-activated receptor alpha agonist; FDR, False Discovery Rate; CON, control group; FC, fold change; *Gnat3, G protein subunit alpha transducin 3*; KO, PPARα-null; *Plc, phospholipase C*; *Prkc, protein kinase C*; *Tas1r2, taste receptor, type 1, member 2*; *Tas1r3, taste receptor, type 1, member 3*; WT, wild-type.