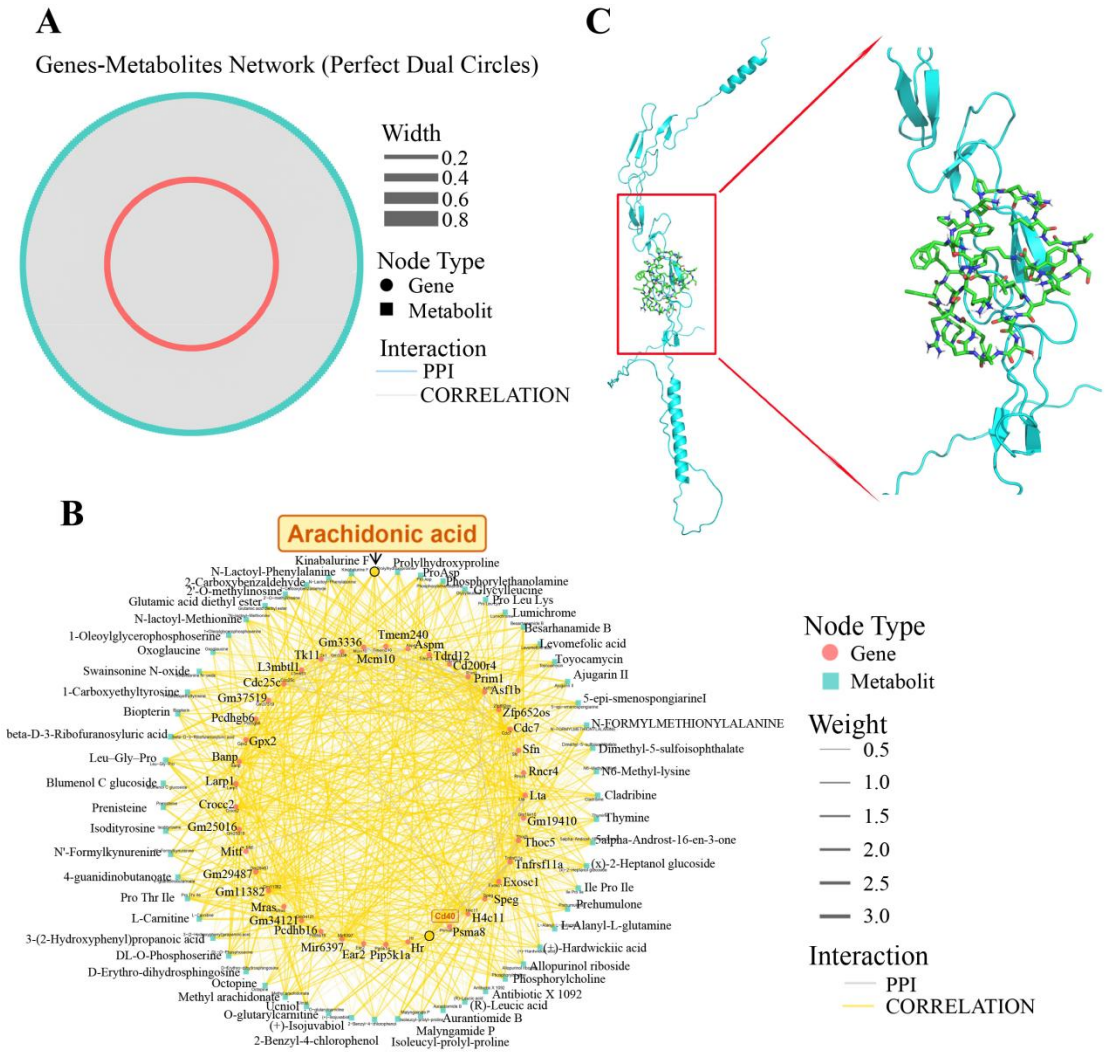
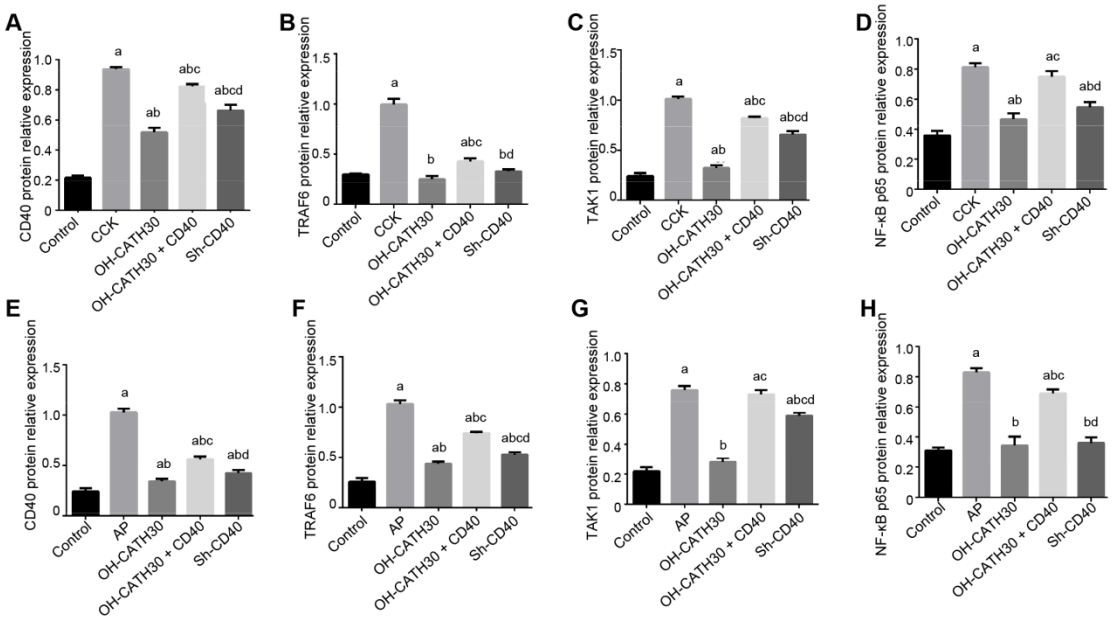
Supplementary material



Supplementary Figure 1 Multi-omics integration identifies CD40 as a candidate target of OH-CATH30, and molecular docking validates their interaction

(A, B) Integrative analysis of transcriptomic and metabolomic data shows strong correlation between NF-κB pathway genes and arachidonic acid (AA) metabolism-related metabolites. The network depicts significant correlations ($|r| \geq 0.8$, $P < 0.01$) between differentially expressed genes (rectangles) and metabolites (circles). Node colors represent expression or abundance levels (red: upregulated in AP; blue: downregulated in AP). CD40 was identified as a central hub gene linking inflammatory signaling to metabolic reprogramming.

(C) Molecular docking simulation of OH-CATH30 with the extracellular domain of mouse CD40 (predicted structure using AlphaFold2). The peptide binds to CD40 with a predicted binding energy of −8.7 kcal/mol. Key interacting residues are shown as sticks: hydrogen bond between Lys12 of OH-CATH30 and Glu117 of CD40 (2.8 Å), salt bridge between Arg14 and Asp84 (3.2 Å), and hydrophobic interactions involving Phe5 and Ile65. These interactions suggest a stable and specific binding mode.



Supplementary Figure 2 Densitometric quantification of CD40 pathway proteins from Figure 6B and 6C

(A–D) Quantitative analysis of CD40 (A), TRAF6 (B), TAK1 (C), and NF-κB p65 (D) protein expression in 266-6 cells corresponding to western blotting results shown in Figure 6B. Protein levels were normalized to that of GAPDH and expressed as relative fold change compared with Control group. Cell groups: Control (untreated); CCK (100 nM CCK for 24 h); OH-CATH30 (100 nM OH-CATH30 after CCK injury); OH-CATH30 + CD40 (AAV-CD40 transfection prior to CCK injury and OH-CATH30 treatment); sh-CD40 (siRNA-mediated CD40 knockdown prior to CCK injury).

(E–H) Quantitative analysis of CD40 (E), TRAF6 (F), TAK1 (G), and NF-κB p65 (H) protein expression in mouse pancreatic tissues corresponding to western blotting results shown in Figure 6C. Protein levels were normalized to that of GAPDH and expressed as relative fold change compared with

Control group. Animal groups: Control (PBS); AP (cerulein-induced); OH-CATH30 (30 μg/kg after AP induction); OH-CATH30 + CD40 (AAV-CD40 tail vein injection prior to AP induction and OH-CATH30 treatment); sh-CD40 (AAV-shCD40 injection prior to AP induction without OH-CATH30 treatment).

All data are presented as mean ± SD (n = 3 independent experiments (A–D) or n = 6 mice per group (E-H)). Statistical analysis was performed using one-way ANOVA followed by Tukey's HSD post hoc test. $^{a}P < 0.05$ vs. Control; $^{b}P < 0.05$ vs. CCK or AP group; $^{c}P < 0.05$ vs. OH-CATH30 group; $^{d}P < 0.05$ vs. OH-CATH30+CD40 group.