Article Title:

Apigenin ameliorates insulin resistance and lipid accumulation by endoplasmic reticulum stress and SREBP-1c/SREBP-2 pathway in palmitate-induced HepG2 cells and high-fat diet-fed mice

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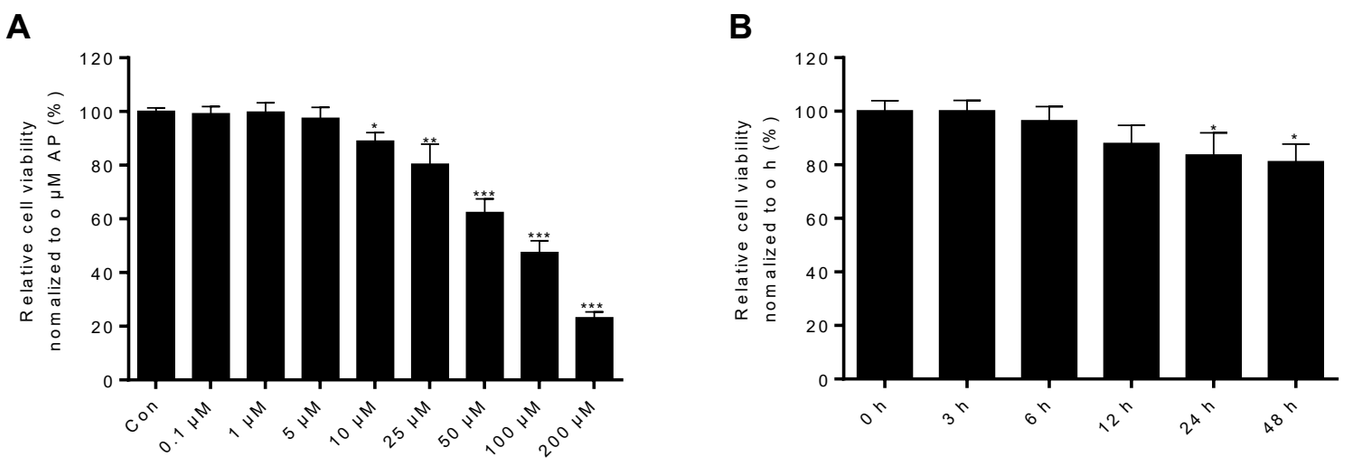
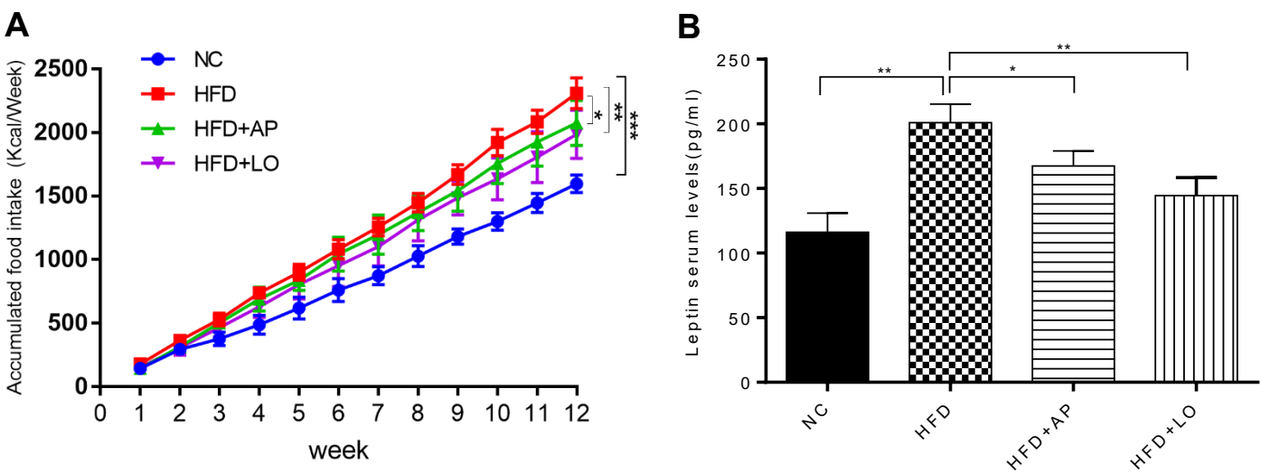
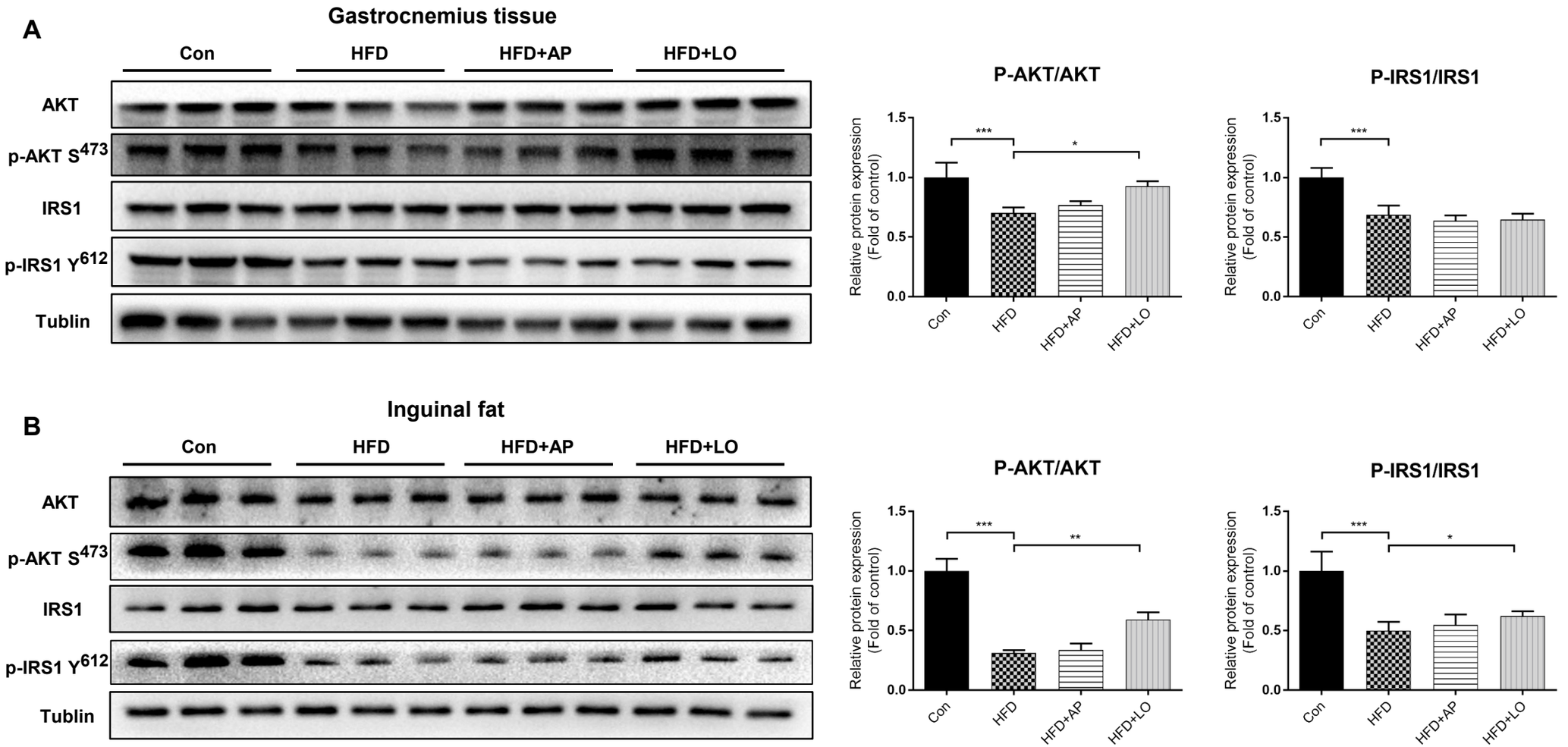


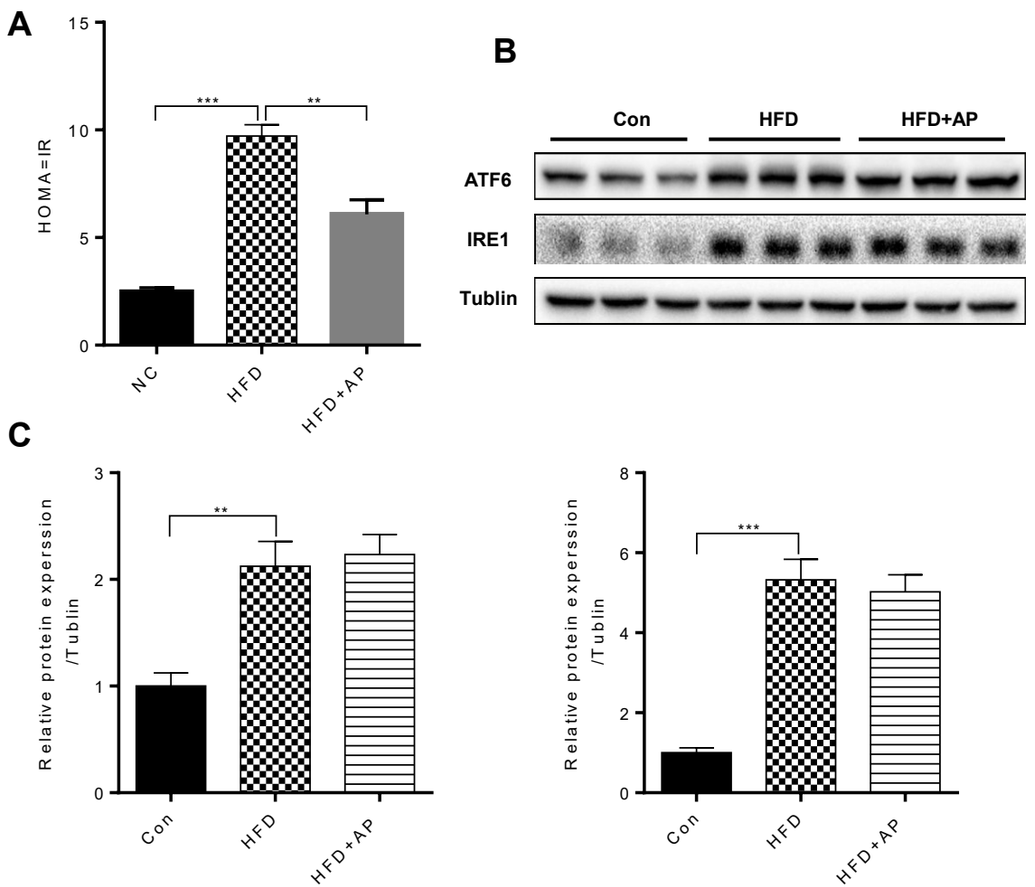
Supplymentary Figure 1



Supplymentary Figure 2



Supplymentary Figure 3



Supplymentary Figure 4

Supplementary Figure 1. Changes in cell viability of HepG2 cells after AP treatment at different concentrations and at different times. (A) HepG2 cells were treated with 0, 0.1, 1, 5, 10, 25, 50, 100, and 200 μM AP for 24h, and cell viability was evaluated by applying CCK-8 assay. **(B)** HepG2 cells were treated with 25μM AP for 3h, 6h, 12h, 24h, 48h, and cell viability was evaluated by applying CCK-8 assay. Data are representative of three independent experiments, and were analyzed by unpaired t-test. Error bars denote SD. $*P < 0.05$; $**P < 0.01$; $***P < 0.001$.

Supplementary Figure 2. Accumulative food intake and leptin serum of mice. (A) Accumulative food intake of per cage was examined for 12 weeks (-3 mice per cage). **(B)** The changes of serum leptin was determined using an Elisa protocol, eight mice in each group. Data are representative of three independent experiments, and were analyzed by unpaired t-test. Error bars denote SD. $*P < 0.05$; $**P < 0.01$.

Supplementary Figure 3. The impacts of AP or LO on p-AKT and P-IRS1 in gastrocnemius muscle and inguinal fat of HFD-fed model mice. The levels of Akt, p-Akt, IRS1 and p-IRS1 were determined by western blotting assays in gastrocnemius muscle **(A)** and inguinal fat **(B)** of the HFD-fed model mice, which were treated with AP or LO. Quantitative analysis of p-Akt and p-IRS1 were conducted based on western blot assay results (Right). Data are representative of three independent experiments, and were analyzed by unpaired t-test. Error bars denote SD. $*P < 0.05$; $**P < 0.01$; $***P < 0.001$.

Supplementary Figure 4. The effects of AP on the ATF6 and IRE1 expressions in HFD-fed model mice. (A) The level of HOMA-IR in the HFD-fed model mice after administration with AP. (B) The levels of ERS-markers proteins (IRE1 and ATF6) were determined through the application of western blot assay in the HFD-fed model mice after administration with AP. (C) Statistical analysis of IRE and ATF6 levels in line with western blot assay results. Data are representative of three independent experiments, and were analyzed by unpaired t-test. Error bars denote SD. $**P < 0.01$; $***P < 0.001$.