

SUPPLEMENTARY TABLE

Table 1-Primers for Real-Time PCR

Gene	Forward (5'-3')	Reverse (5'-3')
Foxo1	AGATGAGTGCCCTGGGCAGC	GATGGACTCCATGTCACAGT
G6Pc	CATTGTGGCTTCCTTGGTCC	GGCAGTATGGGATAAGACTG
Pck	CCATCGGCTACATCCCTAAG	GACCTGGTCCTCCAGATACC
TNF- α	GAGAAAGTCAACCTCCTCTCTG	GAAGACTCCTCCCAGGTATATG
MCP1	CAGGTGTCCCAAAGAAGCTGTAG	GGGTCAGCACAGACCTCTCTCT
Colla1	TAGGCCATTGTGTATGCAGC	ACATGTTTCAGCTTTTGTGGACC
TIMP1	GGCATCCTCTTGTTGCTATCACTG	GTCATCTTGATCTCATAACGCTGG
Elastin	TGGTGACATGATCCCTCTCTCTT	CCAGGGTGTCCCAGATGTG
FASN	GCAAGGTGTAACATTCCCCTCT	ACCGAGTAATGCCATTCAGT
Gck	CCTTCGACCCTCTGTGCGCCG	GCATCACGTCCTCACTGCGG
Hmgcr	CAAGCCTGCCTGCAGATGCT	TGTCCTGCTGCCAAGGCTGC
IRS1	CCCGTTCGGTGCCAAATAGC	GCCACTGGTGAGGTATCCACATAGC
IRS2	ACTTCCCAGGGTCCCCTGCTG	GGCTTTGGAGGTGCCACGATAG
IL6	CCAGAGATACAAAGAAATGATGG	ACTCCAGAAGACCAGAGGAAAT
UQCRC1	ACCAGTGCTACAGAGAGTGAGG	AGCATCTGGGCATCCACCTCCTG
MT-CO1	GTCTGATCCGTACTIONTATTACAG	GCTCATACTATTCTATATAGCCG
Hadha	CGTATGCCATGACTGTCCCA	CCAAATTTCTGCGATTTCAGCAAG
Cpt1a	GCCGATCATGGTTAACAGCAACT	AGACCTTGAAGTAACGGCCTC
VLCAD	CCTTGGTGTTAGCGTTACCCT	GGCTACATCGGATCCACTCG
GSR	CCACGGCTATGCAACATTCG	AATCAGGATGTGTGGAGCGG
Nqo1	CGCCTGAGCCCAGATATTGT	GCACTCTCTCAAACCAGCCT
SOD2	AAGGTCGTTACAGATTGCTGC	AGCGGAATAAGGCCTGTTGTTC
Gclc	CCGCTGTCCAAGGTTGACGA	GTTGCCGCCTTTGCAGATGTC
Glem	CGTGAAGAGCAGGGGAATCA	AGCTGGAGTTAAGAGCCCCT
Cyclophilin	CTAAAGCATACAGGTCTTGGCATCTTG	TGCCATCCAGCCATTCAGTCTTG

SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1-HO1 overexpression regulates Foxo1 and HGP in hepatocytes independent of p38 α . *A*: Hepatocytes isolated from wild-type mice were pre-treated by 10 μ mol/L p38 α inhibitor SB203580 for 0.5 h and then transfected with Adv-GFP or Adv-HO1 for 20 h, followed by the incubation in HGP buffer for 3 h. HGP was normalized to total protein levels. n=4/group. Results are presented as mean \pm SEM. *B*: Hepatocytes isolated from wild-type mice were transfected with scramble siRNA or p38 α siRNA for 12 h and then transfected with Adv-GFP or Adv-HO1 for 20 h. Afterwards, the cells were switched to HGP buffer for 3 h. HGP was normalized to total protein levels. n=6/group. Results are presented as mean \pm SEM.

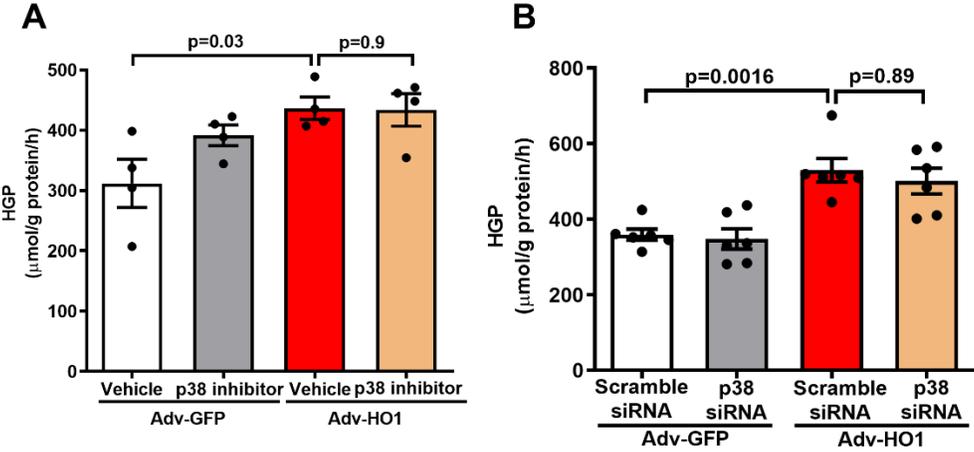
Supplementary Figure 2-HO1 overexpression drives insulin resistance. *A*: AAV8-GFP or AAV8-HO1 was delivered via retro orbital to Foxo1^{fl/fl} or L-FKO mice (male, 8- to 12-week). Serum samples were collected from mice fasted for 16 h by cardiac puncture 14 days after the AAV injection for the measurement of serum insulin level by an ELISA kit. Results are presented as mean \pm SEM. *B*: Hepatocytes isolated from wild-type mice were transfected with Adv-GFP or Adv-HO1 for 24 h. The cells were starved in DMEM with 1% FBS for 1 h prior to the insulin stimulation (100 nmol/L, 1 h). The cell lysates were loaded onto a 10% SDS-PAGE for western blotting analyses to detect pAkt-S473, total Akt, pFoxo1-S253, and total Foxo1. n=3/group.

Supplementary Figure 3-HO1 overexpression does not affect SDO activity or ROS level in hepatocytes. *A*: Hepatocytes isolated from wild-type mice were transfected with Adv-GFP or Adv-HO1 for 24 h. The cell lysates were collected for the measurement of SOD activity by a colorimetric kit. The results are expressed as the inhibition rate of superoxide anion. n=6 mice/group. Results are presented as mean \pm SEM. *B*: Hepatocytes isolated from wild-type mice were transfected with Adv-GFP or Adv-HO1 for 24 h. Intracellular ROS was probed by

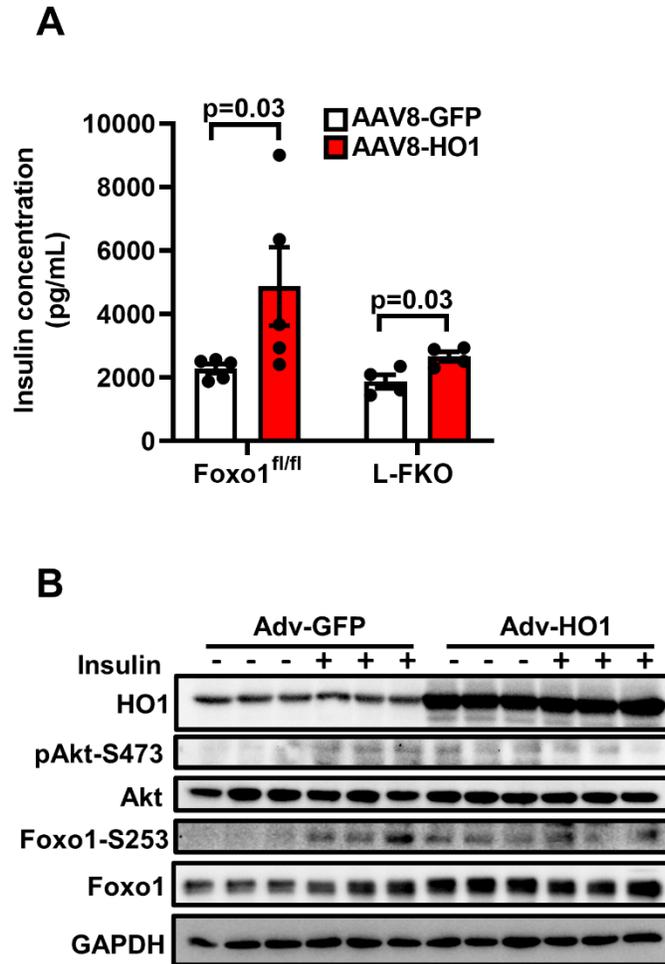
MitoSOX™ Red and visualized by a confocal microscope (Leica Biosystems). *C*: AAV8-GFP or AAV8-HO1 was delivered via retro orbital to Foxo1^{fl/fl} or L-FKO mice (male, 8- to 12-week). Tissues from the mice were collected after 14 days of the AAV8 injection. Total RNA from liver tissues were extracted for reverse transcription and qPCR analyses of antioxidant genes. n=4 mice/group. Results are presented as mean ± SEM.

SUPPLEMENTARY FIGURES

Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3

