**Supplementary Information**

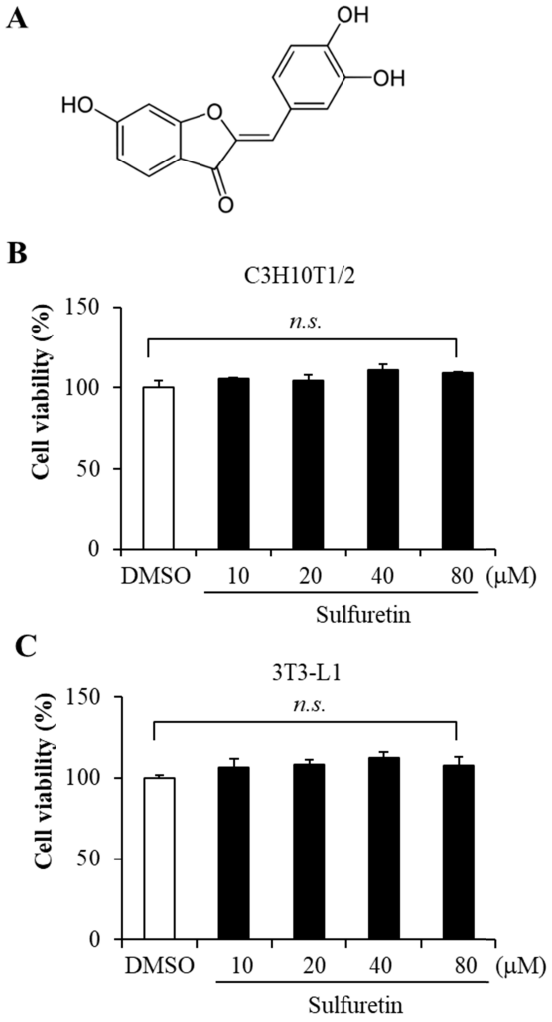


**Fig. S1. Effects of sulfuretin on cell viability.**

(A) Chemical structure of Sulfuretin. (B) C3H10T1/2 and (C) 3T3-L1 cells were treated with DMSO or sulfuretin at the indicated concentrations (10, 20, 40, and 80 μM) for 24 hours and cell viability was assessed by MTT assays. Values are expressed as the means ± s.e.m. from three independent experiments. (n.s; not significant)

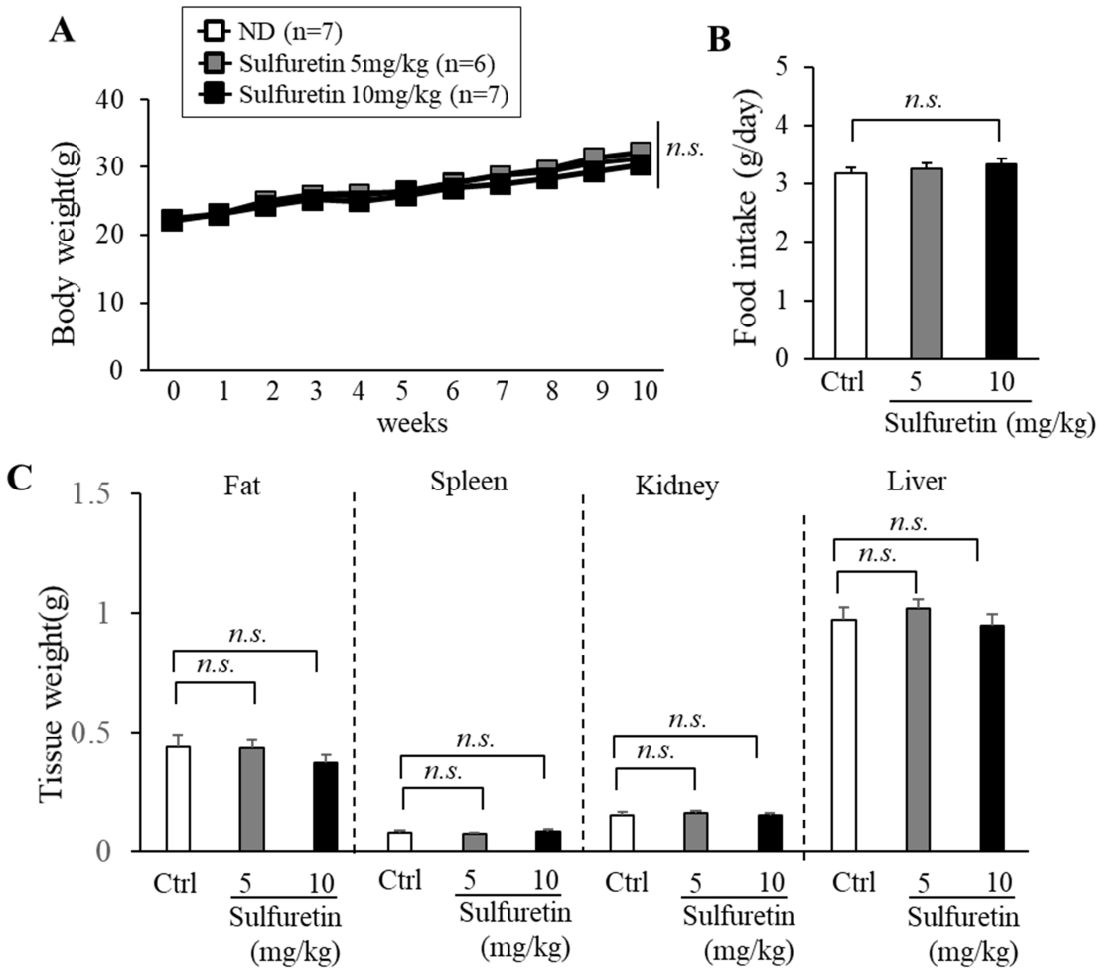


**Figure S2. Body weight, daily food intake in sulfuretin or control treated normal diet fed mice.**

Sulfuretin treatment decreased body weight gain in ND-fed mice. Eight-week-old male C57BL/6J mice were fed a normal diet (ND, 20% fat) and treated with a vehicle or sulfuretin (5 mg/kg or 10 mg/kg) for 10 weeks (n=6-7 per group). Sulfuretin did not affect body weight gains (A), food intake (B), and organ weights (C). Data represent means ± s.e.m. No differences between groups are considered significant with P>0.05 using ANOVA with Dunnett's multiple comparison test (n.s; not significant).

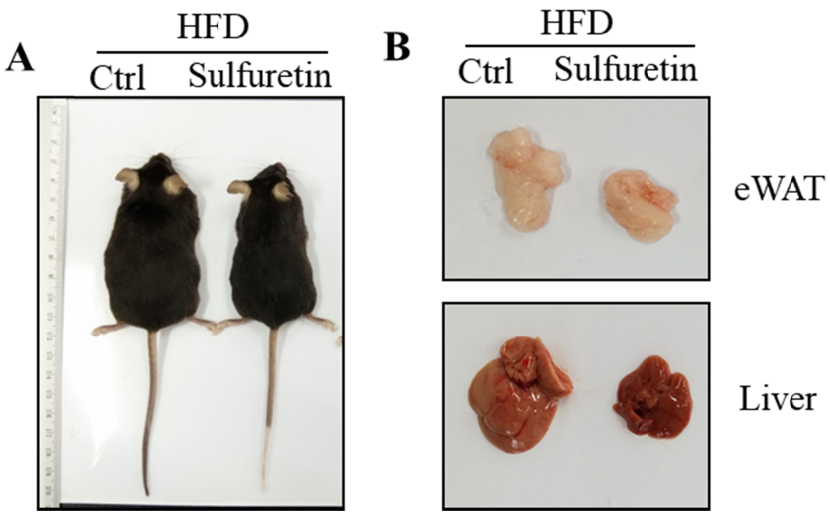


**Fig. S3. Representative photographs of whole body, fat, and liver from sulfuretin treated mice.**

Representative whole body (A), eWAT, and liver (B) pictures collected from control and sulfuretin treated mice fed with HFD for 8 weeks were shown.

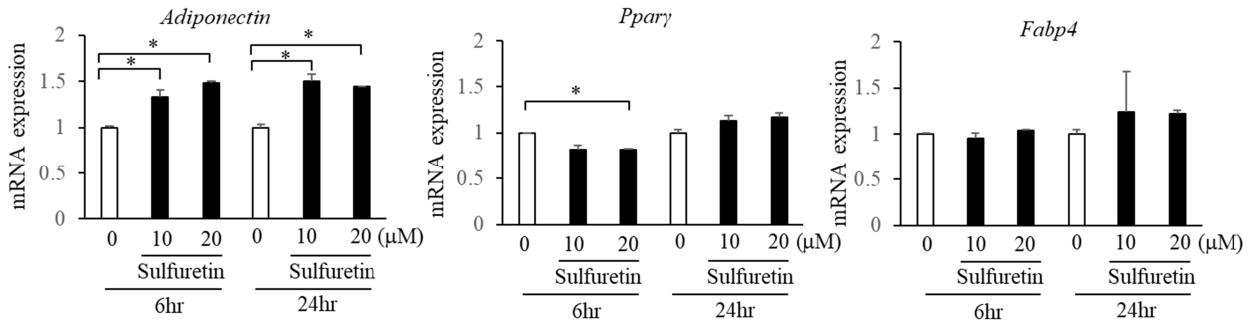


**Fig. S4. Effect of sulfuretin on adiponectin expression in differentiated 3T3-L1 adipocytes.**

Sulfuretin was treated into differentiated 3T3-L1 adipocytes for 6 or 24 hours and expression was analyzed by real time PCR. Values are expressed as the means ± s.e.m. from triplicates. Statistical significance was determined relative to a control by a Student's t-test (* $p<0.05$).

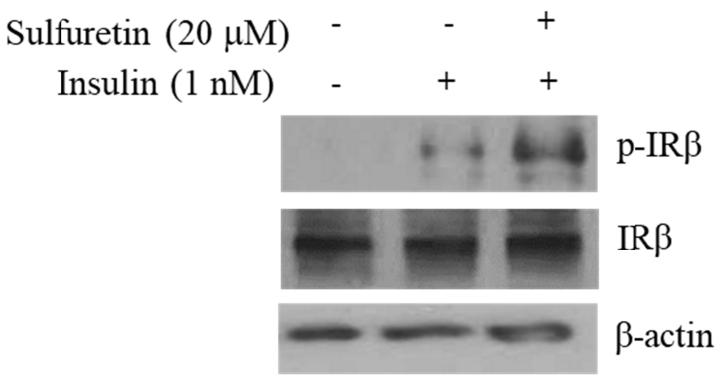


**Fig. S5. Sulfuretin increased insulin receptor phosphorylations in 3T3-L1 adipocytes.**

Western blot analysis of insulin receptor β phosphorylations stimulated by sulfuretin in 3T3-L1 adipocytes. Differentiated 3T3-L1 adipocytes were pretreated with 20 μM sulfuetin for 24 hours and further stimulated with insulin 1 nM for 30 min. Insulin receptor β phosphorylation was determined by anti-phospho insulin receptor β antibody (top panel) and total insulin receptor β was analyzed using anti- insulin receptor β (middle panel). Expression of β-actin is shown (bottom panel).

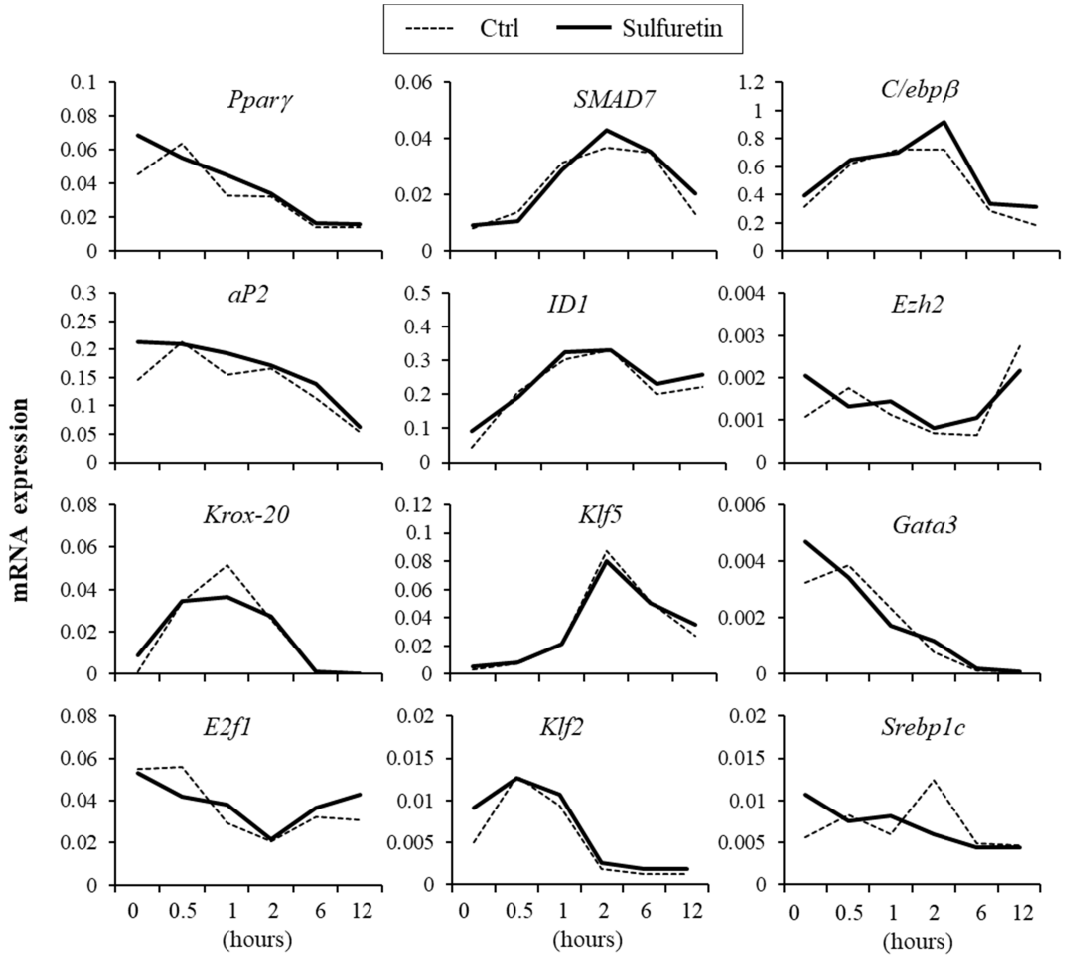


**Fig. S6. Effects of sulfuretin on known adipogenic regulators.**

Sulfuretin treatment at 40 μM for various times did not affect the expression of known adipogenic regulators in 3T3-L1 cells. Gene expression was measured by real-time PCR and normalized to the expression in 36b4. Values are expressed as the means ± s.d from three independent experiments.

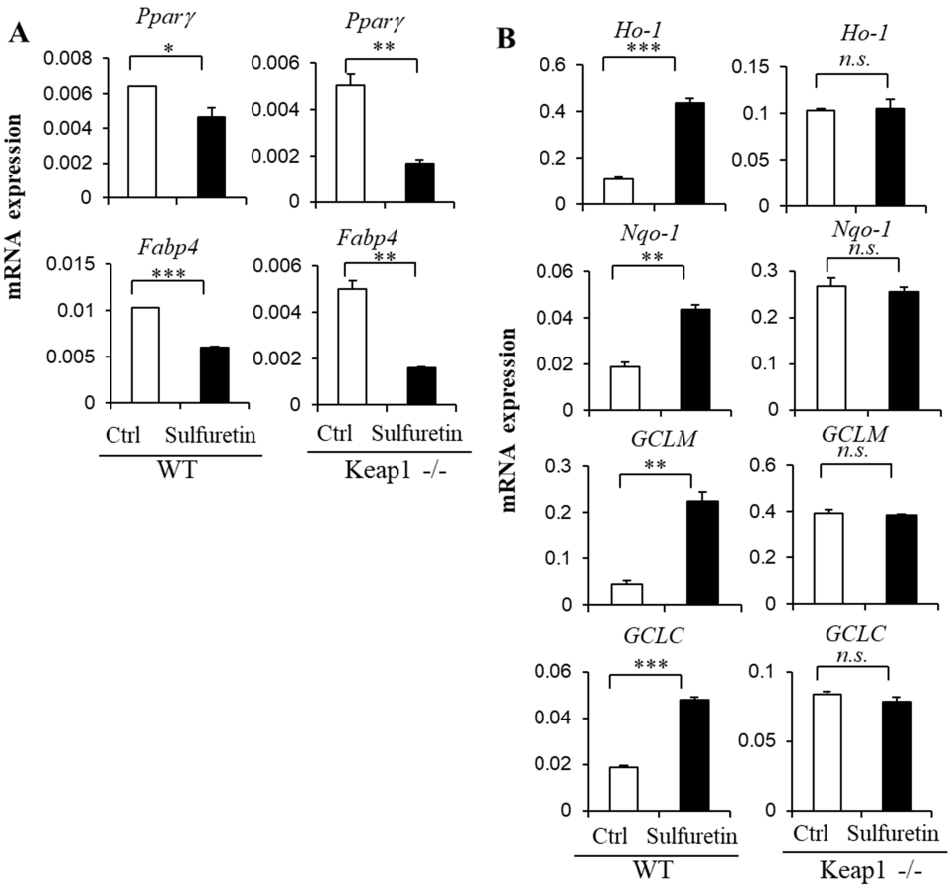


**Fig. S7. Anti-adipogenic effects of sulfuretin in Nrf2 activated Keap1 -/- cells.**

(A, B) Mouse embryonic fibroblasts were isolated from wild type and Keap1 -/- mice and treated with sulfuretin for 4 days. (A) Expression of *Pparγ* and *FABP4* was measured by real time PCR. (B) Nrf2 target genes were measured in sulfuretin-treated wild type and Keap1 -/- cells. Sulfuretin induced the expression of Nrf2 target genes in cells isolated from wild type mice. However, sulfuretin failed to induce the expression of NRf2 target genes in Keap 1-/- cells. Gene expression was measured by real-time PCR and normalized to the expression of 36b4. Values are expressed as the means ± s.d from three independent experiments. Statistical significance was determined relative to a control by a Student's t-test (* $p<0.05$, ** $p<0.005$, n.s; not significant).

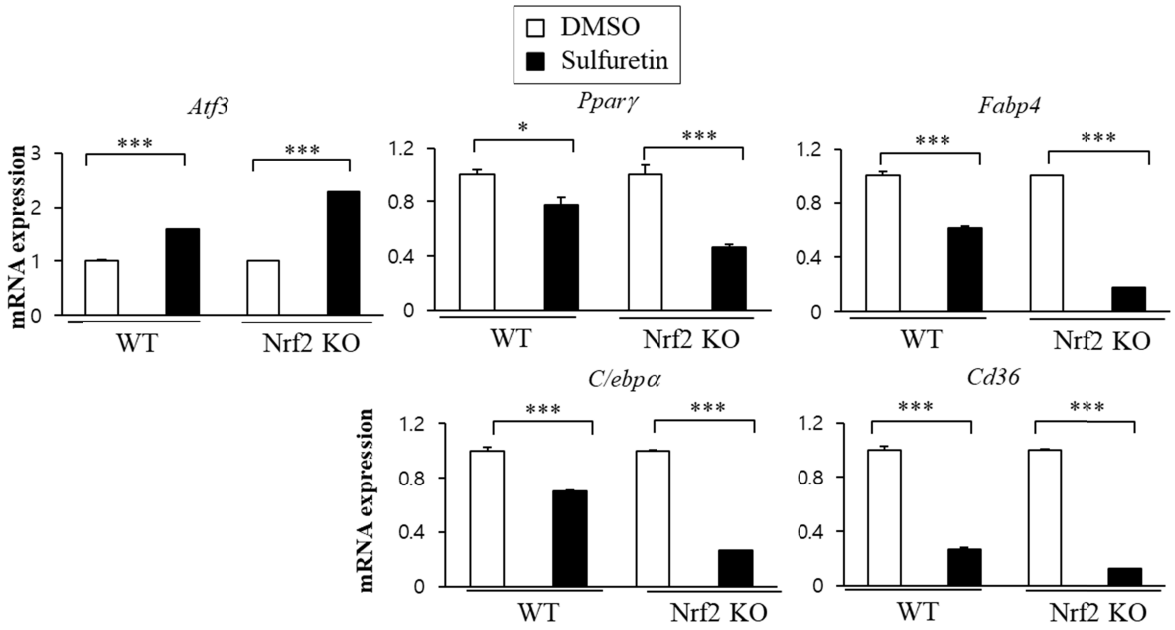


**Fig. S8. Anti-adipogenic effects of sulfuretin in Nrf2 -/- cells.**

Mouse embryonic fibroblasts (MEF) were isolated from wild type, Nrf2 knockout mice and treated with sulfuretin for 96 hours. Expression of *Atf3*, *Pparγ*, and *C/ebpα* was measured by real-time PCR. Gene expression was measured by real-time PCR and normalized to the expression levels of 36b4. Values are expressed as the means ± s.d of three replicates. Statistical significance was determined relative to a control by the Student's t-test (* $p<0.05$, ** $p<0.005$, *** $p< 0.0005$, n.s. not significant; n.d.: not detectable).

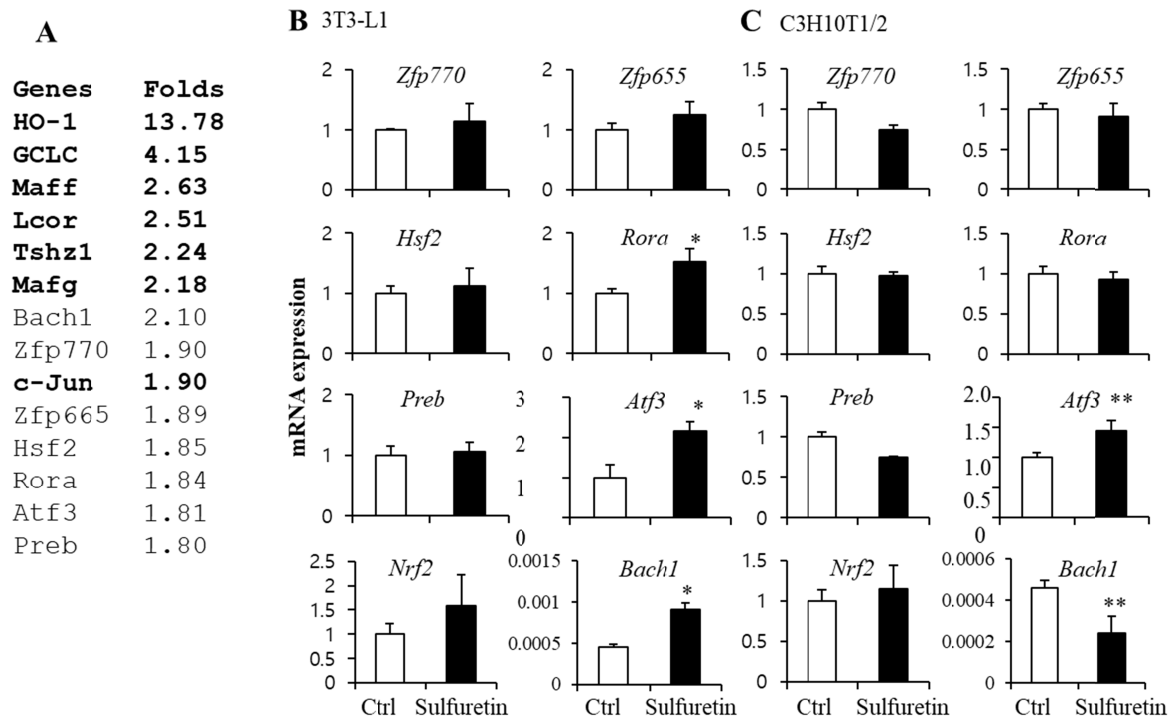


**Fig. S9. Induction of *Atf3* by sulfuretin in 3T3-L1 and C3H10T1/2 cells.**

(A) Transcriptional regulators (>1.8-fold increase) induced by sulfuretin were shown. The highlighted genes are known Nrf2 downstream regulators (*Maff*, *Lcor*, *Tshz1*, *Mafg*, and *c-Jun*). Acute induction of Atf3 by treatment with sulfuretin for 2 hours in 3T3-L1 (B) and C3H10T1/2 cells (C). Sulfuretin failed to induce the expression of *Zfp770*, *Zfp655*, *HSF2*, *Preb*, and *Nrf2* in both 3T3-L1 and C3H10T1/2 cells. Gene expression was measured by real-time PCR and normalized to the expression in 36b4. Values are expressed as the means ± s.d from three independent experiments. Statistical significance was determined relative to a control by a Student's t-test (* $p<0.05$, ** $p<0.005$).

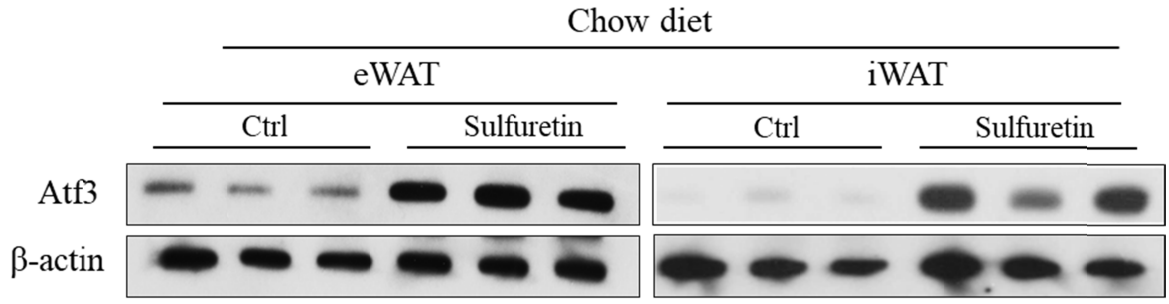


**Fig S10. Induction of Atf3 in adipose tissue from chow-diet-fed lean mice.**

Induction of Atf3 protein by sulfuretin in the epididymal (eWAT) and inguinal (iWAT) white adipose tissue from sulfuretin treated chow-diet-fed lean mice. Sulfuretin was treated at a daily dose of 10 mg/kg for 8 weeks (n=3 per group).

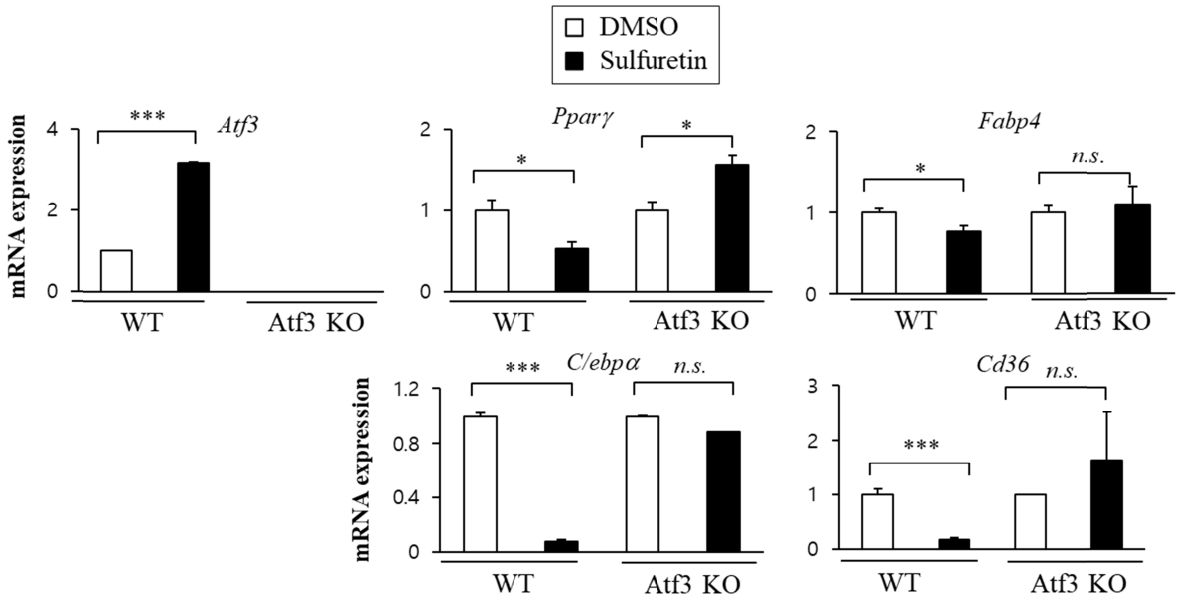


**Fig. S11. Anti-adipogenic effects of sulfuretin in Atf3 -/- cells.**

Mouse embryonic fibroblasts (MEF) were isolated from wild type or Atf3 -/- mice and treated with sulfuretin for 4 days followed by gene expression analysis. Gene expression was measured by real-time PCR and normalized to the expression in 36b4. Values are expressed as the means ± s.d from three independent experiments. Statistical significance was determined relative to a control by a Student's t-test (* $p<0.05$, ** $p<0.005$, n.s; not significant).