**Supplementary Figure S1**



**Supplementary Figure S1**. Effects of ethanol consumption and SAMC co-treatment on mice diet intake, respiratory exchange ratio (RER), and energy expenditure (n = 4; two-way ANOVA).

**Supplementary Figure S2**



**Supplementary Figure S2.** Effects of ethanol consumption and SAMC co-treatment on mice hepatic insulin receptor and insulin receptor substrate-1 expression, at both transcriptional and translational levels (n = 4; two-way ANOVA).

**Supplementary Figure S3**



**Supplementary Figure S3.** Effects of ethanol consumption and SAMC co-treatment on mice white adipose tissue (WAT) lipolysis. Changes of (A) abdominal WAT tissue weight and (B) adipocyte size (diameter) in mice treated with NIAAA model in the absence or presence of SAMC (n = 4). (C) Fatty acid release from epididymal WAT cut from mice and them cultured in Dulbecco’s modified Eagle’s medium for 2 hrs. (D) Key markers expression from epididymal adipose tissue extracted from mice at both transcriptional (n = 4) and translational levels (n = 3) (two-way ANOVA). The immunoblot bands were quantified by densitometry analysis.

**Supplementary Figure S4**



**Supplementary Figure S4.** SAMC dose-selection and contribution of ethanol (EtOH) or palmitate acid (PA) to cell injury. (A) SAMC dosage optimization test in AML-12 cell with or without ethanol plus palmitate acid challenge, by the measurements of cell viability, apoptotic ratio, Oil Red O/MTT ratio, and the activity of caspase-3/7 (n = 4). (B) Contribution of EtOH or PA to AML-12 injury, in the absence or presence of SAMC (250 μM) co-incubation (n = 4). Statistical analysis was performed using two-way ANOVA.

**Supplementary Figure S5**



**Supplementary Figure S5.** Effects of ethanol+PA challenge and SAMC co-treatment on AML-12 cell insulin receptor and insulin receptor substrate-1 expression, at both transcriptional and translational levels (n = 4; two-way ANOVA).

**Supplementary Figure S6**



**Supplementary Figure S6.** Administration of IGF-1 partially alleviated ALD-induced liver damage in mice, in coordination with SAMC. Changes of mice (A) serum chemistry, including ALT, AST, TC, and TG; (B) liver histology stained with H&E or Oil Red O; and (C) hepatic parameters including NAS score, TG, TNF-α and IL-6 contents after NIAAA induction with or without IGF/SAMC co-administration. (Scale bar = 20 μm; n = 4; two-way ANOVA)

**Supplementary Figure S7**



**Supplementary Figure S7.** Long-term (90-d) safety check of SAMC administration in healthy mice. (A) Histology of the liver, kidneys, spleen, and heart; and (B) key health parameters including serum ALT, AST, free fatty acid (FFA), and blood urea nitrogen (BUN) were tested (n = 6; two-way ANOVA). (Scale bar = 20 μm)

**Supplementary Figure-uncropped WB data**



**Supporting information Table S1.** Primer sequence information for quantitative real-time PCR assay

|  |  |  |  |
| --- | --- | --- | --- |
| Target gene | Direction | Primer sequence (5’-3’) | A. Temp. (oC) |
| *Adiponection* | Forward | TGTTCCTCTTAATCCTGCCCA | 56 |
|  | Reverse | CCAACCTGCACAAGTTCCCTT |  |
| *ACC* | Forward | ATGGGCGGAATGGTCTCTTTC | 56 |
|  | Reverse | TGGGGACCTTGTCTTCATCAT |  |
| *ATGL* | Forward | GAGCCCCGGGGTGGAACAAGAT | 56 |
|  | Reverse | AAAAGGTGGTGGGCAGGAGTAAGG |  |
| *CPT1* | Forward | CTCCGCCTGAGCCATGAAG | 56 |
|  | Reverse | CACCAGTGATGATGCCATTCT |  |
| *GAPDH* | Forward | CTGGGCTACACTGAGCACC | 58 |
|  | Reverse | AAGTGGTCGTTGAGGGCAATG |  |
| *HSL* | Forward | GCCGGTGACGCTGAAAGTGGT | 57 |
|  | Reverse | CGCGCAGATGGGAGCAAGAGGT |  |
| *InsR* | Forward | ATGGGCTTCGGGAGAGGAT | 57 |
|  | Reverse | GGATGTCCATACCAGGGCAC |  |
| *IRS1* | Forward | CGATGGCTTCTCAGACGTG | 56 |
|  | Reverse | CAGCCCGCTTGTTGATGTTG |  |
| *PPARg* | Forward | TCGCTGATGCACTGCCTATG | 56 |
|  | Reverse | GAGAGGTCCACAGAGCTGATT |  |
| *SREBP-1c* | Forward | GATGTGCGAACTGGACACAG | 57 |
|  | Reverse | CATAGGGGGCGTCAAACAG |  |

A. Temp.: Annealing temperature