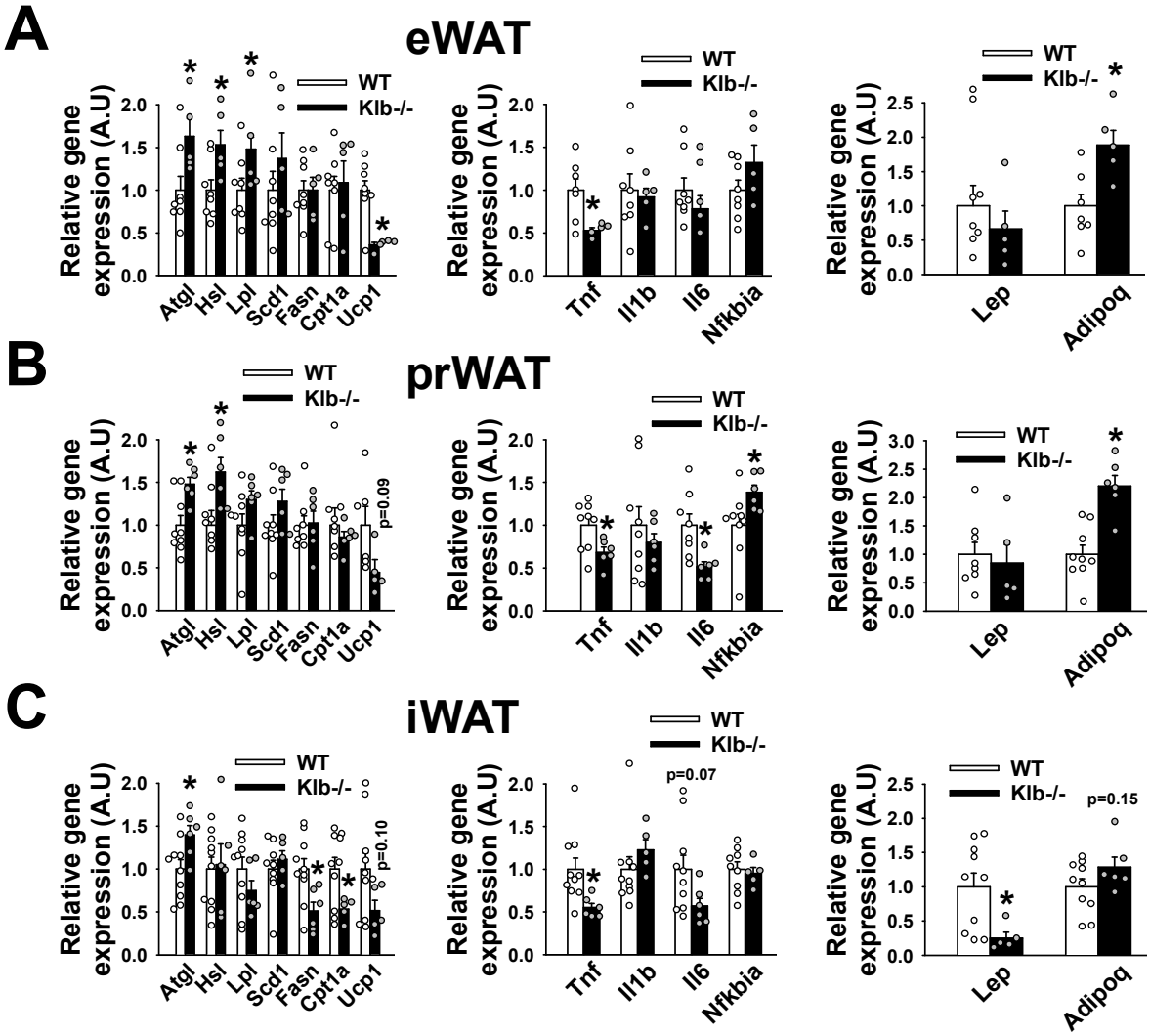
Supplemental table 1. Primers list for quantitative real-time PCR.

Targeted gene	Forward	Reverse
Acaca	5'-AGGAAGATGGCGTCCGCTCTG-3'	5'-GGTGAGATGTGCTGGGTCAT-3'
Adipoq	5'-GCACTGGCAAGTTCTACTGCAA-3'	5'-GTAGGTGAAGAGAACGGCCTTGT-3'
Agrp	5'-AGCTTTGGCGGAGGTGCTA-3'	5'-GCGACGCGGAGAACGA-3'
Atgl	5'-GTCCTTCACCATCCGCTTGTT-3'	5'-CTCTTGGCCCTCATCACCAG-3'
Cd36	5'-AGATGACGTGGCAAAGAACAG-3'	5'-CCTTGGCTAGATAACGAACTCTG-3'
Cidea	5'-TGCTCTTCTGTATCGCCCAGT-3'	5'-GCCGTGTTAAGGAATCTGCTG-3'
Cpt1a	5'-AACCCAGTGCCTTAACGATG-3'	5'-GAACTGGTGGCCAATGAGAT-3'
Crh	5'-CAACCTCAGCCGGTTCTGA-3'	5'-CCCCAGGCGGAGGAAGTA-3'
Cyp7a1	5'-GCCTCTGAAGAAGTGAATGG-3'	5'-CTAGTACTGGCAGGTTGTTTAG-3'
Cyp7b1	5'-CTGCAGTCAACAGGTCAAA-3'	5'-GCCTCAGAACCTCAAGAATAG-3'
Cyp8b1	5'-CTGGCTTCCTGAGCTTATTC-3'	5'-CCCAGTAGGGAGTAGACAAA-3'
Cyp27a1	5'-CAACCTCCTTTGGGACTTAC-3'	5'-TGATCCATGTGGTCTCTTATTG-3'
Dgat2	5'-TGGGCCTTGGTGGTTTCTTAC-3'	5'-GACTGCCCTTGCCCAGCTA-3'
Dio2	5'-CAGTGTGGTGCACGTCTCCAATC-3'	5'-TGAACCAAAGTTGACCACCAG-3'
Elovl3	5'-TCCGCGTTCTCATGTAGGTCT-3'	5'-GGACCTGATGCAACCCTATGA-3'
Fasn	5'-CATGACCTCGTGATGAACGTGT-3'	5'-CGGGTGAGGACGTTTACAAAG-3'
Fgf21	5'-TCTATGGATCGCCTCACTTTGA-3'	5'-CCTCCAGCAGCAGTTCTCTGA-3'
Fgfr1	5'-CCAAACCGTAGGCCTGTAGCT-3'	5'-CATGCAGTTTCTTCTCCATTTTCTC-3'
Fgfr4	5'-CCAGAGTGACGTGTGGTCTTTC-3'	5'-GCCCCCGAGGGTGAAG-3'
Hnf4a	5'-GGTAGGGGAGAATGCGACTC-3'	5'-AAACTCCAGGGTGGTGTAGG-3'
Hmgcr	5'-CTTGTGGAATGCCTTGTGATTG-3'	5'-AGCCGAAGCAGCACATGAT-3'
Hmgcs1	5'-GCCGTGAACTGGGTCGAA-3'	5'-GCATATATAGCAATGTCTCCTGCAA-3'
Hsl	5'-TCTATGCGCAGGAGTGTGTC-3'	5'-TTGACATCAGAGGGTGTGGA-3'
Il1b	5'-GATGAAGGGCTGCTTCCAAAC-3'	5'-GTGCTGCTGCGAGATTTGAA-3'
Il6	5'-CCTTCAGAGAGATACAGAAACTCTAATTCA-3'	5'-CTGTTAGGAGAGCATTGGAAATTG-3'
Ikbkb	5'-GGCACCTTGGATGACCTAGA-3'	5'-CCATATCCTGGCTGTCACCT-3'
Lep	5'-CACACACGCAGTCGGTATCC-3'	5'-TTGGACTTCATTCCTGGGCT-3'
Lpl	5'-TTGCCCTAAGGACCCCTGAA-3'	5'-TTGAAGTGGCAGTTAGACACAG-3'
Lrh1	5'-GATGTCCCTACTGTCGATTCAAAA-3'	5'-TGGAAGCCGTAAGAGCCG-3'
Nfkbia	5'-TGCCTGGCCAGTGTAGCAGTCTT-3'	5'-CAAAGTCACCAAGTGCTCCACGAT-3'
Npy	5'-TCTGCGACACTACATCAATCTCATC-3'	5'-GTGTCTCAGGGCTGGATCTCTT-3'
Nr1h3 (Lxr)	5'-AGGAGTGTCGACTTCGCAAA-3'	5'-CTCTTCTTGCCGCTTCAGTTT-3'
Nr1h4 (Fxr)	5'-CATCGGCAGGCAGAATAAA-3'	5'-ACGGCGTTCTTGGTAATG-3'
Nrip (RIP140)	5'-TCAGCTTCCTTTCCCACATAGC-3'	5'-TCATCTTTCGTTGCTCACCAAA-3'
Pgc1a	5'-GCACGAGAAGCGGGAGTCT-3'	5'-CAGAAGCAGAAAGCAATTGAAGAG-3'
Pomc	5'-TGCTTCAGACCTCCATAGATGTGT-3'	5'-GGATGCAAGCCAGCAGGTT-3'
Rps29	5'-GCCAGGGTTCTCGCTCTTG-3'	5'-GGCACATGTTCAGCCCGTAT-3'
Shp	5'-CACTGTGTGAAGTCTTGGAG-3'	5'-ATGATAGGGCGGAAGAAGA-3'
Shp2	5'-TCCATGGTCACTTGTCTGGA-3'	5'-GACGTGGGTCACTTTGGACT-3'
Scd1	5'-AGATCTCCAGTTCTTACACGACCAC-3'	5'-GACGGATGTCTTCTTCCAGGTG-3'
Socs3	5'-TGCGCCTCAAGACCTTCAG-3'	5'-GCTCCAGTAGAATCCGCTCTC-3'
Srebp1c	5'-GGAGCCATGGATTGCACATT-3'	5'-GGCCCGGGAAGTCACTGT-3'
Srebp2	5'-GGCGCCCCACTCAGAACACC-3'	5'-CAGGAACGGCGGTCACCCAC-3'
Tnf	5'-CCACGCTCTTCTGTCTACTGAACTT-3'	5'-GATGAGAGGGAGGCCATTTG-3'
Ucp1	5'-CCTCACTCAGGATTGGCCTCTA-3'	5'-CTTCAGGGAGAGAAACACCTGC-3'
Ucp3	5'-GACCTACGACATCATCAAGGAGAAGT-3'	5'-CTCCAAAGGCAGAGACAAAGTGA-3'
Pan-bacteria	5'-GCAGGCCTAACACATGCAAGTC-3'	5'-CTGCTGCCTCCCGTAGGAGT-3'
Bacteroidetes	5'-CRAACAGGATTAGATACCCT-3'	5'-GGTAAGGTTCCTCGCGTAT-3'
Firmicutes	5'-TGAAACTYAAAGGAATTGACG-3'	5'-ACCATGCACCACCTGTC-3'
Gammaproteobacteria	5'-TCGTCAGCTCGTGTYGTGA-3'	5'-CGTAAGGGCCATGATG-3'

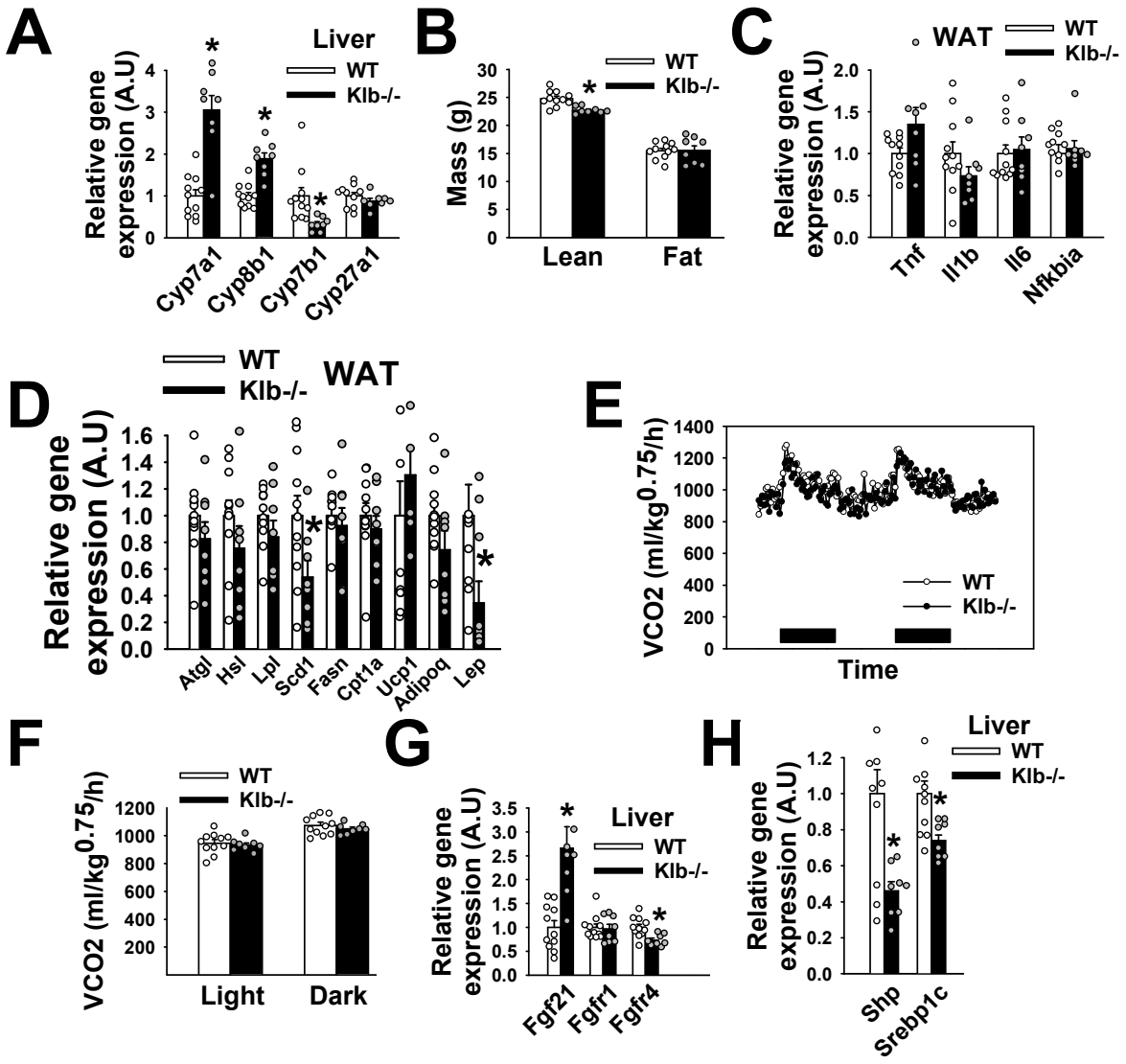
SUPPLEMENTAL FIGURE 1



Supplemental Figure 1: Transcriptional changes in white adipose tissue (WAT) depots in *Klb*$^{-/-}$ mice on high-fat diet (HFD).

A) Epididymal WAT (eWAT) mRNA levels of metabolic enzymes, transporters, inflammatory markers and adipokines (A.U).
B) Perirenal WAT (prWAT) mRNA levels of metabolic enzymes, transporters, inflammatory markers and adipokines (A.U).
C) Inguinal WAT (iWAT) mRNA levels of metabolic enzymes, transporters, inflammatory markers and adipokines (A.U).
Results are expressed as means ± SEM. N=5-6 *Klb*$^{-/-}$ and N=9-10 WT male mice on HFD per group. *p < 0.05 vs. WT determined by unpaired *t* test.

SUPPLEMENTAL FIGURE 2



Supplemental Figure 2: Antibiotic-mediated (Vancomycin=VCM) blockade of deoxycholic acid (DCA) production abrogates resistance to high-fat diet (HFD)-induced obesity in *Klb*$^{-/-}$ mice.

A) Hepatic mRNA levels of BAs synthesis enzymes (A.U).
B) Lean and fat mass (g).
C) eWAT mRNA levels of inflammatory markers (A.U).
D) eWAT mRNA levels of metabolic enzymes and adipokines (A.U).
E) VCO_2 curves (ml/kg$^{0.75}$/h) representing two consecutive days.
F) VCO_2 means (ml/kg$^{0.75}$/h) during light and dark phases.
G) Hepatic mRNA levels of ligand and receptors of the FGF signaling pathway (A.U).
H) Hepatic mRNA levels of transcriptional regulators (A.U).
Results are expressed as means ± SEM. N=8 *Klb*$^{-/-}$ and N=11 WT male mice per group. *p < 0.05 vs. WT determined by unpaired *t* test. Individual values not represented (outside the range of the Y-axis): Panel D (2.14, 2.34 for Ucp1 in WT group; 1.91 for Ucp1 in Klb-/-

group; 2.22, 2.01 for Lep in WT group); Panel G (5.41 for Fgf21 in Klb-/- group); Panel H (1.59, 1.50 for Shp in WT group; 1.51 for Srebp1c in WT group).