Supplemental Figures and Tables

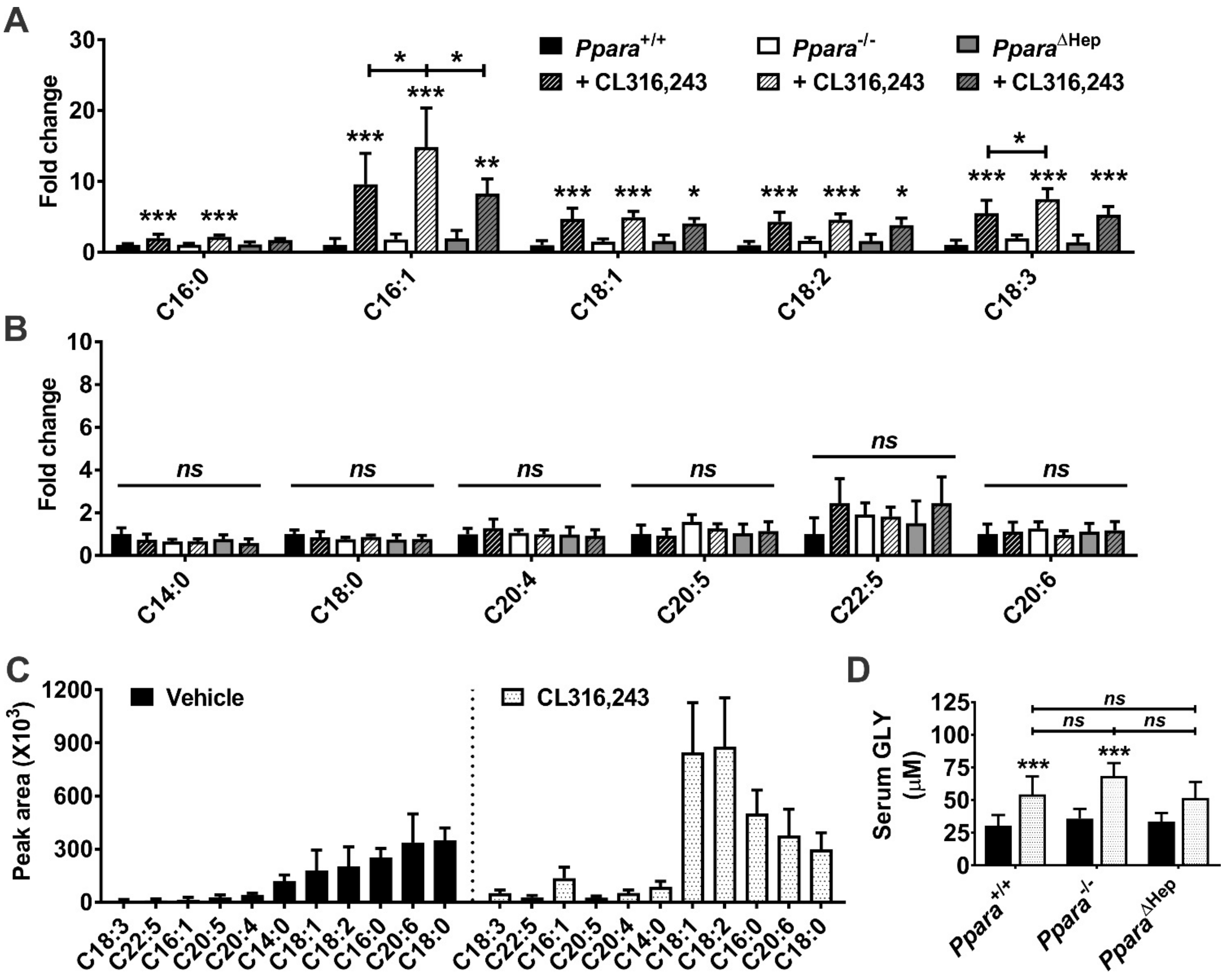

Figure S1. Extrahepatic *Ppara* normalizes serum FA response in CL316,243 treated *Ppara*$^{\Delta Hep}$ mice. Mice were given an intraperitoneal injection of either the *Adrb3* receptor agonist CL316,243 or vehicle. One hour later serum was collected for analysis. *Ppara*-dependent (A) and -independent (B) changes in serum FAs after CL316,243 treatment in *Ppara*$^{+/+}$, full-body *Ppara* KO (*Ppara*$^{-/-}$), and hepatocyte-specific *Ppara* KO (*Ppara*$^{\Delta Hep}$) mice. Mean MS peak area data indicating relative abundance of individual FAs in vehicle and CL316,243 treated wild-type (*Ppara*$^{+/+}$) mouse serum (C). Serum glycerol (GLY) in vehicle and CL316,243 treated mice (D). Fold change data are shown as mean fold change ± standard deviation (SD; n = 5) vs vehicle treated wild-type groups. '*' above bars indicate significance vs fed group of the same genotype (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; ns, not significant).

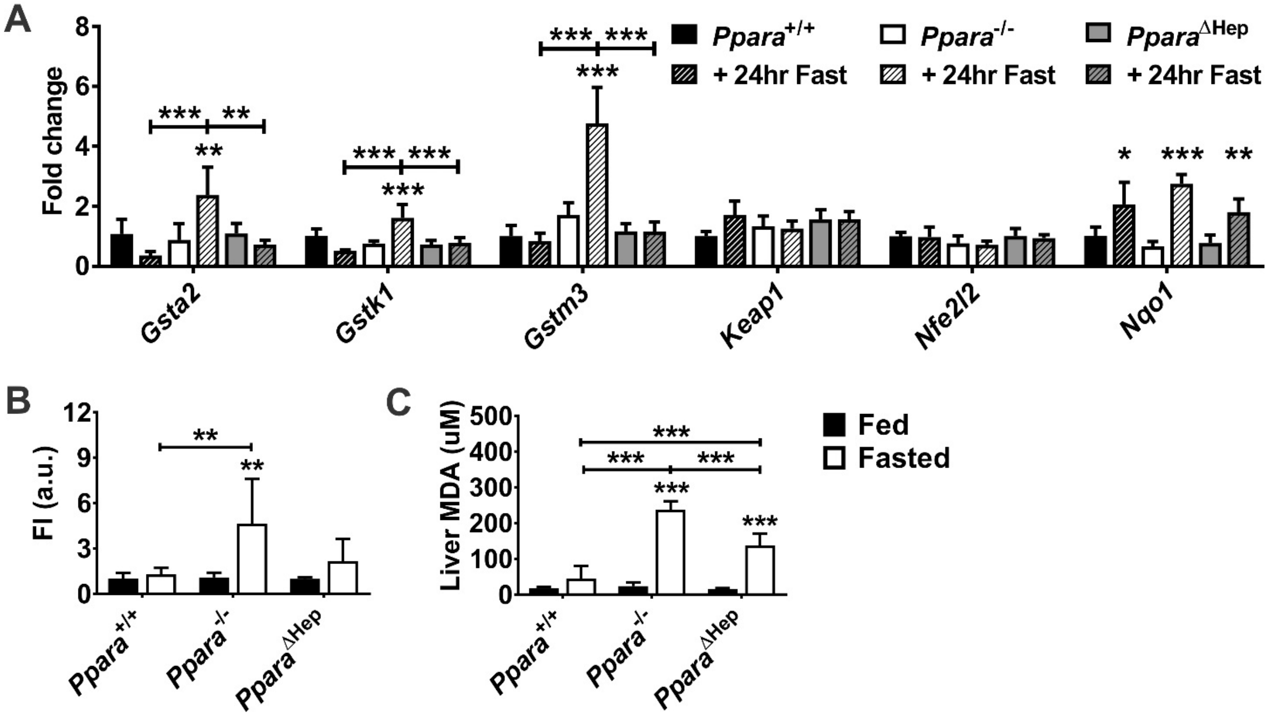

Figure S2. Extrahepatic PPARA activity prevents fasting-induced oxidative stress and lipotoxicity in the liver. Wild-type (*Ppara*$^{+/+}$), full-body KO (*Ppara*$^{-/-}$), and hepatocyte-specific KO (*Ppara*$^{\Delta \mathrm{Hep}}$) mice fed *al libitum* or fasted for 24 hours then livers collected for RNA isolation and lysate preparation. Oxidative stress marker (*Gsta2*, *Gstk1*, *Gstm3*, *Keap1*, *Nfe2l2*, *Nqo1*) expression was measured by qRT-PCR (A). Hepatic reactive oxygen species (ROS) were measured by 2',7'-dichlorofluorescin diacetate (DCFDA) assays (B). Malondialdehyde (MDA) levels were determined as an indicator of lipid peroxidation (LPO) (C). qRT-PCR data were normalized to beta actin (*Actb*) and expressed as fold change wild-type control. Data are mean ± standard deviation (SD; n = 5). '*' above bars indicate significance vs fed group of the same genotype (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$).

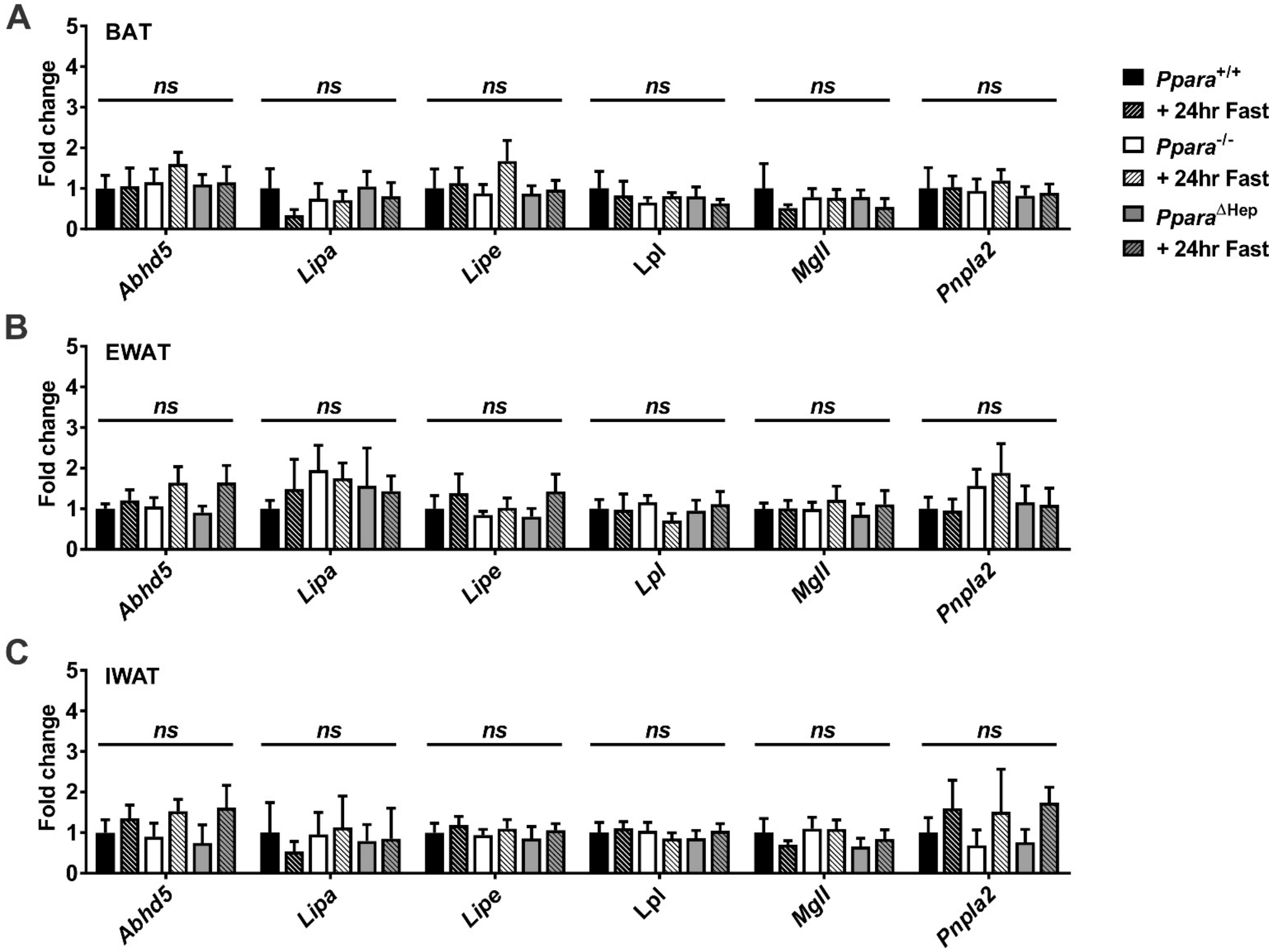

Figure S3. ***Ppara*** **does not impact lipase expression in adipose depots.** Mice were fasted for 24 hours then tissues collected for RNA isolation and qRT-PCR analysis. Expression of adipose lipases (*Abhd5*, *Lipa*, *Lipe*, *Lpl*, *MglI*, *Pnpla2*) were measured in brown adipose tissue (BAT) (A), epididymal white adipose tissue (EWAT) (B), and inguinal white adipose tissue (IWAT) (C). Data normalized to beta actin (*Actb*) and expressed as fold change wild-type control. Data are mean ± standard deviation (SD; n = 5). '*' above bars indicate significance vs fed group of the same genotype (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; ns, not significant).

Table S1. GC-MS mass parameters

Peak ID	Fatty acid	C:D[a]	Qualifier (m/z)	RT (min)	R^2 (1-100 μg/ml)
1	Decanoate	C10:0	74/87/143/155/186	8.4	0.9732
2	Dodecanoate	C12:0	74/87/143/171/183/214	10.4	0.9972
3	Tridecanoate	C13:0	143/185	11.5	0.9526
4	Myristoleate	C14:1 (9Z)	166/208/240	12.6	0.9865
5	Myristate	C14:0	74/87/143/199	12.7	0.9941
6	Pentadecanoate	C15:0	185/199/213/225/256	13.9	0.9654
7	Palmitoleate	C16:1 (9Z)	50/69/74/ 236/194/268	14.8	0.9912
8	Palmitate	C16:0	74/87/227/270	15.1	0.9904
9	gamma-Linolenate	C18:3 (6Z,9Z,12Z)	79/93/107/121/150/194/292	16.8	0.9865
10	Elaidate	C18:1 (9E)	180/152/235/253/194/143/128/123	17.1	0.9734
11	Arachidonate	C20:4 (5Z,8Z,11Z,14Z)	79/91/119//105/133/150	18.8	0.9610
12	cis-5,8,11,14,17-Eicosapentaenoate	C20:5 (5Z,8Z,11Z,14Z,17Z)	79/91/119/147/247/273	18.9	0.9523
13	Heneicosanoate	C21:0	241/297/309/340	20.5	0.9824
14	cis-4,7,10,13,16,19-Docosahexaenoic acid	C22:6 (4Z,7Z,10Z,13Z,16Z,19Z)	71/91/119/131/255/273	20.8	0.9885
15	cis-13-Docosenoate	C22:1 (13Z)	180/236/278/320/352	21.2	0.9684
16	Benenate	C22:0	143/199/255/311/323/354	21.5	0.9924
17	Tricosanoate	C23:0	129/185/255/269/311/354	22.4	0.9932
18	Nerovonate	C24:1 (15Z)	264/277/306/348/380	23.1	0.9904
19	Myristic acid-d27 (ISTD)	--	281/73/133/177/193/249	5.6	--

[a] C:D; Length of fatty acid chain : Number of double bonds

Table S2. List primer sets used for qRT-PCR analysis of gene expression

Gene Symbol	**Forward Primer**	**Reverse Primer**
Acadl	TGCACACATACAGACGGTGC	CATGGAAGCAGAACCGGAGT
Acadm	GAACCAGACCTACAGTCGCA	GCTCCACTAGCAGCTTTCCA
Acox1	GGGCACGGCTATTCTCACAG	CATCAAGAACCTGGCCGTCT
Abhd5	TTCCTACCTGGTGTCCCACA	TGTAAGTGCAGGGGACACATTT
Apob	GGTGTATGGCTTCAACCCTGA	GCTTGAGTTCGTACCTGGACA
Apoc2	GATGTTGGGAAATGAGGTCCAG	CCTTGGCAGAGGTCCAGTAAC
Apoe	CACATTGCTGACAGGATGCC	AGCGCAGGTAATCCCAGAAG
Cd36	GATTAATGGCACAGACGCAGC	CAGATCCGAACACAGCGTAGA
Cpt1b	GAACACAAATGTGCAAGCAGC	GCCATGACCGGCTTGATCTC
Cpt2	CGTACCCACCATGCACTACC	TTCTGTCTTCCTGAACTGGCTG
Cyp2b9	TGAGGATGGAGAAGGAGAAGTCA	AGGACTCCATAGTGGAGGGT
Cyp8b1	TTGCAAATGCTGCCTCAACC	TAACAGTCGCACACATGGCT
Ehhadh	CGGTCAATGCCATCAGTCCAA	TGCTCCACAGATCACTATGGC
Etnppl	ACATCAGAGGTGTCGGCCTT	GGCACTGAGAAGTACCCCCT
Fgf21	GCTCTCTATGGATCGCCTCA	TGGTTTGGGGAGTCCTTCTG
Gsta2	AGGACTCTCACTAGACCGTGA	CCTGATGCACTCCATTCTGC
Gstk1	GGTCCTATGCAGATACCAACAC	GTACTGGCCTTTTCGGGGAA
Gstm3	GGAAGCACAACCTGTGTGGAG	GCAGCAGACTATCATGAGCTGTA
Keap1	GCGTGGAGAGATATGAGCCA	CATACAGCAAGCGGTTGAGC
Lcn2	TCTGTCCCCACCGACCAAT	GGAAAGATGGAGTGGCAGACA
Lcn13	GACCTGGTGGATTACTCTGGG	ACTGTGGTCTCCAAGTCTCCT
Lipa	CTGGTGAGGAACACTCGGTC	CTGGGACCTTTGCCAAAATGG
Lipe	TGTGACCTGCTTGGTTCAACT	ATCTGGCACCCTCACTCCAT
Lpl	CAGCAGACGCGGGAAGAGATT	TGGTTGAAGTGGCAGTTAGACA
MglI	CTGGTCAATGCAGACGGACA	GACACAAAGATGAGGGCCTTGG
Nfe2l2	GGTTGCCCACATTCCCAAAC	GCAAGCGACTCATGGTCATC
Nqo1	CATCACAGGTGAGCTGAAGGA	ACAATATCTGGGCTCAGGCG
Pdk4	TTCCAGGCCAACCAATCCAC	TGGCCCTCATGGCATTCTTG
Pnpla2	GACTCGTGTTTCAGACGGAGA	CATAGCGCACCCCTTGGAG
Slc27a4	TCCCATCAGCAACTGTGACC	GGACGCTAGGGCTCTGAATC
Slc27a5	CTACGCTGGCTGCATATAGATG	CCACAAAGGTCTCTGGAGGAT