

SUPPLEMENTARY FIGURES

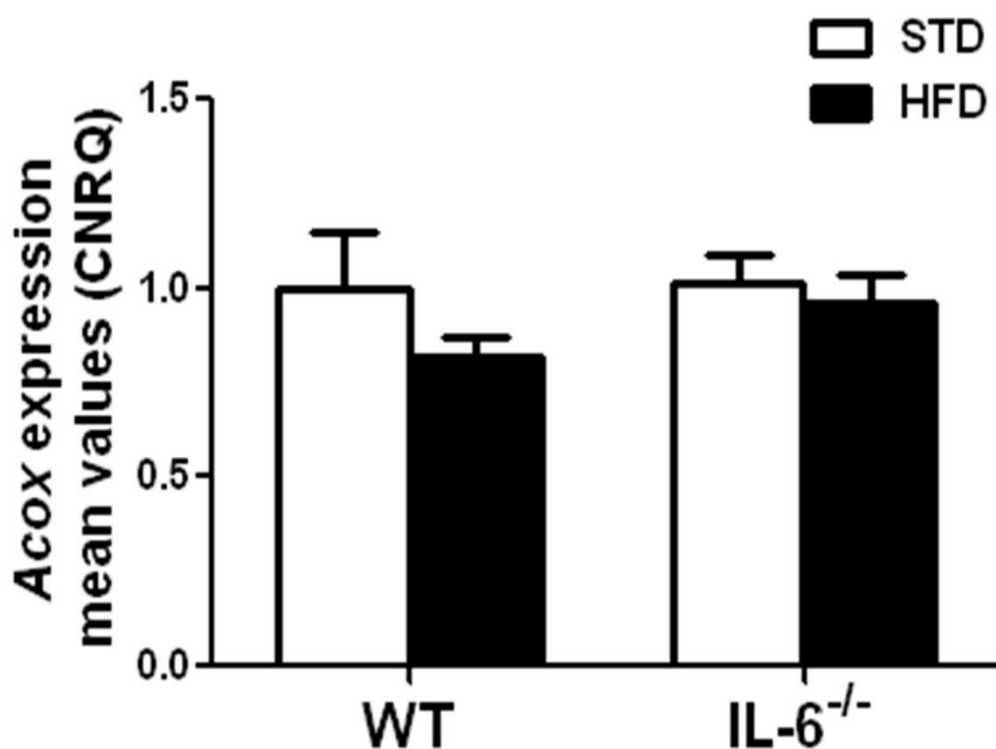


Figure S1. Effect of a HFD on the *Acox* gene expression in the livers of WT and IL-6^{-/-} mice. Expression of *Acox* in the livers of WT and IL-6^{-/-} mice fed STD or HFD determined through qPCR analysis. The Graph represents CNRQ means \pm SEM (n=4 animals per group) and gene expression was normalized using Biogazelle's qbase^{PLUS} software with *Gapdh* and *Gus β* as reference genes. Comparisons between groups were analyzed using two-way ANOVA analysis and Bonferroni *post-hoc* tests. The analysis revealed no significant effect of diet or genotype and no interaction between both factors.

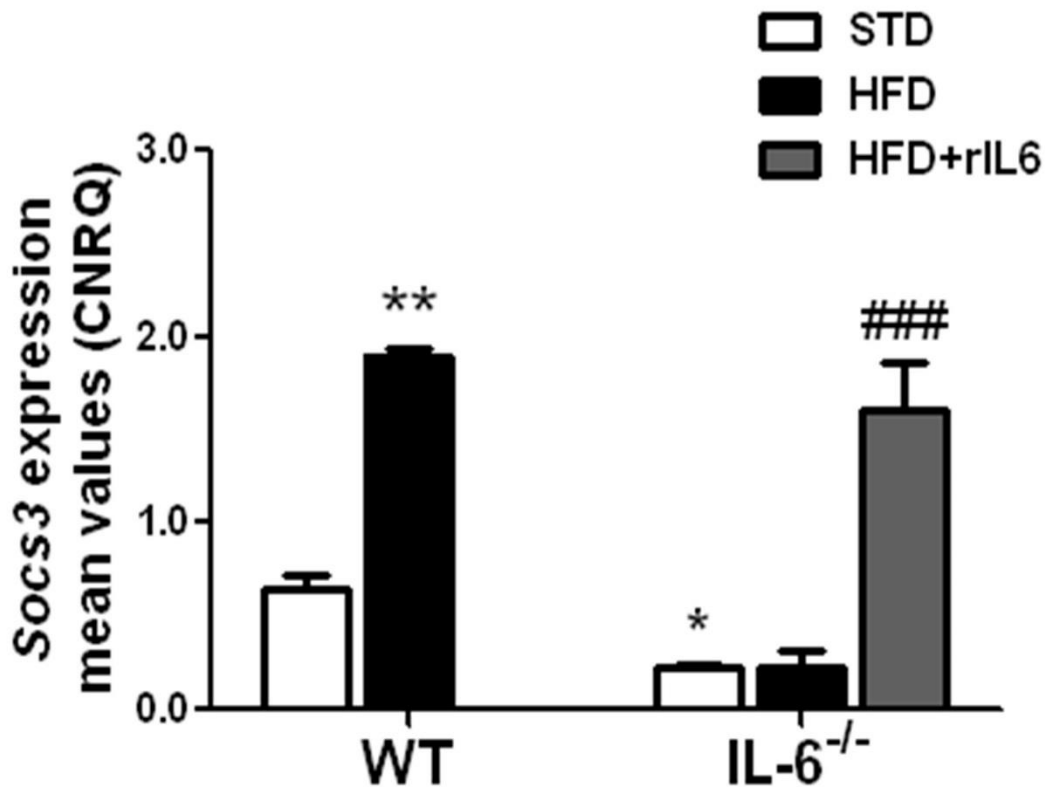


Figure S2. Effect of IL-6 replacement on the *Socs3* gene expression in the livers of IL-6^{-/-} mice fed HFD. Expression of *Socs3* in the livers of WT and IL-6^{-/-} mice fed STD or HFD. The *Socs3* expression in IL-6^{-/-} mice fed HFD and chronically treated with rIL-6 is also depicted. The gene expression was determined through qPCR analysis and normalized using Biogazelle's qbase^{PLUS} software with *Gapdh* and *Gusβ* as reference genes. The columns represent CNRQ means \pm SEM (n=4 animals per group) and comparisons between two groups were analyzed using Student's *t* test. **P*<0.05, and ***P*<0.01 denote significant differences compared with the WT mice STD-fed group. ###*P*<0.001 denotes significant differences between IL-6^{-/-} mice fed HFD and HFD + rIL-6 treated groups.

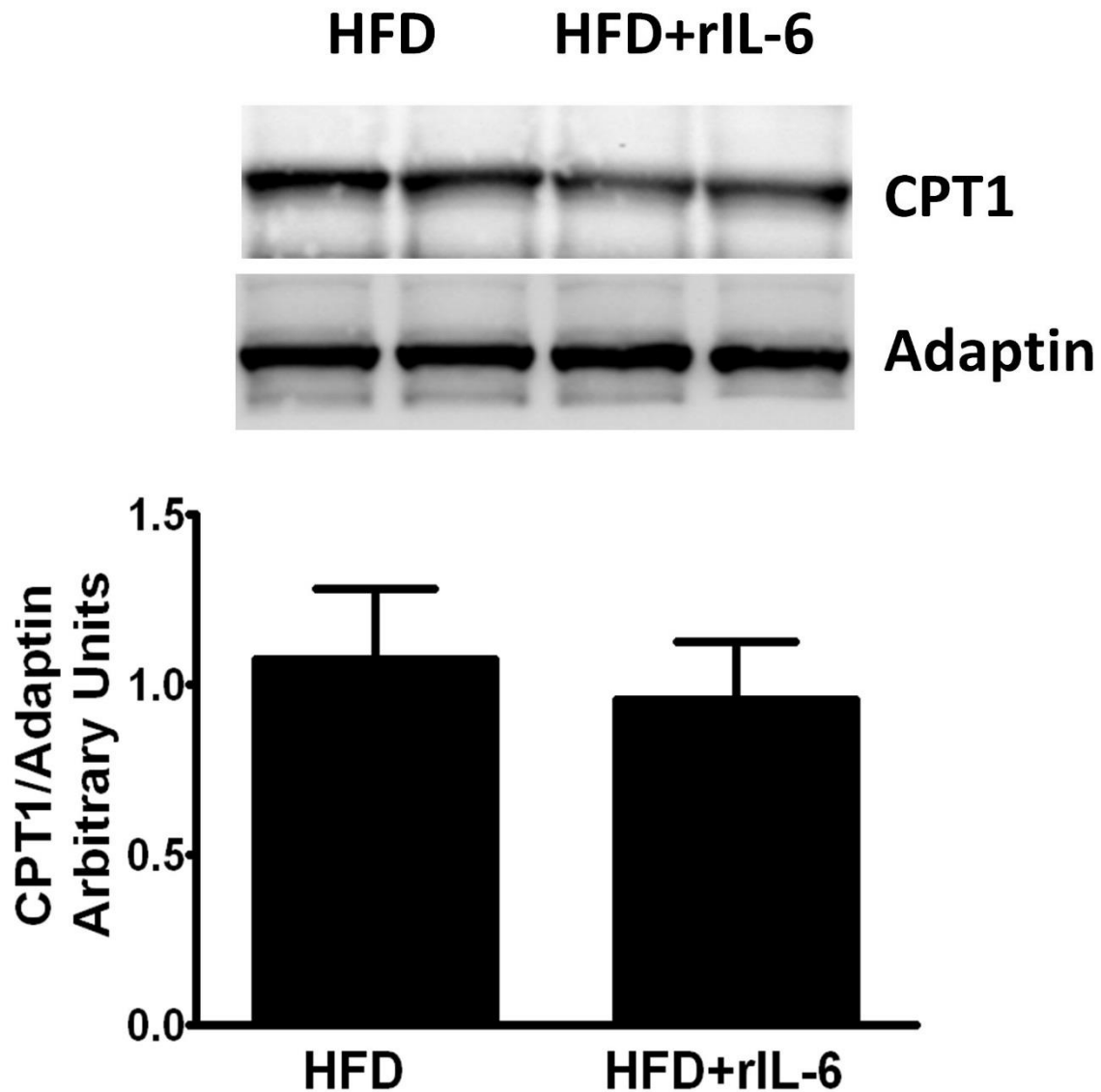


Figure S3. Effect of rIL-6 treatment on the hepatic CPT1 protein expression in IL-6^{-/-} mice fed HFD. Western blot analysis of the CPT1 protein expression in liver samples from WT and IL-6^{-/-} mice fed STD or HFD. Representative blot of protein from two samples per group is shown in the upper panel. The corresponding expression of Adaptin is also shown as a loading control per lane. The histogram depicts the means ± SEM (n=4 animals per group) of CPT1/Adaptin densitometric values. Analysis by Student's *t* test showed no significant differences between groups.

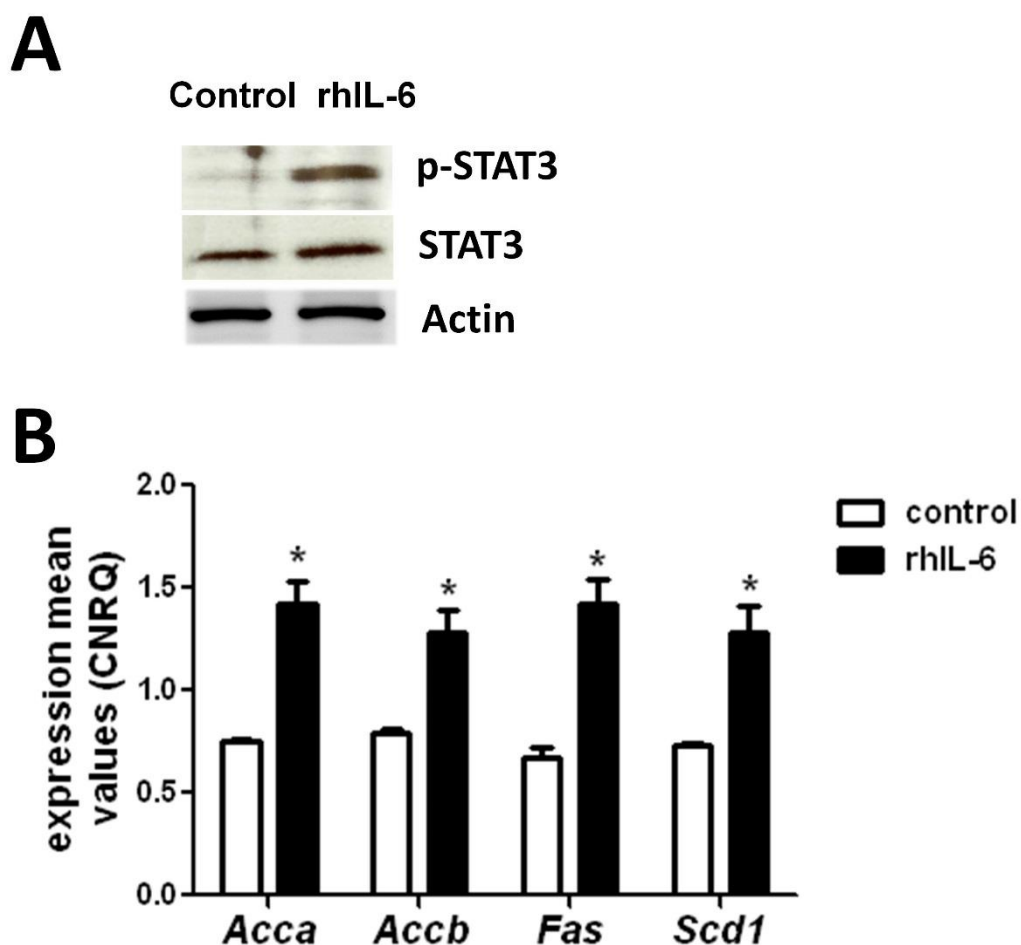


Figure S4. Ability of recombinant human IL-6 to induce expression of lipogenic enzymes in HepG2 cells. (A) Western blot of STAT3 and p-STAT3 expression after 1 h of rhIL-6 exposure in HepG2 cells compared with untreated sample (control). The corresponding expression of Actin is shown as a loading control per lane. (B) The histogram represents the expression of human *Acaca*, *Acacb*, *Fasn* and *Scd1* genes in the HepG2 cells untreated (control) or treated with hrIL-6 for 6 h. The gene expression was determined through qPCR analysis and was normalized using Biogazelle's qbase^{PLUS} software with *Gapdh* and *Gusβ* as reference genes. The columns represent CNRQ means \pm SEM (n=3 samples per group). Comparisons between control and hrIL-6 treated samples were analyzed using Student's *t* test. * $P < 0.05$ denotes significant differences between hrIL-6-treated samples and the corresponding control.

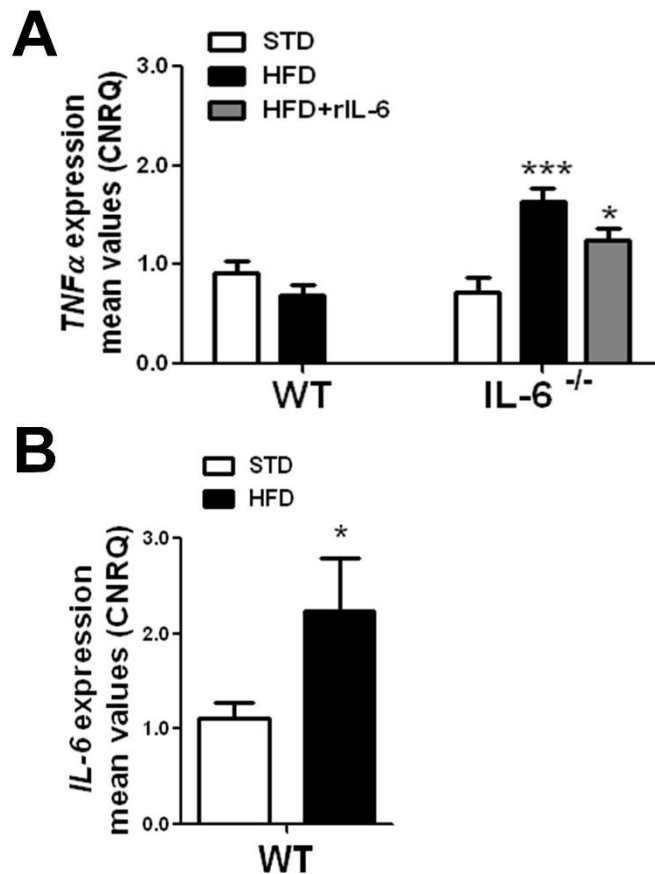


Figure S5. Gene expression of *TNFα* and *IL-6* in the livers of WT and *IL-6*^{-/-} mice fed HFD. (A) Hepatic *TNFα* gene expression in WT and *IL-6*^{-/-} mice fed STD and HFD. The effect of IL-6 replacement on *TNFα* expression in *IL-6*^{-/-} mice fed HFD group is also shown. The *TNFα* expression was determined through qPCR analysis and was normalized using Biogazelle's qbase^{PLUS} software with *Gapdh* and *Gusβ* as reference genes. The columns represent CNRQ means ± SEM (n=4 animals per group) and significance of differences between groups HFD fed and the corresponding groups STD fed was analyzed by Student's *t* test. **P*<0.05, and ****P*<0.001 denote significant differences compared with the *IL-6*^{-/-} mice STD-fed group. (B) Endogenous expression of the *IL-6* gene in liver samples from STD and HFD fed WT mice, determined through qPCR analysis as indicated in panel A. Student's *t* test analysis showed significant differences (**P*<0.05) between STD-fed and HFD-fed groups.

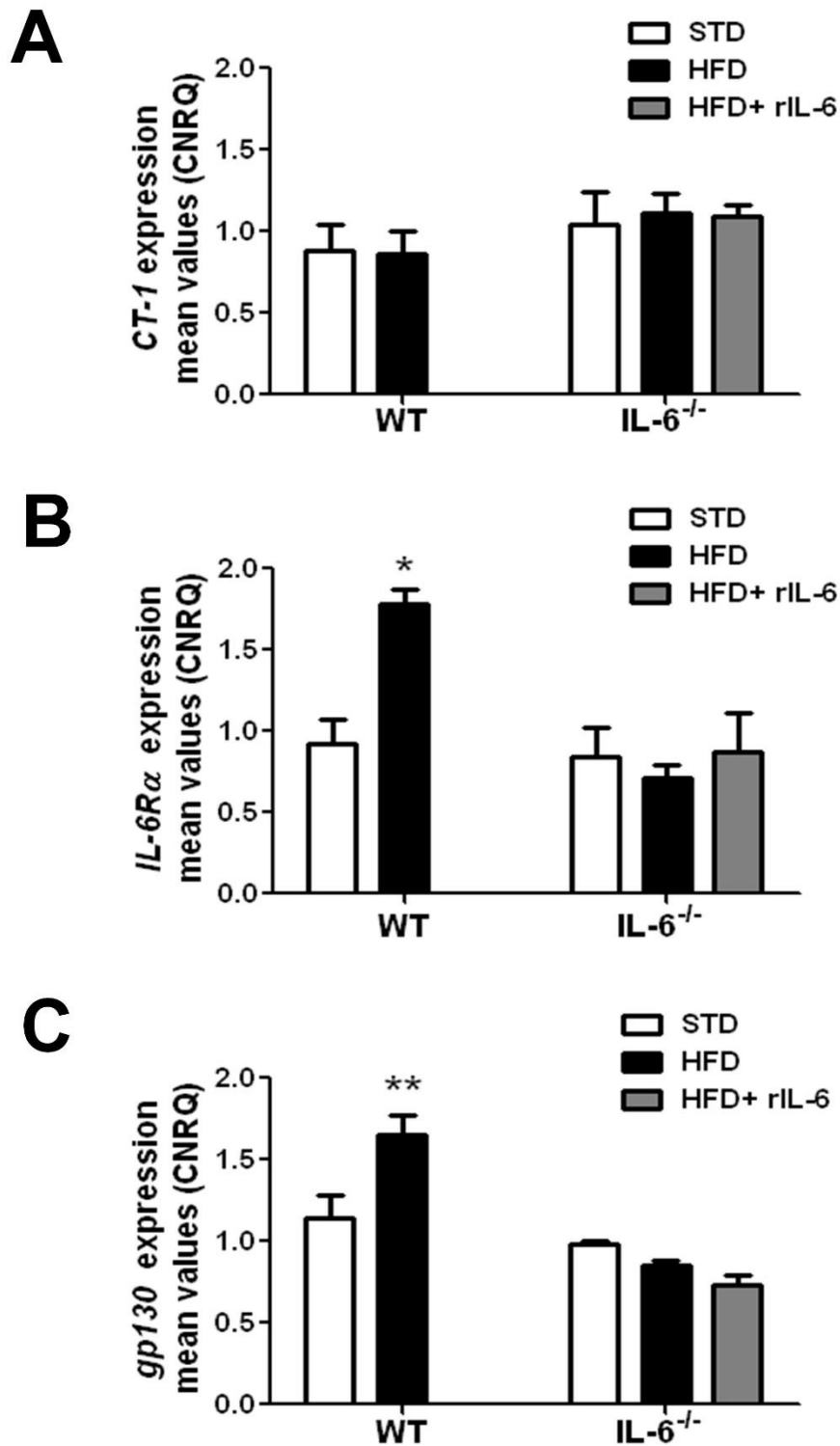


Figure S6. Hepatic *CT-1* and *IL-6R/gp130* gene expression in WT and *IL-6*^{-/-} mice fed HFD. Analysis by qPCR for *CT-1* (A), *IL-6R* (B) and *gp130* (C) gene expression in livers of WT and *IL-6*^{-/-} mice fed STD and HFD. Analysis of the effect of IL-6 replacement on the

hepatic expression of each gene in IL-6^{-/-} mice fed HFD is also shown in the corresponding histogram. The gene expression was normalized by means of Biogazelle's qbase^{PLUS} software using *Gapdh* and *Gusβ* as reference genes. The columns represent CNRQ means ± SEM (n=4 animals per group) and comparisons between two groups were analyzed by Student's *t* test. **P*<0.05, and ***P*<0.001 denote significant differences compared with the WT mice STD-fed group.

Table S1. Effect of genotype and diet on serum lipid parameters

	WT		IL-6 ^{-/-}	
	STD	HFD	STD	HFD
Cholesterol (mg/dl)	86.25 ± 3.84	129.00 ± 7.65***	99.00 ± 7.65	209.00 ± 17.01***, ###
HDL (mg/dl)	21.00 ± 2.45	24.00 ± 2.12	22.00 ± 1.22	19.00 ± 3.24
Triglyceride (mg/dl)	60.00 ± 6.30	45.00 ± 13.25	131.00 ± 28.25&&&	77.00 ± 8.03 ***,#

Data represent means ± SEM (n=4 animals per group)

*** $P < 0.001$; significant difference compared to the corresponding STD-fed group.

&&& $P < 0.001$; significant difference between both STD-fed groups.

$P < 0.05$; ### $P < 0.001$; significant difference between both HFD-fed groups.

Table 2S.

Mouse primer sequences used for qPCR

<i>Gene Symbol</i>	<i>Gene ID</i>		Primer sequence 5' to 3'	GeneBank AN*	Amplicon length
<i>Acaca</i>	107476	Fw	GCGTCGGGTAGATCCAGTT	NM_133360.2	70
		Re	CTCAGTGGGGCTTAGCTCTG		
<i>Acacb</i>	100705	Fw	TGAATCTCACGCGCCTACTA	NM_133904.2	61
		Re	GCCTCTCTTCACCAGATGGA		
<i>Fasn</i>	14104	Fw	GCTGCTGTTGGAAGTCAGC	NM_007988.3	76
		Re	AGTGTTTCGTTCCCTCGGAGTG		
<i>Scd1</i>	20249	Fw	TCCCTCCTGCAAGCTCTAC	NM_009127.4	62
		Re	CAGAGCGCTGGTCATGTAGT		
<i>Tnfa</i>	21926	Fw	TCTTCTCATTCTGCTTGTGG	NM_013693	128
		Re	GGTCTGGGCCATAGAACTGA		
<i>CT-1</i>	13019	Fw	GCCTCCGACTCCCAATTT	NM_007795.1	75
		Re	CATGAGACAAAGTAAGGGTTACACA		
<i>Gapdh</i>	14433	Fw	CGTCCCGTAGACAAAATGGT	NM_008084	125
		Re	TCAATGAAGGGGTCGTTGAT		
<i>Gusβ</i>	110006	Fw	CTCTGGTGGCCTTACCTGAT	NM_010368.1	73
		Re	CAGTTGTTGTCACCTTCACCTC		

Mouse primer sequences used for TaqMan® Gene Expression Assays (Applied Biosystems)

<i>Gene Symbol</i>	<i>Gene ID</i>		Assay ID	GeneBank AN*	Amplicon length
<i>IL-11</i>	16156		Mm00434162_m1	NM_008350.4	130
<i>OSM</i>	18413		Mm1193966_m1	NM_001013365	82
<i>IL-6</i>	16193		Mm00446190_m1	NM_031168.1	78
<i>Gapdh</i>	14433		Mm99999915_g1	NM_008084	107
<i>Gusβ</i>	110006		Mm01197698_m1	NM_010368.1	71

* Accession number

Fw=Forward

Rev=Reverse

Table S3. Human primer sequences used for qPCR

<i>Gene Symbol</i>	Gene ID		Primer sequence 5' to 3'	GeneBank AN*	Amplicon length
<i>Acaca</i>	31	Fw	TGCCGGCCAGTGCTATGCTG	NM_198834.1	60
		Re	TGCTCCAGGTCGCTTGACGT		
<i>Acacb</i>	32	Fw	AGCGGGCCATCCGGTTTGTT	NM_001093.3	63
		Re	TGCTCCAGGTCGCTTGACGT		
<i>Fasn</i>	2194	Fw	CAGGCACACACGATGGAC	NM_004104.4	92
		Re	CGGAGTGAATCTGGGTTGAT		
<i>Scd1</i>	6319	Fw	CCTACCTGCAAGTTCTACACCTG	NM_005063	85
		Re	GACGATGAGCTCCTGCTGTT		
<i>Gusβ</i>	2990	Fw	CGCCCTGCCTATCTGTATTC	NM_000181.3	91
		Re	TCCCCACAGGGAGTGTGTAG		
<i>Rpl19</i>	6143	Fw	GCTCTTTCCTTTCGCTGCT	NM_000981.3	122
		Re	CATTGGTCTCATTGGGGTCT		

* Accession number

Fw=Forward

Rev=Reverse