Supplemental Fig 1.- Hypothalamic gene expression of orexigenic (*Npy* and *Agrp*) and anorexigenic (*Cart* and *Pomc*) neuropeptides of *ob/ob* and C57BL6/J mice subcutaneously treated with oxytocin (50nmol/day) or vehicle (saline) during 14 days, considering the levels in the C57BL6/J saline-treated group as a log2 fold change of 0 (A) or 100% (B), N=7-8. ***p*<0.01, ****p*<0.001 *vs.* C57 Sal; †*p*<0.05, ††*p*<0.01, †††*p*<0.001 *vs.* C57 Oxt.

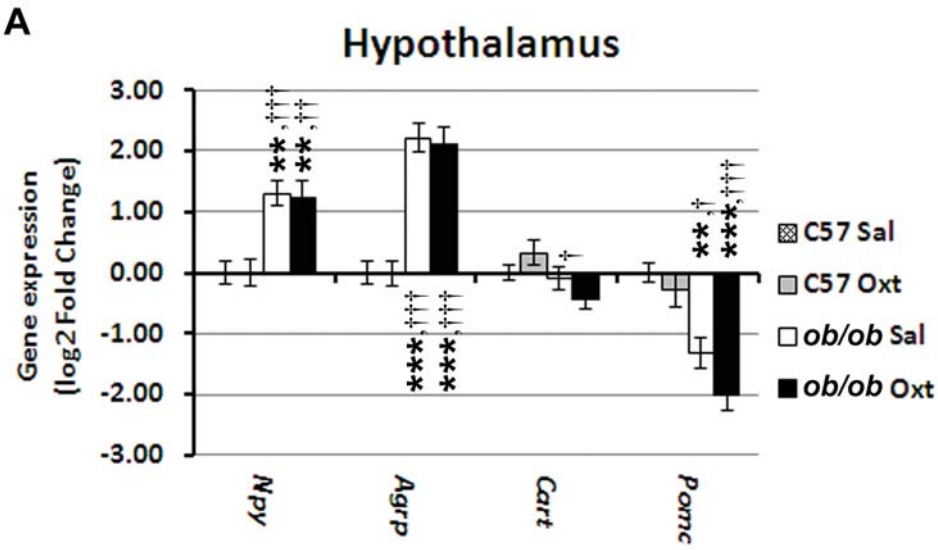
Supplemental Fig 2.- Food intake-dependent and –independent effects of oxytocin, as determined by using a pair-fed control group. *Ob/ob* mice were treated with vehicle (saline), oxytocin (50nmol/day) or vehicle (saline), but receiving the same amount of food as oxytocin-treated mice (PF, pair-fed group) during 14 days. (*A*) Delta body composition between the beginning and the end of the treatment measured by magnetic resonance imaging, N=6-20. (*B*) Epididymal white adipose tissue (eWAT) weight, N=6-7. (*C*) eWAT gene expression of lipolytic (*Hsl*), lipogenic (*Fasn*) lipid uptake (*Lpl*) and glyceroneogenic (*Pepck*) enzymes, as well as of the oxytocin receptor (*Oxtr)*, considering the levels in the *ob/ob* Sal group as 100%, N=6-7. (*D*) FASN activity in eWAT, N=6-7. (*E*) Expression of the macrophage marker *Emr1* in eWAT, considering the levels in the *ob/ob* Sal group as 100%, N=6. (*F*) Representative merged immunofluorescence images of the macrophage marker MAC-2 in the red channel and the nuclear marker, Hoechst 33258 in the blue channel and quantification of the immunofluorescence in percent of MAC-2 positive cells over all cells present on the slice, scale white bar: 100 um, N=6-7. (*G*) Representative hepatic hematoxylin and eosin staining from animals with the different treatments, scale black bar: 100 um. (*H*) Quantification of hepatic triglyceride content, N=6-7. (*I*) Representative hepatic oil red O staining from animals with the different treatments, scale black bar: 100 um. (*J*) Hepatic gene expression of gluconeogenic (*G6pc*, *Fbp1* and *Pepck*) and glycolytic (*Gck*, *Pfkb1* and *Pklr*) enzymes, N=6-7. (*K-L*) Glycemia (*K*, N=6-17) and insulinemia (*L*, N=6-7) during a glucose tolerance test. **p*<0.05, ***p*<0.01, ****p*<0.001 *vs. ob/ob* Sal; †*p*<0.05, ††*p*<.0.01 *vs. ob/ob* Oxt.

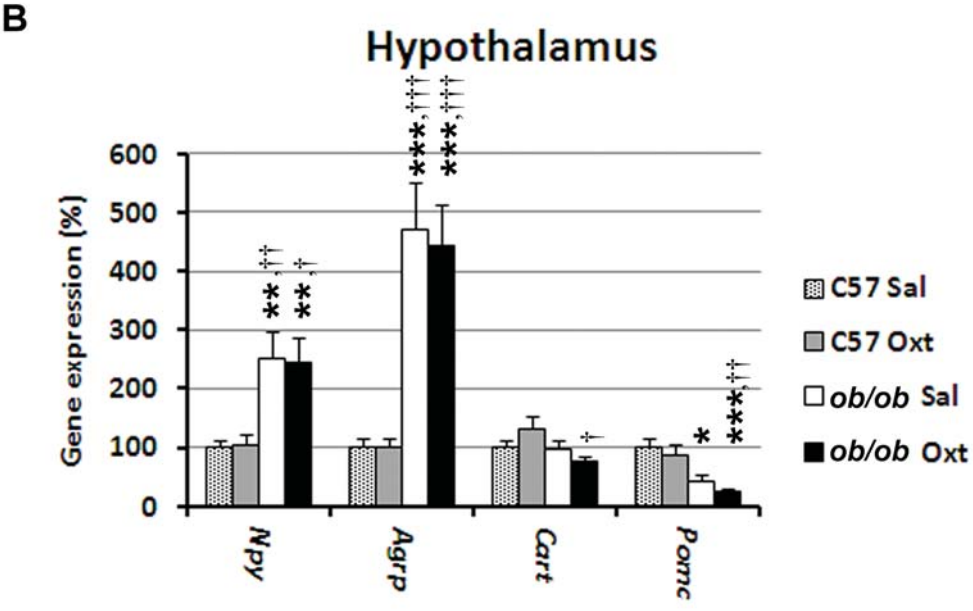
Supplemental Fig 3 Hepatic glycogen content and related genes in C57BL6/J and *ob/ob* mice. (A-B) Quantification of hepatic glycogen content, (C-D) Hepatic gene expression of glycogen synthase (*Gys2*) and phosphorylase (*Pygl*). Mice were *ob/ob* (*A* and *C*) or C57BL6/J (*B* and *D*) subcutaneously treated with oxytocin (50nmol/day) or vehicle (saline) during 14 days. N=6-8. **p*<0.05, ****p*<0.001..

Supplemental Fig 4 *Oxtr* mRNA expression and plasma oxytocin levels in C57BL6/J and *ob/ob* mice. (*A*) *Oxtr* levels in different mouse tissues, according to the BioGPS database (24). (*B*) eWAT gene expression of *Oxtr* in saline-treated C57BL6/J and *ob/ob* mice, considering the levels in the C57BL6/J group as 100%, N=7-8. (*C*) Plasma oxytocin levels of saline-treated C57BL6/J and *ob/ob* mice, N=5-6. ****p*<0.001.

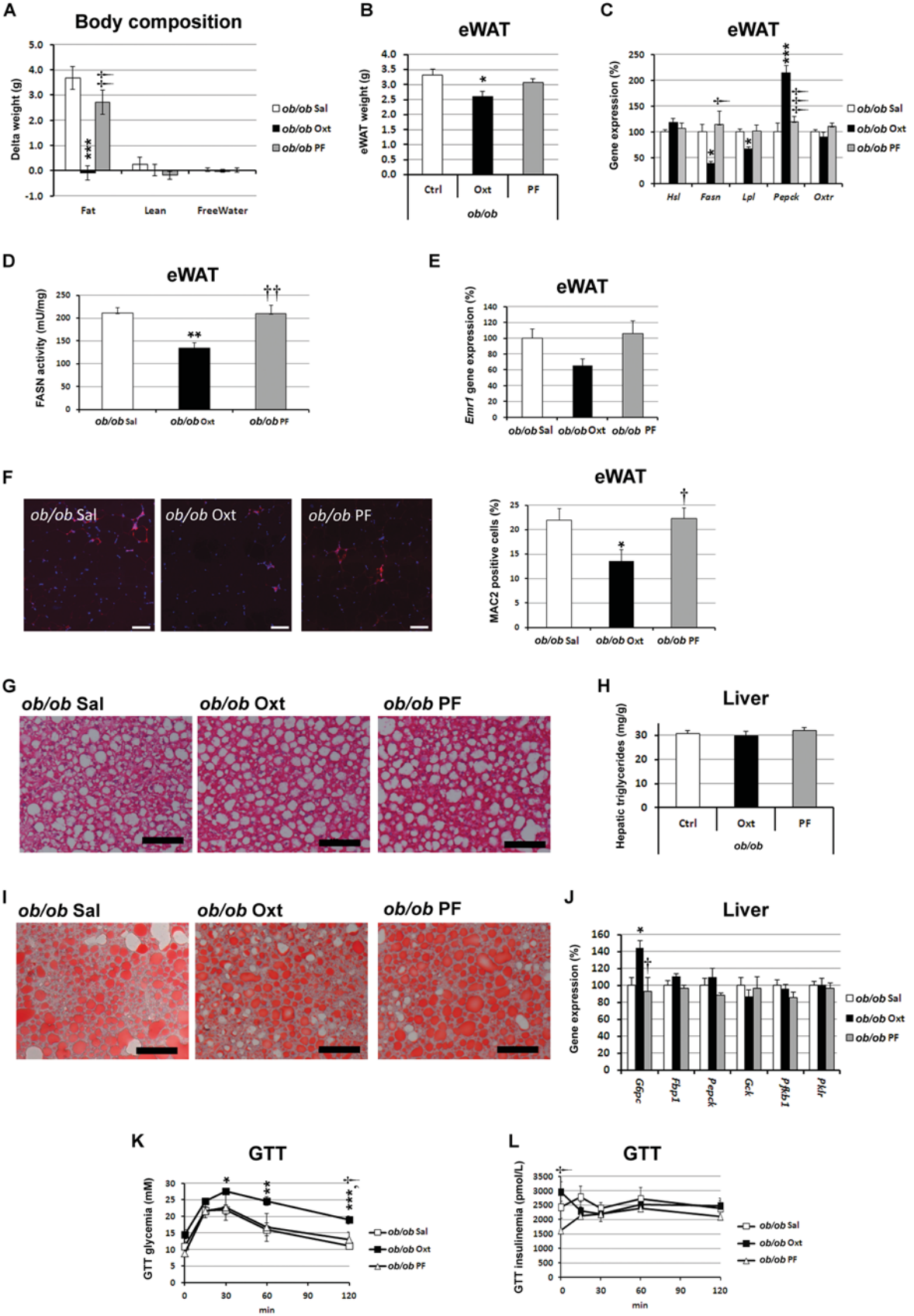
Supplmental Table 1.- Sequence of primers used for the Real Time PCR.

Sup Fig 1

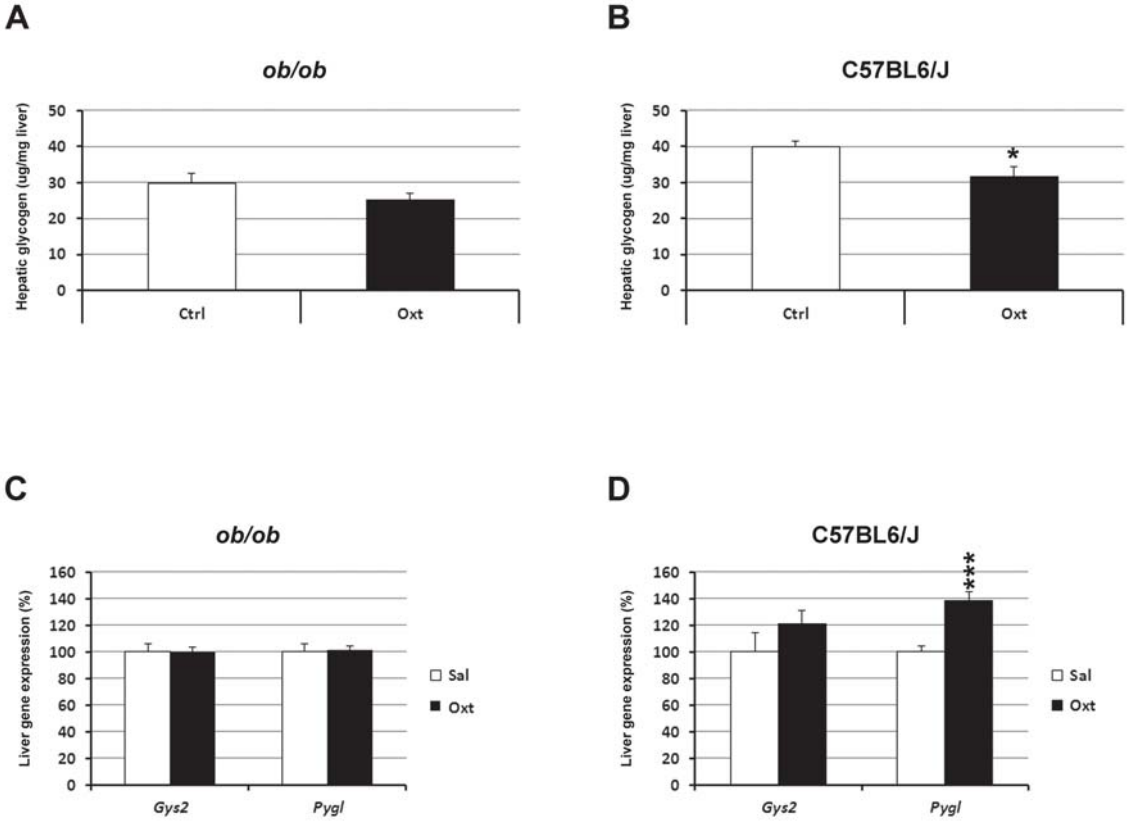

A
Hypothalamus
Gene expression (log2 Fold Change)
3.00
2.00
1.00
0.00
-1.00
-2.00
-3.00
**,†††
**,††
***,†††
***,†††
**,†
***,†††
Npy
Agrp
Cart
Pomc
C57 Sal
C57 Oxt
ob/ob Sal
ob/ob Oxt


B
Hypothalamus
Gene expression (%)
600
500
400
300
200
100
0
**,††
**,†
***,†††
***,†††
*
***,††
Npy
Agrp
Cart
Pomc
C57 Sal
C57 Oxt
ob/ob Sal
ob/ob Oxt

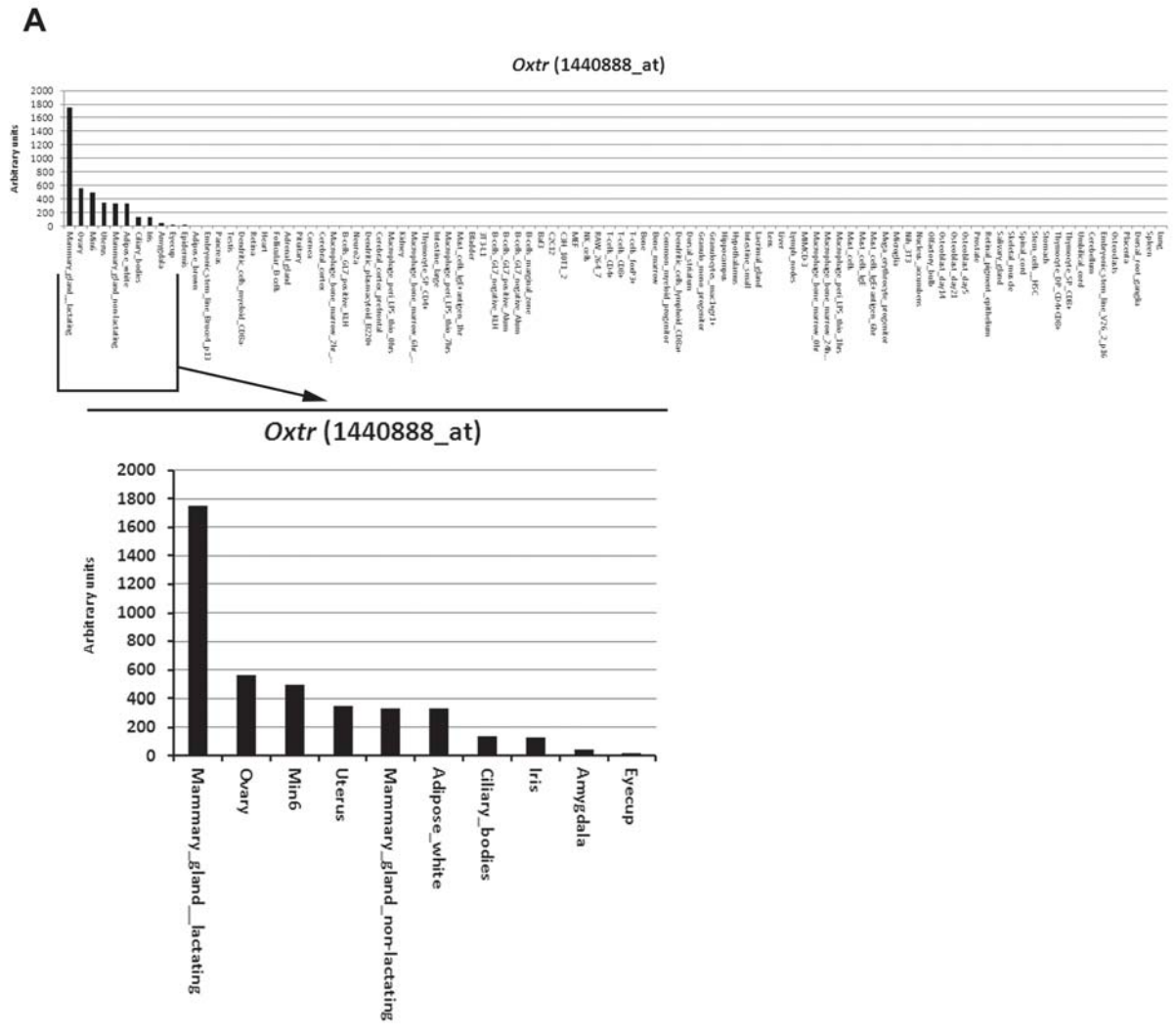
Sup Fig 2

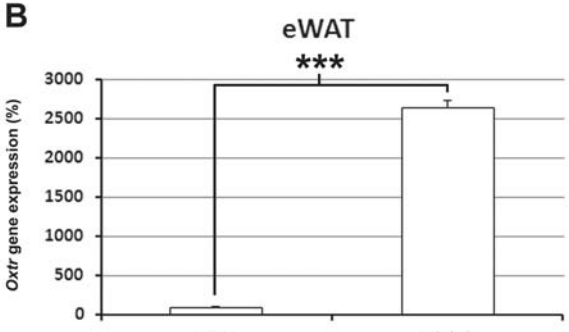

A
Body composition
Delta weight (g)
Fat
Lean
FreeWater
ob/ob Sal
ob/ob Oxt
ob/ob PF
B
eWAT
eWAT weight (g)
Ctrl
Oxt
PF
ob/ob
C
eWAT
Gene expression (%)
Hsl
Fasn
Lpl
Pepck
Oxtr
D
eWAT
FASN activity (mU/mg)
E
eWAT
Emr1 gene expression (%)
F
ob/ob Sal
ob/ob Oxt
ob/ob PF
eWAT
MAC2 positive cells (%)
G
ob/ob Sal
ob/ob Oxt
ob/ob PF
H
Liver
Hepatic triglycerides (mg/g)
I
ob/ob Sal
ob/ob Oxt
ob/ob PF
J
Liver
Gene expression (%)
G6pc
Fbp1
Pepck
Gck
Pfkb1
Pklr
K
GTT
GTT glycemia (mM)
min
L
GTT
GTT insulinemia (pmol/L)
min

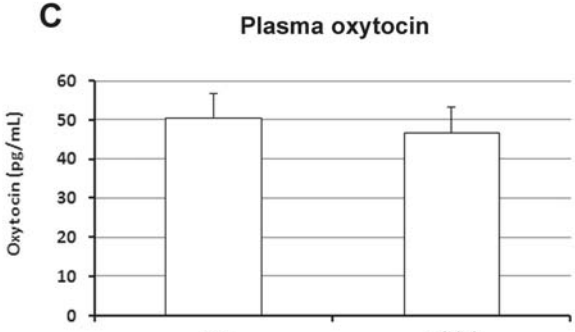
Sup Fig 3


A
ob/ob
Hepatic glycogen (ug/mg liver)
50
40
30
20
10
0
Ctrl
Oxt
B
C57BL6/J
Hepatic glycogen (ug/mg liver)
*
Ctrl
Oxt
C
ob/ob
Liver gene expression (%)
160
140
120
100
80
60
40
20
0
Gys2
Pygl
Sal
Oxt
D
C57BL6/J
Liver gene expression (%)
***
Gys2
Pygl
Sal
Oxt

Sup Fig 4


A
Oxtr (1440888_at)
Arbitrary units
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Mammary_gland__lactating
Ovary
Min6
Uterus
Mammary_gland_non-lactating
Adipose_white
Ciliary_bodies
Iris
Amygdala
Eyecup
Oxtr (1440888_at)
Arbitrary units
2000
1800
1600
1400
1200
1000
800
600
400
200
0
Mammary_gland__lactating
Ovary
Min6
Uterus
Mammary_gland_non-lactating
Adipose_white
Ciliary_bodies
Iris
Amygdala
Eyecup


B
eWAT
***
Oxtr gene expression (%)
3000
2500
2000
1500
1000
500
0
C57
ob/ob


C
Plasma oxytocin
Oxytocin [pg/mL]
60
50
40
30
20
10
0
C57
ob/ob

Sup Table-Primers

	Genes	Forward	Reverse
White adipose tissue genes	*Hsl* (official name *Lipe*)	GGAGCACTACAAACGCAACGA	CCACCGGTAAAGAGGGAACTG
	Fasn	GCCAACCGGCTCTCTTTCTT	GGCTGTGTCCAGGGCAAT
	Lpl	TTCCAGCCAGGATGCAACA	CCACGTCTCCGAGTCCTCTCT
	Oxtr	CATCACCTTCCGCTTCTACGG	ATGCCCACCACCTGCAAGTA
	Emr1 (also known as F4/80)	CAGATACAGCAATGCCAAGCA	GATTGTGAAGGTAGCATTCACAAGTG
Liver genes	*G6pc*	GGAGTCTTGTCAGGCATTGCT	CGGAGGCTGGCATTGTAGAT
	Fbp1	GCACTCTGGTATATGGAGGGATCT	AGCAGCCGCAGCTTTCC
	Pepck1(official name *Pck1*)	CCACAGCTGCTGCAGAACAC	GAAGGGTCGCATGGCAAA
	Pfkb1	TGATCTGTCACCAGGCTGTCA	AGGGCAGCTCATCTGAACTTTT
	Pklr	GAACCATGAAGGCGTGAAGAA	CCCCGAGCCACCATGAT
	Gck	TGGATGGCTCCGTGTACAAG	GATTTCGCAGTTGGGTGTCA
	Gys2	GAGTCCTTATCCAGGCTTAATTTCC	GGCAGGCATGATGAAAAACA
	Pygl	CGGTGAACGGTGTAGCAAAGA	CTAGCTCGCTGAAGTCCTTGAAT
Hypothalamic genes	*Cart*	CTGCAATTCTTTCCTCTTGAAGTG	GGGAATATGGGAACCGAAGGT
	Agrp	CCGCTTCTTCAATGCCTTTT	AGGTGCGACTACAGAGGTTCGT
	Pomc	GCAGAGGCAAACAAGATTGGA	CAGAGAGCTGCCTTTCCGCGACAG
	Npy	AAAACGCCCCCAGAACAAG	CGGGAGAACAAGTTTCATTTCC
Housekeeping gene	*Rps29*	GCAAATACGGGCTGAACATGT	TCCAACTTAATGAAGCCTATGTCCTT

Sequence of primers used for the Real Time PCR.