Supplemental Figure Legends

Supplemental Figure 1: Characterization of Tadipo mice on chow diet

a-b) qPCR analysis of TLR4 and IL1 β mRNA expression in various tissue normalized to TLR4 $^{fl/fll}$. **c)** 10 week body weight follow up (n=10~15). **d)** oral glucose tolerance test (2.5 mg/g BW). **e)** insulin tolerance test (0.75 mU/g BW). **f)** triglyceride clearance test (15ml/kg BW of 20% intralipid) (n=4). **g)** glucose infusion rate during hyperinsulinemic euglycemic clamp (n=4~5). **h)** glucose infusion rate after acute lard infusion during hyperinsulinemic euglycemic clamp (n=4~5). *p<0.05 compared to TLR4 $^{fl/fll}$. Data are presented as means ± SEM

Supplemental Figure 2: β3 adrenergic receptor stimulation and average adipocyte size

a) Circulating NEFA (non-esterified fatty acid) (left) and triglyceride concentrations (right) in male TLR4$^{f/f}$ and Tadipo mice during a β-3 adrenergic agonist sensitivity test (1 mg per kg body weight) CL316,243 intraperitoneally, *n* = 5 TLR4$^{f/f}$, n=10 Tadipo) on chow diet.

b) Circulating NEFA (left) and triglyceride concentrations (right) in male TLR4$^{f/f}$ and Tadipo mice during a β-3 adrenergic agonist sensitivity test (*n* = 6 TLR4$^{f/f}$, n=7 Tadipo) after chronic HFD.

c) Average adipocytes sized (n≥105).

Supplemental Figure 3: Insulin levels during hyperinsulinemic euglycemic clamps

a-c) plasma insulin measured at basal and steady state during hyperinsulinemic euglycemic clamp after 3 week HFD, chronic HFD, and lard infusion. **d-f)** hepatic glucose production during hyperinsulinemic euglycemic clamp after 3 week HFD, chronic HFD, and lard infusion. *p<0.05 compared to TLR4 $^{fl/fll}$. Data are presented as means ± SEM

Supplemental Figure 4: Plasma and tissue sphingolipid analysis with and without HFD challenge

a-b) plasma. **c-d)** liver. **e-f)** sWAT ceramide level after 8 weeks Dox chow or HFD induction.

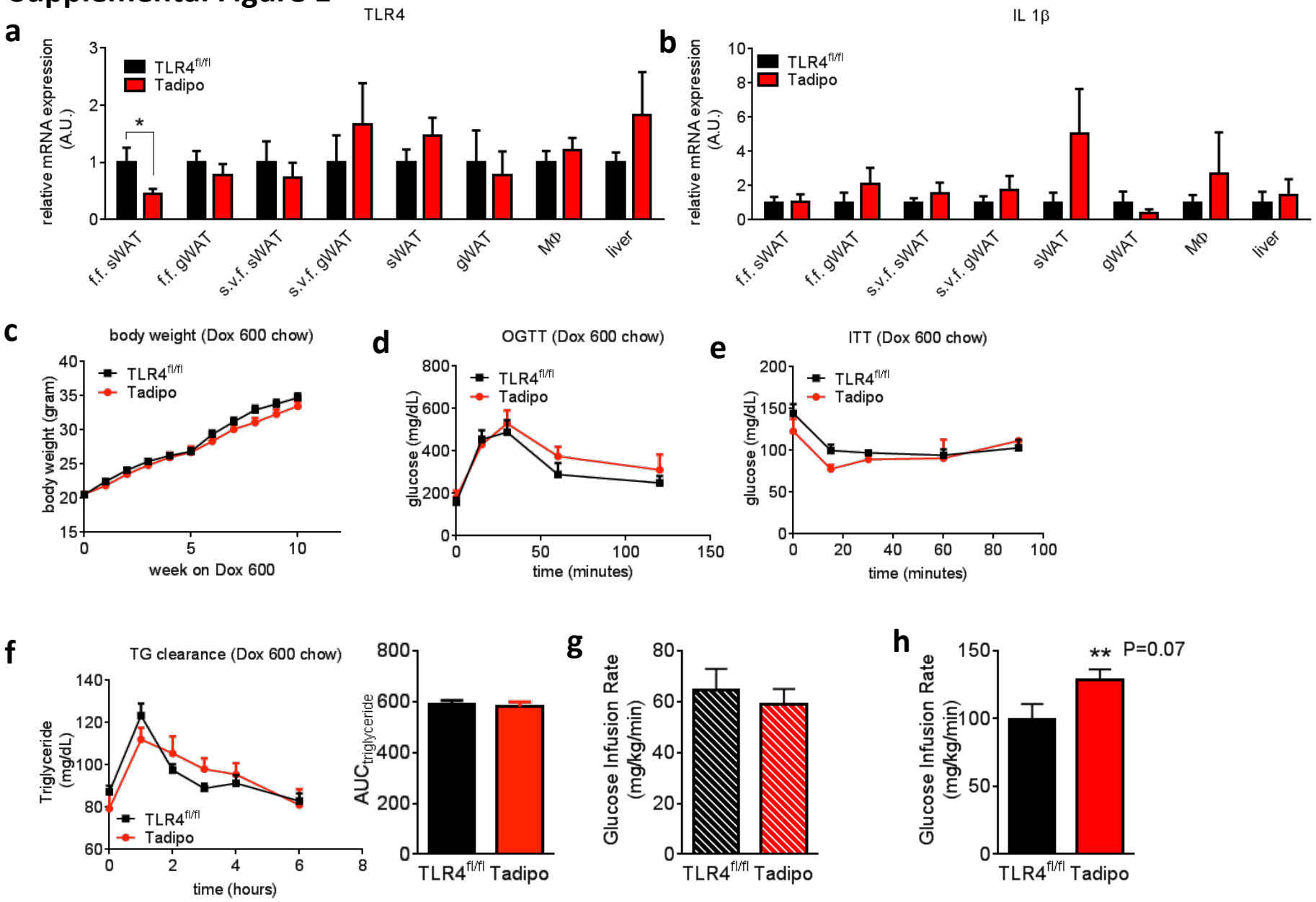
Supplemental Table 1: Primer sets for qPCR analysis

Gene	Forward primer	Reverse primer
Acc1	TGGACAGACTGATCGCAGAGAAAG	TGGAGAGCCCCACACACA
Acox 1	TCCCGATCTGCGCAAGGAGC	CTGGTGAAGCAAGGTGGGCA
β-actin	TACCACAGGCATTGTGATGG	TTTGATGTCACGCACGATTT
Fas	GCTGCGGAAACTTCAGGAAAT	AGAGACGTGTCACTCCTGGACTT
IL 1β	CAACCAACAAGTGATATTCTCCATG	GATCCACACTCTCCAGCTGCA
Scd1	CCGGAGACCCCTTAGATCGA	TAGCCTGTAAAAGATTTCTGCAAACC
SREBP1-c	GGAGCCATGGATTGCACATT	CAGGAAGGCTTCCAGAGAGG
TLR4	GACACCAGGAAGCTTGAATCC	TGATCCATGCATTGGTAGGTAA

Supplemental Table 2: Primer sets to screen TLR4 deletion

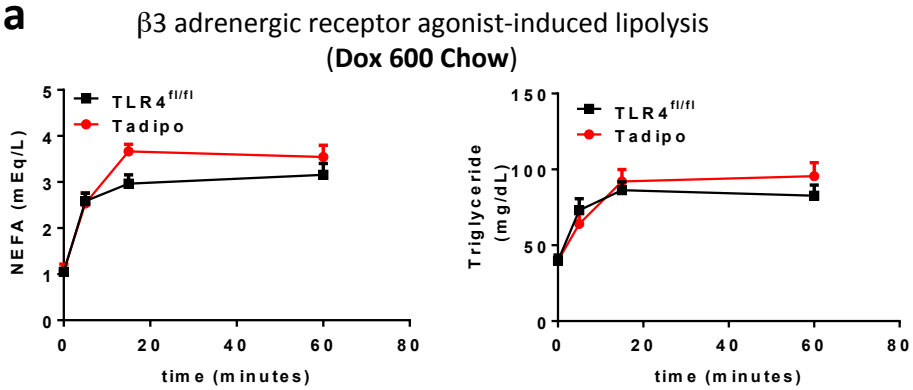
Gene	Forward primer	Reverse primer
fl/fl	GACTTGAGAGTTATGTAACACCTG	TCCTATAGACCAGTCTGGCCTTAA
Tadipo	GACTTGAGAGTTATGTAACACCTG	GTGGCTATGTTCCAGTTTGAATG

Supplemental Figure 1

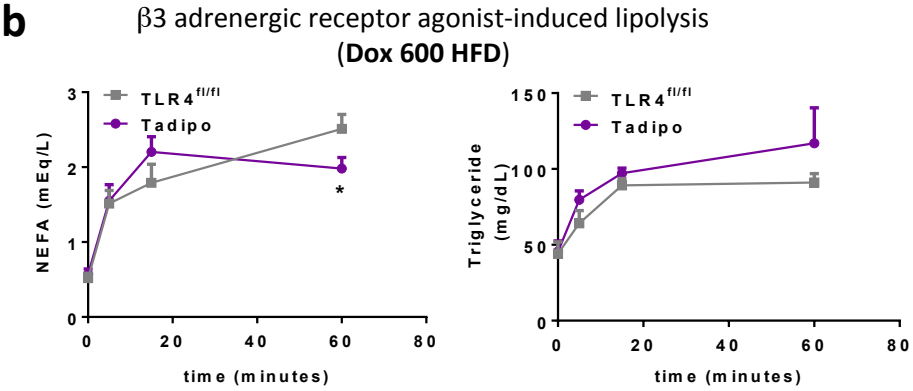


Supplemental Figure 2

a



b



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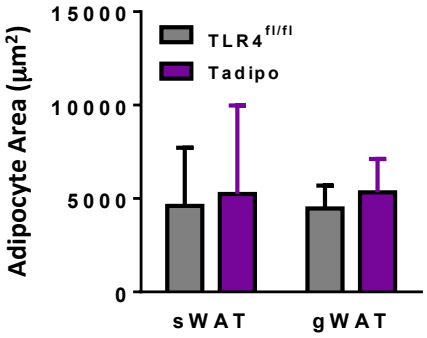
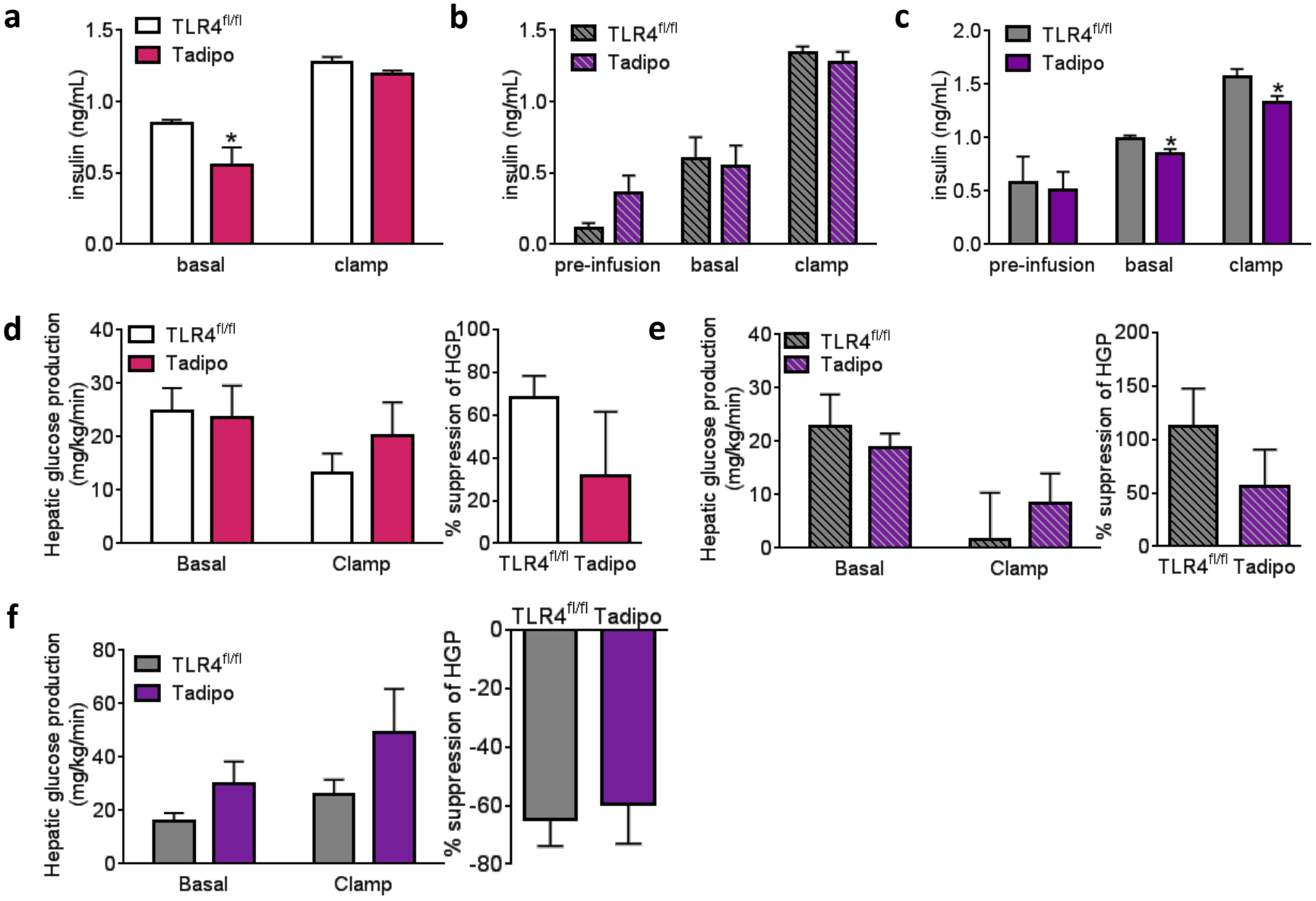
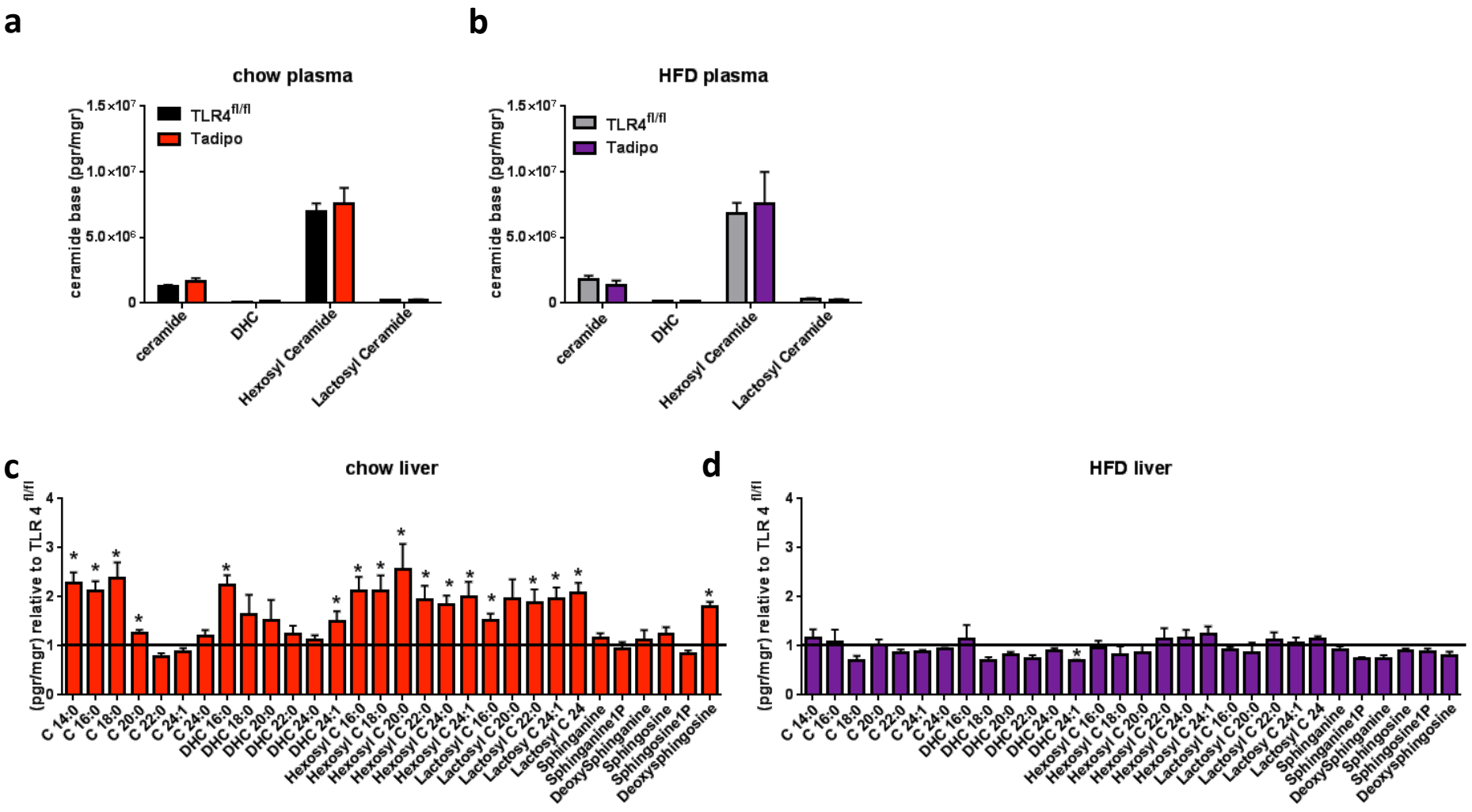


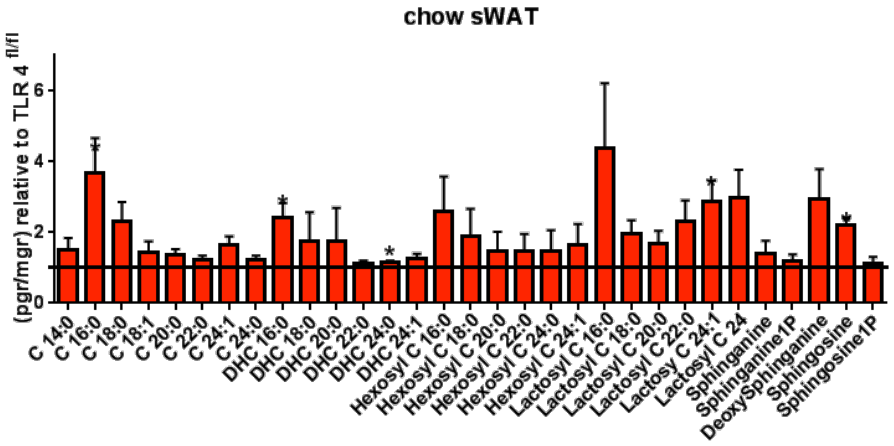
Supplemental Figure 3



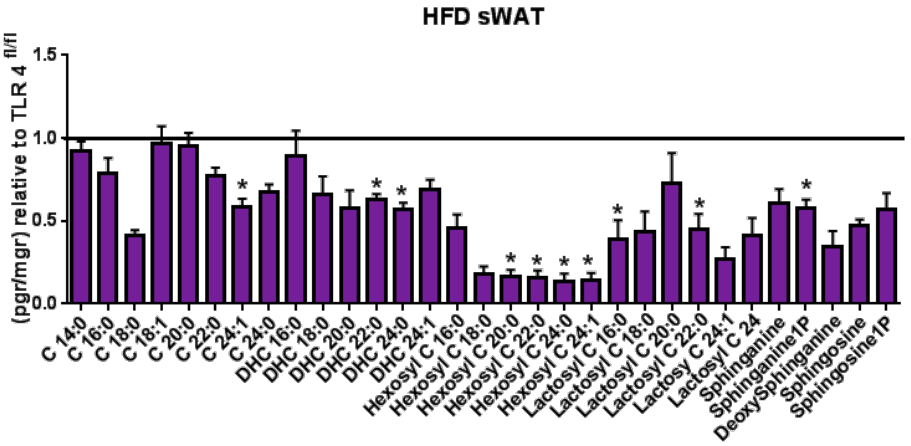
Supplemental Figure 4



e


chow sWAT
(pgr/mgr) relative to TLR 4 fl/fl
0
2
4
6
C 14:0
C 16:0
C 18:0
C 18:1
C 20:0
C 22:0
C 24:1
C 24:0
DHC 16:0
DHC 18:0
DHC 20:0
DHC 22:0
DHC 24:0
DHC 24:1
Hexosyl C 16:0
Hexosyl C 18:0
Hexosyl C 20:0
Hexosyl C 22:0
Hexosyl C 24:0
Hexosyl C 24:1
Lactosyl C 16:0
Lactosyl C 18:0
Lactosyl C 20:0
Lactosyl C 22:0
Lactosyl C 24:1
Lactosyl C 24
Sphinganine
Sphinganine1P
DeoxySphinganine
Sphingosine
Sphingosine1P

f


HFD sWAT
(pgr/mgr) relative to TLR 4 fl/fl
0.0
0.5
1.0
1.5
C 14:0
C 16:0
C 18:0
C 18:1
C 20:0
C 22:0
C 24:1
C 24:0
DHC 16:0
DHC 18:0
DHC 20:0
DHC 22:0
DHC 24:0
DHC 24:1
Hexosyl C 16:0
Hexosyl C 18:0
Hexosyl C 20:0
Hexosyl C 22:0
Hexosyl C 24:0
Hexosyl C 24:1
Lactosyl C 16:0
Lactosyl C 18:0
Lactosyl C 20:0
Lactosyl C 22:0
Lactosy C 24:1
Lactosyl C 24
Sphinganine
Sphinganine1P
DeoxySphinganine
Sphingosine
Sphingosine1P