Supplementary Figure 1 Generation of Tg-FABP4-RORα4 mice.

(A) Western blot analysis of total RORα protein level in inguinal adipose tissue from WT and *tg/*+ Tg-FABP4-RORα4 mice. Densitometry scanning was performed for RORα protein level relative to TATA binding protein (TBP) loading control (n=2 littermate pairs). (B) C2C12 cells were transiently co-transfected with SG5 vector, VP16 vector, SG5-RORα4 construct, or VP16-RORα4 construct with a mPCP2tkluc positive control (Lau et al., 2008) luciferase reporter construct (n=3 technical replicates). Luciferase activity was measured and represented as the mean ± S.E.M. fold-activation. Statistical analysis was performed using a one-way ANOVA with Bonferroni's post-test applied where *P<0.05. (C) Representative images of dissected WT and *tg/*+ littermate pair (16 week chow). (D) Mean relative mass/total weight ± S.E.M. of adipose tissues (SAT, visceral epididymal, and interscapular brown adipose tissues) dissected from WT and *tg/*+ littermate pairs (n=7 littermate pairs, 32 week chow). Statistical analyses were performed using unpaired two-tailed Student's t-tests but no significance was observed.

Supplementary Figure 2 Analysis of homozygous tg/tg Tg-FABP4-RORα4 mice.

(A) Total RORα mRNA expression in SAT of WT and tg/+ (n= 7 littermate pairs) and WT and tg/tg (n=3 littermate pairs) was performed using TaqMan assays with 18s rRNA as the endogenous control. (B) Body weight (in grams) of male WT (black) and *tg/tg* (blue, n=5 littermate pairs) mice measured weekly up to 14 weeks of age. (C) Mean relative mass/total weight ± S.E.M. of adipose tissues dissected from WT and and *tg/tg* (n=3 littermate pairs) mice. Statistical analyses were performed using unpaired two-tailed Student's t-test applied but results were not significant. (D) Fasting blood glucose levels from 6 h-fasted WT (white) and *tg/tg* (black) mice (n=3 littermate pairs) in the chow study. Statistical analysis was performed using unpaired two-tailed Student's t-test where **P<0.01. (E and F) Blood glucose was measured at various times after intra-peritoneal administration of (E) glucose or (F) insulin (t=0) on 6 h-fasted WT (black) and *tg/tg* (blue) littermates in the chow study. Statistical analysis was performed using two-way ANOVAs with Bonferroni's post test applied where **P<0.01;***P<0.001 for *tg/tg* versus WT (n=3 littermate pairs).

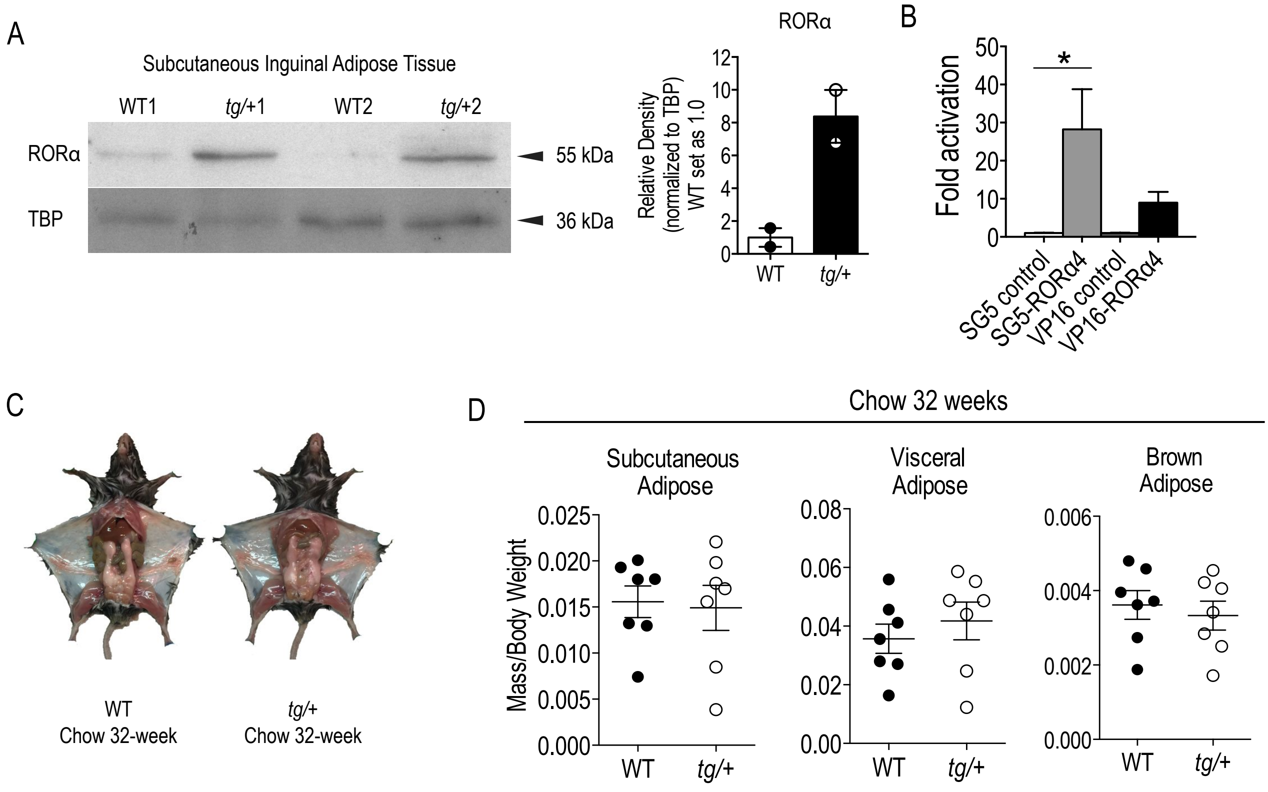
Supplementary Figure 3

(A) H&E staining of HFD livers. Formalin-fixed and paraffinized livers from HFD-fed WT and *tg/+* mice were sectioned at 0.7 μm-step intervals and stained for morphology using H&E. Representative images acquired from n=4 littermate pairs are shown. (B) Top 25 significantly enriched biological processes identified in DAVID analysis of HFD liver. P-value was set at <0.05.

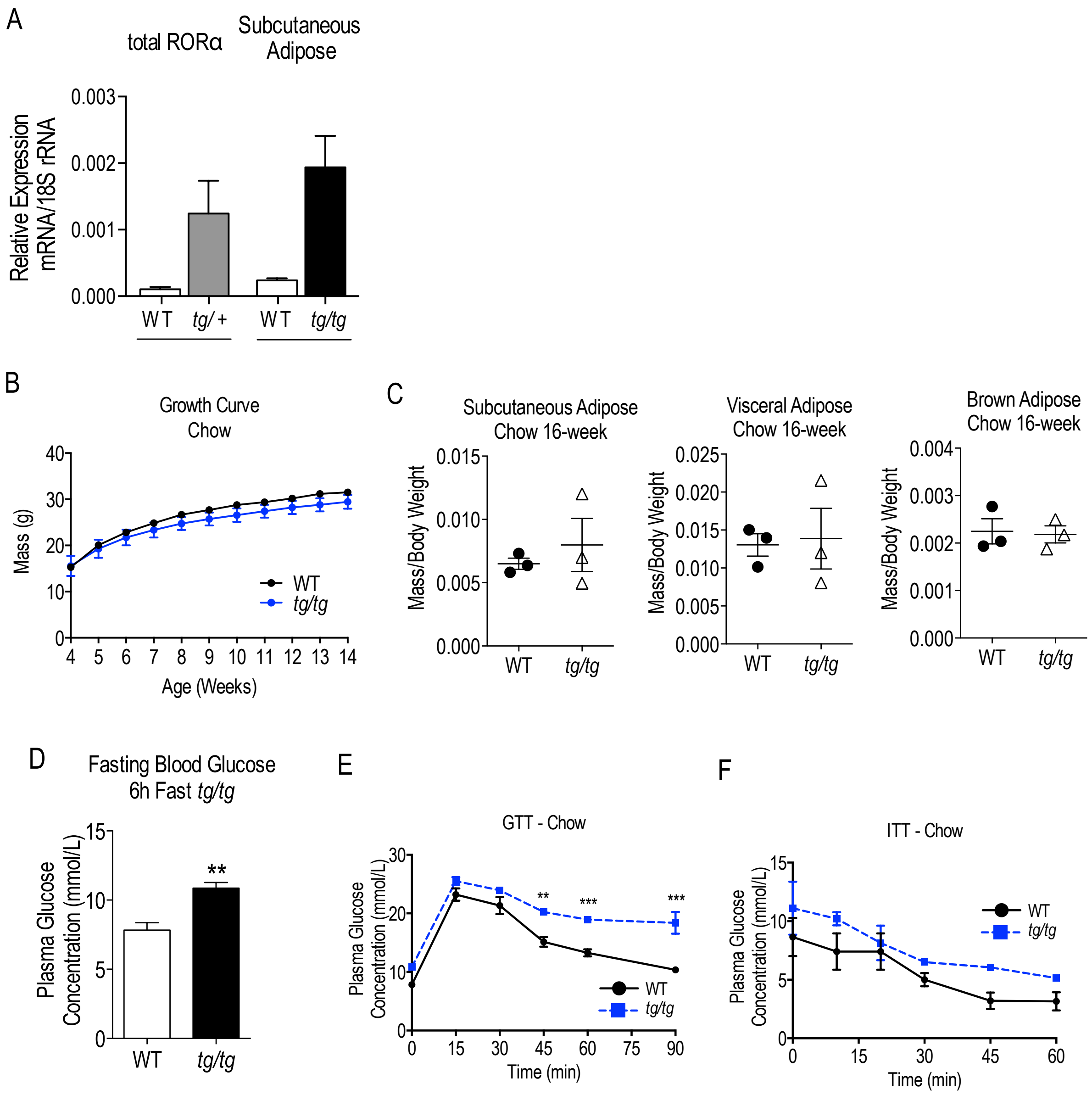
Supplementary Figure 4 qPCR analysis of genes involved in thermogenesis program in brown adipose tissue.

Relative gene expression of the thermogenic transcriptional regulators, *Ehmt1*, *Tle3*, and *Prdm16,* in brown adipose tissue from (A) chow and (C) HFD fed 32-week *tg/+* Tg-FABP4-RORα4 and WT mice (n=5 littermate pairs). Quantitative PCR was performed on RNA fractionated from interscapular brown adipose tissue, and measured *Ehmt1*, *Tle3*, and *Prdm16* expression (using TaqMan assays), and presented as relative gene expression normalized against *Gusb*. Relative gene expression of *Acot11*, *Dio2*, *Erra*, *Mcpt1* and *Pparα* in brown adipose tissue from (B) chow and (D) HFD fed 32-week *tg/+* Tg-FABP4-RORα4 and WT littermates (n=5). Quantitative PCR was performed on RNA fractionated from interscapular brown adipose tissue (using SYBR assays), and expression presented as relative gene expression normalized against *Rplp0*. Statistical analysis was performed using unpaired two-tailed Student's t-test where *P<0.05; **P<0.01; ***P<0.001.

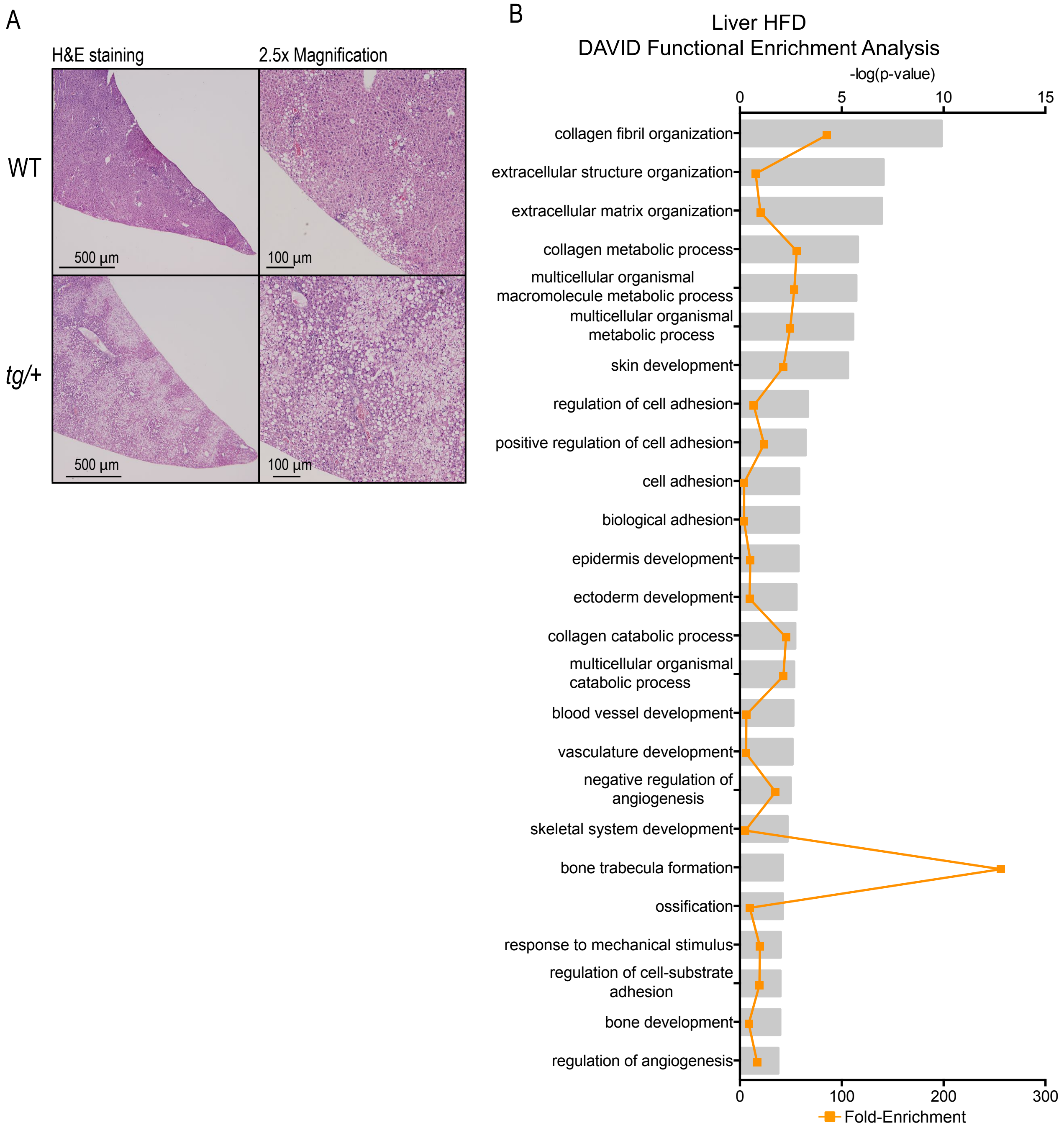
Supplementary Fig 1



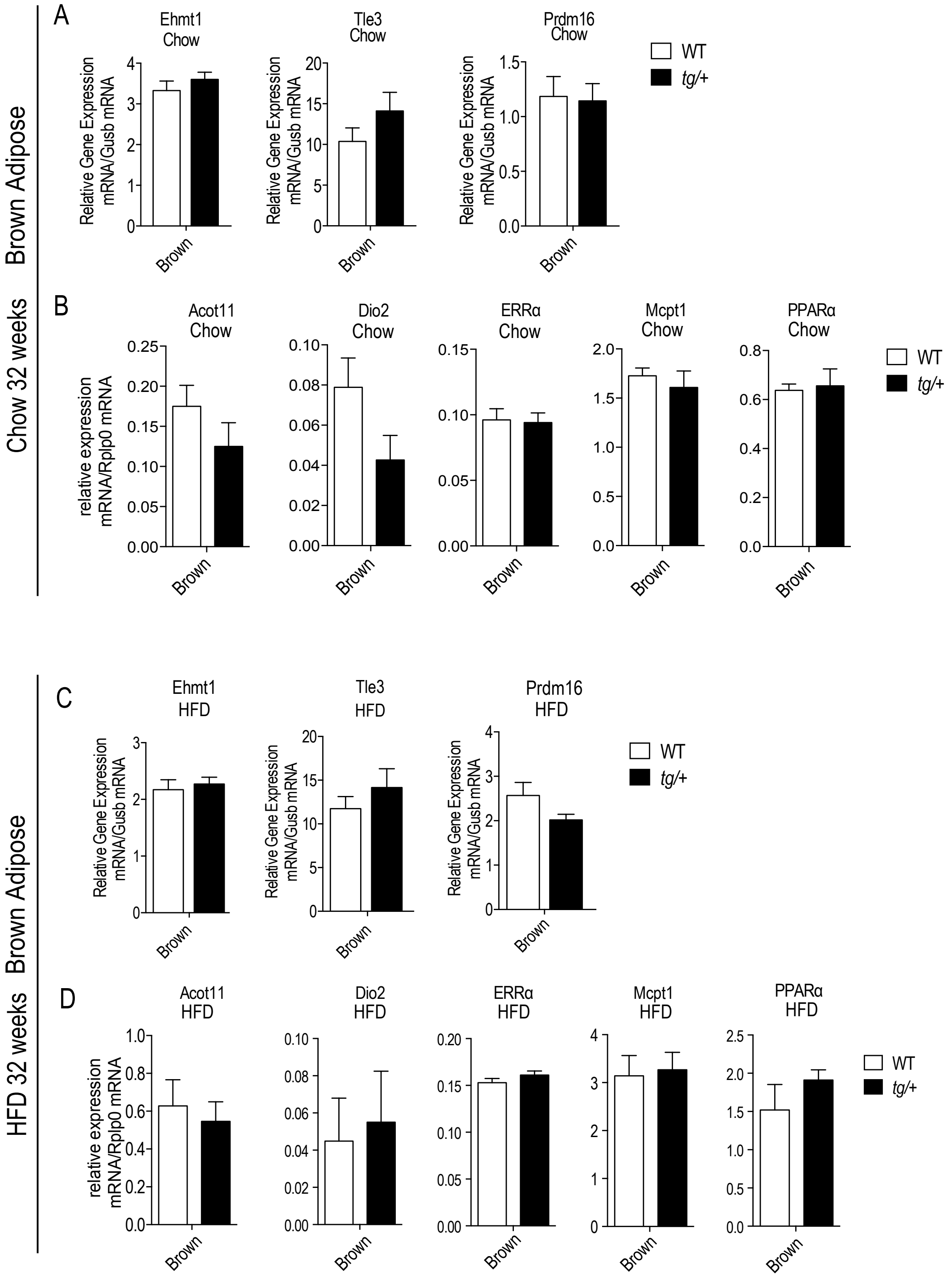
Supplementary Fig 2



Supplementary Fig 3



Supplementary Fig 4



Supplemental Table 1

Top 50 up-regulated genes RNA-seq profiling in subcutaneous inguinal adipose tissue (HFD).

Regulation	Gene	Log_2Fold-change	P Value	Corrected P Value
Up	Liph	5.5426	1.64E-27	9.55E-25
Up	Serpinb1a	5.5275	3.78E-206	1.91E-202
Up	Muc13	5.4333	2.77E-74	8.41E-71
Up	Dsc3	5.1485	4.14E-15	6.48E-13
Up	Fgf14	4.8117	5.94E-30	4.50E-27
Up	Wdr52	4.7363	8.51E-14	1.16E-11
Up	Dsg2	4.4730	3.31E-17	6.97E-15
Up	Pla2g5	4.3257	7.59E-59	1.65E-55
Up	Serpinb9	4.3041	3.13E-282	2.37E-278
Up	Pkp3	4.2785	4.93E-28	2.99E-25
Up	Tmem102	4.1994	2.99E-10	2.15E-08
Up	Aldh3a1	4.0965	6.67E-12	6.89E-10
Up	Hebp2	4.0734	7.03E-51	1.19E-47
Up	Sytl5	4.0024	9.30E-12	9.23E-10
Up	Sult2b1	3.9897	1.78E-26	9.32E-24
Up	Ndst3	3.9373	2.00E-18	5.22E-16
Up	Dock3	3.8142	2.00E-11	1.82E-09
Up	Oprk1	3.8065	2.79E-10	2.02E-08
Up	Serpinb1b	3.7357	5.38E-10	3.63E-08
Up	Ly6d	3.6874	4.81E-18	1.20E-15
Up	Hpcal4	3.6575	1.97E-11	1.81E-09
Up	Tnnt1	3.6133	2.82E-20	9.29E-18
Up	Serpina1e	3.6130	1.11E-10	8.68E-09
Up	Mgarp	3.5284	6.69E-10	4.37E-08
Up	Serpinb1c	3.5276	2.75E-07	1.04E-05
Up	Lad1	3.4636	1.61E-09	9.73E-08
Up	Cdcp1	3.4304	9.96E-08	4.20E-06
Up	Brinp2	3.4003	2.38E-08	1.17E-06
Up	Extl1	3.3997	4.10E-10	2.91E-08
Up	Ugt8a	3.3792	8.08E-10	5.18E-08
Up	**Rora**	**3.3398**	**1.60E-92**	**6.08E-89**
Up	Zfp92	3.3110	8.93E-10	5.69E-08
Up	Tmem56	3.2757	8.87E-08	3.78E-06
Up	Ap1m2	3.2592	3.01E-06	8.34E-05
Up	2900052N01Rik	3.1674	1.29E-07	5.24E-06
Up	Adamdec1	3.1222	1.67E-06	5.05E-05
Up	Nt5c1a	3.0410	1.18E-10	9.15E-09
Up	Gm6484	3.0166	1.10E-10	8.61E-09
Up	Plekhb1	2.9907	1.47E-24	6.98E-22
Up	Dapl1	2.9809	6.39E-11	5.22E-09

Up	Plch2	2.9570	1.79E-06	5.33E-05
Up	Grem1	2.9094	5.61E-05	1.02E-03
Up	1810041L15Rik	2.8964	2.81E-05	5.73E-04
Up	Cbs	2.8862	5.73E-23	2.48E-20
Up	Fam150b	2.8663	3.81E-17	7.51E-15
Up	Bspry	2.8482	2.68E-05	5.49E-04
Up	Colq	2.8387	3.81E-05	7.47E-04
Up	Akr1c14	2.8386	1.18E-22	4.99E-20
Up	Eps8l2	2.7981	9.00E-19	2.44E-16
Up	Gm9696	2.7917	8.74E-11	7.01E-09

Top 50 down-regulated genes RNA-seq profiling in inguinal adipose tissue (HFD).

Regulation	**Gene**	**Log_2Fold-change**	**P Value**	**Corrected P Value**
Down	Peg10	-3.4101	1.46E-13	1.98E-11
Down	Mucl1	-3.3138	2.63E-06	7.43E-05
Down	Gabrr2	-3.2133	2.48E-39	3.13E-36
Down	Zim1	-3.1328	2.34E-19	6.97E-17
Down	Acta1	-3.0988	1.20E-11	1.18E-09
Down	Peg3os	-2.6731	2.18E-04	3.09E-03
Down	Slc13a3	-2.6298	5.41E-11	4.49E-09
Down	Thbs1	-2.5967	3.23E-30	2.58E-27
Down	Aldh1a2	-2.5509	9.83E-11	7.81E-09
Down	Acta2	-2.5034	1.00E-33	1.09E-30
Down	Ttc36	-2.4985	4.40E-08	2.04E-06
Down	Bpifb6	-2.4156	3.85E-08	1.83E-06
Down	Peg3	-2.3643	6.69E-27	3.62E-24
Down	**Sfrp5**	**-2.3506**	**3.38E-59**	**8.55E-56**
Down	Optc	-2.3107	2.04E-07	7.94E-06
Down	Alb	-2.3085	1.70E-04	2.52E-03
Down	Ear2	-2.3065	1.50E-04	2.28E-03
Down	4933417O13Rik	-2.2999	4.81E-04	5.82E-03
Down	Tmem178	-2.2589	4.88E-07	1.74E-05
Down	Slc22a2	-2.2267	3.07E-11	2.69E-09
Down	Stac	-2.1650	1.89E-09	1.13E-07
Down	Pkhd1	-2.1609	4.81E-04	5.82E-03
Down	4932435O22Rik	-2.1187	9.54E-05	1.58E-03
Down	2810459M11Rik	-2.0778	1.33E-03	1.28E-02
Down	Timp4	-2.0464	6.04E-12	6.32E-10
Down	Nexn	-2.0428	4.31E-20	1.39E-17
Down	Map3k7cl	-2.0350	4.16E-07	1.52E-05
Down	Gfi1b	-2.0111	1.94E-03	1.72E-02
Down	Clrn1	-1.9958	4.11E-06	1.08E-04
Down	Fgf21	-1.9940	4.28E-05	8.16E-04
Down	Abcc2	-1.9674	1.14E-03	1.15E-02
Down	Slc9b2	-1.9430	1.76E-06	5.29E-05
Down	Trpc3	-1.9368	1.96E-11	1.81E-09
Down	Abat	-1.9278	4.40E-23	1.96E-20
Down	P2rx5	-1.9239	2.89E-17	6.27E-15
Down	Kcnt1	-1.9140	6.76E-04	7.65E-03
Down	Syt14	-1.8809	1.89E-05	4.12E-04
Down	Fcamr	-1.8803	3.79E-10	2.71E-08
Down	Calr4	-1.8582	1.92E-07	7.51E-06
Down	Mogat2	-1.8540	3.95E-06	1.04E-04
Down	Ccr2	-1.8453	1.21E-21	4.60E-19
Down	Slc9a4	-1.8151	1.57E-05	3.53E-04
Down	Ankrd23	-1.8129	3.00E-11	2.65E-09

Down	Hspb7	-1.8031	2.06E-06	6.03E-05
Down	Pmfbp1	-1.7930	9.17E-04	9.57E-03
Down	Gls2	-1.7911	2.58E-03	2.13E-02
Down	Prkag3	-1.7644	2.23E-06	6.45E-05
Down	Fam47e	-1.7467	1.98E-03	1.74E-02
Down	Fam83d	-1.7467	3.45E-04	4.45E-03
Down	Gadd45b	-1.7454	4.89E-10	3.36E-08

Up-regulated genes RNA-seq profiling in liver (HFD).

Regulation	**Gene**	**Log$_2$Fold-change**	**P Value**	**Corrected P Value**
Up	Cx3cr1	2.6468	6.69E-20	8.78E-16
Up	Col1a1	2.4141	1.47E-13	4.82E-10
Up	Ephb2	1.9752	3.05E-10	5.01E-07
Up	Serpinb6b	1.9191	9.38E-14	4.10E-10
Up	Gpr98	1.8520	1.02E-10	1.91E-07
Up	Col3a1	1.8205	1.45E-12	3.80E-09
Up	Col1a2	1.7669	1.23E-15	8.09E-12
Up	Mmp13	1.7544	4.49E-05	1.53E-02
Up	Chil3	1.6898	1.76E-05	7.69E-03
Up	Mgl2	1.5795	2.65E-04	4.76E-02
Up	Ubd	1.5703	5.41E-05	1.73E-02
Up	Sdcbp2	1.5677	1.70E-04	3.59E-02
Up	Aqp7	1.5219	1.87E-04	3.83E-02
Up	Lrrc39	1.4752	1.13E-05	5.51E-03
Up	Cd63	1.4121	1.13E-04	2.97E-02
Up	Itgax	1.4089	2.88E-05	1.11E-02
Up	Ccdc120	1.4027	1.56E-04	3.54E-02
Up	Serpinb9	1.3954	8.90E-11	1.91E-07
Up	Sema4d	1.3574	8.51E-05	2.38E-02
Up	Col5a2	1.3563	4.79E-05	1.57E-02
Up	S100a9	1.2746	4.55E-05	1.53E-02
Up	Tnc	1.2352	4.11E-05	1.46E-02
Up	Thbs1	1.2269	7.73E-07	7.80E-04
Up	Adamts12	1.2252	2.32E-04	4.28E-02
Up	Col6a3	1.2194	1.06E-06	9.30E-04
Up	Haus8	1.1894	1.01E-06	9.30E-04
Up	Loxl1	1.1689	1.63E-04	3.56E-02
Up	Col6a2	1.1649	7.38E-06	4.21E-03
Up	Mmp2	1.1616	2.46E-05	1.01E-02
Up	Adamts9	1.1514	1.75E-04	3.64E-02
Up	Serpina7	1.1460	5.66E-07	6.19E-04
Up	Tubb2a	1.1238	2.93E-06	2.19E-03
Up	Kctd17	1.1236	6.04E-05	1.89E-02
Up	Uap1l1	1.1211	1.22E-04	3.07E-02
Up	Cntnap1	1.1138	3.13E-05	1.14E-02
Up	Adamts2	1.0852	2.71E-05	1.08E-02
Up	Anxa2	1.0593	2.30E-07	2.74E-04
Up	Tnxb	1.0582	5.94E-06	3.71E-03
Up	Fbn1	1.0017	3.00E-05	1.12E-02
Up	Ngfr	0.9833	2.73E-04	4.85E-02
Up	Olfml3	0.9581	7.33E-05	2.19E-02
Up	Trim47	0.9498	1.25E-04	3.08E-02
Up	Col5a1	0.9374	3.34E-06	2.19E-03
Up	Col4a2	0.9301	1.59E-09	2.32E-06
Up	Matn2	0.9203	9.64E-05	2.63E-02
Up	Jun	0.9025	1.65E-04	3.56E-02
Up	Pdgfrb	0.8927	3.07E-06	2.19E-03
Up	Plk3	0.8786	1.56E-05	7.31E-03
Up	Ltbp1	0.8729	6.99E-05	2.13E-02
Up	Apoa4	0.8573	1.18E-04	3.05E-02
Up	Anxa5	0.8401	1.55E-04	3.54E-02
Up	Sparc	0.8364	7.30E-06	4.21E-03
Up	Fstl1	0.8351	1.92E-04	3.83E-02

Up	Lcn2	0.8334	1.41E-04	3.43E-02
Up	Col4a1	0.8293	7.73E-08	1.01E-04
Up	Ccdc80	0.8213	1.05E-05	5.29E-03
Up	Pdk4	0.7954	1.93E-04	3.83E-02
Up	Serpinh1	0.7854	2.17E-05	9.19E-03
Up	Phldb1	0.7621	2.24E-04	4.24E-02
Up	Tmem43	0.6858	2.80E-04	4.90E-02
Up	Col14a1	0.6458	1.97E-04	3.85E-02
Up	Tgm2	0.5549	2.39E-04	4.35E-02
Up	Myo9b	0.5457	7.88E-05	2.30E-02

Down-regulated genes from RNA-seq profiling in liver (HFD).

Regulation	**Gene**	**Log_2Fold-change**	**P Value**	**Corrected P Value**
Down	Cyp2c40	-1.9598	3.31E-06	2.19E-03
Down	Cyp17a1	-1.1833	1.45E-06	1.19E-03
Down	Tsc22d3	-1.0823	1.74E-05	7.69E-03
Down	Cyp2c37	-0.9858	2.26E-04	4.24E-02
Down	BC089597	-0.9473	1.57E-04	3.54E-02
Down	Ces2a	-0.7478	1.01E-05	5.29E-03
Down	Fcna	-0.6940	1.62E-04	3.56E-02
Down	Hsd11b1	-0.6391	1.04E-05	5.29E-03
Down	Pxmp2	-0.5372	8.47E-05	2.38E-02
Down	Afm	-0.5204	1.56E-04	3.54E-02
Down	BC024386	-0.5153	1.11E-04	2.96E-02
Down	Il1rap	-0.4679	2.16E-04	4.17E-02