

## Supporting Information for

### Deletion of *Jazf1* gene causes early growth retardation and insulin resistance in mice

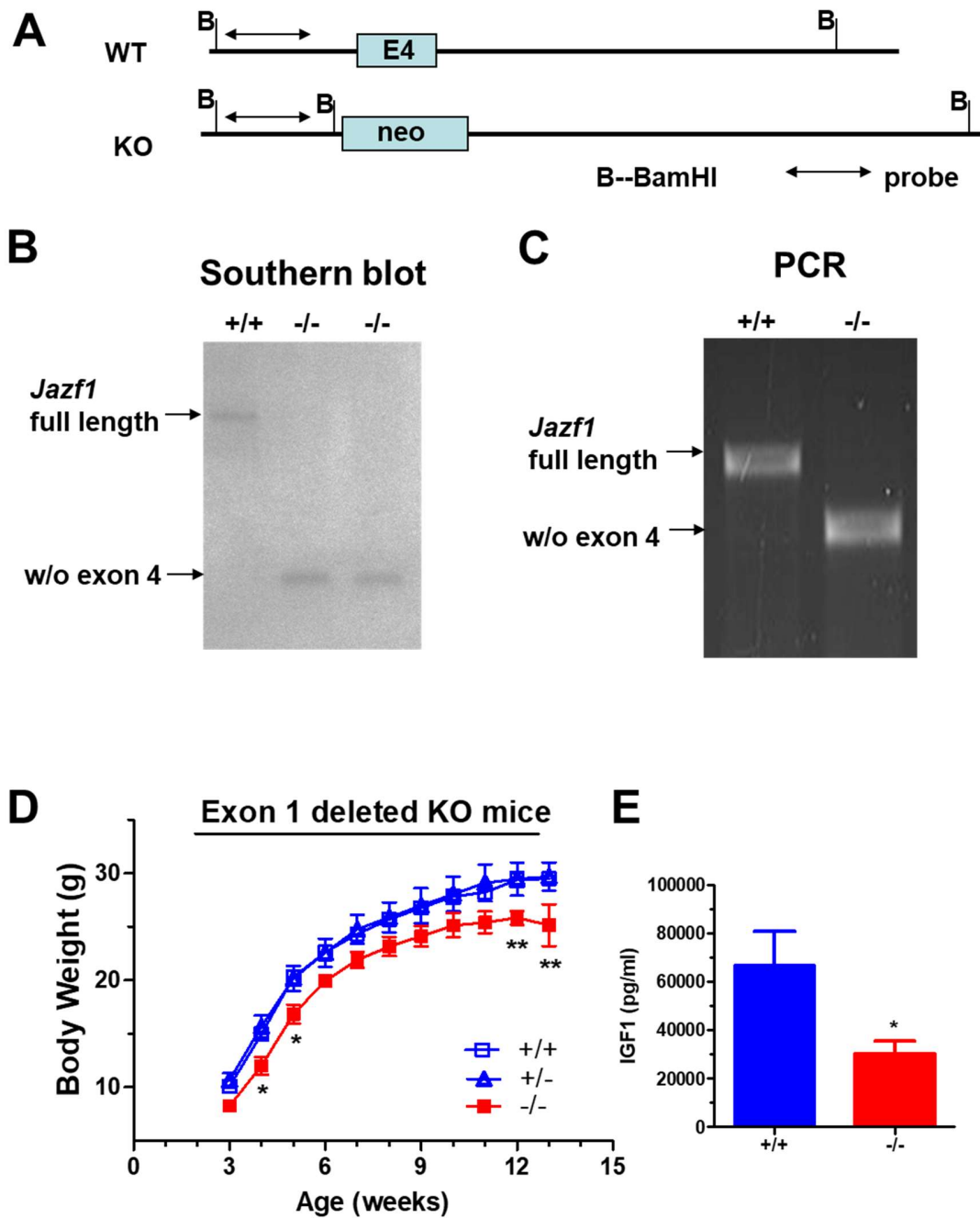
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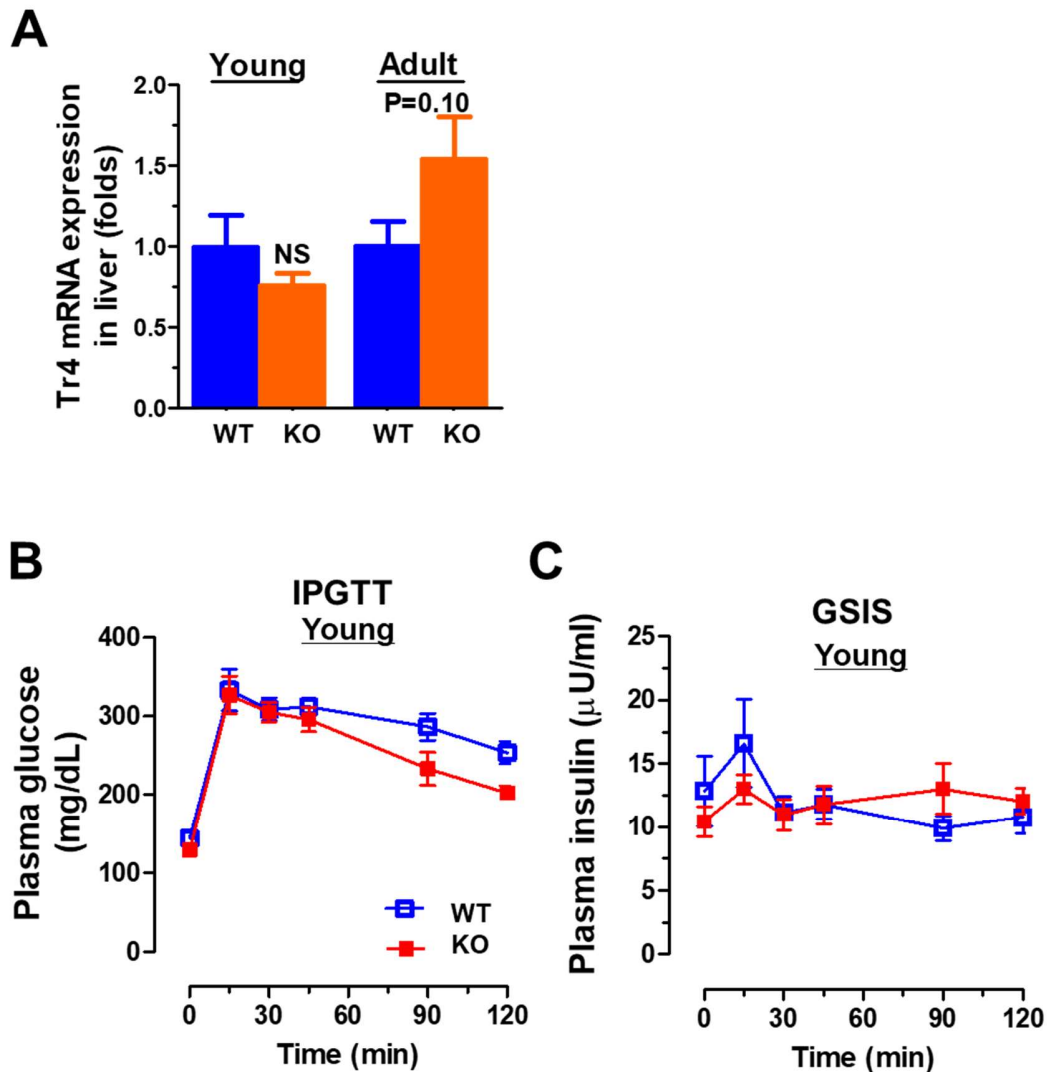
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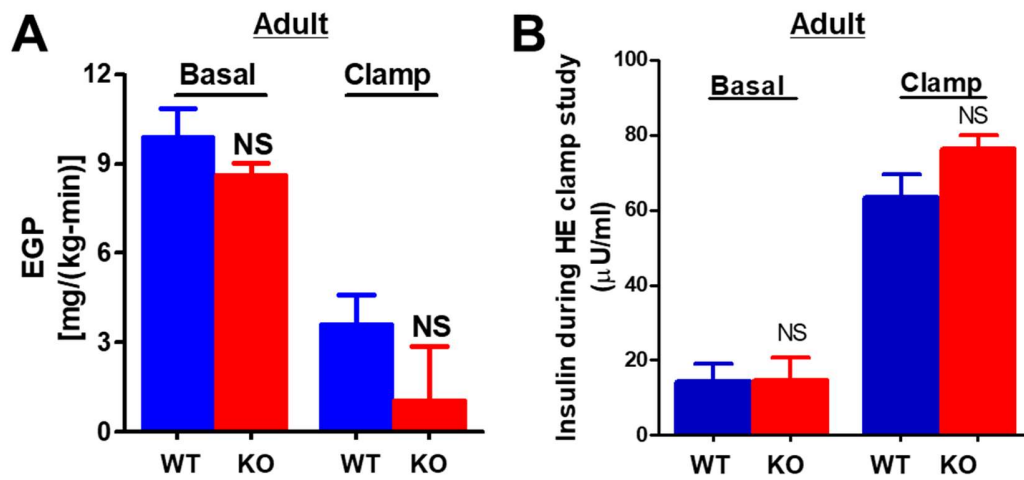
Figures S1 to S4  
Tables S1 to S3



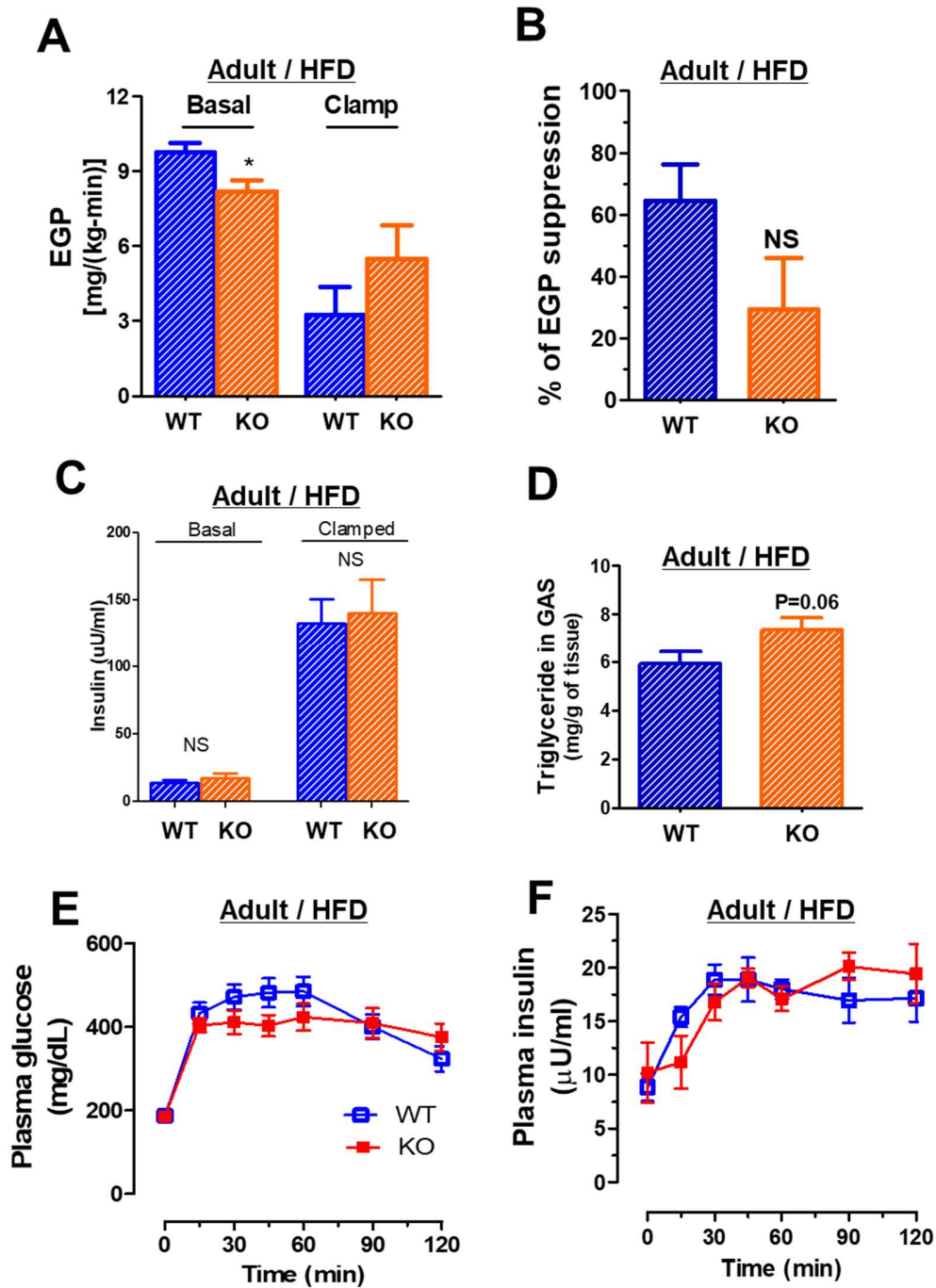
**Fig. S1. Construction of *Jazf1* KO mice. (A)** Genomic structure of the WT *Jazf1* locus surrounding exon 4(E4) and the neo cassette replacing exon 4 in the KO mice and BAMH1 restriction sites that distinguish the WT and KO alleles. Double-headed arrows indicate positions of probes used for Southern blot. **(B)** Correctly targeted ES cell clones were identified by Southern blot analysis using genomic DNA from *Jazf1* +/+ and KO strains were digested by BAMH1 and DNA illustrated in panel A, radiolabelled with <sup>32</sup>P. **(C)** PCR analysis of DNA using the primers illustrated in panel A. **(D)** Body weight curve of WT and *Jazf1* KO mice with 8bp deletion in exon 1. **(E)** Plasma IGF-1 concentration of WT and *Jazf1* KO mice with 8bp deletion in exon 1.



**Fig. S2. TR4 mRNA expression and glucose tolerance test in young animals. (A)** TR4 mRNA expression in liver from WT and KO mice in young (n=5-6 for each group). **(B)** Plasma glucose and **(C)** insulin concentration during IPGTT at age 3 months on regular chow (n=7-8 for each group). All data are mean  $\pm$  SEM. NS, not significant by two tailed student t-test, compared to WT mice.



**Fig. S3. Hyperinsulinemic-euglycemic clamp study on regular chow in adult mice.** Animals were fed on regular chow and overnight fasted before hyperinsulinemic-euglycemic clamp study (n=5-6 for each group). The clamp study performed in 7 month-old *Jazf1* KO mice and age/weight-matched WT mice. **(A)** Basal and insulin suppressed endogenous glucose production (EGP) during the clamp study. **(B)** Plasma insulin concentration during the clamp study. All data are mean  $\pm$  SEM. NS, not significant by two tailed student t-test, compared to WT mice.



**Fig. S4. Hyperinsulinemic-euglycemic clamp study and glucose tolerance test on high-fat diet in adult mice.** Animals were fed on high fat diet for 4 weeks and overnight fasted before hyperinsulinemic-euglycemic clamp study. The clamp study performed in 7 month-old *Jazf1* KO mice and age-matched WT mice (n=9 for each group). **(A)** Basal and insulin suppressed (clamp) endogenous glucose production (EGP), **(B)** percentage suppression of EGP during clamp, **(C)** plasma insulin concentration in *Jazf1* KO mice and WT mice during the clamp study, **(D)** Intramuscular triglyceride content in gastrocnemius (GAS) muscle after the clamp study, **(E)** plasma glucose curve and **(F)** insulin concentration curve during IPGTT. All data are mean  $\pm$  SEM. \*P<0.05 by two tailed student t-test.

**Table S1.** 108 Up-regulated genes in *Jazf1* KO mouse liver compared to WT mouse liver (related to Fig.6A).

	Gene	WT1	WT2	KO1	KO2	Mean fold
1	Cyp2d9	11.05	54.83	3151.32	3750.57	176.82
2	Hsd3b5	5.14	2.03	218.72	247.05	82.04
3	Mup20	208.76	464.61	20577.61	29976.97	81.54
4	Elovl3	25.31	18.82	1125.61	1137.77	52.47
5	Serpina1e	250.00	894.67	7830.81	10280.11	21.41
6	C6	30.83	37.22	325.27	471.03	11.60
7	Cyp7b1	19.40	18.61	146.88	258.02	10.72
8	Mup6	8.22	6.20	39.28	75.72	8.49
9	Aox3	52.93	89.49	518.75	503.22	7.71
10	Bcl6	5.78	4.80	38.01	42.16	7.68
11	Hsd3b2	14.65	14.54	71.54	70.15	4.85
12	Srd5a1	7.71	8.08	37.04	38.55	4.79
13	Slco1a1	21.84	18.66	86.55	98.47	4.62
14	Mup3	3737.44	5007.63	20026.30	19107.42	4.59
15	Ces3a	213.26	278.33	980.90	1205.91	4.47
16	Scp2	532.51	730.54	2645.49	2872.94	4.45
17	C8a	76.44	154.96	419.21	523.58	4.43
18	Serpine2	8.22	10.27	37.11	42.37	4.32
19	Cela1	9.25	32.42	58.92	51.22	3.97
20	Ces2c	18.37	27.94	76.91	96.45	3.82
21	Ugt2b1	283.79	334.10	810.79	1351.57	3.45
22	Ociad2	15.55	28.77	69.22	67.82	3.41
23	Abcg2	15.16	37.01	70.49	67.45	3.24
24	Nudt7	421.64	451.22	1178.26	1630.07	3.20
25	Clk1	17.86	22.36	76.24	46.56	3.18
26	1600002 H07Rik	9.89	9.12	30.69	29.22	3.15
27	2310001 H17Rik	6.94	24.29	33.30	33.19	3.08
28	Sdr9c7	81.45	62.13	137.17	258.87	2.93
29	Pgp	10.79	12.77	35.40	30.76	2.84
30	Vmo1	7.84	10.27	23.82	23.92	2.68
31	Clec2h	6.81	6.78	17.70	18.40	2.66
32	C9	246.66	295.37	543.69	898.95	2.62
33	Arsa	14.52	16.84	39.73	40.94	2.58
34	Cyp2f2	817.45	881.43	1888.02	2450.43	2.54
35	Tmem19	26.21	34.77	76.17	74.87	2.53
36	Chpt1	46.25	86.94	151.36	153.09	2.52
37	Car3	2595.86	3723.20	7941.70	7285.64	2.51
38	Fxn	6.30	9.96	22.25	14.21	2.48

39	Hao1	109.46	125.46	273.90	302.35	2.46
40	Slc41a2	9.89	8.34	21.21	23.07	2.45
41	Ccnh	7.32	10.89	21.66	21.21	2.45
42	Slc22a7	17.22	19.34	45.85	40.41	2.38
43	Enpp2	5.65	11.42	20.76	12.25	2.37
44	Gm6637	7.07	2.35	6.50	8.80	2.34
45	Stbd1	44.07	40.19	87.96	107.06	2.33
46	Mrpl20	7.97	15.22	25.99	21.21	2.33
47	Fn3k	7.32	5.00	13.37	14.16	2.33
48	Cyp2c67	314.24	286.15	633.22	754.88	2.33
49	Qprt	93.01	94.18	201.09	233.26	2.32
50	Sh3glb2	5.40	5.63	14.19	11.24	2.31
51	Fam195a	22.48	25.90	66.16	43.53	2.31
52	Aox1	22.61	29.71	61.98	55.89	2.31
53	Neat1	5.78	1.67	8.59	5.20	2.30
54	Hspb6	6.42	6.31	14.04	15.11	2.29
55	Slc10a2	6.04	6.98	15.16	14.21	2.27
56	Mea1	13.23	23.77	42.12	32.08	2.27
57	Cox7a2	273.38	705.78	973.73	671.04	2.26
58	C8b	278.01	479.73	682.13	975.94	2.24
59	Minos1	26.98	57.70	89.61	65.22	2.23
60	Per1	7.58	5.00	8.89	16.28	2.21
61	Ndufs6	253.86	403.27	709.84	654.82	2.21
62	Snord118	15.80	6.57	21.21	20.10	2.20
63	Fkbp11	19.14	35.03	46.82	68.40	2.20
64	Jtb	21.71	70.73	74.30	67.08	2.19
65	Gstk1	31.86	56.92	101.63	67.18	2.19
66	Hes6	10.54	17.10	24.57	34.79	2.18
67	Aff4	7.71	8.03	17.55	16.54	2.17
68	Fermt2	22.87	96.74	83.78	64.74	2.17
69	Smim4	64.49	68.18	159.50	126.73	2.17
70	Ugt2b35	109.33	80.63	205.20	197.79	2.16
71	Ugdh	46.64	69.79	126.50	112.15	2.16
72	Slc35g1	12.21	10.11	17.77	28.74	2.15
73	Ftcd	34.43	24.86	67.35	58.12	2.15
74	Gm40826	5.01	13.76	15.46	16.60	2.15
75	Ube2a	11.69	33.57	39.43	30.28	2.14
76	Map1lc3a	14.13	14.07	32.11	27.95	2.13
77	Tspan33	11.05	10.89	18.89	27.47	2.12
78	Dad1	16.96	68.28	58.92	51.38	2.11
79	Slc2a1	5.01	3.91	10.53	8.27	2.11
80	Gm38426	13.10	7.51	16.95	21.90	2.11
81	Vegfb	7.71	6.05	14.04	14.37	2.10

82	Sertad1	8.74	8.18	15.53	19.78	2.10
83	Gdf15	5.52	4.54	11.50	9.44	2.08
84	Cyp8b1	128.73	509.54	432.50	408.51	2.08
85	2010320 M18Rik	6.04	14.54	19.56	13.20	2.07
86	Myeov2	75.16	200.15	241.42	186.17	2.07
87	Tpmt	48.43	66.92	115.07	116.34	2.06
88	Lrrc16a	6.81	5.84	14.79	11.24	2.05
89	Gas2	37.51	60.83	99.09	88.50	2.05
90	Oaf	24.41	63.75	71.39	74.55	2.05
91	Keg1	99.56	102.99	209.38	204.04	2.04
92	Fam188a	16.06	41.91	50.18	40.14	2.04
93	Fam213b	12.21	13.14	27.78	23.70	2.04
94	Fmo5	348.54	490.83	808.33	863.53	2.04
95	Mrpl34	26.34	30.75	65.34	49.05	2.04
96	Guk1	7.97	29.92	25.46	26.25	2.04
97	Rnaseh2c	16.32	16.78	35.99	31.29	2.04
98	Cdh1	14.65	22.83	33.23	40.83	2.03
99	Rarres1	20.43	41.23	47.64	71.00	2.03
100	Anapc16	7.32	14.49	19.56	19.99	2.03
101	Prmt1	16.32	25.49	41.97	37.38	2.02
102	Ndufa13	289.70	310.96	652.56	552.05	2.01
103	Gpr155	20.17	27.52	48.84	44.06	2.01
104	Clk4	9.25	17.62	26.29	20.57	2.00
105	Tiam2	15.03	7.87	13.14	24.60	2.00
106	Car1	9.12	13.08	20.09	23.49	2.00
107	Alas2	73.23	30.70	84.90	87.02	2.00
108	Sirt3	13.10	36.75	40.55	32.98	2.00



**Table S2.** Gene ontology (GO) terms enriched in the 108 up-regulated genes from *Jazf1* KO mouse liver (related to Fig.6B).

GO ID	GO Term	P value
GO:0035634	response to stilbenoid	0.00001
GO:0072523	purine-containing compound catabolic process	0.00158
GO:0006957	complement activation, alternative pathway	0.00004
GO:0010039	response to iron ion	0.00116
GO:0033559	unsaturated fatty acid metabolic process	0.00023
GO:0019369	arachidonic acid metabolic process	0.00307
GO:0035383	thioester metabolic process	0.00105
GO:0006637	acyl-CoA metabolic process	0.00105
GO:0033574	response to testosterone	0.00350
GO:0060416	response to growth hormone	0.00055
GO:0048512	circadian behavior	0.00053
GO:0045475	locomotor rhythm	0.00055
GO:1905953	negative regulation of lipid localization	0.00242
GO:0010883	regulation of lipid storage	0.00280
GO:0010888	negative regulation of lipid storage	0.00047
GO:0045912	negative regulation of carbohydrate metabolic process	0.00036
GO:0031649	heat generation	0.00071
GO:0009060	aerobic respiration	0.00006
GO:0010677	negative regulation of cellular carbohydrate metabolic process	0.00027
GO:0051055	negative regulation of lipid biosynthetic process	0.00381
GO:0070584	mitochondrion morphogenesis	0.00004
GO:0010907	positive regulation of glucose metabolic process	0.00293
GO:0006094	gluconeogenesis	0.00113
GO:0006111	regulation of gluconeogenesis	0.00032
GO:0045721	negative regulation of gluconeogenesis	0.00002
GO:0061179	negative regulation of insulin secretion involved in cellular response to glucose stimulus	0.00039
GO:0046676	negative regulation of insulin secretion	0.00413

**Table S3.** Sequence for RT-PCR primers used in this study.

<b>Gene</b>	<b>Forward primer (5' to 3')</b>	<b>Reverse primer (5' to 3')</b>
Tr4	CATATTCACCACCTCGGACAAC	TGACGCCACAGACCACA
Igf-1	GGACCAGAGACCCTTTGCGGGG	GGCTGCTTTTGTAGGCTTCAGTGG
Igf-1r	ATGACCCAGGGGAGGCTGTGTA	CTTCAGCTTTGCAGGTGCACG
Igfbp3	TGCCGCCCTTCCAAAGGCAG	GGCTCTGCACGCTGAGGCAA
Ghr	TTAGTTTGACCGGGATTTCGTGG	AATCTTTGGAAGTGGGACTGGG
JAZF1	ATCGAGCACATCGAGGACAAC	GAGCTTCGGCTGAATCTTCTT
$\beta$ - actin	TGTGCCCATCTACGAGGGGTATGC	GGTACATGGTGGTGCCGCCAGACA

Testicular receptors 4 (Tr4), Insulin-like growth factor 1 (Igf-1), IGF-1 receptor (Igf-1r), Insulin-like growth factor-binding protein 3 (Igfbp3), Growth hormone receptor (Ghr)