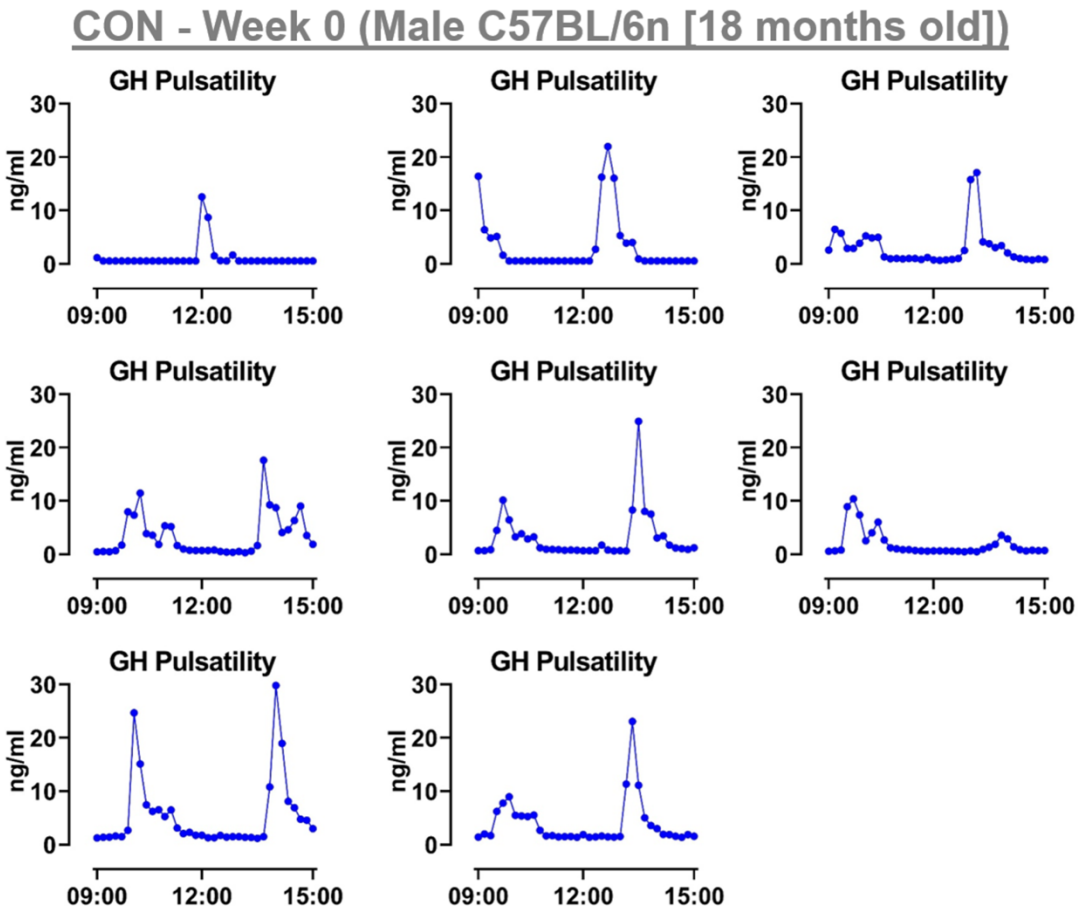
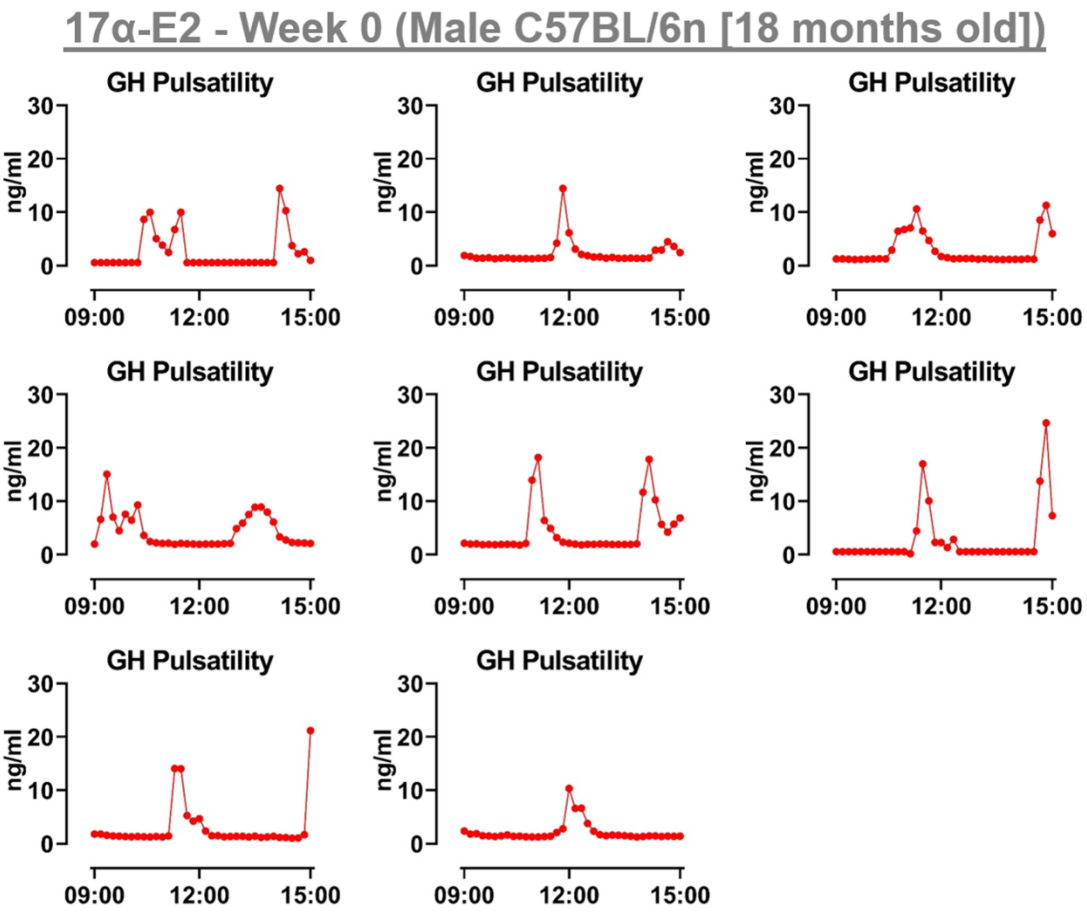
17α-estradiol modulates IGF1 and hepatic gene expression in a sex-specific manner

Supplemental Material

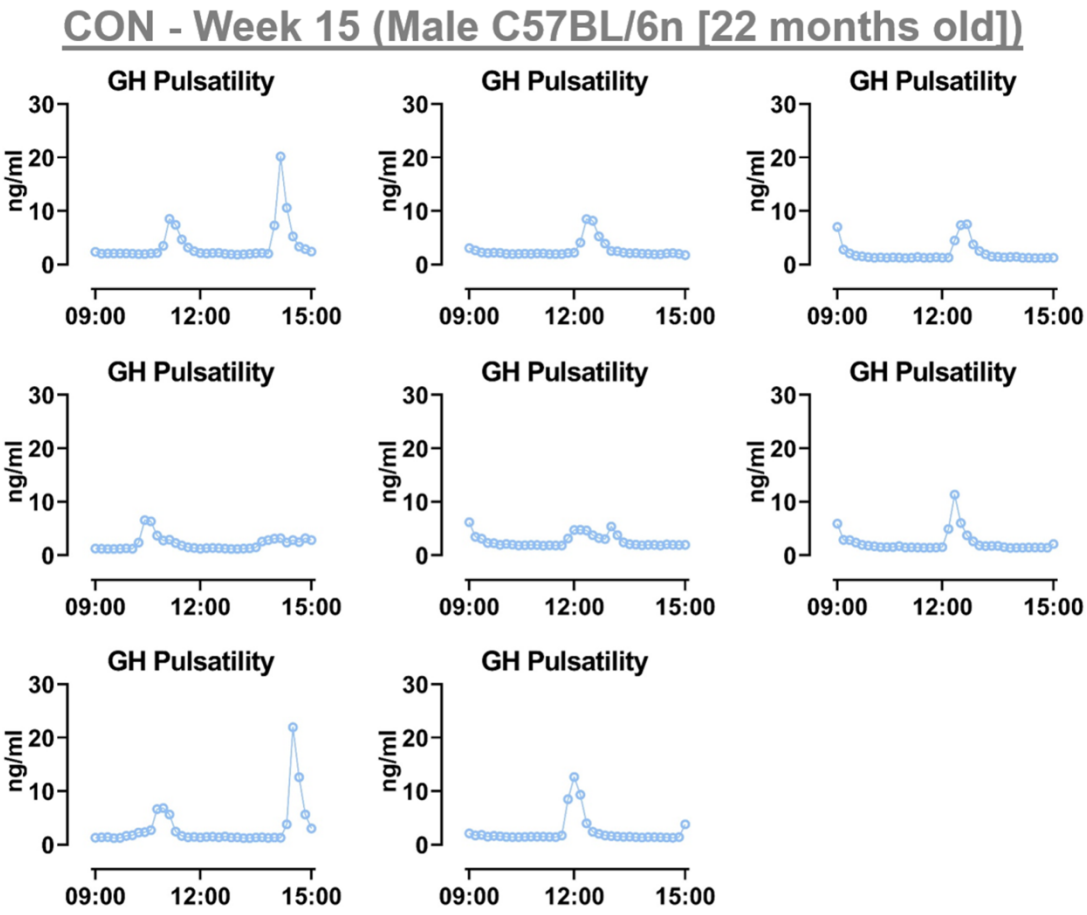
eFigure 1: Individual GH pulse patterns over a 6-hour period in male C57BL6/n control (CON) mice at baseline. n=8/group



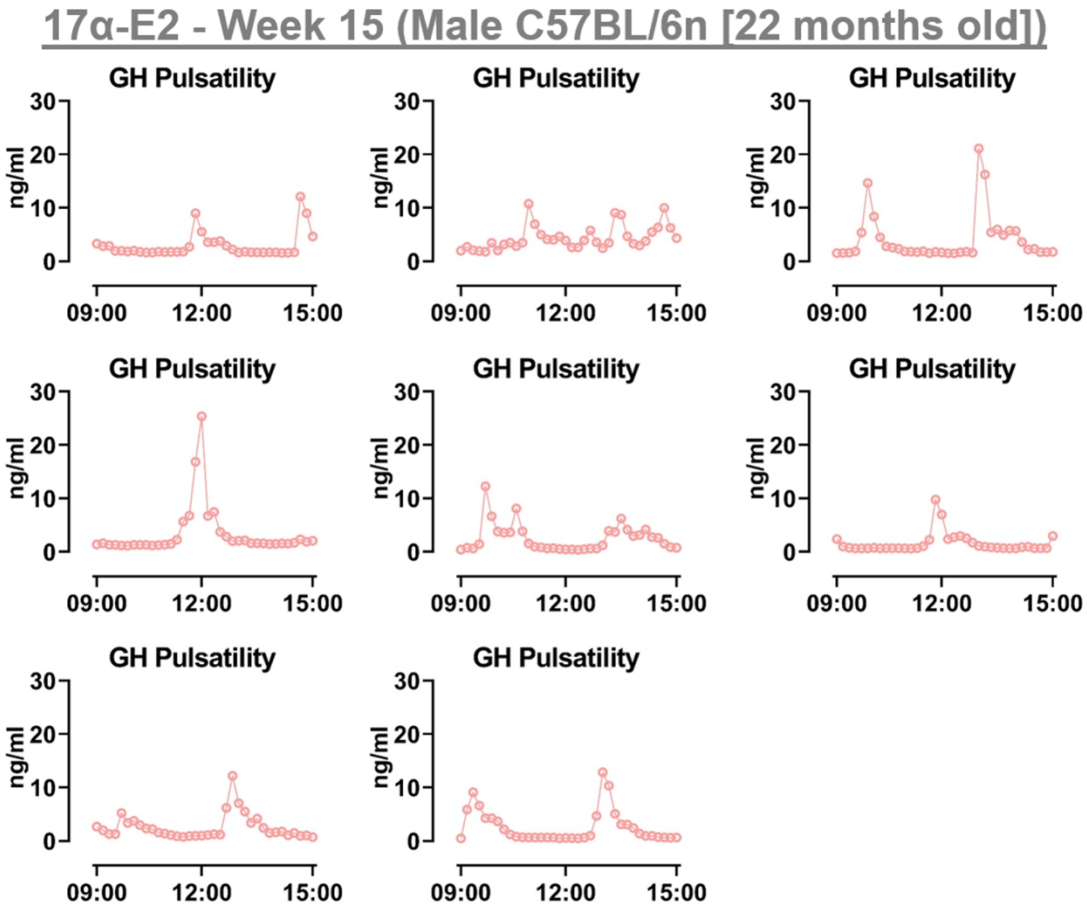
eFigure 2: Individual GH pulse patterns over a 6-hour period in male C57BL6/n mice at baseline prior to 17α-E2 treatment. n=8/group



eFigure 3: Individual GH pulse patterns over a 6-hour period in male C57BL6/n CON mice following the 15 week treatment period. n=8/group



eFigure 4: Individual GH pulse patterns over a 6-hour period in male C57BL6/n mice following 15 weeks of 17α-E2 treatment. n=8/group



eTable 1 – Differentially expressed genes by 17 α estradiol in normal control male mice

Gene	logFC	logCPM	PValue	FDR
Col16a1	3.54	2.94	2.68E-26	3.85E-22
Spon1	5.38	2.32	7.66E-19	5.50E-15
Scd3	8.10	1.91	1.08E-17	5.17E-14
Aff3	3.74	0.55	9.59E-16	3.44E-12
Mmp27	7.49	1.00	1.37E-13	3.94E-10
Med12l	4.01	0.09	2.89E-13	6.92E-10
Arhgap10	2.99	1.25	4.29E-13	8.80E-10
Abcb1a	2.01	3.83	8.79E-13	1.58E-09
Ppard	-2.35	3.54	4.56E-12	7.27E-09
Bnc2	5.38	-0.90	1.32E-11	1.90E-08
Tmem200b	2.57	2.03	4.21E-11	5.49E-08
Pik3c2g	1.18	4.36	1.14E-10	1.36E-07
Osbpl3	3.18	4.01	2.08E-09	2.29E-06
Lmod3	5.16	0.76	2.36E-09	2.42E-06
Serpina7	-2.23	6.72	4.75E-09	4.54E-06
S100g	6.63	1.33	1.24E-08	1.11E-05
Apoc2	1.53	9.32	1.66E-08	1.40E-05
Smtnl2	2.20	0.95	2.68E-08	2.14E-05
Ttc3	0.79	4.76	5.86E-08	4.43E-05
Gpcpd1	1.65	6.08	1.66E-07	1.19E-04
Tspan8	2.98	1.98	1.79E-07	1.21E-04
Insc	-1.54	3.67	1.89E-07	1.21E-04
Prkd1	3.33	-1.03	1.94E-07	1.21E-04
Adam19	2.87	1.58	2.75E-07	1.65E-04
Slc39a4	-1.54	5.65	3.01E-07	1.73E-04
Mme	3.43	4.20	3.45E-07	1.91E-04
Aldh1b1	-1.29	6.06	3.98E-07	2.12E-04
Mfge8	1.56	4.03	5.95E-07	3.05E-04
Nnmt	-3.08	5.75	6.79E-07	3.36E-04
Slc40a1	1.02	7.16	7.76E-07	3.71E-04
Scnn1a	-1.05	5.22	1.38E-06	0.001
Cuedc1	1.58	2.21	3.49E-06	0.002
Pkd2	2.31	3.41	3.81E-06	0.002
Efna3	-2.50	1.11	3.82E-06	0.002
Tmem56	0.89	7.55	5.00E-06	0.002
Nucb2	1.84	1.49	5.56E-06	0.002
H19	5.09	2.78	5.70E-06	0.002
Isyna1	2.71	4.74	5.82E-06	0.002

Tubb4b	-1.19	6.31	6.13E-06	0.002
Ada	2.09	0.78	7.30E-06	0.003
Cd63	2.03	3.50	7.33E-06	0.003
Lsr	-0.76	7.07	8.22E-06	0.003
Slc35f2	3.39	-1.12	8.89E-06	0.003
Tubb2a	-2.00	6.10	9.45E-06	0.003
Cyp2a22	2.89	7.38	1.02E-05	0.003
Dnahc11	2.37	0.90	1.06E-05	0.003
Ier5	-1.61	2.67	1.07E-05	0.003
Syne4	-2.64	1.27	1.14E-05	0.003
E130307A14Rik	1.50	0.13	1.20E-05	0.004
Rundc3b	1.74	-0.31	1.27E-05	0.004
Tbc1d4	1.21	1.98	1.85E-05	0.005
Pak1	2.23	1.61	1.97E-05	0.005
Lima1	0.70	5.83	2.35E-05	0.006
BC089597	-1.42	6.61	2.52E-05	0.007
St5	-1.26	5.11	2.53E-05	0.007
D16Ertd472e	0.91	2.82	2.56E-05	0.007
Snrpa	-0.73	4.79	3.03E-05	0.008
Pnrc1	-1.22	6.37	3.04E-05	0.008
Galc	0.64	2.81	3.09E-05	0.008
Crip2	-1.16	5.99	3.21E-05	0.008
Hif1a	0.65	4.89	3.36E-05	0.008
Fam126b	0.98	4.26	3.38E-05	0.008
Sh3bgrl2	0.60	5.05	3.47E-05	0.008
Tff3	4.13	2.85	3.62E-05	0.008
Zfp704	0.83	3.88	3.85E-05	0.009
Nelfa	-0.67	3.47	3.98E-05	0.009
Slc4a4	0.74	6.83	3.99E-05	0.009
Plekhg5	0.94	3.49	4.05E-05	0.009
Npas2	-3.28	1.77	4.35E-05	0.009
Thtpa	-0.52	4.72	4.99E-05	0.010
Senp6	0.51	5.16	5.05E-05	0.010
Rasl11b	1.45	2.02	5.47E-05	0.011
Lpar1	1.78	-0.05	5.68E-05	0.011
Proser2	-0.81	4.72	5.75E-05	0.011
Gale	-1.50	3.87	5.99E-05	0.011
6430573F11Rik	1.38	1.41	6.01E-05	0.011
Nceh1	0.93	4.86	6.11E-05	0.011
Traf3ip2	0.98	2.15	6.23E-05	0.011

Tceal5	4.00	-1.97	6.32E-05	0.011
Tubb6	-1.19	3.28	6.70E-05	0.012
Tiam1	1.66	0.21	6.77E-05	0.012
Med24	-0.64	4.08	7.03E-05	0.012
Cry1	-1.37	3.03	7.05E-05	0.012
Agpat2	-0.75	7.85	7.25E-05	0.012
Hist2h2be	-0.95	1.11	7.56E-05	0.013
Rybp	0.85	2.63	8.72E-05	0.015
Elovl3	-2.19	5.65	8.94E-05	0.015
Calml4	1.79	-0.05	8.99E-05	0.015
Adam12	1.90	-1.32	9.31E-05	0.015
Ckmt1	3.69	-1.64	1.02E-04	0.016
Myo6	0.52	5.59	1.02E-04	0.016
Nfil3	-1.52	4.77	1.03E-04	0.016
Tet2	0.80	3.58	1.09E-04	0.017
Sgsm1	-1.25	1.79	1.10E-04	0.017
Hist2h3c2	-1.46	1.01	1.11E-04	0.017
Fgfr4	-0.57	5.94	1.11E-04	0.017
Serpina12	2.58	4.10	1.18E-04	0.017
Dbndd2	-0.74	3.46	1.18E-04	0.017
Diap2	0.61	3.87	1.20E-04	0.017
Tuba4a	-0.95	7.30	1.21E-04	0.017
Dcun1d4	0.57	5.36	1.23E-04	0.017
Vil1	3.59	0.09	1.23E-04	0.017
Large	0.82	2.34	1.25E-04	0.017
Tmem9	0.52	4.72	1.28E-04	0.018
Hist2h3c1	-1.19	2.73	1.29E-04	0.018
Parp16	-1.32	5.83	1.32E-04	0.018
Arg2	2.69	-1.49	1.37E-04	0.018
Morc4	1.25	1.71	1.39E-04	0.018
Tbkbp1	-0.71	3.59	1.40E-04	0.018
Plcb4	1.51	-0.76	1.45E-04	0.019
Ctr9	0.42	4.84	1.45E-04	0.019
Rgs7	1.83	-1.09	1.45E-04	0.019
Sptssa	0.58	5.48	1.46E-04	0.019
Mpst	-0.66	6.64	1.48E-04	0.019
Krt4	4.46	-0.64	1.67E-04	0.021
C1rb	-1.62	0.08	1.77E-04	0.022
Fgfr2	0.67	5.44	1.78E-04	0.022
Gdf15	1.75	3.75	1.79E-04	0.022

Cyp2g1	2.19	0.79	1.86E-04	0.022
Uap1l1	1.65	2.70	1.87E-04	0.022
Mrps12	-0.65	4.53	1.94E-04	0.023
Slco2a1	0.87	5.22	1.95E-04	0.023
Gm15441	3.19	0.06	1.97E-04	0.023
Dnmt3b	-1.25	1.64	2.08E-04	0.024
Lrrtm3	4.00	0.51	2.09E-04	0.024
Sigirr	-0.58	4.87	2.10E-04	0.024
Irf5	-1.19	2.59	2.23E-04	0.025
Spsb4	-1.29	3.10	2.27E-04	0.025
Chmp4c	1.64	-0.68	2.38E-04	0.026
Alkbh7	-0.76	4.06	2.46E-04	0.027
Ppa1	-0.60	7.22	2.47E-04	0.027
Hkdc1	3.64	-0.24	2.50E-04	0.027
Tmtc2	0.79	3.63	2.68E-04	0.029
Gfod2	-0.77	3.54	2.83E-04	0.030
Fhdc1	2.71	-1.89	2.85E-04	0.030
2010003K11Rik	-1.24	5.31	2.95E-04	0.031
Rps13	-0.78	6.77	3.00E-04	0.031
C4a	1.21	6.85	3.03E-04	0.031
Josd2	-0.71	4.86	3.04E-04	0.031
Copg1	-0.49	6.40	3.13E-04	0.032
Wnk4	1.49	1.57	3.16E-04	0.032
Gm15348	-3.44	0.29	3.24E-04	0.033
Cd36	1.04	7.46	3.31E-04	0.033
Ndrg1	-1.44	4.59	3.48E-04	0.035
Pnp	-0.71	6.60	3.67E-04	0.036
Peo1	0.51	5.16	3.68E-04	0.036
Sdhaf1	-0.64	4.35	3.70E-04	0.036
Tubb5	-0.67	5.94	3.71E-04	0.036
Rev3l	0.69	3.67	4.04E-04	0.039
Tubb2b	-2.31	-0.12	4.05E-04	0.039
Sparcl1	2.15	2.32	4.11E-04	0.039
Saa2	-5.07	10.10	4.13E-04	0.039
Loxl4	-1.74	-0.26	4.17E-04	0.039
Cyp26a1	-1.82	5.39	4.28E-04	0.040
Dpp9	-0.67	5.77	4.43E-04	0.041
4930404H11Rik	7.07	-0.13	4.52E-04	0.042
Pik3ap1	0.63	5.60	4.68E-04	0.043
Map3k5	0.57	5.16	4.72E-04	0.043

Adra1b	-0.72	6.25	4.77E-04	0.043
Slc13a3	-1.91	4.38	4.98E-04	0.045
Chka	-1.47	5.57	5.20E-04	0.046
Mios	0.76	3.54	5.21E-04	0.046
Atp11a	-1.26	5.65	5.32E-04	0.046
2510049J12Rik	-0.47	4.55	5.33E-04	0.046
Slc35g1	0.72	4.60	5.33E-04	0.046
Tmx4	0.57	3.87	5.39E-04	0.047
Abtb2	-0.93	4.03	5.53E-04	0.048
Muc2	4.99	-1.13	5.61E-04	0.048
Zfp707	-0.48	4.94	5.71E-04	0.049
Sigmar1	-0.61	6.98	5.85E-04	0.049

eTable 2 – Differentially expressed genes by 17 α estradiol in growth hormone receptor knockout male mice

Gene	logFC	logCPM	PValue	FDR
Csrp3	3.27	4.31	2.33E-10	3.35E-06
Slc22a26	3.42	4.81	2.56E-08	1.84E-04
Parp16	-1.82	5.83	2.07E-07	0.001
Pmm1	1.29	2.72	1.07E-06	0.004
Il13ra2	5.60	-2.21	2.06E-06	0.006
Sult3a1	4.36	7.09	4.79E-06	0.011
Paqr9	1.55	6.88	5.40E-06	0.011
Gm4794	5.51	5.19	1.11E-05	0.020
Agtr1a	0.65	5.99	1.58E-05	0.025
Tnfaip8l1	1.02	4.92	2.01E-05	0.026
Adck5	1.02	4.53	2.02E-05	0.026
Col27a1	-1.36	5.75	2.20E-05	0.026
Fetub	1.04	9.22	2.57E-05	0.028
Spon1	2.22	2.32	3.36E-05	0.034
AW549542	1.56	3.62	5.14E-05	0.049

eTable 3 – Differentially expressed genes by 17 α estradiol in normal control female mice

Gene	logFC	logCPM	PValue	FDR
Tspan8	4.57	1.98	7.10E-14	8.33E-10
Tff3	9.42	2.85	1.16E-13	8.33E-10
Apoc2	1.78	9.32	5.59E-11	2.67E-07
Col16a1	1.89	2.94	1.53E-09	5.47E-06
Tmem200b	2.27	2.03	3.74E-09	1.07E-05
Osbpl3	3.08	4.01	6.40E-09	1.53E-05
Marveld3	2.60	1.40	1.52E-08	3.12E-05
Gpr64	2.79	0.87	4.49E-08	8.06E-05
Treh	2.97	0.74	9.96E-08	1.59E-04
Gria3	3.80	-0.49	1.18E-07	1.69E-04
3930402G23Rik	5.23	0.29	1.48E-07	1.93E-04
Gpcpd1	1.64	6.08	1.91E-07	2.29E-04
Bnc2	3.67	-0.90	4.12E-07	4.55E-04
Spink3	7.67	1.31	8.51E-07	0.001
Aldh1l1	-0.91	10.27	9.53E-07	0.001
Mup20	3.15	7.16	1.53E-06	0.001
Sult1e1	3.19	6.20	1.72E-06	0.001
Adcy1	4.99	1.52	2.27E-06	0.002
Lepr	3.26	2.91	2.34E-06	0.002
Serpina12	3.25	4.10	2.54E-06	0.002
Rgs7	2.32	-1.09	2.82E-06	0.002
Cyp4a31	3.56	3.81	2.90E-06	0.002
Lor	2.16	-0.20	3.03E-06	0.002
Ddx3y	4.63	4.38	3.08E-06	0.002
Scd3	3.69	1.91	3.10E-06	0.002
Defb1	3.94	0.79	3.26E-06	0.002
Hspb8	-1.06	7.65	3.30E-06	0.002
Adra1b	-0.95	6.25	3.47E-06	0.002
Mtnr1a	2.06	1.84	4.14E-06	0.002
Serpine1	3.05	2.14	4.26E-06	0.002
Rgs3	1.66	3.35	4.33E-06	0.002
Spon1	2.45	2.32	4.39E-06	0.002
Uty	4.89	2.09	5.66E-06	0.002
Scnn1a	-0.99	5.22	5.89E-06	0.002
Gm4841	-3.31	0.12	5.91E-06	0.002
Cxcl14	3.64	1.41	8.68E-06	0.003
Adh4	-0.89	6.45	9.08E-06	0.004
Tceal5	4.69	-1.97	1.05E-05	0.004

Cyp2d12	3.85	1.70	1.13E-05	0.004
Cntnap1	1.37	2.32	1.26E-05	0.005
Gcat	-0.68	6.61	1.31E-05	0.005
Atp11a	-1.59	5.65	1.40E-05	0.005
Paox	-0.95	4.67	1.66E-05	0.006
Cdh1	2.39	3.36	1.72E-05	0.006
S100a8	3.47	2.61	1.83E-05	0.006
Aff3	1.82	0.55	1.95E-05	0.006
Gla	-0.78	2.67	2.04E-05	0.006
Eif2s3y	4.40	4.47	2.08E-05	0.006
Mfge8	1.32	4.03	2.30E-05	0.007
Omd	2.24	1.31	2.31E-05	0.007
Ehhadh	1.41	8.75	2.48E-05	0.007
Nid1	1.46	3.85	2.60E-05	0.007
Irgm1	-1.31	5.34	2.61E-05	0.007
Ccdc149	1.94	0.42	2.68E-05	0.007
Stat5a	0.77	4.73	2.72E-05	0.007
Zbtb21	-0.83	3.31	2.79E-05	0.007
Isyna1	2.48	4.74	2.83E-05	0.007
Stat1	-1.57	5.68	3.28E-05	0.008
Tmem56	0.80	7.55	3.29E-05	0.008
Rnf32	1.97	-1.94	3.49E-05	0.008
Qpct	0.92	2.72	3.61E-05	0.008
Golm1	1.34	1.46	3.96E-05	0.009
S100a9	3.15	2.84	4.29E-05	0.010
Apol9b	-1.44	6.13	4.38E-05	0.010
Gm15441	3.56	0.06	4.51E-05	0.010
B930025P03Rik	2.97	2.45	4.77E-05	0.010
Lmod3	3.17	0.76	4.79E-05	0.010
B230208H11Rik	1.25	0.18	4.93E-05	0.010
Igtp	-2.24	5.34	4.94E-05	0.010
Abcg8	0.78	7.36	5.05E-05	0.010
Psme2	-0.65	6.42	5.32E-05	0.011
Rgs12	-0.87	3.05	5.77E-05	0.011
Krt4	4.88	-0.64	5.92E-05	0.012
Ntn3	-1.22	1.78	6.65E-05	0.013
Cd177	3.59	-0.93	6.68E-05	0.013
Adh1	-0.69	10.76	7.31E-05	0.014
Ccdc120	1.61	1.43	8.56E-05	0.016
B930041F14Rik	1.80	0.91	8.78E-05	0.016

Acot1	2.52	4.69	9.19E-05	0.017
Cpne2	0.97	2.50	9.31E-05	0.017
Tor1b	0.66	5.44	1.05E-04	0.019
Gm12250	-2.98	2.27	1.08E-04	0.019
4833420G17Rik	0.84	3.23	1.10E-04	0.019
Gpc1	1.99	2.79	1.13E-04	0.019
Gbp6	-2.16	2.13	1.16E-04	0.019
Sel1l3	1.19	3.49	1.17E-04	0.019
Abcg5	0.76	6.79	1.17E-04	0.019
Rasal1	2.75	-1.04	1.27E-04	0.021
Slc6a12	-0.59	6.80	1.33E-04	0.021
Dpysl4	3.09	-2.33	1.35E-04	0.021
Kif12	2.10	-0.67	1.38E-04	0.022
Gpx3	1.64	3.18	1.48E-04	0.023
Hn1l	-0.71	4.37	1.67E-04	0.026
Spp1	1.66	5.30	1.67E-04	0.026
Cblb	0.62	3.56	1.86E-04	0.028
Zfp773	-1.54	-1.34	1.92E-04	0.029
Hif3a	2.00	-2.14	2.06E-04	0.031
Scly	-0.52	6.81	2.12E-04	0.031
Gbp8	-2.17	1.59	2.22E-04	0.032
Isg15	-1.30	2.82	2.24E-04	0.032
Sdf2l1	-1.39	4.92	2.37E-04	0.034
Gbp3	-1.91	3.01	2.48E-04	0.035
Fgf21	2.22	3.76	2.55E-04	0.035
Tmx2	-0.52	5.46	2.56E-04	0.035
Ints1	-0.58	4.86	2.57E-04	0.035
Hsdl2	0.73	6.51	2.61E-04	0.035
Apol9a	-1.50	5.19	2.73E-04	0.037
Plekhb1	-0.73	5.80	2.84E-04	0.037
Elovl2	0.73	8.62	2.87E-04	0.037
Psat1	2.23	-0.52	2.96E-04	0.037
Sprn	1.38	-0.07	2.96E-04	0.037
F3	0.93	2.43	2.98E-04	0.037
Traf3ip2	0.88	2.15	2.99E-04	0.037
Adam11	-1.07	6.62	2.99E-04	0.037
Gpr56	1.49	1.53	3.01E-04	0.037
Ppa1	-0.60	7.22	3.02E-04	0.037
Fbp2	2.17	-1.10	3.12E-04	0.038
Pdia4	-0.78	7.51	3.19E-04	0.039

Tnfrsf14	-0.82	2.79	3.24E-04	0.039
Iqsec1	-0.55	5.74	3.33E-04	0.040
Bik	1.26	3.02	3.43E-04	0.041
Tmem64	0.63	5.27	3.47E-04	0.041
Fam83a	3.40	0.34	3.48E-04	0.041
Ugt2b37	1.98	0.55	3.54E-04	0.041
Gbp1	-1.94	3.32	3.58E-04	0.041
Plk2	1.20	3.09	3.59E-04	0.041
Cml1	-0.81	7.44	3.64E-04	0.041
BC016579	2.98	-2.20	3.65E-04	0.041
Phlda3	2.01	1.33	3.70E-04	0.041
Atg7	-0.59	5.83	3.71E-04	0.041
Peg3	2.21	1.89	3.78E-04	0.041
Sspo	-1.00	1.82	3.83E-04	0.041
Car5a	-0.81	5.68	3.86E-04	0.041
Art4	1.17	0.67	3.87E-04	0.041
Srr	-0.55	5.62	3.91E-04	0.041
Rn45s	-1.49	12.76	3.93E-04	0.041
Ngp	4.45	1.58	4.07E-04	0.042
Rbm14	-0.61	4.45	4.10E-04	0.042
Tmem63a	-0.49	4.28	4.16E-04	0.042
Adamts14	1.22	1.34	4.18E-04	0.042
Adssl1	-0.63	5.26	4.21E-04	0.042
Gpr98	1.45	2.42	4.22E-04	0.042
Baiap2l1	0.79	4.79	4.23E-04	0.042
Gsto2	-1.59	-0.11	4.34E-04	0.043
Plscr1	0.89	4.02	4.39E-04	0.043
2610019F03Rik	0.65	3.64	4.42E-04	0.043
4930539E08Rik	1.73	-0.08	4.45E-04	0.043
Limd2	-0.64	5.55	4.46E-04	0.043
Snai3	3.27	-2.23	4.49E-04	0.043
Htra3	1.56	1.20	4.54E-04	0.043
Rad51d	0.44	4.26	4.60E-04	0.044
Snhg5	0.95	2.35	4.70E-04	0.044
Psmb9	-1.42	4.66	4.83E-04	0.045
Ethe1	-0.91	6.47	4.83E-04	0.045
Fut1	2.35	-0.25	4.91E-04	0.045
Mcu	-0.92	4.84	5.02E-04	0.046
Baat	-0.47	7.92	5.35E-04	0.049
Cirbp	0.79	5.36	5.35E-04	0.049

St3gal5	1.26	7.03	5.41E-04	0.049
Qdpr	-0.62	8.76	5.43E-04	0.049

eTable 4 – Differentially expressed genes by 17 α estradiol in growth hormone receptor knockout female mice

Gene	logFC	logCPM	PValue	FDR
Nrap	-4.58	0.95	1.41E-09	2.03E-05
Ankrd23	-2.93	2.60	1.02E-08	6.62E-05
Mylpf	-4.89	1.71	1.77E-08	6.62E-05
Atp2a1	-6.98	3.30	1.84E-08	6.62E-05
Pygm	-3.53	1.99	6.52E-08	1.87E-04
Cox8b	-6.04	1.07	9.73E-08	2.33E-04
Atp1a2	-5.07	1.79	1.45E-07	2.98E-04
Pgam2	-3.18	0.77	3.39E-07	0.001
Xirp1	-7.22	-0.72	4.78E-07	0.001
Fabp3	-6.21	1.27	5.28E-07	0.001
Des	-2.51	3.24	1.05E-06	0.001
Slc25a4	-2.61	3.47	1.31E-06	0.002
Ttn	-7.67	2.63	1.37E-06	0.002
Ak1	-4.82	0.16	1.77E-06	0.002
Klhl41	-4.17	-0.50	2.58E-06	0.002
Tmem38a	-2.23	1.76	2.70E-06	0.002
Neb	-2.63	3.00	2.89E-06	0.002
Tnni2	-7.75	2.72	3.16E-06	0.003
9530077C05Rik	-4.77	0.57	3.98E-06	0.003
Hhex	-1.12	5.87	3.99E-06	0.003
Slc41a2	-2.47	5.16	5.21E-06	0.004
Mybpc2	-4.64	-0.23	6.77E-06	0.004
Dcstamp	1.49	0.25	7.81E-06	0.005
Rpl3l	-3.55	-0.26	1.42E-05	0.008
Lmcd1	-3.00	-0.67	1.42E-05	0.008
Il15ra	0.84	4.63	1.93E-05	0.011
Tpm1	-1.19	5.42	1.98E-05	0.011
Proser2	-0.85	4.72	2.31E-05	0.012
Myom1	-3.62	1.11	2.84E-05	0.014
Npas2	-3.38	1.77	2.96E-05	0.014
Asap2	-1.41	3.44	3.51E-05	0.016
Gadd45g	-3.26	4.63	3.82E-05	0.017
Cacna1s	-5.51	-0.08	3.90E-05	0.017
Cryab	-1.62	2.11	4.62E-05	0.019
Col15a1	-1.59	3.33	5.42E-05	0.022
Eno3	-1.63	3.01	5.47E-05	0.022
Pkia	-2.62	0.11	6.13E-05	0.024
H19	-4.23	2.78	7.30E-05	0.027

Flnc	-4.96	0.16	7.47E-05	0.027
Nexn	-2.61	-0.36	7.53E-05	0.027
Hk2	-2.34	0.92	7.87E-05	0.028
Me3	-3.05	-1.80	1.00E-04	0.034
Igdcc4	-5.14	1.21	1.07E-04	0.036
Saa2	-5.71	10.10	1.12E-04	0.037
Shisa2	-2.33	-1.27	1.33E-04	0.042

eTable 5 – Regulated KEGG pathways by 17 α estradiol in normal control male mice

Pathway	stat.mean	p.val	set.size
mmu03040 Spliceosome	-2.843	0.003	117
mmu03050 Proteasome	-2.566	0.007	41
mmu00190 Oxidative phosphorylation	-2.268	0.012	106
mmu00100 Steroid biosynthesis	-2.211	0.018	15
mmu00900 Terpenoid backbone biosynthesis	-2.171	0.020	14
mmu04070 Phosphatidylinositol signaling system	2.065	0.020	67
mmu00240 Pyrimidine metabolism	-1.978	0.025	92
mmu04141 Protein processing in endoplasmic reticulum	-1.952	0.026	151
mmu04012 ErbB signaling pathway	1.942	0.027	75
mmu03030 DNA replication	-1.951	0.028	35
mmu04976 Bile secretion	1.901	0.030	61
mmu04122 Sulfur relay system	-2.047	0.031	10
mmu04614 Renin-angiotensin system	2.020	0.031	12
mmu02010 ABC transporters	1.781	0.039	40
mmu00250 Alanine, aspartate and glutamate metabolism	-1.742	0.044	28
mmu04612 Antigen processing and presentation	-1.705	0.046	57
mmu00140 Steroid hormone biosynthesis	1.671	0.050	40

eTable 6 – Regulated KEGG pathways by 17 α estradiol in growth hormone receptor knockout (GHRKO) control male mice

Pathway	stat.mean	p.val	set.size
mmu03030 DNA replication	-3.567	3.34E-04	35
mmu04110 Cell cycle	-3.431	3.60E-04	117
mmu04672 Intestinal immune network for IgA production	2.303	0.012	31
mmu04270 Vascular smooth muscle contraction	2.232	0.013	91
mmu04630 Jak-STAT signaling pathway	2.201	0.015	101
mmu04640 Hematopoietic cell lineage	2.155	0.017	65
mmu04514 Cell adhesion molecules (CAMs)	1.997	0.024	100
mmu03420 Nucleotide excision repair	-1.916	0.030	43
mmu00590 Arachidonic acid metabolism	1.856	0.033	61
mmu00500 Starch and sucrose metabolism	-1.860	0.033	40
mmu04660 T cell receptor signaling pathway	1.839	0.034	95
mmu03440 Homologous recombination	-1.871	0.034	25
mmu00230 Purine metabolism	-1.797	0.037	141
mmu04020 Calcium signaling pathway	1.778	0.038	116
mmu04610 Complement and coagulation cascades	1.752	0.041	68
mmu00900 Terpenoid backbone biosynthesis	-1.818	0.041	14
mmu04973 Carbohydrate digestion and absorption	-1.732	0.044	32
mmu00100 Steroid biosynthesis	-1.766	0.045	15
mmu00480 Glutathione metabolism	-1.711	0.045	49
mmu04114 Oocyte meiosis	-1.682	0.047	91
mmu00380 Tryptophan metabolism	-1.680	0.049	33

eTable 7 – Regulated KEGG pathways by 17 α estradiol in normal control female mice

Pathway	stat.mean	p.val	set.size
mmu04612 Antigen processing and presentation	-5.098	7.30E-07	57
mmu00980 Metabolism of xenobiotics by cytochrome P450	-3.372	4.94E-04	66
mmu00982 Drug metabolism - cytochrome P450	-3.362	4.96E-04	75
mmu04141 Protein processing in endoplasmic reticulum	-3.155	0.001	151
mmu04145 Phagosome	-3.000	0.001	130
mmu03050 Proteasome	-2.798	0.003	41
mmu00190 Oxidative phosphorylation	-2.700	0.004	106
mmu00100 Steroid biosynthesis	-2.916	0.004	15
mmu03320 PPAR signaling pathway	2.635	0.005	66
mmu04672 Intestinal immune network for IgA production	-2.658	0.005	31
mmu04623 Cytosolic DNA-sensing pathway	-2.507	0.007	40
mmu04115 p53 signaling pathway	2.259	0.013	59
mmu00052 Galactose metabolism	-2.231	0.015	24
mmu00900 Terpenoid backbone biosynthesis	-1.983	0.029	14
mmu03040 Spliceosome	-1.833	0.034	117
mmu00330 Arginine and proline metabolism	-1.819	0.036	45
mmu04512 ECM-receptor interaction	1.807	0.037	69
mmu04666 Fc gamma R-mediated phagocytosis	-1.795	0.037	80
mmu00053 Ascorbate and aldarate metabolism	-1.813	0.040	21
mmu04973 Carbohydrate digestion and absorption	-1.769	0.041	32
mmu00591 Linoleic acid metabolism	-1.740	0.044	29
mmu00514 Other types of O-glycan biosynthesis	-1.697	0.048	31

eTable 8 – Regulated KEGG pathways by 17 α estradiol in growth hormone receptor knockout (GHRKO) control female mice

Pathway	stat.mean	p.val	set.size
mmu04974 Protein digestion and absorption	-2.824	0.003	52
mmu04260 Cardiac muscle contraction	-2.682	0.005	53
mmu04145 Phagosome	-2.598	0.005	130
mmu04146 Peroxisome	2.521	0.007	75
mmu00010 Glycolysis / Gluconeogenesis	-2.226	0.014	53
mmu00071 Fatty acid metabolism	2.162	0.017	44
mmu04540 Gap junction	-2.083	0.020	67
mmu04510 Focal adhesion	-1.994	0.024	171
mmu04970 Salivary secretion	-1.740	0.043	55
mmu04020 Calcium signaling pathway	-1.727	0.043	116
mmu04612 Antigen processing and presentation	-1.702	0.046	57
mmu04512 ECM-receptor interaction	-1.695	0.046	69
mmu00770 Pantothenate and CoA biosynthesis	1.749	0.046	14
mmu04514 Cell adhesion molecules (CAMs)	-1.652	0.050	100