

Note to readers with disabilities: *EHP* strives to ensure that all journal content is accessible to all readers. However, some figures and Supplemental Material published in *EHP* articles may not conform to [508 standards](#) due to the complexity of the information being presented. If you need assistance accessing journal content, please contact ehp508@niehs.nih.gov. Our staff will work with you to assess and meet your accessibility needs within 3 working days.

Supplemental Material

Neonatal Genistein Exposure and Glucocorticoid Signaling in the Adult Mouse Uterus

Shannon D. Whirlledge, Edwina P. Kisanga, Robert H. Oakley, and John A. Cidlowski

Table of Contents

Figure S1. Relative mRNA expression of *Ppib*, *Gilz*, and *Fkbp5* measured by qRT-PCR in total RNA isolated from the uterus of adult, intact C57Bl/6 mice following neonatal exposure to control (corn-oil) or 50 mg/kg genistein. Bar graphs show the mean \pm SEM from 4-5 animals.

Figure S2. Uterine/body weight ratios were determined by measuring the uterine and body weight (g) in adrenalectomized and ovariectomized C57Bl/6 mice 24 hr following intraperitoneal injection of vehicle (saline) or 10 μ g/kg E₂. Bar graphs show the mean \pm SEM from 4-7 animals. **p<0.01 as determined by ANOVA with Tukey's post-hoc analysis.

Figure S3. Canonical glucocorticoid receptor (GR) signaling distinct following neonatal exposure to genistein. Ingenuity Pathway Analysis identified GR signaling as the top canonical pathway regulated by dexamethasone (Dex) in the uteri of control and genistein-exposed mice. Comparison of differentially expressed genes was visualized from the control and genistein-exposed groups. Red represents induction of gene expression and green indicates repression of gene expression.

Figure S4. IPA comparison analysis of the 1033 significantly regulated genes common to the control and genistein groups. The top five canonical pathways and diseases and biological functions were ranked and assigned an activation z-score (orange = induced; blue = repressed).

Figure S5. Reference protein β -actin protein expression in vehicle and genistein-treated mice. Arbitrary values from genistein-exposed mice were set relative to values from control mice. The results represent the mean of 4 animals \pm SEM.

Table S1. TaqMan Real-Time PCR Primers.

Table S2. Antibodies.

Table S3. ChIP qPCR Primer-Probe Sets.

Table S4. Expression of Glucocorticoid Responsive Genes in the Mouse Uterus at Postnatal Day 5, Postnatal Day 21, and Postnatal Day 56 Following Early-Life Genistein Exposure Dexamethasone.

Table S5. The Top Ten Induced and Repressed Genes as Determined by Fold Change in the Uteri of Neonatal Genistein Exposed Mice Compared to Control.

Table S6. Genes Differentially Regulated by Glucocorticoids in the Uterus of Control and Neonatal Genistein Exposed Mice.

Table S7. The Top Ten Diseases and Biological Functions Enriched in Glucocorticoid-Responsive Genes from the Uteri of Control and Neonatal Genistein Exposed Mice.

Table S8. Gene Ontology Analysis of Genes Differentially Regulated in Response to Dexamethasone from Uterine Tissue of Postnatal Control Animals.

Table S9. Gene Ontology Analysis of Genes Differentially Regulated in Response to Dexamethasone from Uterine Tissue of Postnatal Genistein Treated Animals.

Table S10. Anti-correlated genes commonly regulated in control and genistein-exposed mice.

Supplemental Data and Figures

Figure S1

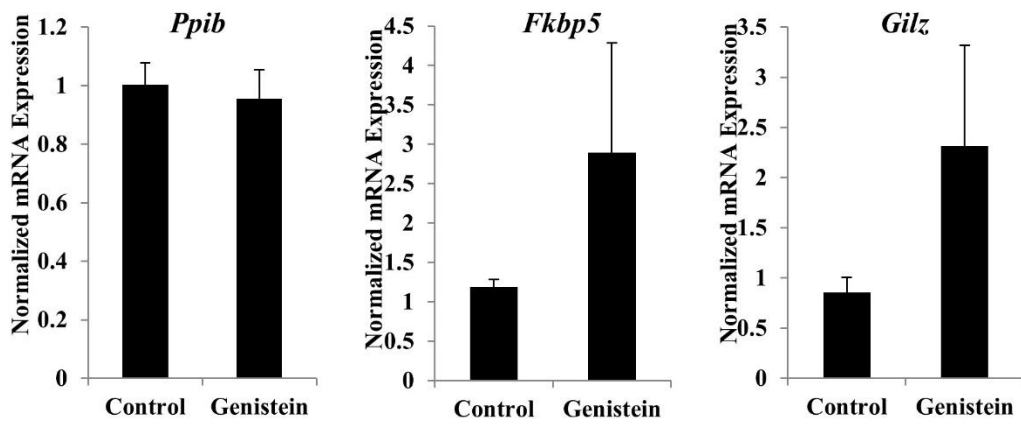


Figure S1. Relative mRNA expression of *Ppib*, *Gilz*, and *Fkbp5* measured by qRT-PCR in total RNA isolated from the uterus of adult, intact C57Bl/6 mice following neonatal exposure to control (corn-oil) or 50 mg/kg genistein. Bar graphs show the mean \pm SEM from 4-5 animals.

Figure S2

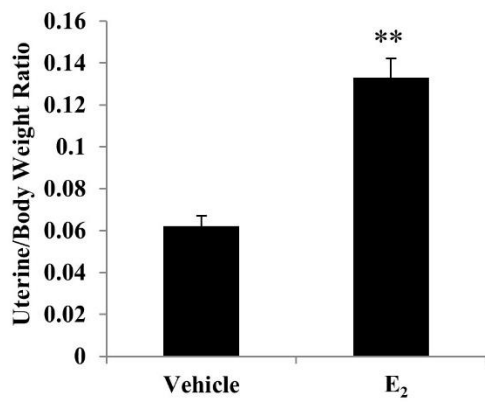
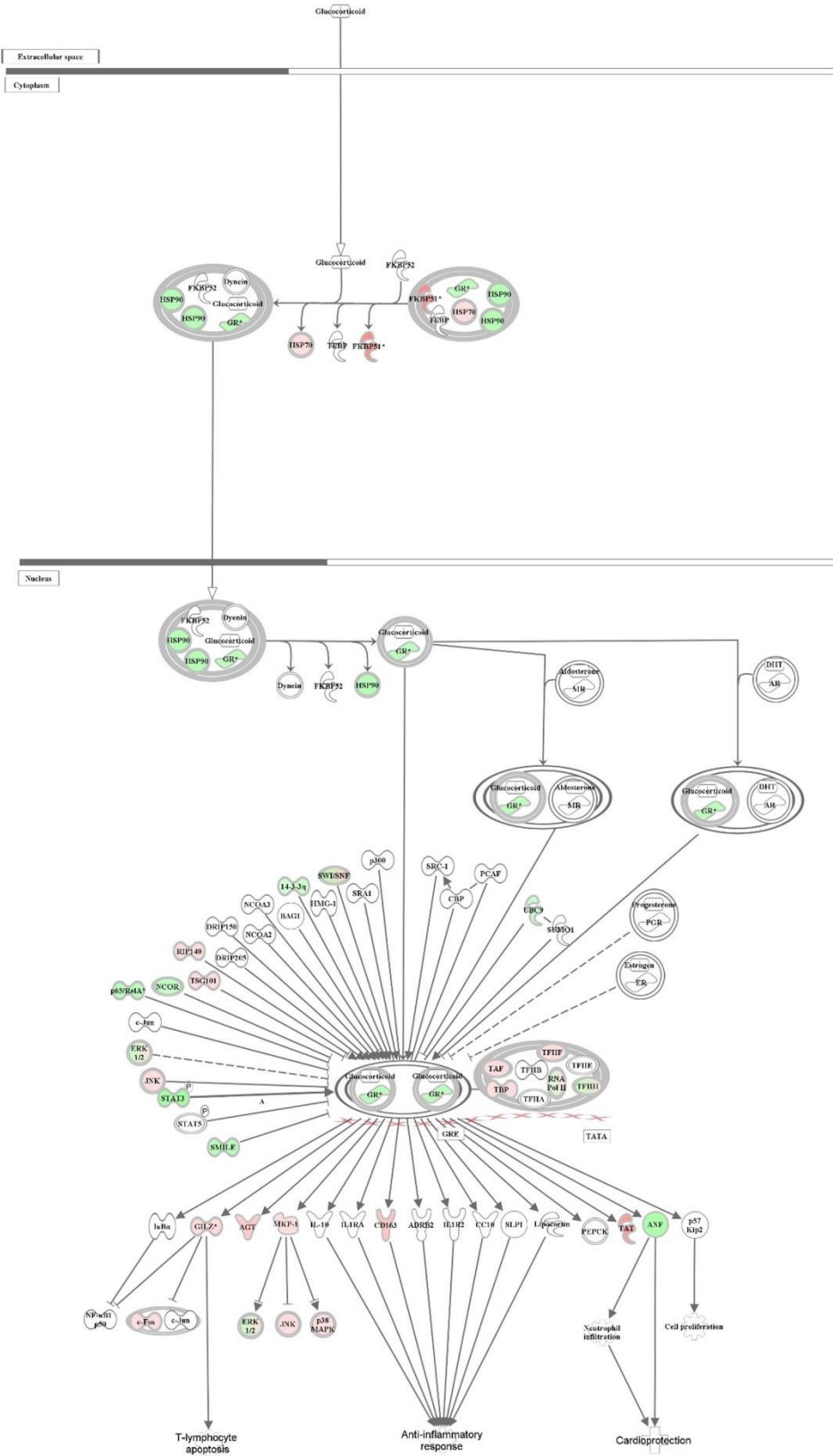


Figure S2. Uterine/body weight ratios were determined by measuring the uterine and body weight (g) in adrenalectomized and ovariectomized C57Bl/6 mice 24 hr following intraperitoneal injection of vehicle (saline) or 10 µg/kg E₂. Bar graphs show the mean ± SEM from 4-7 animals. **p<0.01 as determined by ANOVA with Tukey's post-hoc analysis.

Figure S3

A Control



B Genistein

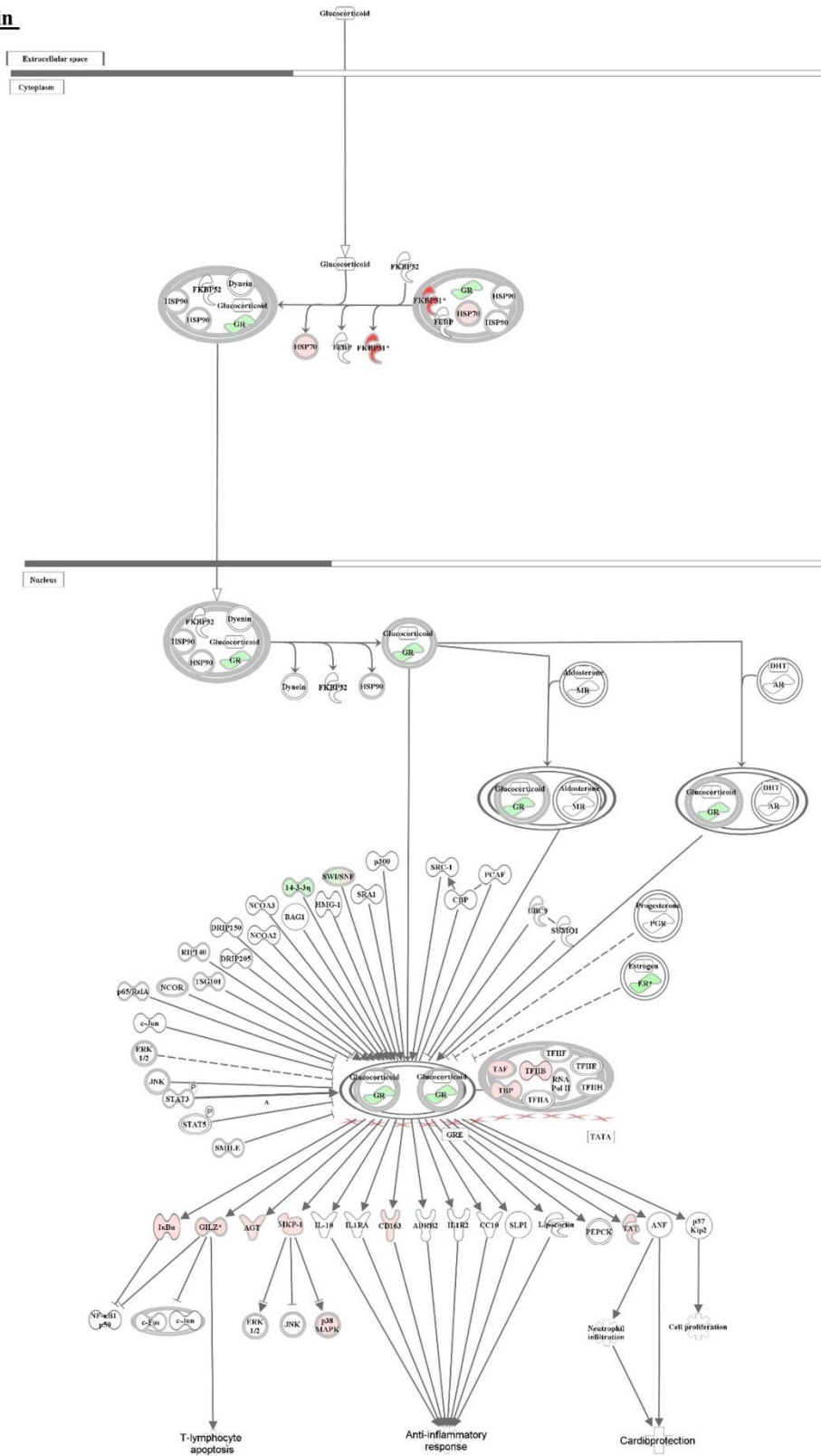
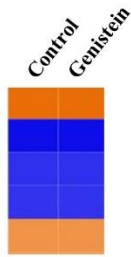


Figure S3. Canonical glucocorticoid receptor (GR) signaling distinct following neonatal exposure to genistein. Ingenuity Pathway Analysis identified GR signaling as the top canonical pathway regulated by dexamethasone (Dex) in the uteri of control and genistein-exposed mice. Comparison of differentially expressed genes was visualized from the control and genistein-exposed groups. Red represents induction of gene expression and green indicates repression of gene expression.

Figure S4

Canonical Pathways

1. Cardiac Hypertrophy Signaling
2. Gαi Signaling
3. Calcium-induced T Lymphocyte Apoptosis
4. PCKθ Signaling in T Lymphocytes
5. mTOR Signaling



Diseases and Biological Functions

1. Cell Movement of Granulocytes
2. Cell Movement of Neutrophils
3. Homing of Leukocytes
4. Cell Movement of Leukocytes
5. Chemotaxis of Phagocytes

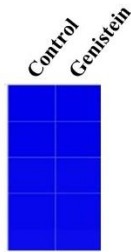


Figure S4. IPA comparison analysis of the 1033 significantly regulated genes common to the control and genistein groups. The top five canonical pathways and diseases and biological functions were ranked and assigned an activation z-score (orange = induced; blue = repressed).

Figure S5

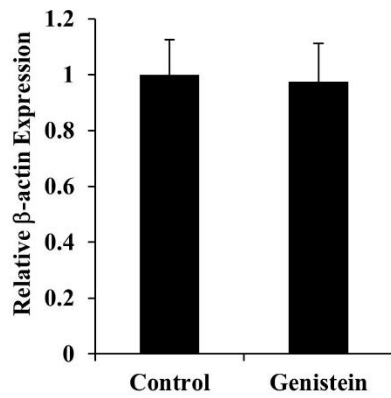


Figure S5. Reference protein β -actin protein expression in vehicle and genistein-treated mice. Arbitrary values from genistein-exposed mice were set relative to values from control mice. The results represent the mean of 4 animals \pm SEM.

Table S1: TaqMan Real-Time PCR Primers

Primer	Gene	Description	Amplicon Length	Assay Design
Mm01326794_m1	<i>Adamtsl2</i>	ADAMTS Like 2	69	Probe spans exons
Mm01151063_m1	<i>Dnmt1</i>	DNA (cytosine-5)-methyltransferase 1	58	Probe spans exons
Mm00432881_m1	<i>Dnmt3a</i>	DNA (cytosine-5)-methyltransferase 3A	58	Probe spans exons
Mm01240113_m1	<i>Dnmt3b</i>	DNA (cytosine-5)-methyltransferase 3B	83	Probe spans exons
Mm00487406_m1	<i>Fkpb5</i>	FK506 binding protein 5	74	Probe spans exons
Mm00726417_s1	<i>Gilz</i>	Glucocorticoid-induced leucine zipper	66	Both primers and probe map within a single exon
Mm02745760_g1	<i>Hdac1</i>	Histone deacetylase 1	74	Probe spans exons
Mm00515108_m1	<i>Hdac2</i>	Histone deacetylase 2	62	Probe spans exons
Mm00439613_m1	<i>Ihh</i>	Indian Hedgehog	64	Probe spans exons
Mm00727486_s1	<i>Klf13</i>	Kruppel-like factor 13	128	Both primers and probe map within a single exon
Mm00521967_m1	<i>Mbd2</i>	Methyl-CpG-binding domain protein 2	71	Probe spans exons
Mm01193537_g1	<i>Mecp2</i>	Methyl-CpG-binding protein 2	99	Probe spans exons
Mm00801489_m1	<i>Ovgp1</i>	Oviduct-specific glycoprotein	70	Probe spans exons
Mm00501813_m1	<i>Per1</i>	Period circadian clock 1	106	Probe spans exons
Mm00441380_m1	<i>Sgk1</i>	Serum/glucocorticoid regulated kinase 1	71	Probe spans exons
Mm00478295_m1	<i>Ppib</i>	Peptidylprolyl isomerase B	82	Probe spans exons
Mm00445641_m1	<i>Retn</i>	Resistin	80	Probe spans exons

Table S2: Antibodies

Antibody ID	Antibody	Source	Catalog Number	Purpose
AB_11179215	Glucocorticoid Receptor (D8H2) XP® Rabbit mAb	Cell Signaling Technologies, Beverly, MA	3660S	Immunofluorescence (1:500) Western blotting (1:1,000) ChIP (1:175)
AB_2620142	Ki-67 (D3B5) Rabbit mAb (Alexa Fluor® 488 Conjugate)	Cell Signaling Technologies, Beverly, MA	12202	Immunofluorescence (1:400)
AB_2223041	Anti-Actin Antibody, clone C4	Millipore, Temecula, MA	MAB1501	Western blotting (1:10,000)
AB_10956389	Goat anti-rabbit IRDye 680-conjugated secondary antibody	LI-COR Biosciences, Lincoln, NE	926-68171	Western blotting (1:10,000)
AB_10793856	Goat anti-mouse IRDye 800-conjugated secondary antibody	LI-COR Biosciences, Lincoln, NE	827-08364	Western blotting (1:10,000)
AB_145841	Normal rabbit IgG	Millipore, Temecula, MA	12-370	ChIP (1:700)

Table S3: ChIP qPCR Primer-Probe Sets

Gene	Description	Primer DNA Sequences	Probe Sequence
<i>Gilz</i>	Glucocorticoid-induced leucine zipper	5'-ACCCTTGTGGTCATGGAATG-3' 5'-AGAAACCAGTGTGCTGAAAGA-3'	5'AGTACACTGAGCACACAACGTGCC-3'
<i>Klf13</i>	Kruppel-like factor 13	5'-AGGGAACACAACGTCCCATATGCT-3' 5'-ATTCAATCCCGGTGAGGGCTTT-3'	5'-ACTGAGAACATGCTGTTCCCGCCA-3'
<i>Per1</i>	Period circadian clock 1	5'-CCCTTCCTCCTAACTGTCTCT-3' 5'-TCGTGTTCTCTTGGCTGATG-3'	5'-TTTGTACAGGACCGCTGTCGTTGG-3'
<i>Sgk13</i>	Serum/glucocorticoid regulated kinase 1	5'-TCTAACTCGCCACCTCCT-3' 5'-GAACATTCTGTTCTTTCCGCATAA-3'	5'-ACGTGTTCTTGGCATGGCTAGGAT-3'

Table S4. Expression of Glucocorticoid Responsive Genes in the Mouse Uterus at Postnatal Day 5, Postnatal Day 21, and Postnatal Day 56 Following Early-Life Genistein Exposure Dexamethasone

Gene	PND 5 Dex/Veh		PND 21 Dex/Veh		PND 56 Dex/Veh	
	Control ^a	Genistein ^b	Control ^a	Genistein ^b	Control ^a	Genistein ^b
<i>Gilz</i>	+++	+++	+++	+++	+++	++
<i>Fkbp5</i>	+++	+++	+++	+++	+++	+
<i>Sgk1</i>	+++	+++	+++	+++	+++	+
<i>Per1</i>	+++	+++	+++	+++	+++	+++

^a+++ represents a high degree of regulation of the respective glucocorticoid responsive gene in control mice as determined by comparing expression in dexamethasone-treated mice versus vehicle-treated mice at the postnatal day indicated.

^b+++ represents a high degree of regulation of the respective glucocorticoid responsive gene in genistein-exposed mice as determined by comparing expression in dexamethasone-treated mice versus vehicle-treated mice at the postnatal day indicated. ++ represents a moderate degree of regulation of the respective glucocorticoid responsive gene in genistein-exposed mice as determined by comparing expression in dexamethasone-treated mice versus vehicle-treated mice at the postnatal day indicated. + represents a low degree of regulation of the respective glucocorticoid responsive gene in genistein-exposed mice as determined by comparing expression in dexamethasone-treated mice versus vehicle-treated mice at the postnatal day indicated.

Table S5. The Top Ten Induced and Repressed Genes as Determined by Fold Change in the Uteri of Neonatal Genistein Exposed Mice Compared to Control

GeneName	GeneSymbol	Fold-Change
Potassium channel, subfamily K, member 10	<i>Kcnk10</i>	6.52
Glycogen synthase 2	<i>Gys 2</i>	5.93
Major urinary protein 2	<i>Mup2</i>	5.50
Olfactory receptor 447	<i>Olfr447</i>	4.79
Carbonic anhydrase 3	<i>Car3</i>	4.37
Klotho beta	<i>Klb</i>	4.27
Cytochrome P450, family 11, subfamily a, polypeptide 1	<i>Cyp11a1</i>	4.22
Solute carrier family 36 (proton/amino acid symporter), member 1	<i>Slc36a1</i>	4.18
Vomeronasal 1 receptor 22	<i>Vmn1r22</i>	3.92
Leptin	<i>Lep</i>	3.82
G1 to S phase transition 1	<i>Gspt1</i>	-3.58
UV radiation resistance associated gene	<i>Uvrug</i>	-3.72
SR-related CTD-associated factor 4	<i>Scaf4</i>	-3.76
Solute carrier family 39 (metal ion transporter), member 8	<i>Slc39a8</i>	-3.86
Activating transcription factor 7	<i>Atf7</i>	-3.87
Phosphodiesterase 6H, cGMP-specific, cone, gamma	<i>Pde6h</i>	-4.00
Cytochrome P450, family 3, subfamily a, polypeptide 25	<i>Cyp3a25</i>	-4.01
Matrix metalloproteinase 16	<i>Mmp16</i>	-4.14
Ankyrin repeat domain 55	<i>Ankrd55</i>	-4.41

Table S6. Genes Differentially Regulated by Glucocorticoids in the Uterus of Control and Neonatal Genistein Exposed Mice

Gene Name	Gene Symbol	Control Dex/Veh ^a	Genistein Dex/Veh ^a
Interleukin 13 receptor, alpha 2	<i>Il13ra2</i>	28.984	85.706
L-amino acid oxidase 1	<i>Lao1</i>	21.778	33.203
Osteomodulin	<i>Omd</i>	20.522	10.118
Dipeptidase 1 (renal)	<i>Dpep1</i>	17.526	34.233
ADAMTS-like 2	<i>Adamtsl2</i>	16.238	7.237
Tyrosine aminotransferase	<i>Tat</i>	16.165	4.3715
Family with sequence similarity 107, member A	<i>Fam107a</i>	15.610	37.563
RIKEN cDNA 6030422H21 gene	<i>6030422H21Rik</i>	14.278	19.329
Glutathione S-transferase, alpha 3	<i>Gsta3</i>	11.449	4.106
FK506 binding protein 5	<i>Fkbp5</i>	11.371	18.787
Tachykinin 4	<i>Tac4</i>	10.093	4.826
Hydroxysteroid 11-beta dehydrogenase 2	<i>Hsd11b2</i>	9.822	20.277
CD163 antigen	<i>Cd163</i>	9.567	5.267
Angiotensinogen (serpin peptidase inhibitor, clade A, member 8)	<i>Agt</i>	8.384	2.768
RIKEN cDNA E030003E18 gene	<i>E030003E18Rik</i>	8.239	4.352
D4, zinc and double PHD fingers family 1	<i>Dpfl</i>	8.101	4.712

Cytochrome P450, family 1, subfamily b, polypeptide 1	<i>Cyp1b1</i>	7.445	2.613
RIKEN cDNA E230001N04 gene	<i>E230001N04Rik</i>	6.907	16.070
Nuclear factor, interleukin 3, regulated	<i>Nfil3</i>	6.765	3.447
Carcolipin	<i>Sln</i>	6.741	3.672
Abhydrolase domain containing 15	<i>Abhd15</i>	5.866	3.452
Mitogen-activated protein kinase kinase kinase 6	<i>Map3k6</i>	5.502	8.894
Pancreatic lipase-related protein 2	<i>Pnliprp2</i>	5.477	10.191
Serum/glucocorticoid regulated kinase 1	<i>Sgk1</i>	5.092	2.836
Transcription factor 23	<i>Tcf23</i>	4.888	9.674
Membrane-spanning 4-domains, subfamily A, member 6D	<i>Ms4a6d</i>	4.562	2.199
Immunoglobulin superfamily, member 21	<i>Igsf21</i>	4.392	2.391
Family with sequence similarity 65, member B	<i>Fam65b</i>	4.145	7.447
Coagulation factor II (thrombin) receptor	<i>F2r</i>	4.042	7.856
Signal peptide, CUB domain, EGF-like 2	<i>Scube2</i>	3.953	8.107
Family with sequence similarity 159, member B	<i>Fam159b</i>	3.769	1.636
Spondin 1, (f-spondin) extracellular matrix protein	<i>Spon1</i>	3.649	9.735
Sulfotransferase family 1A, phenol-preferring, member 1	<i>Sult1a1</i>	3.502	7.393
Adenylate cyclase 1	<i>Adcy1</i>	3.271	6.035
Family with sequence similarity 169, member A	<i>Fam169a</i>	3.098	5.464
Phospholipase D1	<i>Pld1</i>	3.041	5.052
Copine VII	<i>Cpne7</i>	2.895	6.577
Circadian associated repressor of transcription	<i>Ciart</i>	2.894	5.451
Solute carrier family 25 (mitochondrial carrier, palmitoylcarnitine transporter), member 2	<i>Slc25a29</i>	2.819	4.912
Potassium voltage-gated channel, Shal-related family, member 2	<i>Kcnd2</i>	2.758	5.104
RIKEN cDNA B230114P17 gene	<i>B230114P17Rik</i>	2.685	5.384
Unc-13 homolog C (C. elegans)	<i>Unc13c</i>	2.511	-2.094
Potassium voltage-gated channel, subfamily G, member 4	<i>Kcng4</i>	2.434	5.388
Hedgehog interacting protein-like 1	<i>Hhip1</i>	2.292	5.164
Eyes absent 4 homolog (Drosophila)	<i>Eya4</i>	2.193	-2.762
Opa interacting protein 5	<i>Oip5</i>	1.789	-1.347
6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 1	<i>Pfkfb1</i>	1.601	-1.467
Phosphatidic acid phosphatase type 2 domain containing 2	<i>Ppapdc2</i>	1.555	-1.272
RIKEN cDNA 1700096K18 gene	<i>1700096K18Rik</i>	1.350	-1.188
cDNA sequence BC037034	<i>BC037034</i>	-1.143	1.192
Growth factor receptor bound protein 2	<i>Grb2</i>	-1.145	1.180
Cleavage and polyadenylation specific factor 4	<i>Cpsf4</i>	-1.175	1.203
ADP-ribosylation factor GTPase activating protein 1	<i>Arfgap1</i>	-1.179	1.147
Zinc finger, CCHC domain containing 3	<i>Zcchc3</i>	-1.324	1.449

Eukaryotic translation initiation factor 2B, subunit 4 delta	<i>Eif2b4</i>	-1.405	1.422
Huntingtin interacting protein 1	<i>Hip1</i>	-1.737	1.786
Neurexophilin and PC-esterase domain family, member 5	<i>Nxpe5</i>	-2.235	-4.825
Hydroxycarboxylic acid receptor 2	<i>Hcar2</i>	-2.989	-5.793
Olfactomedin 3	<i>Olfm3</i>	-3.092	-6.161
Hydrocarboxylic acid receptor 1	<i>Hcar1</i>	-3.100	-5.999
Dickkopf homolog 2 (<i>Xenopus laevis</i>)	<i>Dkk2</i>	-3.297	-5.527
Guanylate binding protein 4	<i>Gbp4</i>	-5.159	-2.612
Prion protein dublet	<i>Prnd</i>	-5.600	-14.574
Polyamine modulated factor 1 binding protein 1	<i>Pmfbp1</i>	-6.139	-3.679
Tissue inhibitor of metalloproteinase 1	<i>Timp1</i>	-6.375	-3.453
Leucine rich repeat containing 55	<i>Lrrc55</i>	-6.540	-16.515
CD83 antigen	<i>Cd83</i>	-6.741	-2.990
S100 calcium binding protein A9 (calgranulin B)	<i>S100a9</i>	-7.008	-4.985
Death-associated protein kinase 2	<i>Dapk2</i>	-7.103	-4.162
Spondin 2, extracellular matrix protein	<i>Spon2</i>	-7.170	-4.955
G-protein coupled receptor 88	<i>Gpr88</i>	-7.531	-12.142
Complement component 1, q subcomponent-like 2	<i>C1ql2</i>	-7.821	-3.100
Chemokine (C-C motif) ligand 2	<i>Ccl2</i>	-8.850	-5.163
Chemokine (C-C motif) ligand 4	<i>Ccl4</i>	-9.014	-3.427
Chemokine (C-X-C motif) ligand 5	<i>Cxcl5</i>	-10.506	-14.323
Chemokine (C-C motif) ligand 7	<i>Ccl7</i>	-15.957	-6.943

^aValues represent the fold change in gene regulation by glucocorticoids in dexamethasone-treated mice compared to vehicle-treated mice.

Table S7. The Top Ten Diseases and Biological Functions Enriched in Glucocorticoid-Responsive Genes from the Uteri of Control and Neonatal Genistein Exposed Mice

Control			
Rank	Diseases and Biological Functions	No. of Molecules	p-value
1	Organismal Survival	757	4.14E-32 - 3.47E-07
2	Cancer	2583	2.85E-27 - 1.41E-05
3	Organismal Injury and Abnormalities	2616	2.85E-27 - 1.47E-05
4	Gastrointestinal Disease	2322	2.53E-25 - 1.41E-05
5	Cellular Growth and Proliferation	1126	6.24E-23 - 8.66E-06
6	Cell Death and Survival	941	3.42E-18 - 1.67E-05
7	Hematological System Development and Function	583	3.4E-17 - 1.51E-05
8	Tissue Morphology	602	3.4E-17 - 1.65E-05
9	Cell Morphology	719	9.58E-17 - 1.63E-05
10	Connective Tissue Disorders	321	1.03E-16 - 5.72E-12

Genistein

Rank	Diseases and Biological Functions	No. of Molecules	p-value
1	Cancer	1566	1.65E-22 - 2.04E-05
2	Organismal Injury and Abnormalities	1582	1.65E-22 - 2.04E-05
3	Cellular Growth and Proliferation	706	5.44E-21 - 1.58E-05
4	Hematological System Development and Function	407	2.53E-20 - 2.04E-05
5	Tissue Morphology	453	2.53E-20 - 1.71E-05
6	Gastrointestinal Disease	1409	9.22E-19 - 1.45E-05
7	Cellular Movement	384	2.33E-18 - 1.97E-05
8	Lymphoid Tissue Structure and Development	284	7.14E-18 - 6.58E-06
9	Connective Tissue Development and Function	344	8.92E-18 - 1.02E-05
10	Organismal Survival	446	1.47E-17 - 2.22E-06

Bolded rows represent functions unique to treatment within the top ten diseases and biological functions enriched in glucocorticoid-responsive genes from the uteri of control and genistein-exposed mice.

Table S8. Gene Ontology Analysis of Genes Differentially Regulated in Response to Dexamethasone from Uterine Tissue of Postnatal Control Animals

#	Annotation	No. of Genes	Bayes factor	p value
1	GO:0007606 [6]: sensory perception of chemical stimulus	13	120.91	<0.0001
2	GO:0007608 [7]: perception of smell	13	114.29	<0.0001
3	GO:0007600 [5]: sensory perception	28	104.03	<0.0001
4	GO:0009581 [5]: detection of external stimulus	30	101.34	<0.0001
5	GO:0050877 [4]: neurophysiological process	45	91.75	<0.0001
6	GO:0009605 [4]: response to external stimulus	104	84.53	<0.0001
7	GO:0007186 [6]: G-protein coupled receptor protein signaling pathway	94	67.09	<0.0001
8	GO:0050896 [3]: response to stimulus	184	59.5	<0.0001
9	GO:0050874 [3]: organismal physiological process	168	44.51	<0.0001
10	GO:0050875 [3]: cellular physiological process	1167	41.17	<0.0001
11	GO:0008152 [3]: metabolism	855	28.63	<0.0001
12	GO:0007166 [5]: cell surface receptor linked signal transduction	180	28.58	<0.0001
13	GO:0044237 [4]: cellular metabolism	804	25.3	<0.0001
14	GO:0044238 [4]: primary metabolism	766	21.01	<0.0001
15	GO:0050789 [2]: regulation of biological process	375	13.39	<0.0001
16	GO:0050793 [3]: regulation of development	45	9.66	<0.0001
17	GO:0007275 [2]: development	270	8.33	<0.0001
18	GO:0050794 [3]: regulation of cellular process	112	7.4	<0.0001
19	GO:0007154 [3]: cell communication	379	6.94	<0.0001
20	GO:0007242 [5]: intracellular signaling cascade	125	6.42	<0.0001

21	GO:0009653 [3]: morphogenesis	189	6.35	<0.0001
22	GO:0040008 [4]: regulation of growth	24	6.33	<0.0001
23	GO:0050791 [3]: regulation of physiological process	322	6.1	<0.0001
24	GO:0006793 [5]: phosphorus metabolism	115	5.97	<0.0001
25	GO:0006796 [6]: phosphate metabolism	115	5.97	<0.0001
26	GO:0006464 [7]: protein modification	188	5.4	0.0001
27	GO:0006915 [6]: apoptosis	75	5.33	0.0001

Table S9. Gene Ontology Analysis of Genes Differentially Regulated in Response to Dexamethasone from Uterine Tissue of Postnatal Genistein Treated Animals

#	<u>Annotation</u>	<u>No. of Genes</u>	<u>Bayes factor</u>	<u>p value</u>
1	GO:0007606 [6]: sensory perception of chemical stimulus	5	76.5	<0.0001
2	GO:0007608 [7]: perception of smell	5	72.5	<0.0001
3	GO:0007600 [5]: sensory perception	15	62.5	<0.0001
4	GO:0009581 [5]: detection of external stimulus	16	61.21	<0.0001
5	GO:0050877 [4]: neurophysiological process	26	53.36	<0.0001
6	GO:0009605 [4]: response to external stimulus	75	34.49	<0.0001
7	GO:0007186 [6]: G-protein coupled receptor protein signaling pathway	60	33.71	<0.0001
8	GO:0050896 [3]: response to stimulus	125	22.55	<0.0001
9	GO:0050874 [3]: organismal physiological process	105	21.53	<0.0001
10	GO:0050875 [3]: cellular physiological process	695	17.94	<0.0001
11	GO:0007166 [5]: cell surface receptor linked signal transduction	115	11.39	<0.0001
12	GO:0007275 [2]: development	177	9.08	<0.0001
13	GO:0006915 [6]: apoptosis	55	8.23	<0.0001
14	GO:0012501 [5]: programmed cell death	55	7.72	<0.0001
15	GO:0050794 [3]: regulation of cellular process	76	7.63	<0.0001
16	GO:0008152 [3]: metabolism	493	7.06	<0.0001
17	GO:0050789 [2]: regulation of biological process	227	6.6	<0.0001
18	GO:0050793 [3]: regulation of development	30	6.53	<0.0001
19	GO:0009653 [3]: morphogenesis	122	5.52	0.0001
20	GO:0030154 [3]: cell differentiation	48	5.38	0.0001
21	GO:0008219 [4]: cell death	55	5.37	0.0001
22	GO:0016265 [3]: death	55	5	0.0002

Table S10. Anti-correlated genes commonly regulated in control and genistein-exposed mice

Gene Symbol	Gene Name	Control Fold-Change	Genistein Fold-Change
BC037034	cDNA sequence BC037034	-1.14348	1.19282
Grb2	growth factor receptor bound protein 2	-1.14571	1.18027
Cpsf4	cleavage and polyadenylation specific factor 4	-1.17573	1.20376
Arfgap1	ADP-ribosylation factor GTPase activating protein 1	-1.17986	1.14785

Zcchc3	zinc finger, CCHC domain containing 3	-1.32435	1.44911
Eif2b4	eukaryotic translation initiation factor 2B, subunit 4 delta	-1.40553	1.42271
Hip1	huntingtin interacting protein 1	-1.73779	1.78622
Unc13c	unc-13 homolog C (C. elegans)	2.51197	-2.09401
Eya4	eyes absent 4 homolog (Drosophila)	2.1935	-2.76218
Oip5	Opa interacting protein 5	1.78929	-1.34715
Pfkfb1	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 1	1.60198	-1.46713
Ppapdc2	phosphatidic acid phosphatase type 2 domain containing 2	1.55539	-1.27298
1700096K18Rik	RIKEN cDNA 1700096K18 gene	1.35091	-1.18865