Table 1. Antibodies used for immunohistochemistry

Antibody	Provider	Cat #	Lot #	Clone	Concentration	Serum
Primary						
SIX1	Sigma-Aldrich	HPA001893	C75776 C104244	Rabbit polyclonal	0.2 µg/mL	Donkey
P63	Santa Cruz Biotechnology	sc-8343	C2012	Rabbit polyclonal	0.4 µg/mL	Goat
CK14	Covance	PRB-155P	D13EF01483	Rabbit polyclonal	0.8 µg/mL	Donkey
CK18	Santa Cruz Biotechnology	sc-51582	H2714	Mouse monoclonal	8 µg/mL	Horse
Dual CK14 CK18	Covance Santa Cruz Biotechnology	PRB-155P sc-51582	D15LF02399 H2714	See above	0.2 µg/mL 8 µg/mL	Antibody blocker/ diluent
CD44	Lifespan Biosciences	LS-B5508	71714	Mouse monoclonal	2 µg/mL	Rabbit
ERα	Biocare Medical	ACA054	011215	Mouse monoclonal	2 µg/mL	Horse
PGR	Lifespan Biosciences	LS-B5236	38639	Mouse monoclonal	1 µg/mL	Horse

Secondary						
Donkey anti-rabbit (SIX1, CK14)	Jackson Immunoresearch	711-065-152	124459	-	2.4 µg/mL	-
Goat anti-rabbit (P63)	Vector Laboratories	BA-1000	ZA0924	-	3 µg/mL	-
Horse anti-mouse (CK18, ERα, PGR)	Vector Laboratories	BA-2001	Z0421	-	0.5 µg/mL	-
Rabbit anti-rat (CD44)	Vector Laboratories	BA-4001	Y0809	-	1 µg/mL	-
Multiview Plus Kit Mouse-HRP and Rabbit-AP (Dual CK14/18)	Enzo Life Sciences	ENZ-KIT181	37CR13	-	Ready-to-use	-

Negative Control						
Rabbit IgG (P63, SIX1, CK14)	Calbiochem	NIO1	D00168753	-	Equivalent Dilution	-
Mouse IgG1 (CK18, ERα, PGR)	BD Biosciences	557273	4241584	-	Equivalent Dilution	-
Rat IgG2b (CD44)	BD Biosciences	559478	3297579	-	Equivalent Dilution	-
Rabbit IgG and Mouse IgG1 (Dual CK14/18)	Calbiochem BD Biosciences	NIO1 557273	D00168753 4241584	-	Equivalent Dilution	-

Table 2. **Incidence of uterine glandular epithelial lesions over time following neonatal exposure to GEN or DES.**

	CON				GEN				DES			
Age (mo)	**2-3**	**6**	**12**	**18**	**2-3**	**6**	**12**	**18**	**2-3**	**6**	**12**	**18**
Diagnosis	**Incidence (%)**				**Incidence (%)**				**Incidence (%)**			
Glandular cystic dilation	0/13 (0%)	2/33 (6%)	7/29 (24%)	15/30 (50%)	0/10 (0%)	12/30[b] (40%)	23/30[c] (77%)	27/30[b] (90%)	0/9 (0%)	4/31 (13%)	10/26 (38%)	29/30[c] (97%)
Adenomyosis	0/13 (0%)	0/33 (0%)	3/29 (10%)	4/30 (13%)	1/10 (10%)	6/30[a] (20%)	10/30 (33%)	13/30[a] (43%)	1/9 (11%)	13/31[c] (42%)	13/26[b] (50%)	18/30[c] (60%)
Squamous metaplasia	0/13 (0%)	1/33 (3%)	0/29 (0%)	0/30 (0%)	0/10 (0%)	11/30[c] (37%)	16/30[c] (53%)	24/30[c] (80%)	0/9 (0%)	7/31[a] (23%)	12/26[c] 46%	14/30[c] (47%)
Severity grade	0.0	0.0	0.0	0.0	0.0	0.4	0.8	1.2	0.0	0.3	0.6	0.8
Basal cell metaplasia	1/13 (8%)	3/33 (9%)	2/29 (7%)	0/30 (0%)	7/10[b] (70%)	19/30[c] (63%)	26/30[c] (87%)	30/30[c] (100%)	8/9[c] (89%)	30/31[c] (97%)	25/26[c] (96%)	29/30[c] (97%)
Severity grade	0.1	0.1	0.1	0.0	0.7	0.7	1.7	1.7	0.9	1.5	2.0	1.7
Atypical hyperplasia	0/13 (0%)	0/33 (0%)	0/29 (0%)	0/30 (0%)	0/10 (0%)	3/30 (10%)	9/30[b] (30%)	15/30[c] (50%)	0/9 (0%)	14/31[c] (45%)	14/26[c] (54%)	18/30[c] (60%)
Carcinoma	0/13 (0%)	0/33 (0%)	0/29 (0%)	0/30 (0%)	0/10 (0%)	2/30 (7%)	7/30[b] (23%)	10/30[c] (33%)	0/9 (0%)	5/31[a] (16%)	9/26[c] (35%)	12/30[c] (40%)

Incidence data for 6, 12, and 18 mo time points were previously reported by Suen et al. 2016.

Abbreviations: CON, control; GEN, genistein; DES, diethylstilbestrol

Severity values indicate average grade across the entire group (0-4).

[a] P<0.05, [b] P<0.01, and [c] P<0.001 compared with corresponding age-matched control group using a two-tailed Fisher exact test

Table 3. Immunohistochemical expression of differentiation markers in the uterine epithelium following neonatal exposure to GEN or DES

Table 3A.

		Age (mo)					
		2-3			18		
Marker	**Site**	**CON**	**GEN**	**DES**	**CON**	**GEN**	**DES**
SIX1	Cervix: non-neoplastic	13/13 (100%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	10/10 (100%)	12/12 (100%)
	Labeling score	2.2	1.9	2.0	1.9	1.4	1.6
	Endometrium: non-neoplastic	1/13 (8%)	9/10[c] (90%)	9/9[c] (100%)	0/9 (0%)	10/10[c] (100%)	12/12[c] (100%)
	Labeling score	0.1	1.1	1.2	0.0	2.2	2.6
	Endometrium: neoplastic	na	na	na	na	10/10 (100%)	12/12 (100%)
	Labeling score	na	na	na	na	2.0	2.5
P63	Cervix: non-neoplastic	13/13 (100%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	10/10 (100%)	12/12 (100%)
	Labeling score	2.7	3.0	2.7	2.6	2.7	2.8
	Endometrium: non-neoplastic	1/13 (8%)	8/10[c] (80%)	8/9[c] (89%)	4/9 (44%)	10/10[a] (100%)	12/12[b] (100%)
	Labeling score	0.1	0.8	0.9	0.4	2.0	2.5
	Endometrium: neoplastic	na	na	na	na	10/10 (100%)	12/12 (100%)
	Labeling score	na	na	na	na	2.1	1.8

Abbreviations: CON, control; GEN, genistein; DES, diethylstilbestrol; na, not applicable. Cervix includes stratified squamous epithelium, mucification layer if present, and transition zone with uterine body; endometrium includes glands and epithelium lining central lumen. IHC labeling score represents a qualitative average (0-4) within each group.
Letters indicate [a] $P<0.05$, [b] $P<0.01$, and [c] $P<0.001$ compared with corresponding age-matched control group using a two-tailed Fisher exact test.

Table 3. Immunohistochemical expression of differentiation markers in the uterine epithelium following neonatal exposure to DES or GEN

Table 3B.		Age (mo)					
		2-3			18		
Marker	**Site**	**CON**	**GEN**	**DES**	**CON**	**GEN**	**DES**
CK14	Cervix: non-neoplastic	13/13 (100%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	10/10 (100%)	12/12 (100%)
	Labeling score	4.0	4.0	4.0	4.0	4.0	4.0
	Endometrium: non-neoplastic	1/13 (8%)	10/10[c] (100%)	9/9[c] (100%)	4/9 (44%)	10/10[a] (100%)	12/12[b] (100%)
	Labeling score	0.1	1.2	1.0	0.4	2.5	2.7
	Endometrium: neoplastic	na	na	na	na	10/10 (100%)	12/12 (100%)
	Labeling score	na	na	na	na	3.5	3.2
CK18	Cervix: non-neoplastic[#]	9/13 (69%)	0/10[b] (0%)	2/9 (22%)	1/9 (11%)	5/10 (50%)	5/12 (42%)
	Labeling score	0.9	0.0	0.2	0.1	0.5	0.4
	Endometrium: non-neoplastic	13/13 (100%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	10/10 (100%)	12/12 (100%)
	Labeling score	3.8	4.0	4.0	4.0	3.9	3.9
	Endometrium: neoplastic	na	na	na	na	10/10 (100%)	12/12 (100%)
	Labeling score	na	na	na	na	3.1	2.8
Dual CK14/18	Cervix: non-neoplastic[#]*	6/10 (60%)	0/10[a] (0%)	1/9 (11%)	4/9 (44%)	0/10[a] (0%)	2/11 (18%)
	Labeling score	0.8	0.0	0.1	0.4	0.0	0.2
	Endometrium: non-neoplastic*	4/9 (44%)	10/10[a] (100%)	9/9[a] (100%)	2/9 (22%)	10/10[c] (100%)	10/11[b] (91%)
	Labeling score	0.4	1.2	1.1	0.2	1.0	0.9
	Endometrium: neoplastic*	na	na	na	na	9/9 (100%)	11/11 (100%)
	Labeling score	na	na	na	na	2.1	2.1

Abbreviations: CON, control; GEN, genistein; DES, diethylstilbestrol; na, not applicable. Cervix includes stratified squamous epithelium, mucification layer if present, and transition zone with uterine body; endometrium includes glands and epithelium lining central lumen. IHC labeling score represents average (0-4) within each group.

* Tissues from some uteri were not present in section.

[#] CK18 labeling in the cervix was most commonly observed in a superficial mucification layer, which was often not present in GEN or DES mice.

Letters indicate [a] P<0.05, [b] P<0.01, and [c] P<0.001 compared with corresponding age-matched control group using a two-tailed Fisher exact test.

Table 3. Immunohistochemical expression of differentiation markers in the uterine epithelium following neonatal exposure to DES or GEN

Table 3C.		Age (mo)					
		2-3			18		
Marker	**Site**	**CON**	**GEN**	**DES**	**CON**	**GEN**	**DES**
CD44	Cervix: non-neoplastic	13/13 (100%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	10/10 (100%)	12/12 (100%)
	Labeling score	2.3	3.0	3.0	2.8	2.7	2.8
	Endometrium: non-neoplastic	6/13 (46%)	10/10[b] (100%)	9/9[a] (100%)	9/9 (100%)	10/10 (100%)	11/12 (92%)
	Labeling score	0.6	1.1	1.4	1.2	1.0	1.0
	Endometrium: neoplastic	na	na	na	na	9/10 (90%)	8/12 (67%)
	Labeling score	na	na	na	na	1.3	1.0
TUNEL	Cervix: non-neoplastic*	7/10 (70%)	10/10 (100%)	9/9 (100%)	8/8 (100%)	9/9 (100%)	10/11 (91%)
	Labeling score	0.9	1.2	1.0	1.4	1.0	1.0
	Endometrium: non-neoplastic*	7/9 (78%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	9/10 (90%)	11/11 (100%)
	Labeling score	1.7	1.2	1.2	1.8	0.9	1.0
	Endometrium: neoplastic*	na	na	na	na	9/10 (90%)	10/11 (91%)
	Labeling score	na	na	na	na	0.9	0.9

Abbreviations: CON, control; GEN, genistein; DES, diethylstilbestrol; na, not applicable.
Cervix includes stratified squamous epithelium, mucification layer if present, and transition zone with uterine body; endometrium includes glands and epithelium lining central lumen.
IHC labeling score represents average (0-4) within each group.
* Tissues from some uteri were not present in section.
Letters indicate [a] P<0.05, [b] P<0.01, and [c] P<0.001 compared with corresponding age-matched control group using a two-tailed Fisher exact test.

Table 3. Immunohistochemical expression of differentiation markers in the uterine epithelium following neonatal exposure to DES or GEN

Table 3D.

		Age (mo)					
		2-3			18		
Marker	**Site**	**CON**	**GEN**	**DES**	**CON**	**GEN**	**DES**
ERα	Cervix: non-neoplastic	13/13 (100%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	10/10 (100%)	12/12 (100%)
	Labeling score	2.4	2.0	2.0	2.8	2.0	2.3
	Endometrium: non-neoplastic*	12/12 (100%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	10/10 (100%)	12/12 (100%)
	Labeling score	3.2	3.9	3.9	3.3	3.7	4.0
	Endometrium: neoplastic	na	na	na	na	10/10 (100%)	12/12 (100%)
	Labeling score	na	na	na	na	3.3	3.5
PGR	Cervix: non-neoplastic	13/13 (100%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	10/10 (100%)	12/12 (100%)
	Labeling score	2.5	3.5	3.4	2.1	2.7	2.4
	Endometrium: non-neoplastic*	12/12 (100%)	10/10 (100%)	9/9 (100%)	9/9 (100%)	10/10 (100%)	12/12 (100%)
	Labeling score	1.3	1.6	1.8	2.0	2.2	2.1
	Endometrium: neoplastic	na	na	na	na	10/10 (100%)	12/12 (100%)
	Labeling score	na	na	na	na	1.8	1.7

Abbreviations: CON, control; GEN, genistein; DES, diethylstilbestrol; na, not applicable.
Cervix includes stratified squamous epithelium, mucification layer if present, and transition zone with uterine body; endometrium includes glands and epithelium lining central lumen.
IHC labeling score represents average (0-4) within each group.
* Tissues from some uteri were not present in section.
Letters indicate [a] P<0.05, [b] P<0.01, and [c] P<0.001 compared with corresponding age-matched control group using a two-tailed Fisher exact test.