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Supplemental Material

Multi- and Transgenerational Outcomes of an Exposure to a Mixture of Endocrine-Disrupting Chemicals (EDCs) on Puberty and Maternal Behavior in the Female Rat

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Figure S2. Fold enrichment of gene ontology (GO) annotations using David pathway analysis across compared groups (CTL vs EDC) in the MBH-PoA of F3 generation females at P21. The gene enrichment analysis grouped the differentially expressed genes using GO annotations data. We selected enriched GO annotations using 2-fold enrichment criteria as a threshold and identifying annotations that were involved in brain and behavioral processes. Those annotations were then categorized in upregulated (orange) or downregulated (blue) annotations.

Figure S3. *Nr3c1*, *Crh*, *Grin2d*, *Grid2* and *Avp* mRNA expression in the female rat ancestrally (F3 generation) exposed to an EDC mixture or vehicle in the MBH-PoA of infant (P6), prepubertal (P1) and adult (P60) female rats as determined by qPCR (n=6/group). AU = arbitrary units. RNA expression data were normalized by dividing each individual value by the average of the control group at every time point. Bars represent mean \pm s.e.m. (*P < 0.05, **P < 0.01, ***P < 0.001 vs. CTL, Student's t-test). Summary data are reported in Table S5.

Figure S4. Abundance of the TrxG-dependent activating marks H3K4me3 and H3K9ac and the PcG-dependent repressive mark H3K27me3 and H3K9me3 at the *Kiss1*, *Esr1*, *Oxt*, *Pomc*, *Cart*, *Nr3c1*, *Crh* and *Grin2d* promoter in the prepubertal MBH-PoA of females EDC and control from the F3 generation, as measured by ChIP (n=6/group). Dotted red lines represent repressive histone modifications while green lines represent activatory histone modifications. All data was normalized to control. Bars represent mean \pm s.e.m. (*P < 0.05, **P < 0.01, ***P < 0.001 vs. CTL, Student's t-test). Summary data are reported in Table S5.

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Figure S6. Maternal behavior displayed by F1 female rats exposed *in utero* to a mixture of EDC or vehicle. Data shows time spent by dams displaying in-nest behavior (nest building, Arched-back, blancked and passive nursing; and total time spent in-nest) or off-nest behaviors (eating/drinking, self-grooming, being active and total time off-nest) from P2 to P8. Plotted lines represent average of time \pm s.e.m. Summary data are reported in Table S5.

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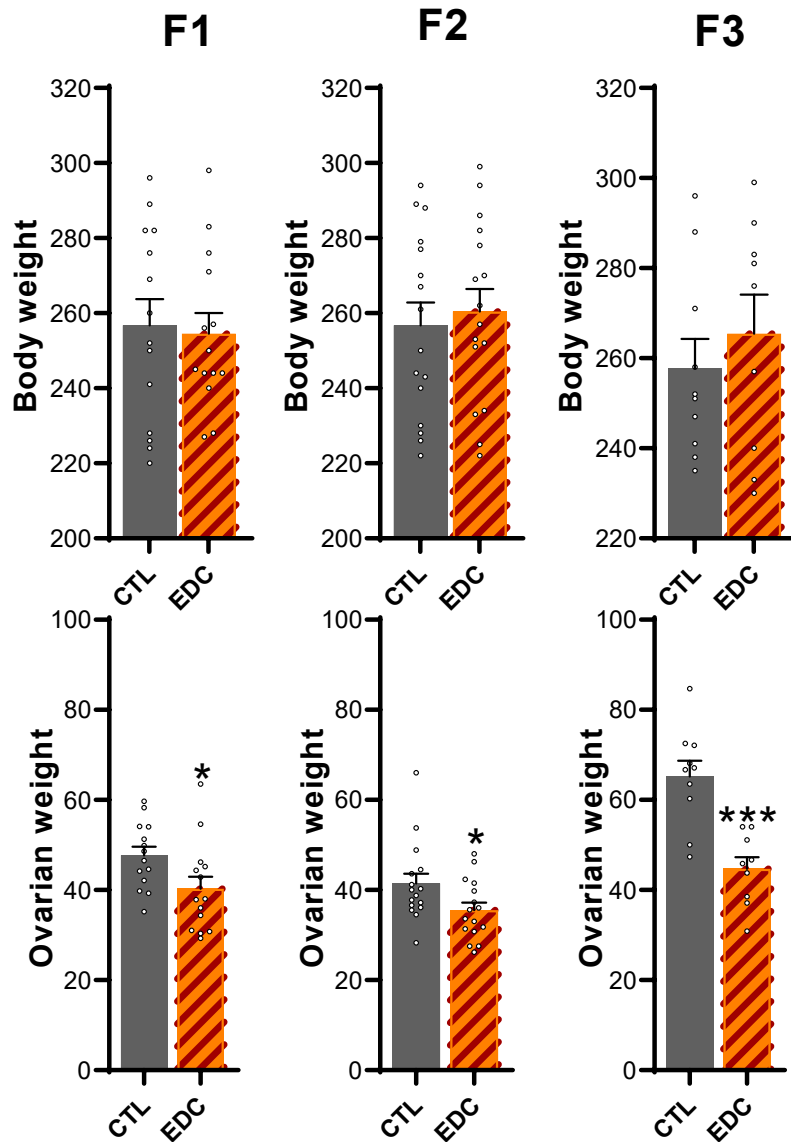


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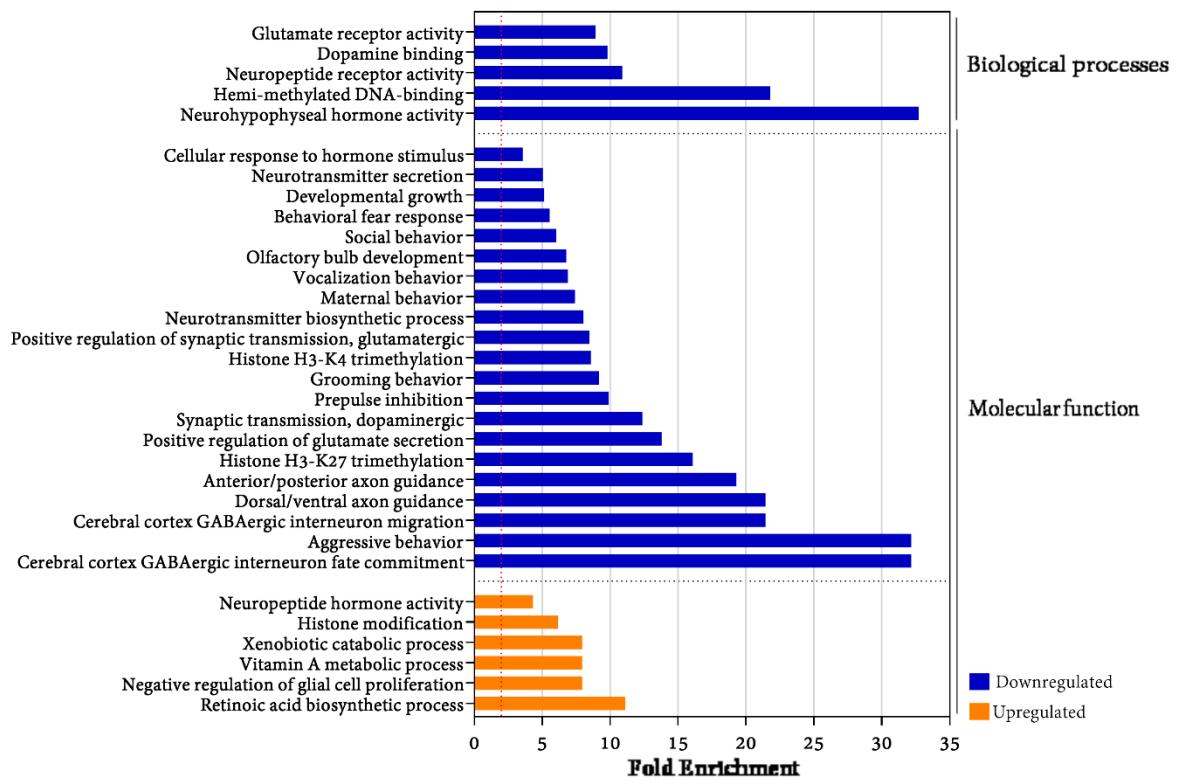


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F3 MBH mRNA validation

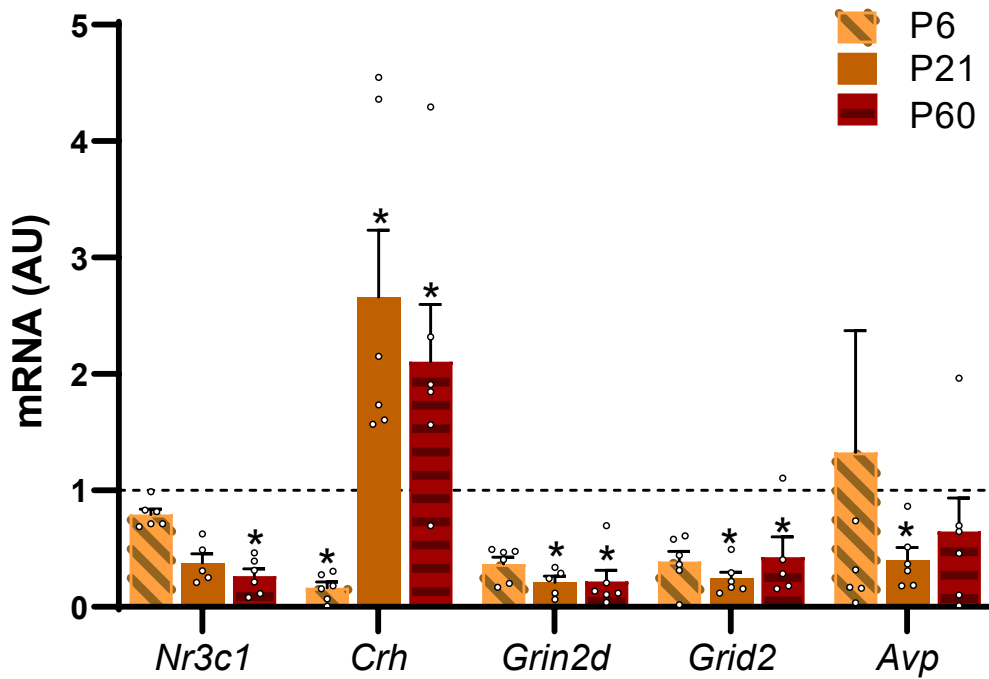


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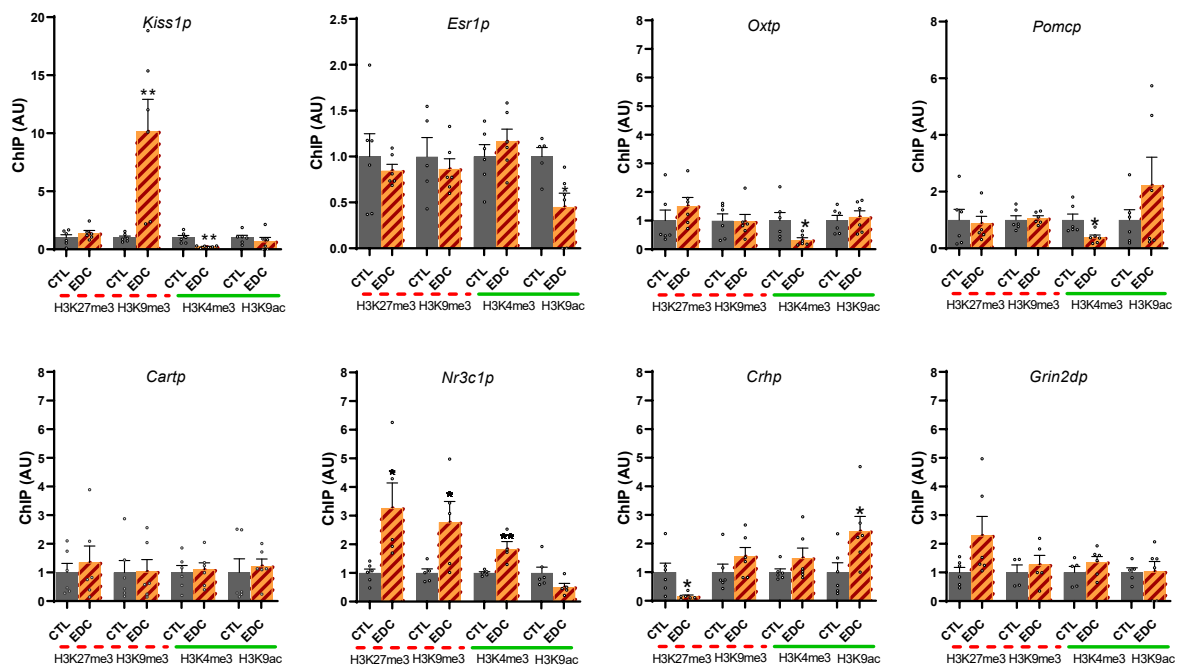


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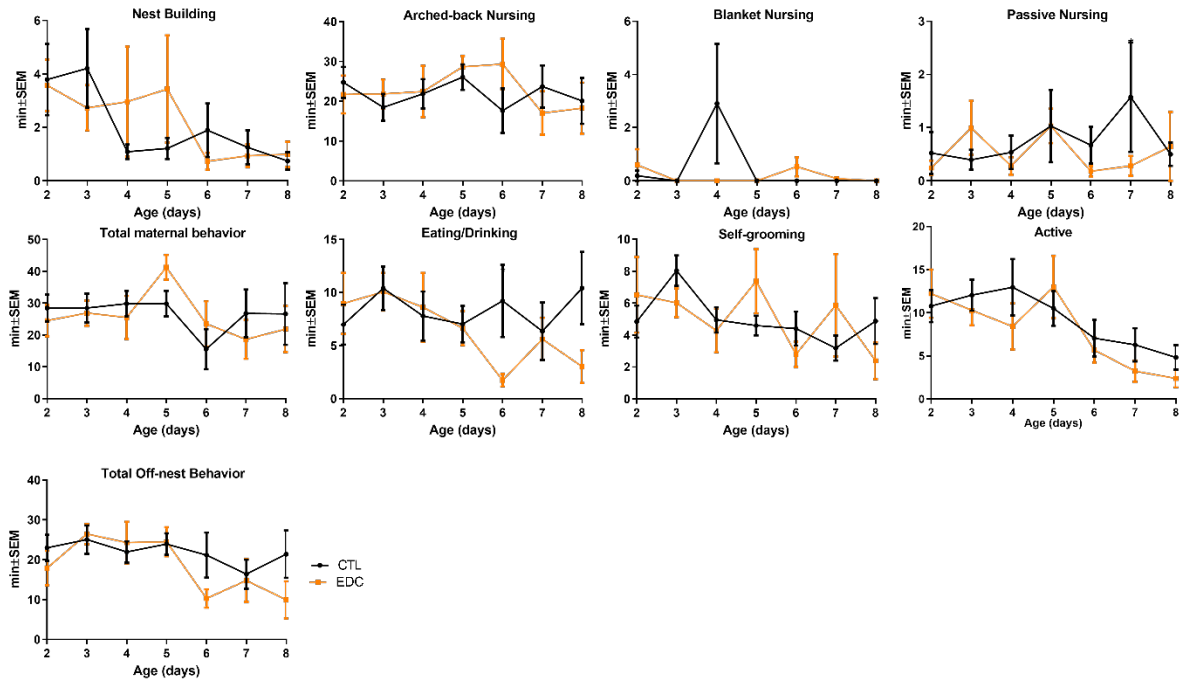


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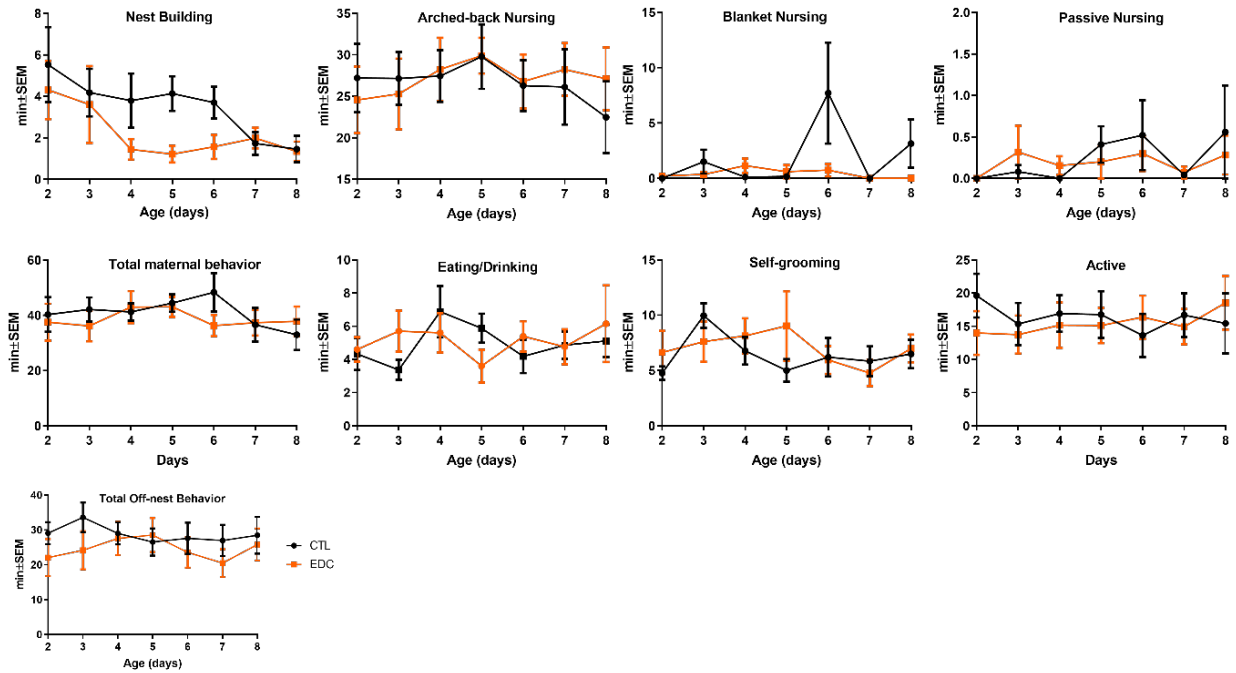


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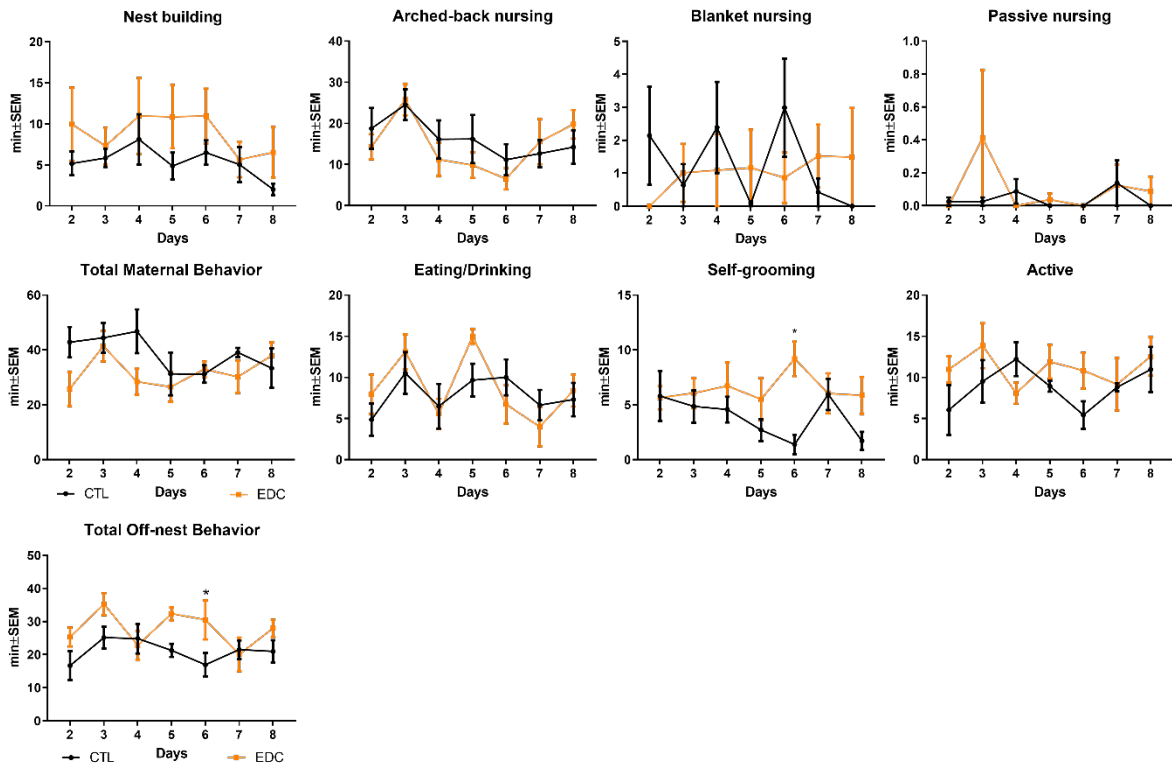


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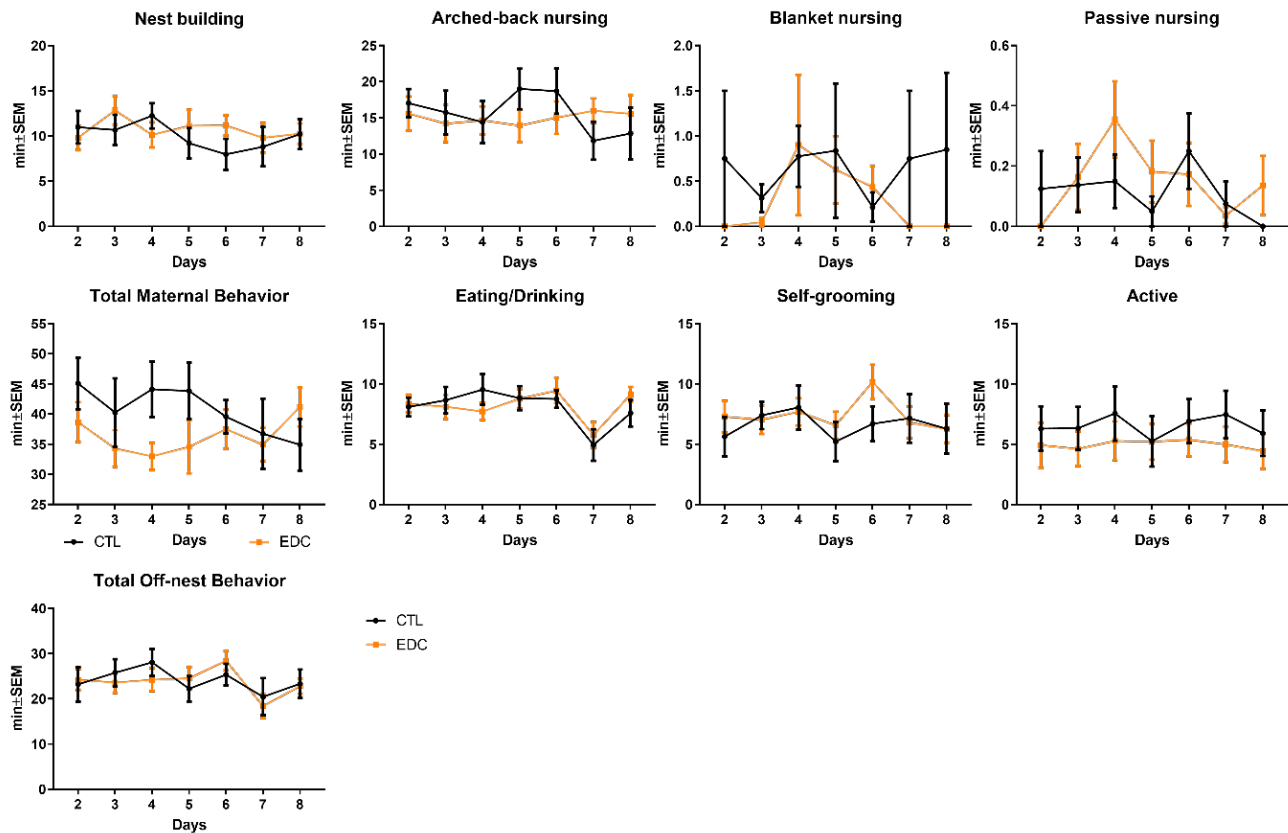


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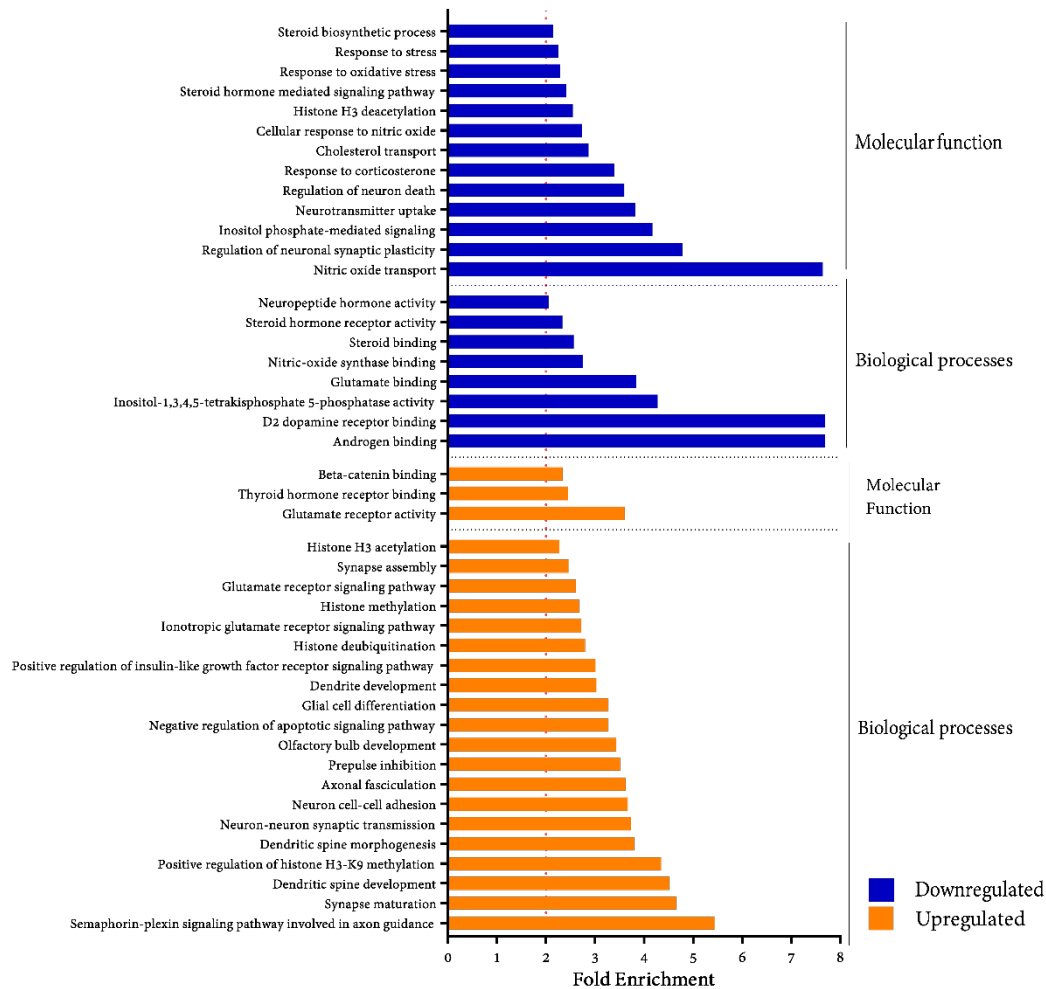


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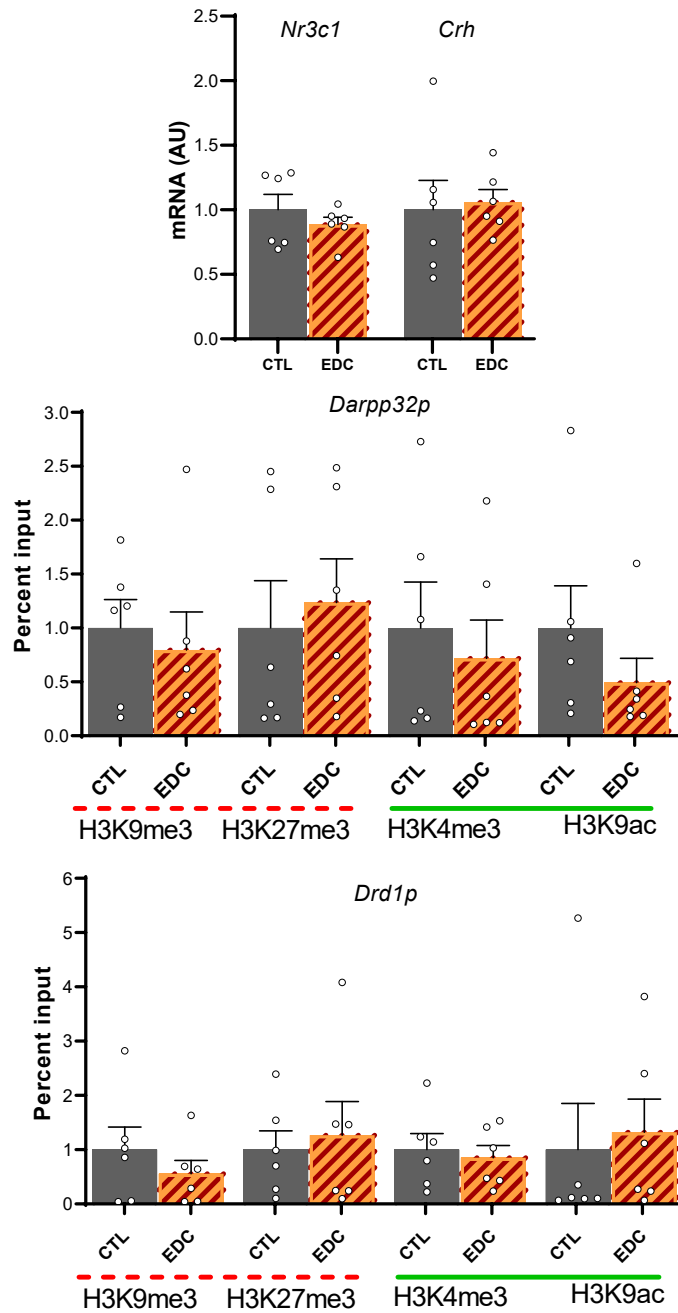


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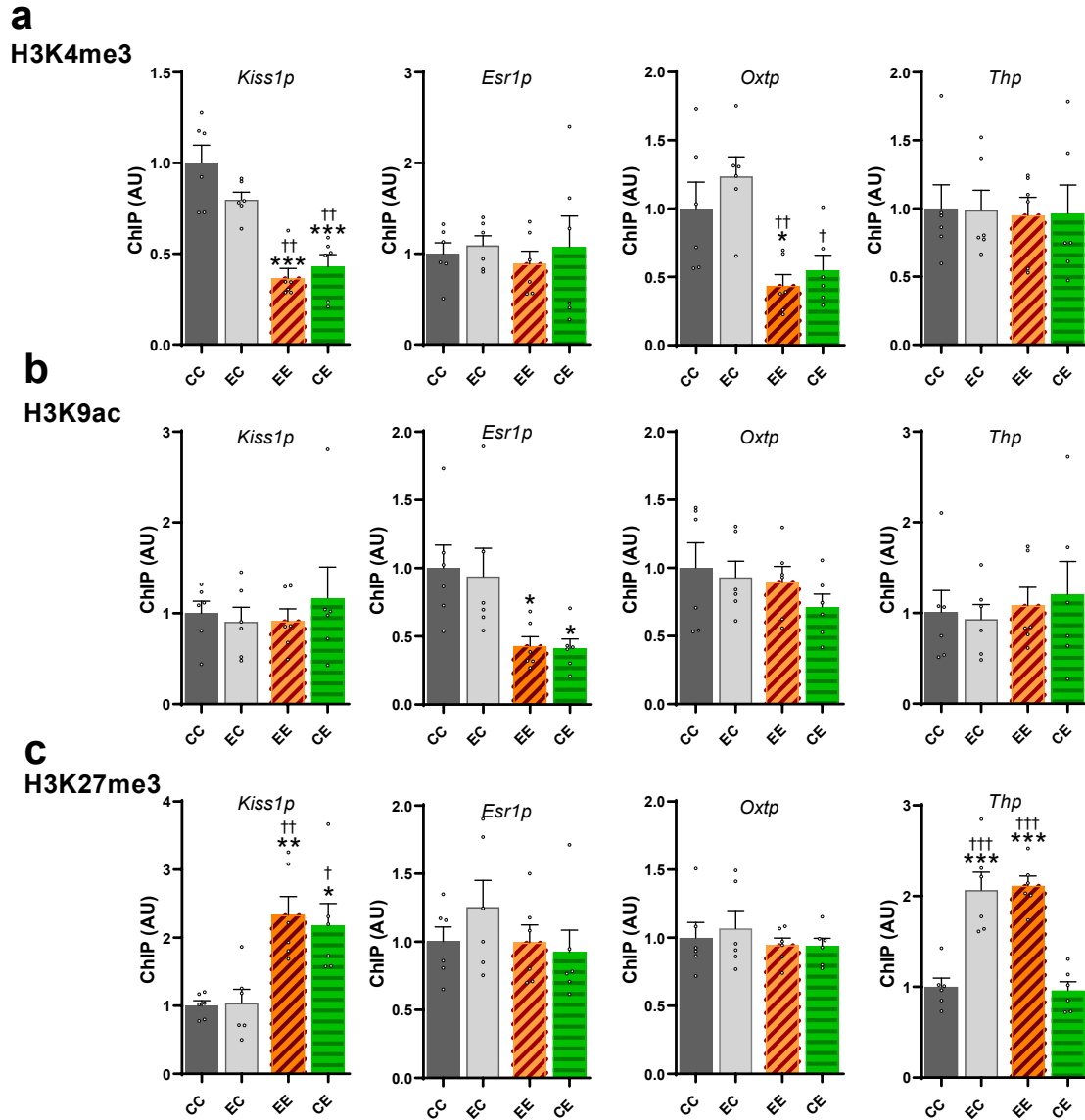


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Table S1. Primer Sequence

Gene	Primer	Accession number	Amplicon size	Use
<i>Kiss1</i>	F <i>TGGTGAACCCTGAACCCACAGGC</i>	NM_181692.1	136	qPCR
	R <i>CGGCGGGCATGGCGATGTT</i>			
<i>Esr1</i>	F <i>CGCTCTGCCTTGATCACACA</i>	NM_012689.1	188	qPCR
	R <i>GCCGAGGTACAGATTGGCTT</i>			
<i>Oxt</i>	F <i>GCTGCCAGGAGGAGAACTAC</i>	NM_012996.3	175	qPCR
	R <i>ATCATCACAAAGCGGGCTCA</i>			
<i>Pomc</i>	F <i>CTTTCCGCGACAGAGCCT</i>	NM_139326.2	113	qPCR
	R <i>CCAGCTCCACACGTCTATGG</i>			
<i>Th</i>	F <i>CCTTCCAGTACAAGCACGGT</i>	NM_012740.3	109	qPCR
	R <i>TGGGTAGCATAGAGGCCCTT</i>			
<i>Cart</i>	F <i>GCGCTGTGTTGCAGATTGAA</i>	NM_017110.1	105	qPCR
	R <i>CGTCACACATGGGGACTTGG</i>			
<i>Nr3c1</i>	F <i>GGTGATTGAACCCGAGGTGT</i>	NM_012576.2	147	qPCRR
	R <i>TTTCTGAAGCCTGGTATCGCC</i>			
<i>Crh</i>	F <i>CAAGGGAGGAGAAGAGAGCG</i>	NM_031019.1	160	qPCR
	R <i>AAGAAATTCACGGCTGCGG</i>			
<i>Grin2d</i>	F <i>AGCTCTGCGACCTGCTGT</i>	NM_022797.1	190	qPCR
	R <i>CCAAGCTGCAGGAAGGTGGA</i>			
<i>Dnm1</i>	F <i>TCTACAAGGATTACCGGCAGC</i>	NM_080689.4	121	qPCR
	R <i>GCTTTCTCCTTGTCCTCCCAACA</i>			
<i>Drd1</i>	F <i>CCACTCTCCTGGGCAATACC</i>	XM_006253600.3	180	qPCR
	R <i>AAAAGGACCCAAAGGGCCAA</i>			
<i>Darpp32</i>	F <i>CCCAAGGACCGCAAGAAGAT</i>	NM_138521.1	172	qPCR
	R <i>CTCCTGAGGTTCTCTGGTGC</i>			
<i>Grid2</i>	F <i>GTCCCATCGAAAGAGGATGACA</i>	NM_024379.1	97	qPCR
	R <i>ACTGTTTATGGGGGCTGTCTG</i>			
<i>Avp</i>	F <i>AGCGATGAGAGCTGCGTG</i>	NM_016992.2	129	qPCR
	R <i>CTGTACCAGCCTAAGCAGCA</i>			
<i>Kiss1</i>	F <i>TCGGGCAGCCAGATAGAGGAAGC</i>	NM_181692.1	91	ChIP
	R <i>TTGAGGGCCGAGGGAGAAGAG</i>			
<i>Esr1</i>	F <i>GTCCCTCAGCAGCCAGCCAGTCT</i>	NM_012689.1	127	ChIP
	R <i>CTCTCGGGAAGCAGCCAGTAGG</i>			
<i>Oxt</i>	F <i>TGTAGCTTAGGCCTCCCCTT</i>	NM_012996.3	159	ChIP
	R <i>CATGACTGGTCACAGCAGGT</i>			
<i>Pomc</i>	F <i>GCTAAGCCTCTGTCCAGTCC</i>	NM_139326.2	103	ChIP
	R <i>GTTAGCACAGACCCGCTGAA</i>			
<i>Th</i>	F <i>CCGACTGGGGCAGTGAATAG</i>	NM_012740.3	198	ChIP
	R <i>TAACCAAACCAGGGCACACA</i>			
<i>Cart</i>	F <i>TTCCATTTTCATGGGCCCTCC</i>	NM_017110.1	139	ChIP
	R <i>GGCTGGAGCACAGAGAACAA</i>			
<i>Nr3c1</i>	F <i>AAGGGTTAGAAGGAATTTGGGGA</i>	NM_012576.2	180	ChIP
	R <i>TGACGTGCCAGAGCCAATTA</i>			
<i>Crh</i>	F <i>ACGCAATCGAGCTGTCAAGA</i>	NM_031019.1	96	ChIP
	R <i>CAGAGCCCGGAGTGAGATTT</i>			
<i>Grin2d</i>	F <i>TCTGGTTCTGTTCTGGGTTTTTG</i>	NM_022797.1	121	ChIP
	R <i>TGGGGTCAGGGAAGATACAGAGGT</i>			
<i>Th – BS</i>	F <i>TCGTCGGCAGCGTCAGATGTGTATA</i>	NM_012740.3	302	BS-seq
	R <i>AGAGACAGGTTTTTTTTTAGGTATAGTAGG</i> <i>GTCTCGTGGGCTCGGAGATGTGTATAA</i> <i>GAGACAGTATTATTATAGGTACAAAAG</i>			

Table S2. List of primary antibodies

Target	Host	Source	Catalog #	Use
Th	Mouse	ImmunoStar	22941	IHC
H3K27me3	Rabbit	Active Motif	39155	ChIP
H3K9ac	Rabbit	Active Motif	39917	ChIP
H3K4me3	Rabbit	Active Motif	39159	ChIP
H3K9me3	Mouse	Active Motif	61013	ChIP
β -Galatocidase	Rabbit	Cortex Biochem	CR7001RP2	ChIP
β -Galatocidase	Mouse	ICN Biomedical	55976	ChIP

Table S3. Report of descriptive and statistical data.

Measure (unit)	F	N	Average		SD		p-value	Effect Size	Figure
			CTL	EDC	CTL	EDC			
Vaginal Opening (days)	F1	51/56	33.92	33.98	1.71	2.94	0.989	0.02	2a
	F2	50/52	34.73	37.93	1.33	1.58	0.000	2.19	2b
	F3	15/24	34.29	38.20	1.92	1.32	0.000	2.37	2c
	F4	47/64	31.36	34.50	1.36	1.40	0.000	2.27	2d
GnRH IP (min)	F1	4	44.38	43.75	1.25	1.44	0.537	0.47	2a
	F3		42.03	44.06	0.94	1.08	0.030	2.01	2c
Regular cycle (%)	F1	20	88.75	89.38	27.77	26.06	0.921	0.02	3a left
Proestrus (%)			23.93	23.31	4.06	5.18	0.679	0.13	
Estrus (%)			26.58	28.78	6.16	12.48	0.483	0.22	
Diestrus (%)			49.49	47.91	5.70	8.47	0.674	0.22	
Regular cycle (%)	F2	15	89.17	60.83	24.49	42.75	0.034	0.81	3b left
Proestrus (%)			23.75	22.50	3.30	4.13	0.744	0.33	
Estrus (%)			26.04	40.42	4.96	17.34	0.001	1.13	
Diestrus (%)			50.21	37.08	5.60	15.12	0.002	1.15	
Regular cycle (%)	F3	15/14	90.83	49.11	22.89	45.85	0.004	1.15	3c left
Proestrus (%)			24.08	17.73	5.24	8.87	0.048	0.87	
Estrus (%)			26.29	37.79	1.70	12.59	0.000	1.28	
Diestrus (%)			49.65	44.49	4.57	6.81	0.048	0.89	
Folliculogenesis (number/mm ³)									3a middle
Primordial	F1	10/9	17.83	12.40	11.52	8.13	0.629	0.55	
Primary			6.28	6.68	4.41	5.95	0.999	0.08	
Secondary			3.55	2.71	1.84	1.57	0.999	0.49	
Antral			1.23	1.00	0.98	0.89	0.999	0.25	
Atretic			8.42	16.25	3.87	11.70	0.061	0.90	
Corpora lutea			0.02	0.05	0.03	0.05	0.999	0.73	
Cysts			1.11	0.66	0.80	0.36	0.185	0.73	
Folliculogenesis (number/mm ³)									3b middle
Primordial	F2	10/9	21.70	9.09	16.52	7.62	0.038	0.98	
Primary			9.25	9.08	6.73	5.61	0.99	0.03	
Secondary			8.54	7.16	6.50	4.14	0.99	0.25	
Antral			2.55	0.74	1.16	0.88	0.045	1.76	
Atretic			18.08	33.62	6.79	25.12	0.014	0.84	
Corpora lutea			0.01	0.12	0.03	0.16	0.99	0.97	
Cysts			0.63	1.13	1.06	1.36	0.470	0.41	
Folliculogenesis (number/mm ³)									3c middle
Primordial	F3	10/9	25.31	9.96	12.37	5.59	0.033	1.60	
Primary			7.00	8.25	5.37	8.31	0.999	0.18	
Secondary			2.49	3.52	1.98	2.21	0.988	0.49	
Antral			1.20	0.29	0.85	0.37	0.048	1.38	
Atretic			10.64	13.70	10.06	8.08	0.002	0.34	
Corpora lutea			0.04	0.07	0.08	0.12	0.998	0.29	
Cysts			1.13	1.02	0.60	1.31	0.128	0.10	
Normalized ovarian Weight (ratio)	F1	14	47.69	40.33	7.34	9.94	0.035	0.84	3a right
	F2	16	41.44	35.54	8.85	6.61	0.041	0.76	3b right
	F3	10/9	65.24	44.67	10.90	7.96	0.000	2.16	3c right

Notes: Effect size was calculated using Cohen's *d*. AU= arbitrary units. F= generation. N=sample size. SD: standard deviation.IP: interpulse interval.

Table S3. Report of descriptive and statistical data (continuation)

Measure (unit)	F	N	Average		SD		p-value	Effect Size	Figure
			CTL	EDC	CTL	EDC			
<i>Kiss1</i> P6 (AU)	F3	6	1	0.39	0.13	0.23	0.002	3.27	4a
<i>Kiss1</i> P21 (AU)			1	0.51	0.34	0.29	0.034	1.56	
<i>Kiss1</i> P70 (AU)			1	0.38	0.07	0.34	0.026	2.52	
<i>Esr1</i> P6 (AU)			1	0.85	0.15	0.24	0.792	0.76	
<i>Esr1</i> P21 (AU)			1	0.32	0.50	0.32	0.019	1.61	
<i>Esr1</i> P70 (AU)			1	0.21	0.07	0.16	0.013	6.40	
<i>Oxt</i> P6 (AU)			1	0.22	0.75	0.16	0.012	1.44	
<i>Oxt</i> P21 (AU)			1	0.23	1.26	0.19	0.018	0.86	
<i>Oxt</i> P70 (AU)			1	0.36	0.09	0.33	0.043	2.64	
<i>Cart</i> P6 (AU)			1	0.77	0.10	0.78	0.543	0.41	
<i>Cart</i> P21 (AU)			1	3.24	0.32	1.66	0.013	1.88	
<i>Cart</i> P70 (AU)			1	0.87	0.16	0.43	0.811	0.41	
<i>Pomc</i> P6 (AU)			1	0.22	0.15	0.15	0.017	5.20	
<i>Pomc</i> P21 (AU)			1	2.60	0.15	1.38	0.023	1.63	
<i>Pomc</i> P70 (AU)			1	1.00	0.17	0.75	0.999	0.01	
<i>Kiss1</i> p H3K27me3 (AU)			1	10.15	0.34	6.78	0.008	1.91	4b
<i>Kiss1</i> p H3K4me3 (AU)			1	0.22	0.46	0.09	0.002	2.38	
<i>Esr1</i> p H3K9ac (AU)			1	0.32	0.69	0.20	0.044	1.33	
<i>Oxtp</i> H3K4me3 (AU)			1	0.32	0.69	0.20	0.044	1.33	
<i>Pomcp</i> H3K4me3 (AU)			1	0.38	0.51	0.21	0.021	1.58	
Licking (min)	F0	15	6.52	5.14	2.64	3.07	0.218	0.49	5a
	F1	10/11	9.18	5.84	3.27	3.59	0.038	0.97	5b
	F2	11	11.93	6.38	3.72	3.49	0.008	1.54	5c
	F3	11	13.79	9.71	2.40	2.79	0.004	1.57	5d
Resting alone (min)	F0	15	0.57	0.24	1.09	0.35	0.369	0.41	5a
	F1	10/11	0.68	1.93	0.93	1.07	0.011	1.24	5b
	F2	11	0.44	1.62	0.43	1.19	0.021	1.30	5c
	F3	11	2.85	3.18	3.20	3.14	0.825	0.10	5d
<i>Th</i> P6 (AU)	F1	6	1	0.65	0.19	0.27	0.547	1.51	6a
<i>Th</i> P21 (AU)			1	0.18	0.64	0.10	0.031	1.79	
<i>Th</i> P60 (AU)			1	0.11	0.22	0.13	0.013	4.93	
<i>Dnm1</i> P6 (AU)			1	0.30	0.24	0.14	0.565	3.58	
<i>Dnm1</i> P21 (AU)			1	0.33	0.10	0.26	0.039	3.40	
<i>Dnm1</i> P60 (AU)			1	1.15	0.29	0.66	0.495	0.29	
<i>Drd1</i> P6 (AU)			1	1.22	0.22	0.33	0.999	0.79	
<i>Drd1</i> P21 (AU)			1	3.41	0.24	1.70	0.016	1.99	
<i>Drd1</i> P60 (AU)			1	0.95	0.14	0.76	0.999	0.09	
<i>Darpp32</i> P6 (AU)			1	0.75	0.17	0.29	0.775	1.05	
<i>Darpp32</i> P21 (AU)			1	0.26	0.73	0.19	0.095	1.39	
<i>Darpp32</i> P60 (AU)			1	0.19	0.30	0.09	0.002	3.64	
<i>Thp</i> methylation CpG site 1	F1	6	0,89	0,88	0,01	0,02	0,097	1,19	6b
CpG site 2			0,84	0,84	0,01	0,01	0,981	0,02	
CpG site 3			0,74	0,72	0,02	0,01	0,143	1,09	
CpG site 4			0,73	0,72	0,02	0,03	0,727	0,24	
CpG site 5			0,77	0,76	0,01	0,02	0,289	0,73	
CpG site 6			0,84	0,83	0,01	0,01	0,154	1,02	
CpG site 7			0,79	0,79	0,01	0,02	0,971	0,02	
CpG site 8			0,63	0,62	0,01	0,03	0,457	0,50	
CpG site 9			0,66	0,66	0,02	0,02	0,936	0,06	
CpG site 10			0,70	0,69	0,03	0,02	0,691	0,28	
CpG site 11			0,55	0,53	0,03	0,01	0,177	1,01	
CpG site 12			0,83	0,84	0,01	0,01	0,648	0,32	
CpG site 13			0,83	0,82	0,01	0,01	0,310	0,74	

Notes: Effect size was calculated using Cohen's *d*. AU= arbitrary units. F= generation. N=sample size. SD: standard deviation. qPCR and ChIP data were normalized to the control group.

Table S3. Report of descriptive and statistical data (continuation)

Measure (unit)	F	N	Average		SD		p-value	Effect Size	Figure
			CTL	EDC	CTL	EDC			
<i>Thp</i> H3K27me3 (AU)	F1	6	1	3.12	0.52	2.10	0.019	1.39	6c
<i>Thp</i> H3K9me3 (AU)			1	1.32	1.12	1.27	0.657	0.26	
<i>Thp</i> H3K4me3 (AU)			1	1.19	0.27	0.77	0.581	0.33	
<i>Thp</i> H3K9ac (AU)			1	1.21	0.64	0.67	0.591	0.32	
<i>Th</i> -ir SN (number)			92.7	87.64	21.05	21.15	0.687	0.24	6e
<i>Th</i> -ir VTA (number)			125.3	116.20	26.47	24.22	0.549	0.36	
<i>Th</i> -ir mPoA (number)			3.98	2.53	0.61	0.36	0.001	2.90	
<i>Th</i> P6 (AU)	F3		1	0.40	0.89	0.37	0.248	0.88	6f
<i>Th</i> P21 (AU)			1	0.36	0.16	0.17	0.040	3.8	
<i>Th</i> P60 (AU)			1	0.46	0.91	0.44	0.395	0.77	
<i>Drd1</i> P6 (AU)			1	0.36	0.58	0.23	0.486	1.45	
<i>Drd1</i> P21 (AU)			1	0.47	0.11	0.15	0.042	4.03	
<i>Drd1</i> P60 (AU)			1	0.15	0.17	0.25	0.001	3.98	
<i>Thp</i> methylation CpG site 1	F3		0,92	0,92	0,02	0,02	0,782	0,18	6g
CpG site 2			0,88	0,89	0,02	0,02	0,749	0,21	
CpG site 3			0,76	0,77	0,04	0,04	0,475	0,47	
CpG site 4			0,77	0,81	0,02	0,03	0,018	1,78	
CpG site 5			0,83	0,85	0,04	0,01	0,286	0,71	
CpG site 6			0,86	0,89	0,02	0,01	0,023	1,69	
CpG site 7			0,83	0,80	0,03	0,03	0,170	0,94	
CpG site 8			0,66	0,66	0,04	0,05	0,883	0,10	
CpG site 9			0,74	0,68	0,04	0,05	0,062	1,33	
CpG site 10			0,76	0,80	0,03	0,06	0,110	1,11	
CpG site 11			0,55	0,62	0,02	0,04	0,004	2,37	
CpG site 12			0,86	0,86	0,03	0,04	0,940	0,05	
CpG site 13			0,90	0,89	0,04	0,04	0,650	0,30	
<i>Thp</i> H3K27me3 (AU)			1	2.16	0.47	1.62	0.124	0.97	6h
<i>Thp</i> H3K9me3 (AU)			1	2.17	0.38	1.13	0.037	1.38	
<i>Thp</i> H3K4me3 (AU)			1	0.90	0.36	0.43	0.657	0.26	
<i>Thp</i> H3K9ac (AU)			1	1.04	0.33	0.51	0.888	0.08	

Notes: Effect size was calculated using Cohen's d . AU= arbitrary units. F= generation. N=sample size. SD: standard deviation. qPCR and ChIP data were normalized to the control group.

Table S4. Report of descriptive data and statistical analysis of crossfostering data.

Measure (unit)	F	N	Group	Average	SD	Comparison	p-value	Effect Size	Figure
Vaginal opening (days)	F2-C	16/19	CC	34.67	1.56	CC vs. CE	0.003	1.29	7a
			CE	37.05	2.09	CC vs. EE	0.003	1.46	
			EE	37.13	1.81	CE vs. EC	0.001	1.30	
			EC	34.72	1.45	EE vs. EC	0.001	1.47	
Regular cycle (%)		10	CC	85.00	18.34	CC vs. CE	0.485	0.23	7b
			CE	75.00	27.50	CC vs. EE	0.775	0.42	
			EE	75.00	23.90	CE vs. EC	0.813	0.30	
			EC	88.33	17.66	EE vs. EC	0.715	0.51	
Proestrus (%)			CC	21.25	3.65	CC vs. CE	0.999	0.04	
			CE	19.58	6.53	CC vs. EE	0.999	0.03	
			EE	22.08	4.83	CE vs. EC	0.999	0.07	
			EC	22.92	2.95	EE vs. EC	0.988	0.03	
Estrus (%)			CC	23.33	3.51	CC vs. CE	0.997	0.12	
			CE	25.83	6.15	CC vs. EE	0.008	1.13	
			EE	32.50	10.90	CE vs. EC	0.587	0.23	
			EC	26.25	4.41	EE vs. EC	0.916	0.62	
Diestrus (%)			CC	55.42	6.23	CC vs. CE	0.999	0.04	
			CE	54.58	8.21	CC vs. EE	0.002	1.30	
			EE	45.42	8.88	CE vs. EE	0.008	1.07	
			EC	50.83	4.30	EE vs. EC	0.299	0.42	
<i>Kiss1</i> (AU)		6	CC	1.00	0.19	CC vs. CE	0.001	2.94	7c
			CE	0.46	0.18	CC vs. EE	0.012	2.03	
			EE	0.61	0.20	CE vs. EC	0.000	2.96	
			EC	1.05	0.22	EE vs. EC	0.004	2.13	
<i>Esr1</i> (AU)			CC	1.00	0.41	CC vs. CE	0.015	2.12	7d
			CE	0.36	0.12	CC vs. EE	0.038	1.84	
			EE	0.44	0.13	CE vs. EC	0.006	2.03	
			EC	1.07	0.48	EE vs. EC	0.017	1.79	
<i>Oxt</i> (AU)			CC	1.00	0.22	CC vs. CE	0.003	2.68	7e
			CE	0.42	0.22	CC vs. EE	0.005	2.87	
			EE	0.44	0.17	CE vs. EC	0.001	2.17	
			EC	1.06	0.36	EE vs. EC	0.002	2.22	
<i>Th</i> (AU)			CC	1.00	0.10	CC vs. CE	0.001	3.42	7f
			CE	1.14	0.26	CC vs. EE	0.000	5.02	
			EE	0.37	0.15	CE vs. EE	0.000	3.68	
			EC	0.52	0.17	CE vs. EC	0.000	2.83	
<i>Kiss1</i> (AU)	F3-C		CC	1.00	0.35	CC vs. CE	0.027	1.42	7c
			CE	0.56	0.26	CC vs. EE	0.043	1.47	
			EE	0.59	0.18	CE vs. EC	0.007	2.53	
			EC	1.09	0.14	EE vs. EC	0.011	3.08	
<i>Esr1</i> (AU)			CC	1.00	0.20	CC vs. CE	0.001	3.09	7d
			CE	0.29	0.26	CC vs. EE	0.002	3.15	
			EE	0.32	0.23	CE vs. EC	0.002	2.15	
			EC	0.97	0.36	EE vs. EC	0.003	2.12	
<i>Oxt</i> (AU)			CC	1.00	0.20	CC vs. EC	0.275	0.42	7e
			CE	0.57	0.11	CC vs. EE	0.057	0.42	
			EE	0.56	0.16	CE vs. EC	0.003	1.49	
			EC	1.27	0.52	EE vs. EC	0.003	2.63	
<i>Th</i> (AU)			CC	1.00	0.25	CC vs. EC	0.000	2.89	7f
			CE	1.00	0.22	CC vs. EE	0.000	3.22	
			EE	0.37	0.12	CE vs. EE	0.000	3.50	
			EC	0.32	0.22	CE vs. EC	0.000	3.05	
<i>Kiss1</i> p H3K27me3 (AU)			CC	1.00	0.18	CC vs. CE	0.011	2.05	7c
			CE	2.18	0.79	CC vs. EE	0.004	0.74	
			EE	2.33	0.67	EE vs. EC	0.005	2.17	
			EC	1.04	0.50	CE vs. EC	0.015	1.72	
<i>Esr1</i> p H3K9ac (AU)			CC	1.00	0.41	CC vs. CE	0.039	1.86	7d
			CE	0.41	0.17	CC vs. EE	0.046	1.81	
			EE	0.43	0.17	CE vs. EC	0.744	0.24	
			EC	0.94	0.51	EE vs. EC	0.999	0.12	
<i>Oxt</i> p H3K4me3 (AU)			CC	1.00	0.48	CC vs. CE	0.428	0.01	7e
			EC	1.24	0.35	CC vs. EE	0.044	1.54	
			EE	0.44	0.20	CE vs. EC	0.012	2.19	
			CE	0.55	0.27	EE vs. EC	0.003	2.78	
<i>Th</i> p H3K27me3 (AU)			CC	1.00	0.24	CC vs. CE	0.000	0.17	7f
			CE	0.96	0.23	CC vs. EE	0.000	4.46	
			EE	2.11	0.26	EE vs. EC	0.000	0.12	
			EC	2.07	0.48	CE vs. EC	0.000	2.91	

Notes: Effect size was calculated using Cohen's *d*. AU= arbitrary units. F= generation. N=sample size. SD: standard deviation. IP: interpulseinterval.

Table S5. Report of descriptive and statistical data from supplementary material.

Measure (unit)	F	N	Average		SD		p-value	Effect Size	Figure
			CTL	EDC	CTL	EDC			
Body weight (g)	F1	14	256.79	254.50	25.21	19.92	0.80	0.10	S1
Ovarian weight (mg)		14	47.69	40.33	7.34	9.94	0.03	0.84	
Body weight (g)	F2	16	256.80	260.40	24.47	23.97	0.67	0.15	
Ovarian weight (mg)		16	41.44	35.54	8.85	6.61	0.04	0.76	
Body weight (g)	F3	10/9	257.70	265.40	20.91	26.02	0.48	0.33	
Ovarian weight (mg)			65.24	44.67	10.90	7.96	0.00	0.33	
<i>Nr3c1</i> P6 (AU)		6	1.00	0.79	0.46	0.10	0.95	0.62	S3
<i>Nr3c1</i> P21 (AU)			1.00	0.38	0.31	0.16	0.16	2.54	
<i>Nr3c1</i> P60 (AU)			1.00	0.26	0.74	0.14	0.04	1.58	
<i>Crh</i> P6 (AU)			1.00	0.17	0.38	0.11	0.03	3.01	
<i>Crh</i> P21 (AU)			1.00	2.66	0.47	1.28	0.02	1.72	
<i>Crh</i> P60 (AU)			1.00	2.11	0.63	1.10	0.04	1.24	
<i>Grin2d</i> P6 (AU)			1.00	0.37	0.99	0.13	0.09	2.17	
<i>Grin2d</i> P21 (AU)			1.00	0.21	0.39	0.10	0.04	2.74	
<i>Grin2d</i> P60 (AU)			1.00	0.22	0.42	0.22	0.05	2.33	
<i>Grid2</i> P6 (AU)			1.00	0.39	0.36	0.20	0.25	2.09	
<i>Grid2</i> P21 (AU)			1.00	0.24	0.36	0.13	0.04	2.80	
<i>Grid2</i> P60 (AU)			1.00	0.43	0.26	0.35	0.08	1.39	
<i>Avp</i> P6 (AU)			1.00	1.33	0.71	2.34	0.77	0.19	
<i>Avp</i> P21 (AU)			1.00	0.40	0.21	0.23	0.05	0.99	
<i>Avp</i> P60 (AU)			1.00	0.65	0.67	0.64	0.86	0.54	
<i>Kiss1p</i> H3K27me3 (AU)			1.00	1.39	0.63	0.56	0.29	0.65	S4
<i>Kiss1p</i> H3K9me3 (AU)			1.00	10.15	0.34	6.78	0.01	1.90	
<i>Kiss1p</i> H3K4me3 (AU)			1.00	0.22	0.46	0.09	0.00	2.38	
<i>Kiss1p</i> H3K9ac (AU)			1.00	0.69	0.52	0.81	0.45	0.45	
<i>Esr1p</i> H3K27me3 (AU)			1.00	0.85	0.61	0.17	0.56	0.34	
<i>Esr1p</i> H3K9me3 (AU)			1.00	0.86	0.46	0.27	0.56	0.36	
<i>Esr1p</i> H3K4me3 (AU)			1.00	1.17	0.32	0.32	0.39	0.52	
<i>Esr1p</i> H3K9ac (AU)			1.00	0.45	0.22	0.37	0.02	1.80	
<i>Oxtp</i> H3K27me3 (AU)			1.00	1.51	0.90	0.73	0.31	0.62	
<i>Oxtp</i> H3K9me3 (AU)			1.00	0.96	0.58	0.61	0.92	0.06	
<i>Oxtp</i> H3K4me3 (AU)			1.00	0.32	0.69	0.20	0.04	1.33	
<i>Oxtp</i> H3K9ac (AU)			1.00	1.13	0.44	0.53	0.66	0.26	
<i>Pomcp</i> H3K27me3 (AU)			1.00	0.87	0.92	0.63	0.79	0.16	
<i>Pomcp</i> H3K9me3 (AU)			1.00	1.06	0.37	0.21	0.72	0.21	
<i>Pomcp</i> H3K4me3 (AU)			1.00	0.38	0.51	0.21	0.02	1.58	
<i>Pomcp</i> H3K9ac (AU)			1.00	2.22	0.89	2.44	0.27	0.67	
<i>Cartp</i> H3K27me3 (AU)			1.00	1.35	0.78	1.41	0.61	0.30	
<i>Cartp</i> H3K9me3 (AU)			1.00	1.03	1.03	1.02	0.96	0.03	
<i>Cartp</i> H3K4me3 (AU)			1.00	1.09	0.60	0.60	0.79	0.16	
<i>Cartp</i> H3K9ac (AU)			1.00	1.22	1.16	0.61	0.69	0.24	
<i>Nr3c1p</i> H3K27me3 (AU)			1.00	3.27	0.34	1.97	0.02	1.61	
<i>Nr3c1p</i> H3K9me3 (AU)			1.00	2.76	0.46	1.27	0.05	1.84	
<i>Nr3c1p</i> H3K4me3 (AU)			1.00	0.45	0.22	0.37	0.01	1.80	
<i>Nr3c1p</i> H3K9ac (AU)			1.00	0.51	0.50	0.28	0.09	1.20	
<i>Crhp</i> H3K27me3 (AU)			1.00	0.16	0.77	0.11	0.02	1.54	
<i>Crhp</i> H3K9me3 (AU)			1.00	1.56	0.69	0.74	0.21	0.78	
<i>Crhp</i> H3K4me3 (AU)			1.00	1.49	0.28	0.86	0.21	0.77	
<i>Crhp</i> H3K9ac (AU)			1.00	2.44	0.80	1.25	0.04	1.37	
<i>Grin2dp</i> H3K27me3 (AU)			1.00	2.29	0.44	1.63	0.09	1.08	
<i>Grin2dp</i> H3K9me3 (AU)			1.00	1.27	0.52	0.73	0.55	0.43	
<i>Grin2dp</i> H3K4me3 (AU)			1.00	1.36	0.46	0.48	0.24	0.76	
<i>Grin2dp</i> H3K9ac (AU)			1.00	2.22	0.89	2.44	0.27	0.67	

Notes: Effect size was calculated using Cohen's *d*. AU= arbitrary units. F= generation. N=sample size. SD: standard deviation.

Table S5. Report of descriptive and statistical data from supplementary material (continuation).

Measure (unit)	F	N	Average		SD		p-value	Effect Size	Figure
			CTL	EDC	CTL	EDC			
Nest-building (minutes)	F0	12/15	2.18	2.19	1.83	1.96	0.99	0.01	S5
Arched-back nursing (minutes)			22.69	22.76	8.78	12.18	0.99	0.01	
Blanket nursing (minutes)			0.46	0.17	1.20	0.31	0.44	0.33	
Passive nursing (minutes)			0.63	0.52	0.73	0.58	0.69	0.17	
Total maternal behavior (minutes)			28.03	26.03	9.33	12.42	0.65	0.18	
Eating/drinking (minutes)			8.24	6.38	4.06	4.19	0.27	0.45	
Self-grooming (minutes)			5.29	5.04	1.38	3.48	0.80	0.10	
Active (minutes)			9.76	7.90	3.65	4.11	0.24	0.48	
Total off-nest behavior (minutes)			22.36	18.31	6.66	5.65	0.12	0.66	
Nest-building (minutes)	F1	10/11	3.51	2.21	1.32	1.42	0.05	0.94	S6
Arched-back nursing (minutes)			26.64	27.16	7.26	3.42	0.84	0.09	
Blanket nursing (minutes)			1.81	0.44	2.79	0.48	0.15	0.68	
Passive nursing (minutes)			0.23	0.19	0.34	0.24	0.77	0.14	
Total maternal behavior (minutes)			40.85	38.73	10.97	9.71	0.66	0.20	
Eating/drinking (minutes)			5.11	4.95	1.28	1.88	0.82	0.10	
Self-grooming (minutes)			6.44	7.02	1.76	2.70	0.59	0.25	
Active (minutes)			16.34	15.40	7.51	8.18	0.80	0.12	
Total off-nest behavior (minutes)			28.76	24.61	8.35	11.28	0.38	0.42	
Nest-building (minutes)	F2	8	5.36	8.89	1.54	7.13	0.20	0.68	S7
Arched-back nursing (minutes)			16.26	14.72	5.83	4.54	0.87	0.29	
Blanket nursing (minutes)			1.24	1.02	1.05	0.85	0.90	0.23	
Passive nursing (minutes)			0.04	0.09	0.06	0.15	0.23	0.48	
Total maternal behavior (minutes)			38.43	31.88	7.81	7.13	0.24	0.88	
Eating/drinking (minutes)			7.93	8.67	1.68	3.11	0.55	0.30	
Self-grooming (minutes)			3.85	6.43	1.22	1.91	0.02	1.61	
Active (minutes)			8.84	11.05	2.51	1.14	0.06	1.13	
Total off-nest behavior (minutes)			21.06	27.76	3.43	5.70	0.12	1.43	
Nest-building (minutes)	F3	8/11	10.01	10.73	2.62	2.37	0.56	0.29	S8
Arched-back nursing (minutes)			15.66	14.99	6.23	4.89	0.81	0.12	
Blanket nursing (minutes)			0.64	0.29	0.69	0.46	0.22	0.60	
Passive nursing (minutes)			0.11	0.15	0.06	0.08	0.29	0.55	
Total maternal behavior (minutes)			40.64	36.30	9.14	6.06	0.26	0.56	
Eating/drinking (minutes)			8.05	8.19	1.61	1.48	0.86	0.09	
Self-grooming (minutes)			6.63	7.40	3.76	2.66	0.63	0.24	
Active (minutes)			6.53	4.97	3.74	3.13	0.36	0.45	
Total off-nest behavior (minutes)			24.07	23.74	6.70	4.88	0.91	0.06	
<i>Nr3c1</i> (AU)	F1	6	1.00	0.89	0.29	0.14	0.41	0.49	S10 top
<i>Crh</i> (AU)			1.00	1.06	0.56	0.24	0.82	0.14	
<i>Darpp32p</i> H3K9me3 (AU)			1.00	0.80	0.65	0.86	0.65	0.27	S10 middle
<i>Darpp32p</i> H3K27me3 (AU)			1.00	1.24	1.08	0.99	0.70	0.23	
<i>Darpp32p</i> H3K4me3 (AU)			1.00	0.72	1.05	0.87	0.62	0.29	
<i>Darpp32p</i> H3K9ac (AU)			1.00	0.49	0.96	0.55	0.29	0.65	
<i>Drd1p</i> H3K9me3 (AU)			1.00	0.56	1.02	0.60	0.38	0.53	S10 bottom
<i>Drd1p</i> H3K27me3 (AU)			1.00	1.24	1.08	0.99	0.70	0.23	
<i>Drd1p</i> H3K4me3 (AU)			1.00	0.72	1.05	0.87	0.62	0.29	
<i>Drd1pp</i> H3K9ac (AU)			1.00	0.49	0.96	0.55	0.29	0.65	

Notes: Effect size was calculated using Cohen's *d*. AU= arbitrary units. F= generation. N=sample size. SD: standard deviation.

Table S6. Report of descriptive data and statistical analysis of crossfostering data from the supplementary material.

Measure (unit)	F	N	Group	Average	SD	Comparison	p-value	Effect Size	Figure
<i>Kiss1p</i> H3K4me3 (AU)	F2-C	6	CC	1.00	0.24	CC vs. CE	0.00	2.77	S11a
			CE	0.43	0.16	CC vs. EE	0.00	3.27	
			EE	0.37	0.13	CE vs. EC	0.01	2.72	
			EC	0.80	0.10	EE vs. EC	0.00	3.70	
<i>Esr1p</i> H3K4me3 (AU)			CC	1.00	0.30	CC vs. CE	0.99	0.11	
			CE	1.07	0.84	CC vs. EE	0.98	0.34	
			EE	0.89	0.34	CE vs. EC	1.00	0.03	
			EC	1.09	0.26	EE vs. EC	0.89	0.66	
<i>Oxtp</i> H3K4me3 (AU)			CC	1.00	0.48	CC vs. CE	0.13	1.17	
			CE	0.55	0.27	CC vs. EE	0.04	1.54	
			EE	0.44	0.20	CE vs. EC	0.01	2.19	
			EC	1.24	0.35	EE vs. EC	0.00	2.77	
<i>Thp</i> H3K4me3 (AU)			CC	1.00	0.43	CC vs. CE	1.00	0.08	
			CE	0.96	0.52	CC vs. EE	1.00	0.13	
			EE	0.95	0.32	CE vs. EC	1.00	0.05	
			EC	0.99	0.36	EE vs. EC	1.00	0.11	
<i>Kiss1p</i> H3K9ac (AU)			CC	1.00	0.33	CC vs. CE	0.94	0.26	S11b
			CE	1.17	0.84	CC vs. EE	0.99	0.26	
			EE	0.91	0.33	CE vs. EC	0.82	0.40	
			EC	0.91	0.39	EE vs. EC	1.00	0.02	
<i>Esr1p</i> H3K9ac (AU)			CC	1.00	0.41	CC vs. CE	0.04	1.86	
			CE	0.41	0.17	CC vs. EE	0.05	1.81	
			EE	0.43	0.17	CE vs. EC	0.07	1.40	
			EC	0.94	0.51	EE vs. EC	0.08	1.35	
<i>Oxtp</i> H3K9ac (AU)			CC	1.00	0.45	CC vs. CE	0.43	0.80	
			CE	0.71	0.23	CC vs. EE	0.95	0.27	
			EE	0.90	0.27	CE vs. EC	0.64	0.84	
			EC	0.93	0.29	EE vs. EC	1.00	0.11	
<i>Thp</i> H3K9ac (AU)			CC	1.01	0.59	CC vs. CE	0.95	0.26	
			CE	1.21	0.89	CC vs. EE	1.00	0.13	
			EE	1.08	0.50	CE vs. EC	0.87	0.40	
			EC	0.93	0.40	EE vs. EC	0.98	0.33	
<i>Kiss1p</i> H3K27me3 (AU)			CC	1.00	0.18	CC vs. CE	0.01	2.05	S11c
			CE	2.18	0.79	CC vs. EE	0.00	2.69	
			EE	2.33	0.67	CE vs. EC	0.01	1.72	
			EC	1.04	0.50	EE vs. EC	0.01	2.17	
<i>Esr1p</i> H3K27me3 (AU)			CC	1.00	0.27	CC vs. CE	0.98	0.23	
			CE	0.92	0.40	CC vs. EE	1.00	0.02	
			EE	0.99	0.32	CE vs. EC	0.44	0.75	
			EC	1.25	0.48	EE vs. EC	0.64	0.63	
<i>Oxtp</i> H3K27me3 (AU)			CC	1.00	0.27	CC vs. CE	0.97	0.28	
			CE	0.94	0.14	CC vs. EE	0.97	0.26	
			EE	0.95	0.13	CE vs. EC	0.76	0.54	
			EC	1.07	0.31	EE vs. EC	0.79	0.52	
<i>Thp</i> H3K27me3 (AU)			CC	1.00	0.24	CC vs. CE	1.00	0.17	
			CE	0.96	0.24	CC vs. EE	0.00	4.46	
			EE	2.11	0.26	CE vs. EC	0.00	2.91	
			EC	2.07	0.48	EE vs. EC	0.99	0.12	

Notes: Effect size was calculated using Cohen's *d*. AU= arbitrary units. F= generation. N=sample size. SD: standard deviation